Respiratory Muscles, Exercise Performance and Health in Overweight and Obese Subjects

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Originally published at:
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Abstract

PURPOSE:: Overweight and obese subjects often perceive increased breathlessness during minor exertion and therefore avoid exercise. Respiratory muscle endurance training (RMET) can reduce the perception of breathlessness. We hypothesized that RMET one month prior to and during a 6-month (3months supervised + 3months unsupervised) exercise and nutrition counseling program (EN) would improve the benefits of EN. METHODS:: 26 overweight and obese subjects with significant perception of breathlessness during exercise (age: 33+/-9y; body mass index [BMI]: 31.3+/-4.9kg.m) were randomized to RMET+EN (R+EN) or EN alone. R+EN performed 30min of normocapnic hyperpnea 5wk prior to and 2wkduring EN. EN consisted of two strength and three endurance training sessions per week, as well as prescribed nutritional composition and a 2.1kJ (=500kcal) energy deficit per day. Both groups had an equal number of lab visits during the 7 months. Before, and after 4 and 7 months, subjects performed a 12-min time trial (TT; 6+6min, 2min pause) and an incremental cycling test (ICT) to exhaustion and blood lipids were assessed. RESULTS:: Weight loss was significant and similar in both groups (-4.2 vs -3.7kg; both p<0.05). During the first 4 months, distance covered in 12min improved more (p<0.05) with R+EN (1678 vs 1824m; p<0.001) than with EN alone (1638 vs 1698m; p<0.05), while after R+EN, breathlessness during the ICT was reduced. Blood lipids of the pooled group improved in those subjects with pathologic values before the study. Despite reduced training compliance during the unsupervised period, subjects of both groups maintained the benefits attained during the supervised period. CONCLUSION:: R+EN improved TT-performance more than EN alone, despite similar weight loss, possibly due to reduced perception of breathlessness.
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Accepted for Publication: 11 August 2010
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Running title: Respiration, exercise, health and overweight

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Financial support was provided by a grant from the Swiss Federal Office of Sport and the Swiss Federal Sports Commission.
ABSTRACT

Purpose: Overweight and obese subjects often perceive increased breathlessness during minor exertion and therefore avoid exercise. Respiratory muscle endurance training (RMET) can reduce the perception of breathlessness. We hypothesized that RMET one month prior to and during a 6-month (3months supervised + 3months unsupervised) exercise and nutrition counseling program (EN) would improve the benefits of EN. Methods: 26 overweight and obese subjects with significant perception of breathlessness during exercise (age: 33±9y; body mass index [BMI]: 31.3±4.9kg·m⁻²) were randomized to RMET+EN (R+EN) or EN alone. R+EN performed 30min of normocapnic hyperpnea 5wk⁻¹ prior to and 2wk⁻¹ during EN. EN consisted of two strength and three endurance training sessions per week, as well as prescribed nutritional composition and a 2.1kJ (=500kcal) energy deficit per day. Both groups had an equal number of lab visits during the 7 months. Before, and after 4 and 7 months, subjects performed a 12-min time trial (TT; 6+6min, 2min pause) and an incremental cycling test (ICT) to exhaustion and blood lipids were assessed. Results: Weight loss was significant and similar in both groups (-4.2 vs -3.7kg; both p<0.05). During the first 4 months, distance covered in 12min improved more (p<0.05) with R+EN (1678 vs 1824m; p<0.001) than with EN alone (1638 vs 1698m; p<0.05), while after R+EN, breathlessness during the ICT was reduced. Blood lipids of the pooled group improved in those subjects with pathologic values before the study. Despite reduced training compliance during the unsupervised period, subjects of both groups maintained the benefits attained during the supervised period. Conclusion: R+EN improved TT-performance more than EN alone, despite similar weight loss, possibly due to reduced perception of breathlessness.

Keywords: Respiration, training, breathlessness, metabolism, sleep, quality of life
INTRODUCTION

**Paragraph Number 1** Obesity is a widespread and growing problem worldwide. The prevalence of overweight (body mass index [BMI] ≥ 25 kg·m⁻²), including obesity (BMI ≥ 30 kg·m⁻²), has increased by 40% from 1980 to 2004 in the United States (17). In Europe, the prevalence of overweight and obesity varies, depending on country, from 28 to 79% (overweight) and from 5 to 35% (obesity; 39). Obesity is associated with multiple chronic health conditions, including coronary heart disease, hypertension, hyperlipidemia, type 2 diabetes mellitus, depression, and obstructive sleep apnea, and is responsible for a large proportion of the health burden of Europe (38). In addition, health-related quality of life is impaired in overweight and obese subjects (34), independent of the prevalence of co-morbidities (28). Weight loss (5 - 15% of the body weight) in obese individuals improves the risk factors associated with obesity (37).

**Paragraph Number 2** Recommendations for the treatment of adults who are overweight or obese focus on energy balance with lifestyle modifications designed to reduce daily energy intake and increase physical activity. While reducing daily energy intake is the most effective method for decreasing weight and total fat mass rapidly (30), physical activity is crucial for long-term weight management (9,40) and may play a role in preventing obesity or preventing established obesity worsening (30).

**Paragraph Number 3** However, physical activity alone is of limited benefit in inducing weight loss (9). Reasons might be lack of time or motivation to engage in the high volume of activity required to lose a relevant amount of weight (40) or an increased level of breathlessness during physical exertion, rendering exercise too unpleasant. Babb et al. (6) showed, for example, that more than 37% of otherwise healthy young obese women suffer from an elevated perception
of breathlessness in response to moderate exercise. Because of this limitation, overweight and obese people may avoid intense daily activities and exercise – a vicious circle.

**Paragraph Number 4** Respiratory muscle endurance training (RMET) improves respiratory muscle and exercise endurance (16,22,35) and reduces the perception of breathlessness and respiratory exertion during volitional as well as during exercise-induced hyperpnea in healthy, normal weight subjects (35). Thus, it is an interesting concept for overweight and obese subjects embarking on a weight-reduction program, consisting of an exercise and nutrition counseling program (EN), to commence isolated RMET before beginning the EN. Furthermore, repeated volitional breathing tasks such as RMET or didgeridoo-practice were shown to reduce snoring (14,26) and to improve the apnea/hypopnea index in subjects with mild obstructive sleep apnea (26). Since overweight and obese subjects have an increased prevalence of sleep apnea (1), RMET in combination with EN may improve sleep quality and daytime sleepiness in this group of subjects. Therefore, the aim of the present study was to assess the effect of RMET, starting one month prior to EN and continuing throughout EN in overweight or obese subjects perceiving a significant amount of breathlessness on exertion, on improvements in exercise performance, quality of life and daytime sleepiness, as well as weight reduction, changes in body fat, lipid profile and insulin sensitivity compared to EN alone.

**Paragraph Number 5** We hypothesized that a reduction in the perception of breathlessness by RMET would make whole-body exercise more enjoyable, increase the level of spontaneous daily activities in addition to the EN program, and increase compliance with the program. This in turn would lead to a greater reduction in body weight and body fat content, and to greater improvements in exercise performance, quality of life, sleep-quality, daytime sleepiness and risk factors associated with coronary heart disease, compared to EN alone.
METHODS

Subjects

Paragraph Number 6 Of 340 people that responded to advertisements, 113 visited the laboratory after detailed information by telephone. Of these, 50 subjects (36 female, 14 male) decided to participate and were enrolled in the study according to all but one inclusion criterion (see below). Inclusion criteria were age between 18 and 50 years, BMI greater than 25 kg·m$^{-2}$, normal lung function, absence of acute or chronic disease, and exercising for less than 3 h per week. Exclusion criteria were smoking, taking regular medication, cardiovascular disease (electrocardiogram during exercise) including elevated resting blood pressure (> 130/85 mmHg), elevated fasting blood glucose (> 6 mmol·L$^{-1}$) and insulin resistance (insulin < 6 mIU/l or > 27 mIU/l), respiratory disease (VC and FEV$_1$ < 90% predicted) including asthma, musculoskeletal disease, and depression. All exclusion criteria were assessed by a detailed medical history and, where noted, by specific measurements. Subjects gave their written informed consent after detailed verbal and written information and after visiting the laboratory. The study was approved by the local ethics committee and conformed to the Declaration of Helsinki.

Paragraph Number 7 A further inclusion criterion was scoring $\geq 5$ for breathlessness during the last stage of the baseline incremental cycling test (ICT). 17 of the enrolled subjects were excluded due to insufficient perception of breathlessness during incremental cycling. A detailed description of the assessment of subjective sensations is given later. Subjects were randomly assigned and counterbalanced (considering age, height, weight and sex) to one of the two study groups: RMET+EN (R+EN) or EN. Of the included subjects, two (1 R+EN, 1 EN) quit the study after the baseline-testing period, another five (3 R+EN, 2 EN) dropped out within the first (supervised) 4 months, and one (R+EN) within the following (unsupervised) 3 months.
Reasons were lack of time (4), change of job description (2), moving (1) and pregnancy (1).

