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Effects of different respiratory muscle training regimes on fatigue-related variables during volitional hyperpnoea

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ABSTRACT

We compared the effects of the most commonly used respiratory muscle (RM) training regimes: RM endurance training (RMET; normocapnic hyperpnoea) and inspiratory resistive training (IMT), on RM performance. Twenty-six healthy men were randomized into 3 groups performing 4 weeks of RMET, IMT or sham-training. Lung function, RM strength and endurance were tested before and after training. RM fatigue during intermittent hyperpnoea was assessed by twitch oesophageal ($P_{oes,tw}$) and gastric pressures with cervical and thoracic magnetic stimulation. Respiratory sensations (visual analogue scale, 0–10) and blood lactate concentrations ([La]) were assessed during hyperpnoea. RMET increased maximal voluntary ventilation while IMT increased maximal inspiratory pressure. Both RMET and IMT increased vital capacity and RM endurance, but only RMET improved the development of inspiratory muscle fatigue (from −31% to −21% $P_{oes,tw}$), perception of respiratory exertion (4.2 ± 0.1 to 2.3 ± 2.3 points) and [La] (1.8 ± 0.4 to 1.3 ± 0.3 mmol l^{-1}) during hyperpnoea. Whether these specific RMET-induced adaptations observed during hyperpnoea would translate into greater improvements in exercise performance compared to IMT remains to be investigated.

1. Introduction

Respiratory muscle training has been used to improve respiratory muscle function in healthy subjects [for review see: (Sheel, 2002)] and in patients [for review see: (Geddes et al., 2005; Padula and Yeaw, 2007)]. In studies with healthy subjects, two different forms of respiratory muscle training have mainly been employed: (i) respiratory muscle endurance training in the form of volitional normocapnic hyperpnoea [RMET (Leith and Bradley, 1976; Boutellier et al., 1992; Boutellier and Piwko, 1992; McMahon et al., 2002; Holm et al., 2004; Leddy et al., 2007; Wylegala et al., 2007)] and (ii) inspiratory muscle training using external resistances or threshold loads [IMT (Leith and Bradley, 1976; Suzuki et al., 1993; Volianitis et al., 2001; Romer et al., 2002a; Gething et al., 2004; Brown et al., 2008)]. While RMET involves high-speed/low-resistance contractions of both inspiratory and expiratory muscles, IMT employs resistance-training principles with high-resistance/low-speed contractions and is confined to inspiratory muscles.

From 'general' skeletal muscle training it is well known that the ability of a training stimulus to improve performance in a target task depends on specific structural and functional adaptations occurring, i.e. the specificity of the muscle groups involved, contraction characteristics (e.g. velocity, strength), neuromuscular coordination and metabolic requirements (Faulkner, 1984). Thus, because RMET and IMT involve to some extent, different muscle groups, muscle loads and speeds of contraction, these training methods are likely to cause different respiratory muscle adaptations, as suggested by specific functional adaptations. Examples of these adaptations are the increased capacity to perform intensive hyperpnoea after RMET only (Leith and Bradley, 1976; Boutellier et al., 1992; Boutellier and Piwko, 1992; McMahon et al., 2002; Holm et al., 2004; Leddy et al., 2007; Wylegala et al., 2007), and the increased maximal inspiratory mouth pressure generation after IMT only (Leith and Bradley, 1976; Suzuki et al., 1993; Volianitis et al., 2001; Romer et al., 2002a; Gething et al., 2004; Brown et al., 2008). Hence the specific muscular adaptations to RMET and IMT may have different effects on muscle fatigue and endurance performance as well as physiological responses (e.g. lactic acid production, respiratory sensations) during hyperpnoea.

Currently, respiratory muscle fatigue is believed to affect whole-body endurance performance by eliciting a metaboreflex (Dempsey et al., 2006). This reflex is thought to originate in fatigued respiratory muscles by stimulating type IV afferents as a result of increased local metabolites, e.g. lactate concentration, which then increase

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muscle sympathetic output causing limb vasoconstriction. Therefore the efficiency of different respiratory muscle training regimes in improving whole-body endurance performance may depend on the ability to prevent or reduce respiratory muscle fatigue and the associated changes in local metabolites during exercise-induced hyperpnoea. The ability and extent to which the different respiratory muscle training regimes applied in current exercise studies specifically affect the development of respiratory muscle fatigue and local metabolism during hyperpnoea is, however, unknown.