**Paragraph Number 8** Finally, 15 subjects (12 female, 3 male) in the R+EN-group and 11 subjects (8 female, 3 male) in the EN-group completed the first 4 months of the study (age R+EN: 34 ± 8 y [mean ± SD], EN: 32 ± 9 y; height: 1.71 ± 0.07 and 1.71 ± 0.09 m; weight: 91.6 ± 15.3 and 93.3 ± 20.5 kg; systolic blood pressure: 116.8 ± 9.7 and 116.1 ± 11.5 mmHg; diastolic blood pressure: 73.1 ± 6.9 and 73.8 ± 6.3 mmHg).

**Protocol overview**

**Paragraph Number 9** The study included three different periods (Fig. 1): i) 1 month RMET or control, ii) 3 months supervised R+EN/EN, iii) 3 months unsupervised R+EN/EN. At baseline, subjects reported to the laboratory on five different occasions (Fig. 2; 5-day testing period), separated by at least 48 h, but within 2 weeks. This 5-day testing period was repeated after the 1-month RMET/control-period, after the 3-month supervised period and after the final 3-month unsupervised period. Tests were performed in the same order (see Fig. 2) and on the same time of day as at baseline. In addition, a reduced test set was carried out (Fig. 2; 2-day testing period) one and two months into the supervised period. Subjects were not permitted to perform any physical exercise the day before the test or to ingest any caffeinated food or drink the day of the test. Sleep duration during the two nights before testing was required to be at least 7 h and the last meal had to be eaten at least 2 h prior to testing. During the entire study period, subjects were requested to maintain their personal physical training at a level comparable to before the study and to complete a logbook where all trainings, including RMET, were recorded with time, duration and intensity. Also, during each training session, subjects were requested to record their heart rate (Polar S610i, Polar Elecor, Kempele, Finland). Logbook and heart rate readouts were regularly checked by the experimenter. During 4 days immediately prior to every
5-day testing period, subjects were requested to record their dietary intake and subjective variables, to wear an accelerometer and to assess sleep quality for two nights at home (for details see later).

Figure 1
Figure 2

Details of the different study periods

1-month RMET/control-period

Paragraph Number 10 During the first month, the R+EN-group performed 20 sessions of normocapnic hyperpnea which were carried out mostly at home with every 5th training session supervised in the laboratory (for details see below). The control group performed no specific training but reported regularly to the laboratory to assess lung function, respiratory muscle strength, skinfold thickness and circumferences. Control subjects did not know that the other group performed RMET during this period and believed that the groups differed with respect to the EN-program. They were informed that these initial measurements were essential baseline measurements before the start of the EN program. Similarly, the RMET-group did not know the details of the program of the 'other' group. Twice during this first month, all subjects visited the fitness center to familiarize themselves with the endurance and strength-training equipment to be used in the following six months of EN.

3-month-supervised R+EN/EN-period

Paragraph Number 11 During the following 12 weeks, R+EN-subjects performed two RMET-sessions per week. All subjects adhered to a prescribed EN (for details see below) with experimenter-contact twice per month when they reported to the laboratory. During these visits, R+EN-subjects performed an RMET or an interval cycling training, in alternating order (for details see below), and EN-subjects performed interval cycling trainings. These supervised
trainings served to control correct performance but also to discuss adherence to and problems with the program, individual achievements and to check training logbooks.

3-month-unsupervised R+EN/EN-period

Paragraph Number 12 For the next 12 weeks, subjects were asked to continue with their respective program, but without arranged contact to the experimenters or testing. Subjects were however free to contact the experimenters at any time with questions or if advice was needed.

Respiratory muscle endurance training (RMET)

Paragraph Number 13 RMET in the form of normocapnic hyperpnea was performed with the SpiroTiger® device (idiag, Fehraltdorf, Switzerland), which records each training session. This device uses partial rebreathing and ensures normocapnia. Tidal volume (V_T) is controlled by feedback, and breathing frequency (f_R) is paced with a duty cycle of 0.5. Target minute ventilation (\( \dot{V_E} \)) was initially set at 50% maximal voluntary ventilation (MVV) and was increased throughout the training period such that the subjects were exhausted at the end of each 30-min training session. For supervised trainings in the laboratory, the training device was connected to the metabolic cart to control for the training technique and to ensure normocapnia was maintained.

Exercise and nutrition counseling program

Paragraph Number 14 Subjects in the present study were requested to exercise on five days per week for 20 – 45 min. The weekly exercise program consisted of three endurance training sessions alternating with two strength training sessions, designed to take place in the fitness center. Subjects were allowed to train more than prescribed if desired, because the study was designed to imitate reality where no upper exercise limit exists. Therefore, rather than restricting subjects to the prescribed exercise program only, the volume of prescribed and
unprescribed exercise was carefully supervised to assess whether RMET and possible resulting reduced perception of breathlessness would motivate subjects to exercise more. During the training sessions, heart rate was recorded not only to assess training compliance but also to give the subject feedback on training intensity. For all sessions, training variables and times were recorded in a logbook.

**Paragraph Number 15** The three endurance training sessions consisted of two constant-load sessions and one interval training with durations starting at 20 min (1st-4th week), increasing to 30 min (5th-8th week) and then to 45 min (from 9th week) for the remainder of the EN. During constant-load training, subjects cycled, walked/ran or rowed at a heart rate corresponding to 45% of peak oxygen consumption ($\dot{V}_{O2peak}$) (1st-6th week) which was then increased to 50% $\dot{V}_{O2peak}$ (7th-15th week) and finally to 55% $\dot{V}_{O2peak}$ (from 16th week) for the remainder of the EN. Interval training was performed on a cycle ergometer, where resistance alternated between a load corresponding to 45% $\dot{V}_{O2peak}$ (80 s, 1st week) and 80% $\dot{V}_{O2peak}$ (40 s, 1st week). Durations of the two loads were then changed to 70 s / 50 s (7th-15th week) and 60 s / 60 s (from 16th week). Durations of the entire interval training sessions changed as noted above.

**Paragraph Number 16** Strength training consisted of leg curls, leg presses, abdominal crunches, torso rotations, lower back extensions, chest presses, lat pull downs and shoulder presses. Each exercise consisted of a concentric phase lasting 4 s, stop at reversal for 2 s and an eccentric phase of 4 s. The load was chosen such that the specific muscle group was exhausted within 60 – 90 s. Once 90 s was reached, the load was increased. Subjects then performed the exercise with this load until they reached 90 s again, and so on. Only one set of each exercise was performed per training session.

**Paragraph Number 17** The energy of the prescribed diet consisted of 20–30% fat, 50–
60% carbohydrates and 10–20% proteins. Diet counseling focused on the use of polyunsaturated fat, whole-grain carbohydrates, fresh fruit and vegetables. The required energy deficit had to be at least 2.1 kJ (= 500 kcal). Energy intake was calculated relative to the daily energy expenditure (for details see below).

Material and measurements

Body weight and body fat

Paragraph Number 18 For body weight and BMI, averages of four measurements (5-day testing period) and of two measurements (2-day testing period) were calculated and compared. Skinfold thicknesses were measured using a skinfold caliper (Siber Hegner, Zurich, Switzerland). Each skinfold was measured at least three times, and the mean of three reproducible values (less than 5% variation) was calculated. To calculate percent body fat according to the Peterson formula (25), the following sites were assessed: triceps, subscapular, suprailiac and mid thigh. Waist circumference was measured at the end of gentle expiration. In addition, hip-circumference was measured. Body fat content was measured during the first and the last 5-day testing period by dual-energy X-ray absorptiometry (DEXA; QDR 4500 Hologic, Bedford, USA).

Resting and daily energy expenditure

Paragraph Number 19 Resting energy expenditure was assessed within the first 5-day testing period by indirect calorimetry. Subjects reported to the laboratory after an overnight fast and reclined in a sun lounger wearing a nose clip and mouthpiece. Gas exchange was recorded continuously (Oxycon mobile, Jaeger, Höchberg, Germany) for at least 10 min or until achieving a respiratory steady state when subjects were sitting in a sun lounger. To calculate daily energy expenditure, resting energy expenditure (2 min of steady state data) was multiplied by subjective
physical activity level, assessed by a questionnaire (8).

**Paragraph Number 20** At each test session, subjects completed an activity questionnaire (7) to retrospectively assess their daily energy expenditure over the duration of the past week. In addition, subjects wore an accelerometer (Actigraph AM 7164, MTI Manufacturing Technology, Fort Walton Beach, FL) for four consecutive days (three weekdays, one weekend day) immediately prior to each 5-day test session to estimate daily energy expenditure more accurately. During the same four days, subjects recorded all details of their food consumption in a logbook. For analysis of the accelerometer data, the following activity levels were chosen: sedentary: 1-99 counts-min\(^{-1}\), light: 100-1951 counts-min\(^{-1}\), moderate: 1952-5724 counts-min\(^{-1}\), heavy: 5725-9498 counts-min\(^{-1}\), very heavy: > 9498 counts-min\(^{-1}\) (13).

**Incremental cycling test (ICT)**

**Paragraph Number 21** Subjects sat on an electromagnetically braked bicycle ergometer (Ergometrics 900, Ergoline, Bitz, Germany) with a nose clip in place, and were connected to the metabolic cart via a mouthpiece to assess ventilation and gas exchange (Oxycon mobile, Jaeger, Höchberg, Germany). Gases were measured by electrochemical O\(_2\)- and CO\(_2\)-sensors that use the principle of heat conductance. After 5 min of rest, subjects started cycling for 2 min at 60 W (women) or 80 W (men). Subsequently, the workload was increased by 20 W every 2 min until exhaustion. The subjects chose their preferred pedaling frequency (between 60 and 100 rpm) during the first two steps of the ICT and this frequency was then held constant during the remainder of this test and during subsequent tests. The test finished when subjects stopped or when the cadence could no longer be sustained within ± 3 rpm of the target. Subjects were not encouraged by the experimenter. Heart rate was measured continuously using a 12-lead electrocardiogram (Oxycon mobile, Jaeger, Höchberg, Germany). At the end of every 2-min
stage, subjects were asked to rate their breathlessness, respiratory exertion, and leg exertion on a visual analogue scale (see below). In addition, at the end of each stage, 20 µl of arterialized venous blood were drawn from an earlobe to assess blood lactate concentration enzymatically (Biosen 5040-lactate analyzer; EKS Industrie Elektronik, Magdeburg, Germany).

**Paragraph Number 22** ICT-data was analyzed at the point of exhaustion: Averages of ventilation, gas exchange and heart rate were calculated over the last 30 s of each test while for blood lactate concentration and rating of sensations the values at the point of exhaustion were taken. Maximal workload (\( W_{\text{max}} \)) was extrapolated proportionally according to time spent at the final workload, and \( \dot{V}_{\text{O}_2\text{peak}} \) was defined as the highest 15 s-average of oxygen consumption (\( \dot{V}_{\text{O}_2} \)). For comparison of physiological variables at submaximal exercise, 6-min averages over the last three iso-stages (iso = at the same time after the start of a test, independent of the total test duration) were calculated.

**Walk/run time trial (TT)**

**Paragraph Number 23** A 12-min walk/run time trial (TT) with 2 min recovery after 6 min was chosen to evaluate endurance performance. This design was chosen because i) walking and running better reflect the daily activities of overweight and obese subjects than other forms of exercise, e.g. cycling, ii) the reliability of a TT is higher compared to time-to-exhaustion tests (21), and iii) the 6-min walking distance is a well-established clinical test (3). To increase the endurance component, subjects performed two 6-min walk/runs with a 2-min recovery period in between. However, subjects were asked to cover the largest distance possible within the first 6 min without thinking of their performance in the second test. In the second test, subjects were requested to do as good as possible in face of having passed an exhaustive first test. For both tests, subjects received no encouragement from the experimenter. However each
minute the remaining number of minutes was shouted. Ventilation and gas exchange were recorded continuously using a face mask (Oxycon mobile, Jaeger, Höchberg, Germany) and heart rate was recorded every 5 s (Polar S610i, Polar Electro, Kempele, Finland). The test was performed in a corridor with a marked distance of 75 m between which subjects walked/ran back and forth. Every 150 m, subjects were asked to rate their level of breathlessness, respiratory exertion and leg exertion between 0 and 10 (see below) by holding up the fingers on both hands. Before the first run as well as at the end of both runs, a 20-µL sample of arterialized capillary blood was drawn from an earlobe for blood lactate analysis (Biosen 5040-lactate analyzer; EKS Industrie Elektronik, Magdeburg, Germany). TT-ventilation, gas exchange, heart rate, and sensations were averaged over the first and second 6-min run separately and over the entire 12-min run. For blood lactate concentration the values at the end of the second run were taken.

Assessment of subjective sensations

Breathlessness, respiratory exertion and leg exertion during exercise (except TT) were assessed by means of a visual analogue scale consisting of three horizontal lines split post-hoc into values between 0 and 10. They were labeled with the three qualities and ranged from “none” on the left-hand side to “maximal” on the right-hand side. Subjects were interviewed extensively prior to the test session regarding their experience and understanding of the different respiratory sensations. Subsequently, they discussed with the experimenter which sensations meant breathlessness (Atemnot, i.e. the sensation of “not getting enough air”) and which meant respiratory exertion (Atmungsanstrengung, i.e. “how difficult it is to breathe”), respectively. This ensured that subjects could distinguish between breathlessness and respiratory exertion (15,20). The definitions were read to the subjects before each exercise test, and the following calibration terms were used as previously discussed with the subjects:
“none” was defined as perceiving no breathlessness, respiratory exertion or leg exertion, similar to the sensation when sitting on a chair at rest; “maximal” was defined as the intensity at which the exercise would have to be stopped immediately due to this particular sensation.

**Quality of life**

*Paragraph Number 25* Subjects completed a German translation of the SF-36 questionnaire (10,29) to evaluate physical and mental aspects of their quality of life. In order to create a reference for data of the SF-36 questionnaire, norm values for the demographics of our study population were calculated from norm values of a German population (10).

*Paragraph Number 26* In addition, subjects scored their level (0-10) of breathlessness, perceived well-being, tiredness and hunger during 4 consecutive days (1 weekend day and 3 week days; same days as dietary protocol) when prompted by the monitor at 10 am, 3 pm and 8 pm by means of a wrist-worn monitor (Actiwatch Score, Cambridge Neurotechnology, Cambridge, UK). For the different subjective sensations that were each assessed at 10 am, 3 pm and 8 pm over 4 days, the average over the four consecutive days of each 5-day testing period was calculated separately.

**Venous blood analysis**

*Paragraph Number 27* The subjects reported to the laboratory after an overnight fast. 30 ml of venous blood were drawn from a cubital vein to assess fasting serum concentrations of insulin, glucose, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides. Blood was drawn into a lithium-heparinate vacutainer for lipid analysis and into a sodium-fluoride/oxalate vacutainer for fasting glucose analysis. The tubes were centrifuged and blood serum was separated from blood cells. The serum was analyzed at the Institute of Clinical Chemistry of the Zurich University Hospital.
(Switzerland) using routine techniques.

Sleep

**Paragraph Number 28** During two consecutive nights within a 5-day testing period, subjects wore, at home, a pocket sized digital recorder (Compass F10, Medcare Flaga, Reykjavik, Iceland) designed to diagnose sleep-disordered breathing and estimate sleep quality from records of nasal pressure (flow), activity, position and oxygen saturation. Furthermore, subjects completed the Epworth Sleepiness Scale to evaluate their daytime sleepiness (18). For sleep analysis, the second of the two nights was analyzed. Apnea was defined as cessation of airflow for ≥ 10 s with decrements in blood oxygen saturation of ≥ 3%. Hypopnea was defined as a reduced airflow for ≥ 10 s with decrements of blood oxygen saturation of ≥ 3% (2).

**Lung function, respiratory muscle strength and airway resistance (R_{aw})**

**Paragraph Number 29** Resting lung function as well as maximal inspiratory mouth pressure (P_{limax}) and maximal expiratory mouth pressure (P_{emax}) were measured in standing position according to standard procedures (4,5). Vital capacity (VC), forced expiratory volume in one second (FEV₁), peak expiratory flow (PEF), and MVV were determined by means of an ergospirometric device (Oxycon mobile, Jaeger, Höchberg, Germany) using a calibrated turbine for volume measurement. P_{limax} from residual volume and P_{emax} from total lung capacity were assessed over 1 s with a small air leak in the measurement device to prevent glottis closure (MicroMPM, Micro Medical, Rochester, UK). A nose clip was used for all efforts. Airway resistance (R_{aw}) was measured in sitting position using the Master Screen Diffusion Device (Jaeger, Höchberg, Germany) according to standard procedures (23). R_{aw} was assessed by using the interrupter technique and was determined by averaging the last five of at least ten reproducible values. R_{aw} was assessed before and after the respiratory endurance test (RET) at
isotime to assess the change in $R_{aw}$ during heavy breathing. For lung function, respiratory muscle
strength and $R_{aw}$, % predicted values were calculated. Due to technical problems some subjects
had to be excluded in the analysis of respiratory muscle strength and $R_{aw}$ (numbers are given in
results where appropriate).

**Respiratory endurance test (RET)**

*Paragraph Number 30* At baseline, subjects (in sitting position) were requested to 
breathe to exhaustion at a given target ventilation using a partial rebreathing device (SpiroTiger®,
idiag, Fehraltdorf, Switzerland) to ensure normocapnia. During the three familiarization sessions 
within the first 5-day testing period, a level of ventilation was chosen by the investigators that 
ensured the subjects could continue for a minimum of 8 min but a maximum of 15 min. This 
resulted in an average target $\dot{V}_E$ of 67 ± 10% MVV for the R+EN-group and 66 ± 4% MVV for 
the EN-group. Subjects were required to maintain this pre-selected $\dot{V}_E$ while holding $V_T$ and $f_R$
constant. If necessary, the test administrator asked the subjects to correct their $V_T$ and $f_R$ that was 
 supervised on the metabolic cart, ensuring normocapnia was maintained. The test was either 
 stopped by the subjects due to exhaustion or by the test administrator when subjects were no 
 longer able to sustain target $V_T$ and $f_R$. In the subsequent RETs, subjects breathed with identical 
 target $\dot{V}_E$ and breathing pattern for the same duration as during the RET at baseline. After a 4-
min break where $R_{aw}$ was measured, they continued breathing until exhaustion at the same level 
of ventilation. These tests were stopped according to the criteria above or after a maximum of 
60 min breathing. Ventilation and end-tidal CO$_2$ partial pressure ($P_{ET}CO_2$) were recorded 
continuously (Oxycon mobile, Jaeger, Höchberg, Germany) and heart rate was recorded every 
5 s (Polar S610i, Polar Electro, Kempele, Finland). Every 2 min, subjects rated their perception
of breathlessness and respiratory exertion on a visual analogue scale, and a 20 μL- sample of arterialized capillary blood was drawn from an earlobe for blood lactate analysis (Biosen 5040-lactate analyzer; EKS Industrie Elektronik, Magdeburg, Germany). Ventilation, P_{ET}CO_2, heart rate, blood lactate concentration, and sensations were averaged over the test-duration of the shortest test, i.e. during identical durations.

Data analysis

*Paragraph Number 31* The number of subjects was different between the supervised and the unsupervised period. To have the largest possible number of subjects available for analysis, within-group comparisons from before to after the supervised period (n=26) and the unsupervised period (n=25) were performed separately by using student’s paired t-test. Between-group comparisons of within group-changes from before to after the supervised/unsupervised-period were performed using unpaired t-tests. The Pearson product-moment correlation was applied for assessing possible relations between changes from before to after the supervised program within groups. Analyses were performed using a computer software package (SPSS 11 for Mac OS X, Chicago, Illinois, USA). Statistical significance was accepted at p < 0.05. We also show statistical trends (i.e. p < 0.1) where appropriate.

RESULTS

Training compliance

*Paragraph Number 32* During the first month of RMET, training-compliance with RMET was 97 ± 6% while it decreased to 63 ± 18% during the supervised period and further to 35 ± 34% during the unsupervised period. Physical training compliance was similar between groups both during the supervised period (R+EN-group: 81 ± 15%; EN-group: 89 ± 8%; p = 0.161) and the unsupervised period (R+EN-group: 51 ± 35%; EN-group: 63 ± 18%;
In both groups, training compliance with physical training significantly decreased during the unsupervised period compared to the supervised period (both: \( p < 0.05 \)). During the supervised period, R+EN-subjects performed an additional \( 10 \pm 8 \) trainings, meaning that they undertook extra trainings (which was allowed in addition to the program). EN-subjects completed an additional \( 21 \pm 23 \) trainings (\( p = 0.104 \)). During the unsupervised period, R+EN-subjects performed \( 11 \pm 18 \) extra trainings and the EN-group an additional \( 13 \pm 16 \) (\( p = 0.813 \)).

**Body weight, body fat content and circumferences**

Paragraph Number 33 Baseline anthropometric data were similar between the two groups (all \( p > 0.05 \); Table 1, Fig. 3). After the first 4 months of supervised training, body weight decreased in both groups by the same magnitude (statistical power 98%; Fig. 3) while body fat content decreased significantly in the R+EN-group and tended to decrease in the EN-group (Table 1). During the following 3-month-unsupervised training period, body weight tended to decrease further with R+EN while it decreased significantly with EN. Body weight and % body fat reduction did not correlate with changes in self-reported energy expenditure, changes in energy intake or with training compliance in either group. Waist circumference significantly decreased with R+EN in the supervised period, while EN had no effect (Table 1). When all subjects were considered as one pooled group (R+EN + EN), waist circumference was reduced significantly after the supervised period (before: \( 1.02 \pm 0.15 \) m, after: \( 0.98 \pm 0.14 \) m, \( p < 0.01 \)) while no further change was observed after the unsupervised period (before: \( 0.97 \pm 0.14 \) m, after: \( 0.96 \pm 0.15 \) m, \( p = 0.170 \)).

Figure 3

Table 1

**Energy intake and expenditure**

Paragraph Number 34 After the 4-month supervised period, R+EN-subjects reported a
larger energy deficit (-1.1 kJ·day⁻¹) than prescribed and the same tendency was observed for EN-subjects (-1.8 kJ·day⁻¹; Table 1). For both groups, fat intake (prescription: 20–30%) stayed at the upper limit during this period (R+EN: 26–43%, EN: 26–40%) and carbohydrate intake (prescription: 50–60%) was too low (R+EN: 37–58%, EN: 42–61%). By the end of the unsupervised period, R+EN subjects reported a calorie intake corresponding to the prescription while that of EN-subjects was significantly lower compared to prescription. The level of self-reported daily energy expenditure increased after the supervised R+EN-period, while it remained the same after EN. The increased energy expenditure during the supervised period compared to baseline is also reflected in the increased duration spent at higher activity (≥ moderate activity) in R+EN (Table 1).

Incremental cycling test (ICT)

Paragraph Number 35 \( \dot{W}_{\text{max}} \) (Fig. 3) and \( \dot{V}_{\text{O}_2}\text{peak} \cdot \text{kg}^{-1} \) significantly increased with R+EN during the 4-month supervised period (R+EN: before: 29 ± 6 mL·min⁻¹·kg⁻¹, after: 32 ± 6 mL·min⁻¹·kg⁻¹, p < 0.01; EN: before: 28 ± 5 mL·min⁻¹·kg⁻¹, after: 29 ± 6 mL·min⁻¹·kg⁻¹, p = 0.235; between groups: p = 0.461). At exhaustion, breathlessness was significantly reduced after R+EN compared to EN alone (R+EN: before: 9.4 ± 1.0, after: 6.4 ± 4.1 points, p < 0.01; EN: before: 8.1 ± 1.7, after: 7.8 ± 1.9 points, p = 0.709; between groups: p < 0.05). Both programs significantly and similarly reduced heart rate (R+EN: before: 180 ± 14 beats·min⁻¹, after: 174 ± 10 beats·min⁻¹, p < 0.01; EN: before: 178 ± 8 beats·min⁻¹, after: 168 ± 14 beats·min⁻¹, p < 0.01; between groups: p = 0.190). Maximal blood lactate concentration remained unchanged after R+EN (before: 9.3 ± 1.5 mmol·L⁻¹, after: 9.3 ± 2.2 mmol·L⁻¹, p = 0.884) and was reduced after EN (before: 8.1 ± 3.0 mmol·L⁻¹, after: 6.6 ± 2.8 mmol·L⁻¹, p < 0.05; between group: p < 0.05). At submaximal levels (Table 2) ventilation and perception of breathlessness were reduced during
the last 6 min of the test. After both R+EN and EN, submaximal heart rate and blood lactate concentration were significantly lower. No further changes were observed in the following unsupervised 3-month period.

**Table 2**

*Paragraph Number 36* In the R+EN-group, reduction in breathlessness during submaximal exercise tended to correlate with changes in $\dot{W}_{max}$ ($r^2 = 0.23, p = 0.072$) and $\dot{V}_{O_{peak}}$ ($r^2 = 0.23, p = 0.067$), but did not correlate with changes in anthropometric data and self-reported energy expenditure. Improvements in $\dot{V}_{O_{peak}} \cdot \text{kg}^{-1}$ correlated with training compliance ($r^2 = 0.42, p < 0.05$). For the pooled group, changes in daily energy expenditure significantly correlated with changes in $\dot{W}_{max}$ ($r^2 = 0.16, p < 0.05$).

**Time trial (TT)**

*Paragraph Number 37* Baseline 12-min distance did not differ significantly between the two groups (R+EN: 1678 ± 269 m, EN: 1638 ± 256 m, $p = 0.704$). After the 4-month supervised period, TT-performance improved significantly more in the R+EN-group (statistical power for improvement 100%) than in the EN-group (Fig. 3, Table 2), while $\dot{V}_E$, perception of breathlessness, respiratory exertion and leg exertion, heart rate, and blood lactate concentration remained unchanged. During the following 3-month unsupervised period, no further changes were observed (Table 2).

*Paragraph Number 38* In the R+EN-group, changes in the perception of breathlessness during the ICT tended to correlate with improvement in TT-performance (12-min distance: $r^2 = 0.22, p = 0.074$; second 6-min run: $r^2 = 0.20, p = 0.095$) after the first 4 months. This correlation was significant when analyzed for the pooled group (12-min distance: $r^2 = 0.24, p < 0.05$; first 6-min run: $r^2 = 0.30, p < 0.01$). TT-performance-changes did not correlate with
changes in anthropometric data or the change in self-reported daily energy expenditure.

**Quality of life**

*Paragraph Number 39* Details of subjective rating of quality of life and daily perception of subjective sensations are given in Table 3. Before the start of the intervention-period, scores of the mental component summary were below or at the 25th percentile for both groups and remained the same during the entire study period. The average score of the physical component summary lay between 25th and 50th percentile in both groups before the start of the intervention period and significantly and similarly increased during the supervised 4-month period (pooled group: before: 49 ± 6, after: 54 ± 5, p < 0.001) and then remained unchanged. Perception of general health improved significantly after R+EN but not after EN (R+EN: before: 63 ± 12, after: 76 ± 12, p < 0.05; EN: before: 70 ± 14, after: 70 ± 14, p = 0.982; between within-group-changes: p < 0.05).

**Table 3**

*Paragraph Number 40* Training compliance, body weight and % body fat did not correlate with improvement in the perception of physical well-being in either group. In the R+EN-group, reduction in breathlessness during submaximal exercise tended to correlate with improvements in the perception of general health (r² = 0.21, p = 0.085), while they did not correlate with changes in the physical component summary. For the pooled group, the improvements in Wmax and the reduction in breathlessness correlated with the change in physical component summary (Wmax: r² = 0.21, p < 0.05; breathlessness: r² = 0.16, p < 0.05).

**Metabolic blood parameters**

*Paragraph Number 41* Values of the different metabolic blood parameters are given in Table 4. Changes did not correlate with absolute changes in body weight, BMI, % body fat,
dietary intake, self-reported energy expenditure nor with the change in fitness level ($\bar{W}_{max}, \dot{V}_{O_{peak}} \text{ / kg, 12-min distances}$) of the pooled group.

Table 4

**Paragraph Number 42** However, if only subjects with pathologic values at the start of the study were included in the analysis of the pooled group, blood lipids tended to improve after the supervised period (total serum cholesterol: before: 5.8 ± 0.8 mmol·L$^{-1}$, after: 5.4 ± 1.2 mmol·L$^{-1}$, $p = 0.080$, $n = 10$; HDL-cholesterol: before: 0.9 ± 0.0 mmol·L$^{-1}$, after: 1.0 ± 0.1 mmol·L$^{-1}$, $p = 0.062$, $n = 3$; LDL-cholesterol: before: 3.7 ± 0.7 mmol·L$^{-1}$, after: 3.4 ± 1.2 mmol·L$^{-1}$, $p < 0.050$, $n = 11$; total serum triglycerides: before: 2.6 ± 0.3 mmol·L$^{-1}$, after 1.9 ± 0.9 mmol·L$^{-1}$, $p = 0.164$; $n = 3$). Insulin levels did not change (insulin: before: 5.0 ± 1.6 mLU·l$^{-1}$, after: 4.8 ± 2.1 mLU·l$^{-1}$, $p = 0.853$, $n = 5$). In this pooled group, correlations were performed only for variables with a large enough number of subjects. The reduction in total serum cholesterol tended to correlate with the improved 12-min TT-performance ($r^2 = 0.38$, $p = 0.056$), but changes in blood lipids did not correlate with changes in body weight.

**Sleep**

**Paragraph Number 43** Although apnea/hypopnea index remained unchanged during the supervised period in both groups (R+EN: before: 2.6 ± 4.1, after: 3.1 ± 3.2, $p = 0.661$; EN: before: 3.3 ± 5.3, after: 3.4 ± 4.6, $p = 0.947$; between within-group-changes: $p = 0.793$), R+EN significantly decreased daytime sleepiness while EN alone had no such effect (Table 3; note: before the intervention period, five subjects of the R+EN-group and one subject of the EN-group reported excessive daytime sleepiness, i.e. Epworth Sleepiness Scale-score $> 10$). In both groups changes in daytime sleepiness did not correlate with changes in body weight, BMI, % body fat, self-reported daily energy expenditure or physical performance (all $p > 0.05$). For the pooled
group, the change in $\dot{V}O_{2\text{peak}}$ /kg correlated significantly with the change in daytime sleepiness ($r^2 = 0.30, p < 0.01$).

Lung function and maximal respiratory muscle strength

Paragraph Number 44 In Table 5 lung function and respiratory muscle strength are shown. Before the start of the intervention period, $R_{aw}$ was higher than predicted in both groups (both groups: $p < 0.01$). After the 4-month supervised program, $R_{aw}$ was significantly lower with R+EN but did not change significantly with EN alone.

Table 5

Respiratory endurance test (RET)

Paragraph Number 45 R+EN Breathing duration increased significantly after the 4-month supervised period while EN alone had no significant effect. However, breathing duration decreased slightly but significantly after the 3-month unsupervised training period (Table 5). Similarly, the perception of breathlessness, respiratory exertion, as well as blood lactate concentration were reduced after R+EN only.

DISCUSSION

Paragraph Number 46 In the present study, we found that overweight and obese subjects with a significant perception of breathlessness during exercise who performed RMET one month prior to and during a 3-month supervised EN program improved their running performance significantly more than a group that performed EN only despite similar weight loss and reduction in % body fat. In addition, maximal cycling performance improved after R+EN but not after EN. This difference between groups may result from the significantly reduced perception of breathlessness or underlying changes, e.g. increased respiratory muscle endurance, in the group that performed RMET. The following 3-month-unsupervised training period did not yield further improvements but neither did performance deteriorate. This is possibly a result of the reduced
training compliance in both groups during the unsupervised training phase. The overall benefit of both training regimes is reflected in improved quality of life, particularly an improved physical component. For the subgroup of subjects that started out with a pathological blood lipid profile, an improvement was seen during the training period. In summary, although the effect of the two programs on body weight loss, amount of energy expenditure, quality of life and long-term compliance with the program was similar between groups, the addition of RMET resulted in a decrease in breathlessness and a greater improvement in performance.

Weight loss

Paragraph Number 47 For both groups of subjects, the weight loss resulting from the daily energy deficit of 2.1 kJ was expected to be 0.5 kg·wk⁻¹ which would, in accordance with Wadden et al. (36), result in a total loss of 12 kg over the 6 months. Given the self-reported larger energy deficit in both groups, weight loss was expected to be greater. However, only four R+EN-subjects (27%) and two EN-subjects (18%) lost ≥6 kg during the supervised period and only two R+EN- and no EN-subjects lost ≥6 kg during the unsupervised period. Although more R+EN-subjects reached the goal, the groups as a whole did not differ in the amount of body weight or body fat lost over time. In fact, the numbers are in the same range as reported in systematic reviews by Shaw et al. (30) with an average weight loss for a 3-month period of 3.4 - 17.7 kg, and Curioni et al. (11), where the average weight loss for a 3-month period was around 4.2 kg.

Exercise performance

Paragraph Number 48 After the supervised intervention period, TT-performance improved more with R+EN than with EN alone. In this period, \( W_{\text{max}} \) improved only with R+EN. Interestingly, clinically relevant improvements of >70 m within 6 min, a number given for
respiratory patients (3), were only achieved in the second of the two 6 min runs (R+EN: +96 ± 45 m, EN: +73 ± 44 m). This could either result from the fact that subjects were not as deconditioned as cardio-respiratory patients (3), resulting in smaller scope for improvement, that the present exercise program mainly improved the longer duration endurance component, or that subjects did not perform to their maximum in the first of the two runs after the first training period. Although it is theoretically possible that subjects paced themselves for 12 min rather than 6 min, it seems unlikely to us. We believe that subjects performed at their maximum during the first 6-min run, as we emphasized prior to each test explaining that subjects had to cover the largest distance possible within the first 6 min. During the unsupervised period, subjects trained less and thus it is not surprising that performance did not continue to improve but remained constant during this period of time.

**Paragraph Number 49** Interestingly physical training did not affect maximal cycling performance of the EN-group during the supervised period. It is likely that the training intensity designed to optimize fat-burning was too low to improve maximal performance.

**Paragraph Number 50** Given the similar amount of physical training between the R+EN and the EN-group during the 3-month supervised period, the greater improvement in exercise performance in the R+EN-group is likely, at least in part, to result from increased respiratory muscle endurance (seen in improved RET-duration and MVV) associated with reduced breathlessness. In addition, the reduction in $R_{aw}$ and FEV$_1$, possibly reflecting increased airway patency, may have reduced resistive respiratory muscle work, reflected in reduced perception of respiratory exertion during the RET. This could have helped to reduce the development of respiratory muscle fatigue in addition to improving the endurance of muscle fibers due to intramuscular adaptations in respiratory muscles. In fact, respiratory muscle fatigue is thought to
impair exercise performance by a so-called metaboreflex (31) impairing leg muscle perfusion, thereby enhancing leg muscle fatigue and compromising performance. The significant reduction in blood lactate accumulation during isolated respiratory muscle work after R+EN suggests this mechanism might indeed have contributed to improved exercise performance since the concentration of lactic acid in respiratory muscles was shown to be one factor causing the metaboreflex (27).

**Quality of life**

*Paragraph Number 51* From a subjective perspective, the most important question is whether improvements in running and cycling performance translate into improved quality of life. Indeed, perception of general health improved after R+EN to a similar degree as breathlessness during respiratory and physical exertion. This might indicate that breathlessness was also reduced during daily living, improving subjects' perception of general health, supported by a trend for a correlation between the two. However, the overall physical component of quality of life improved to a similar degree in both groups. In the pooled group, in fact, the change in breathlessness not only significantly correlated with the change in TT- and ICT-performance but also breathlessness and ICT-performance correlated with the physical component of quality of life, hinting at a possible cause-effect relationship. This is also suggested by Tompkins et al. (33), who found improvements in TT-performance to correlate with improved perception of the physical component of quality of life.

**Blood lipids**

*Paragraph Number 52* Changes in blood lipid profile resulting from the present intervention were smaller than those reported by Shaw et al. (30) in their review (cholesterol: -0.15 to -1.4 mmol·L⁻¹; triglycerides: -0.69 to +0.03 mmol·L⁻¹; HDL: -0.1 to +0.1 mmol·L⁻¹) if all
subjects were considered. However, when only subjects with pathologic values at baseline were included, improvements in blood lipid profile after the supervised period were in a similar range (pooled group: cholesterol: $-0.34 \pm 0.54\text{ mmol}\cdot\text{L}^{-1}$; triglycerides: $-0.73 \pm 0.59\text{ mmol}\cdot\text{L}^{-1}$; HDL: $+0.08 \pm 0.04\text{ mmol}\cdot\text{L}^{-1}$). Blood lipid profile might have been positively affected by a change in visceral fat content, an assumption that is supported by the significant reduction in waist circumferences after the supervised training period in our pooled group, since accumulation of visceral fat is known to be associated with a deterioration in blood lipid profile (12). Also Ohkawara et al. (24) recently showed a dose-response relationship between visceral fat reduction and the amount of exercise performed, showing that about 150 min of moderate activity per week, exactly corresponding to the amount performed by our subjects, was necessary for significant visceral fat reduction. The fact that changes in total serum cholesterol correlated with changes in TT-performance, but did not correlate with changes in body weight, supports the evolving notion that blood lipids are mostly affected by level of fitness rather than the level of overweight or obesity per se. This is in agreement with a recent study by Tjønna et al. (32) suggesting that increasing aerobic capacity is more important than reducing weight for reducing the risk of cardiovascular mortality.

Sleep quality

Paragraph Number 53 In contrast to the findings of King et al. (19), Furrer et al. (14) and Puhan et al. (26), sleep quality remained unchanged after R+EN and EN. However, the discrepancy between the studies likely results from the fact that these investigators studied subjects suffering from impaired sleep quality, while only a few subjects in the present study suffered from reduced sleep quality. Despite the apnea/hypopnea index remaining constant in both groups, daytime sleepiness tended to improve more with R+EN than with EN alone during
the supervised period, the former being associated with a reduced $R_{aw}$ in this group of subjects. However, this difference might result from the fact that more R+EN-subjects (5 vs. 1 EN) suffered from excessive daytime sleepiness at baseline. This, in turn, would render RMET more likely to improve these symptoms (14,26). It seems, however, that the reduction in daytime sleepiness is independent of the change in energy expenditure, body weight or body fat, while the fitness level might affect daytime sleepiness.

Clinical implications

*Paragraph Number 54* The fact that the compliance with RMET during the unsupervised period was very low, may either mean that the subjects had difficulties continuing with RMET without regular contact to a supervisor, or that they were not motivated to continue with RMET regularly as long as the level of breathlessness remained reduced. In this context it is important to note that, despite the reduction in the amount of RMET performed, subjects of the R+EN-group at least maintained the improvements attained after the supervised period in the most important parameters such as body weight and exercise performance. This implies that, in clinical practice, RMET should be supervised initially. As soon as perception of breathlessness is markedly reduced, physical training (with or without a reduction in RMET) may be sufficient.

Limitations of the study

*Paragraph Number 55* A first potential limitation is that the EN-group did not perform sham training before starting the 3-month EN-period. We decided that if EN-subjects did not know about the R+EN-group, their performance 4 months after the start of the program would not be affected by this. In addition, they also had regular contact to the experimenters within the first 1-month period performing 'baseline' tests in the laboratory. Second, blinding of the experimenters was not possible due to restrictions in personnel. As previous studies showed that
a blinded experimenter will know the group-assignment of the subject after the RET, it would have meant to have three different experimenters for RET measurements. This would, in turn, have had the drawback of changing experimenters of the same test. However, as the experimenters were well aware of the potential influence of knowing group assignment, they paid great attention to treat every subject similarly. Also, subjects were not encouraged during exercise tests to limit any expectational influence of the experimenters. A third point is that no objective measure of respiratory muscle fatigue, e.g. phrenic nerve stimulation with assessment of transdiaphragmatic pressure, was performed in this study. We refrained from doing these time-consuming and rather unpleasant tests because the training and testing load was already very high, in particular for this special group of subjects. A fourth point is that we did not exclude variation in menstrual cycle, i.e. women did not perform each particular test at the same time within their respective menstrual cycle in the six different testing periods. We decided not to do so for two reasons: i) we wanted to keep the volume of training and the between-test period similar between subjects rather than having different volumes of training or having similar amounts of training spread over a different time span (since cycle-length is very individual) and ii) it would have been almost impossible to schedule the tests given the number of subjects and the number of tests per subject. Retrospectively we found that days within the menstrual cycle were evenly distributed within each testing period such that we believe this limitation did not affect our results.

Conclusion

**Paragraph Number 56** In overweight and obese subjects perceiving a significant amount of breathlessness during exercise, one month of RMET prior to the start of the 3-month supervised EN-intervention reduced breathlessness during exertion and increased running
performance more than EN alone. Reduced breathlessness was associated with increased daily physical activity and daily energy expenditure. The change in lifestyle (increased activity and reduced energy intake) improved the blood lipid profile in subjects with pathologic values at the beginning of the study. The benefits of the supervised period could be preserved independent of the training regime and despite decreased compliance in both groups. Therefore, RMET can be recommended prior to the start of a lifestyle intervention in overweight and obese subjects to enhance benefits of physical fitness.

ACKNOWLEDGEMENTS

Paragraph Number 57 We would like to thank the subjects for their time and effort dedicated to this study, Daniel Studer and Stefan Trachsler for help with data acquisition, Claudia Notter-Hausmann and Jana Kohl for help with activity and sleep and analyses, the Swiss Federal Office of Sports in Magglingen, especially Dr. Urs Maeder, for lending us the activity monitors and for much helpful advice regarding activity monitoring, Dr. Paolo Colombani for his support with nutrition recording and analysis, Dr. Marco Toigo for his valuable support in defining the strength training program, the fitness center ACTIV FITNESS (Zurich) for offering free entrance to the subjects and the Swiss Federal Office of Sport and the Swiss Federal Sports Commission for providing financial support. The results of the present study do not constitute endorsement by ACSM.
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Figure legends

**FIGURE 1.** Study design.

RMET: respiratory muscle endurance training; EN: exercise and nutrition counseling program; R+EN: RMET+EN.

**FIGURE 2.** Details of the different testing sessions.

**FIGURE 3.** Body weight, maximal workload (\(\dot{W}_{\text{max}}\)) and 12-min time trial distance at baseline, during and after the R+EN- and EN-intervention-period. R+EN: respiratory muscle endurance training + exercise nutrition counseling program; EN: exercise nutrition counseling program. Values are given as mean ± SE. Significances are given for comparisons within groups for the supervised period (baseline - 4\(^{th}\) month, n=15 for R+EN and n=11 for EN) and the unsupervised period (4\(^{th}\) - 7\(^{th}\) month, n=14 for R+EN, n=11 for EN) and for comparisons between changes of the two groups within the supervised and unsupervised period (\(^{'}p < 0.1, *p < 0.05, **p < 0.01, ***p < 0.001\).
### Figure 1

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### 5-day testing period

**1st session**
Medical history*, venous blood sample, body weight*, height*, resting energy expenditure*, breakfast*, interview about subjective sensation*, familiarisation with measurements of lung function*, airway resistance ($R_{aw}$)*, and respiratory muscle strength* and endurance*

**2nd session**
Dual-energy X-ray absorptiometry (DEXA) - measurement*

**3rd session**
Body weight, lung function, questionnaires (daily energy expenditure, daytime sleepiness, quality of life), respiratory muscle strength, skinfold thickness and body circumferences, incremental cycling test (ICT), familiarisation with measurement of respiratory muscle endurance*

**4th session**
Body weight, time trial (TT), familiarisation with measurement of respiratory muscle endurance*

**5th session**
Body weight, $R_{aw}$, respiratory muscle endurance test (RET)

* denotes procedures performed at baseline only; * performed in first and last 5-day testing period only

### 2-day testing period

**1st session**
Body weight, $R_{aw}$, lung function, questionnaires (daily energy expenditure, daytime sleepiness, quality of life), respiratory muscle strength, skinfold thickness and body circumferences

**2nd session**
Body weight, TT
Figure 3
<table>
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<tr>
<th>Measure</th>
<th>(n=15) Baseline</th>
<th>R+EN 4 months supervised</th>
<th>R+EN 4 months unsupervised</th>
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<th>∆ unsup</th>
<th>(n=11) Baseline</th>
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<tr>
<td>Duration ≥ moderately active [min·day⁻¹]</td>
<td>47.7 ± 18.0</td>
<td>64.1 ± 28.1*</td>
<td>67.2 ± 27.6</td>
<td></td>
<td></td>
<td>49.4 ± 16.3</td>
<td>65.5 ± 54.5</td>
<td>68.3 ± 56.9</td>
</tr>
</tbody>
</table>

R+EN: respiratory muscle endurance training and exercise nutrition counseling programme; EN: exercise nutrition counseling programme; BMI: body mass index; DEXA: dual-energy X-ray absorptiometry. Values are given as mean ± SD. Significances are given for comparisons within groups for the supervised period (baseline - 4th month) and the unsupervised period (4th - 7th month) and for comparisons between changes (Δ) of the two groups within the supervised (sup) and unsupervised (unsup) period (*p < 0.1, **p < 0.05, ***p < 0.01) except for body fat (DEXA) which was compared at baseline and 7 months (†p < 0.05).
**TABLE 2.** Incremental cycling (last 3 iso-stages) and 12-min time trial data

<table>
<thead>
<tr>
<th></th>
<th>(n=15)</th>
<th>R+EN (n=14)</th>
<th>(n=11)</th>
<th>EN (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>baseline</td>
<td>4 months supervised</td>
<td>4 months unsupervised</td>
<td>Δ sup</td>
</tr>
<tr>
<td><strong>Incremental cycling test (ICT)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VE [L· min⁻¹]</td>
<td>69 ± 18</td>
<td>62 ± 16**</td>
<td>63 ± 24</td>
<td>64 ± 15</td>
</tr>
<tr>
<td>Breathlessness [points]</td>
<td>5.1 ± 2.1</td>
<td>3.9 ± 2.9*</td>
<td>3.6 ± 3.0</td>
<td>3.7 ± 3.5</td>
</tr>
<tr>
<td>Respiratory exertion [points]</td>
<td>6.0 ± 1.4</td>
<td>5.2 ± 2.2</td>
<td>5.4 ± 2.2</td>
<td>5.3 ± 2.2</td>
</tr>
<tr>
<td>Leg exertion [points]</td>
<td>6.4 ± 1.4</td>
<td>6.8 ± 1.7</td>
<td>6.9 ± 1.5</td>
<td>6.8 ± 1.8</td>
</tr>
<tr>
<td>Heart rate [beats· min⁻¹]</td>
<td>163 ± 14</td>
<td>151 ± 14***</td>
<td>154 ± 15</td>
<td>156 ± 14</td>
</tr>
<tr>
<td>La [mmol· L⁻¹]</td>
<td>5.9 ± 1.2</td>
<td>4.6 ± 1.1***</td>
<td>5.0 ± 1.8</td>
<td>5.4 ± 1.4</td>
</tr>
<tr>
<td><strong>Walk/run Time trial (TT)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VE [L· min⁻¹]</td>
<td>86 ± 23</td>
<td>88 ± 21</td>
<td>87 ± 22</td>
<td>86 ± 20</td>
</tr>
<tr>
<td>Breathlessness [points]</td>
<td>5.6 ± 1.9</td>
<td>5.0 ± 2.0</td>
<td>4.9 ± 2.1</td>
<td>4.6 ± 2.8</td>
</tr>
<tr>
<td>Respiratory exertion [points]</td>
<td>6.2 ± 1.2</td>
<td>5.8 ± 1.2</td>
<td>5.7 ± 1.3</td>
<td>5.6 ± 1.9</td>
</tr>
<tr>
<td>Leg exertion [points]</td>
<td>5.7 ± 1.4</td>
<td>5.9 ± 1.0</td>
<td>5.7 ± 1.0</td>
<td>5.6 ± 1.9</td>
</tr>
<tr>
<td>Heart rate [beats· min⁻¹]</td>
<td>167 ± 11</td>
<td>165 ± 10</td>
<td>164 ± 10</td>
<td>166 ± 9</td>
</tr>
<tr>
<td>La [mmol· L⁻¹]</td>
<td>8.8 ± 3.3</td>
<td>8.0 ± 2.2</td>
<td>8.2 ± 2.3</td>
<td>8.3 ± 2.6</td>
</tr>
<tr>
<td>6-min distance 1st run [m]</td>
<td>888 ± 148</td>
<td>938 ± 142***</td>
<td>919 ± 143</td>
<td>929 ± 154</td>
</tr>
<tr>
<td>6-min distance 2nd run [m]</td>
<td>789 ± 126</td>
<td>885 ± 125***</td>
<td>866 ± 123</td>
<td>878 ± 155</td>
</tr>
</tbody>
</table>

R+EN: respiratory muscle endurance training and exercise nutrition counseling program; EN: exercise nutrition counseling program; VE: minute ventilation; La: blood lactate concentration. Incremental cycling test: 6-min-averages of the last 3 iso-stages; 12-min time trial: 12-min averages. Values are given as mean ± SD. Significances are given for comparisons within groups for the supervised period (baseline - 4th month) and the unsupervised period (4th - 7th month) and for comparisons between changes (∆) of the two groups within the supervised (sup) and unsupervised (unsup) period (*p < 0.05, **p < 0.01, ***p < 0.001). Note: The last 3 iso-stages differed between comparisons in the supervised and unsupervised period.
TABLE 3. Quality of life and daytime sleepiness.

<table>
<thead>
<tr>
<th></th>
<th>(n=15) baseline</th>
<th>R+EN (n=14) 4 months supervised</th>
<th>R+EN (n=14) 4 months unsupervised</th>
<th>R+EN (n=14) 7 months unsupervised</th>
<th>EN (n=11) baseline</th>
<th>EN (n=11) 4 months supervised</th>
<th>EN (n=11) 4 months unsupervised</th>
<th>EN (n=11) 7 months unsupervised</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daytime sleepiness [points]</strong></td>
<td>9.3 ± 4.1</td>
<td>7.2 ± 3.4*</td>
<td>7.3 ± 3.5</td>
<td>7.6 ± 3.5</td>
<td>6.7 ± 3.7</td>
<td>7.2 ± 4.0</td>
<td>7.2 ± 4.0</td>
<td>5.9 ± 3.1*</td>
</tr>
<tr>
<td><strong>Physical component summary [score]</strong></td>
<td>49 ± 5</td>
<td>54 ± 4**</td>
<td>54 ± 4</td>
<td>53 ± 8</td>
<td>50 ± 6</td>
<td>53 ± 6**</td>
<td>53 ± 6</td>
<td>55 ± 4</td>
</tr>
<tr>
<td><strong>Mental component summary [score]</strong></td>
<td>46 ± 11</td>
<td>48 ± 10</td>
<td>47 ± 10</td>
<td>48 ± 12</td>
<td>47 ± 10</td>
<td>47 ± 12</td>
<td>47 ± 12</td>
<td>46 ± 11</td>
</tr>
<tr>
<td><strong>Breathlessness [points]</strong></td>
<td>1.3 ± 1.1</td>
<td>1.4 ± 1.4</td>
<td>0.6 ± 0.7</td>
<td>0.9 ± 1.8</td>
<td>5.9 ± 1.6</td>
<td>7.2 ± 1.9*</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Wellbeing [points]</strong></td>
<td>6.3 ± 1.6</td>
<td>6.6 ± 1.7</td>
<td>3.6 ± 1.8</td>
<td>2.6 ± 2.2*</td>
<td>2.5 ± 1.4</td>
<td>2.1 ± 1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tiredness [points]</strong></td>
<td>4.3 ± 1.3</td>
<td>3.2 ± 1.7*</td>
<td>3.6 ± 1.8</td>
<td>2.6 ± 2.2*</td>
<td>2.5 ± 1.4</td>
<td>2.1 ± 1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hunger [points]</strong></td>
<td>2.9 ± 1.2</td>
<td>3.2 ± 1.7</td>
<td>2.5 ± 1.4</td>
<td>2.1 ± 1.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R+EN: respiratory muscle endurance training and exercise nutrition counseling program; EN: exercise nutrition counseling program. SF-36 norm values for demographics of our population: physical component summary (median [25th-75th percentile]): (54 [47-57]); mental component summary (53 [48-56]). Values are given as mean ± SD. Significances are given for comparisons within groups for the supervised period (baseline - 4th month) and the unsupervised period (4th - 7th month) and for comparisons between changes (Δ) of the two groups within the supervised (sup) and unsupervised (unsup) period (*p < 0.1, **p < 0.05, ***p < 0.01).
<table>
<thead>
<tr>
<th></th>
<th>(n=15) R+EN</th>
<th></th>
<th>(n=14)</th>
<th></th>
<th>(n=11) EN</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>baseline</td>
<td>4 months supervised</td>
<td>4 months unsupervised</td>
<td>7 months</td>
<td>4 months supervised</td>
<td>4 months unsupervised</td>
</tr>
<tr>
<td>Glucose [mmol·L⁻¹]</td>
<td>5.0 ± 0.4</td>
<td>5.2 ± 0.4*</td>
<td>5.2 ± 0.4</td>
<td>5.2 ± 0.5</td>
<td>5.1 ± 0.4</td>
<td>5.1 ± 0.4</td>
</tr>
<tr>
<td>Total serum cholesterol [mmol·L⁻¹]</td>
<td>5.0 ± 0.9</td>
<td>4.9 ± 1.1</td>
<td>4.9 ± 1.1</td>
<td>4.9 ± 0.9*</td>
<td>4.9 ± 0.8</td>
<td>4.6 ± 0.9**</td>
</tr>
<tr>
<td>HDL-cholesterol [mmol·L⁻¹]</td>
<td>1.5 ± 0.3</td>
<td>1.4 ± 0.2*</td>
<td>1.4 ± 0.3</td>
<td>1.5 ± 0.3*</td>
<td>1.5 ± 0.5</td>
<td>1.4 ± 0.5</td>
</tr>
<tr>
<td>LDL-cholesterol [mmol·L⁻¹]</td>
<td>3.0 ± 0.9</td>
<td>3.1 ± 1.0</td>
<td>3.1 ± 1.1</td>
<td>2.9 ± 0.9</td>
<td>2.8 ± 0.9</td>
<td>2.5 ± 0.9*</td>
</tr>
<tr>
<td>Total serum triglycerides [mmol·L⁻¹]</td>
<td>1.0 ± 0.4</td>
<td>1.0 ± 0.3</td>
<td>1.0 ± 0.3</td>
<td>0.9 ± 0.3</td>
<td>1.5 ± 0.8</td>
<td>1.4 ± 0.6</td>
</tr>
<tr>
<td>Insulin [mIU·L⁻¹]</td>
<td>6.8 ± 2.6</td>
<td>6.4 ± 2.4</td>
<td>6.5 ± 2.5</td>
<td>8.2 ± 3.1</td>
<td>10.7 ± 3.2</td>
<td>11.8 ± 6.2</td>
</tr>
</tbody>
</table>

R+EN: respiratory muscle endurance training and exercise nutrition counseling programme; EN: exercise nutrition counseling programme; HDL: high-density lipoprotein; LDL: low-density lipoprotein. Values are given as mean ± SD. Significances are given for comparisons within groups for the supervised period (baseline - 4th month) and the unsupervised period (4th - 7th month) and for comparisons between changes (Δ) of the two groups within the supervised (sup) and unsupervised (unsup) period (*p < 0.05, **p < 0.01).
### TABLE 5. Lung function, respiratory muscle strength and respiratory muscle endurance test data

<table>
<thead>
<tr>
<th></th>
<th>(n=15) Baseline</th>
<th>R+EN 4 months</th>
<th>(n=14) 4 months</th>
<th>7 months</th>
<th>Δ sup 4 months</th>
<th>Δ sup 7 months</th>
<th>EN 4 months</th>
<th>7 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC [% pred]</td>
<td>120 ± 13</td>
<td>123 ± 13</td>
<td>124 ± 13</td>
<td>124 ± 15</td>
<td>113 ± 19</td>
<td>110 ± 11</td>
<td>110 ± 11</td>
<td>112 ± 12</td>
</tr>
<tr>
<td>FEV\textsubscript{1} [% pred]</td>
<td>108 ± 13</td>
<td>111 ± 15</td>
<td>113 ± 15</td>
<td>111 ± 15</td>
<td>101 ± 11</td>
<td>100 ± 9</td>
<td>100 ± 9</td>
<td>101 ± 8</td>
</tr>
<tr>
<td>PEF [% pred]</td>
<td>99 ± 16</td>
<td>100 ± 16</td>
<td>101 ± 16</td>
<td>102 ± 15</td>
<td>95 ± 15</td>
<td>98 ± 13</td>
<td>98 ± 13</td>
<td>99 ± 13</td>
</tr>
<tr>
<td>MVV [% pred]</td>
<td>119 ± 20</td>
<td>129 ± 25**</td>
<td>132 ± 21</td>
<td>134 ± 19</td>
<td>114 ± 17</td>
<td>120 ± 16**</td>
<td>120 ± 16</td>
<td>119 ± 19</td>
</tr>
<tr>
<td>R\textsubscript{aw} [% pred]</td>
<td>137 ± 41</td>
<td>121 ± 39*</td>
<td>119 ± 40</td>
<td>131 ± 45</td>
<td>*</td>
<td>150 ± 32</td>
<td>143 ± 31</td>
<td>143 ± 31</td>
</tr>
<tr>
<td>P\textsubscript{Imax} [% pred]</td>
<td>120 ± 23</td>
<td>127 ± 26</td>
<td>127 ± 28</td>
<td>126 ± 28</td>
<td>110 ± 26</td>
<td>129 ± 33</td>
<td>124 ± 31</td>
<td>130 ± 32</td>
</tr>
<tr>
<td>P\textsubscript{Emax} [% pred]</td>
<td>103 ± 22</td>
<td>96 ± 23*</td>
<td>94 ± 23</td>
<td>97 ± 25</td>
<td>*</td>
<td>88 ± 22</td>
<td>100 ± 33</td>
<td>98 ± 28</td>
</tr>
</tbody>
</table>

**Respiratory muscle endurance test (RET)**

<table>
<thead>
<tr>
<th></th>
<th>(n=14) Baseline</th>
<th>R+EN 4 months</th>
<th>(n=11) 4 months</th>
<th>7 months</th>
<th>Δ sup 4 months</th>
<th>Δ sup 7 months</th>
<th>EN 4 months</th>
<th>7 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing Duration [min]</td>
<td>12.8 ± 4.1</td>
<td>46.8 ± 11.8***</td>
<td>46.7 ± 12.2</td>
<td>40.4 ± 17.9*</td>
<td>13.3 ± 5.6</td>
<td>27.4 ± 15.3</td>
<td>27.4 ± 15.3</td>
<td>33.8 ± 17.7</td>
</tr>
<tr>
<td>Breathlessness [points]</td>
<td>4.0 ± 2.3</td>
<td>1.4 ± 1.4***</td>
<td>1.4 ± 1.5</td>
<td>1.8 ± 2.1*</td>
<td>3.9 ± 2.2</td>
<td>3.3 ± 2.4</td>
<td>3.3 ± 2.4</td>
<td>2.5 ± 2.4</td>
</tr>
<tr>
<td>Respiratory exertion [points]</td>
<td>6.6 ± 1.8</td>
<td>3.0 ± 1.7***</td>
<td>3.1 ± 1.8</td>
<td>3.4 ± 2.3</td>
<td>6.0 ± 1.6</td>
<td>5.3 ± 2.1</td>
<td>5.3 ± 2.1</td>
<td>4.4 ± 2.2</td>
</tr>
<tr>
<td>Heart rate [beats· min\textsuperscript{-1}]</td>
<td>102 ± 18</td>
<td>90 ± 14**</td>
<td>90 ± 14</td>
<td>91 ± 15</td>
<td>109 ± 10</td>
<td>99 ± 14**</td>
<td>99 ± 14</td>
<td>99 ± 15</td>
</tr>
<tr>
<td>L\textsubscript{a} [mmol· L\textsuperscript{-1}]</td>
<td>1.9 ± 0.7</td>
<td>1.3 ± 0.4***</td>
<td>1.3 ± 0.4</td>
<td>1.5 ± 0.7</td>
<td>1.8 ± 0.7</td>
<td>1.5 ± 0.4</td>
<td>1.5 ± 0.4</td>
<td>1.5 ± 0.4</td>
</tr>
<tr>
<td>R\textsubscript{aw,0} [kPa· L\textsuperscript{-1}· s\textsuperscript{-1}]</td>
<td>0.20 ± 0.60</td>
<td>0.08 ± 0.13</td>
<td>0.08 ± 0.14</td>
<td>0.04 ± 0.17</td>
<td>0.08 ± 0.12</td>
<td>-0.03 ± 0.17</td>
<td>-0.02 ± 0.16</td>
<td>0.05 ± 0.07</td>
</tr>
</tbody>
</table>

R+EN: respiratory muscle endurance training and exercise nutrition counseling program; EN: exercise nutrition counseling program; VC: vital capacity; pred: predicted; FEV\textsubscript{1}: forced expiratory volume in 1 s; PEF: peak expiratory flow rate; MVV: maximum voluntary ventilation during 12 s; R\textsubscript{aw}: airway resistance; P\textsubscript{Imax}: maximal inspiratory mouth pressure; P\textsubscript{Emax}: maximal expiratory mouth pressure; L\textsubscript{a}: blood lactate concentration; R\textsubscript{aw,0}: change in airway resistance from rest to isotime in the respiratory endurance test.

Values are given as mean ± SD. Significances are given for comparisons within groups for the supervised period (baseline - 4\textsuperscript{th} month) and the unsupervised period (4\textsuperscript{th} - 7\textsuperscript{th} month) and for comparisons between changes (Δ) of the two groups within the supervised (sup) and unsupervised (unsup) period (*p < 0.05, **p < 0.01, ***p < 0.001).