Therefore, the aim of the present investigation was to compare the effects of the two most frequently used training regimes in healthy subjects: RMET and IMT. Based on the specific characteristics of the ventilatory load applied during hyperpnoea and during inspiratory resistive breathing (Belman et al., 1994), we hypothesized that (i) only RMET would induce endurance training-specific metabolic changes (e.g. reduction in blood lactate concentration), (ii) RMET would reduce the development of inspiratory as well as expiratory muscle fatigue during volitional hyperpnoea and improve endurance performance more than IMT, which would only reduce respiratory muscle fatigue (if at all), and (iii) as a result, during volitional hyperpnoea, adverse respiratory sensations would be reduced to a larger extent after RMET than after IMT.

2. Methods

2.1. Subjects

Twenty-six moderately trained, non-smoking, male volunteers with normal lung function (see results for details) were studied. Subjects were randomly assigned to one of three groups: RMET-group ($n = 8$; age 28 ± 4 years, height 180 ± 5 cm, weight 72 ± 4 kg; performing respiratory muscle endurance training in the form of normocapnic hyperpnoea), IMT-group ($n = 10$; 26 ± 6 years, 183 ± 5 cm, 76 ± 6 kg; performing inspiratory resistive training) and SHAM-group ($n = 8$; 26 ± 6 years, 181 ± 6 cm, 71 ± 7 kg; performing sham-training). Subjects refrained from strenuous physical exercise 2 days before the test sessions and performed no physical exercise the day prior to as well as the day of the test. Caffeinated beverages were forbidden before the test and subjects ate their last meal at least 2 h before each test. Subjects did not receive any financial reimbursement for participating, and all gave their written informed consent. The protocol was approved by the local ethics committee and performed according to the Declaration of Helsinki.

2.2. Protocol

In a preliminary session, subjects were thoroughly familiarized with their respective training device and with the different laboratory procedures, i.e. performance of lung function measurements, respiratory muscle pressure measurements, and performance of normocapnic hyperpnoea as required during the respiratory endurance test (RET; for details see below).

In the first experimental session, maximal inspiratory (MIP) and expiratory (MEP) mouth pressures were determined (from residual volume and total lung capacity, respectively). Pressures were measured via a mouthpiece attached to a non-compliant tubing system, including a 0.4 mm leak to avoid glottis closure, attached to a Validyne pressure transducer (DP45-34; Northridge, CA, USA), and the signal being amplified (CD19A, Validyne, Northridge, CA, USA), ADD-converted (MacLab, ADInstruments, Castle Hill, Austral) and stored (Chart Software 5.0.1, ADInstruments). The manoeuvres were performed according to standard procedures (ATS/ERS, 2002). The level of hyperpnoea to be used in the RET was then determined: subjects breathed with the SpiroTiger (Idiag, Fehraltorf, Switzerland), a partial rebreathing device that ensures normocapnia. This device provides the subject with breath-by-breath feedback of tidal volume (V_T) and respiratory frequency (f_R). Target minute ventilation ($\dot{V}_E$) was first set at 70% of maximal voluntary ventilation in 15 s (MVV_{15}) with V_T at 50–60% of vital capacity (VC, similar to hyperpnoea during intense exercise) and f_R adjusted accordingly. The device was connected to a metabolic cart (Oxycon Alpha, Jaeger, Höchberg, Germany) equipped with a turbine and an infrared absorption sensor for CO_2-measurement to check ventilatory variables and normocapnia. $\dot{V}_E$ was adjusted, if necessary, to allow the subject to just complete 8 min of hyperpnoea (eventually leading to $135 \pm 14\,l\,min^{-1}$ for the RMET-group, $140 \pm 24\,l\,min^{-1}$ for the IMT-group and $140 \pm 17\,l\,min^{-1}$ for the SHAM-group, i.e. $70 \pm 9\%$, $69 \pm 13\%$ and $74 \pm 6\%$ of individual MVV_{15}, respectively).

The second experimental session, which included the RET, took place at least 2 days later. Following this, the subjects started the 30-day training period. For details of both, see below.

At least 2 days after the last training session lung function and maximal mouth pressures were determined, and after at least a further 2 days the RET was repeated.

The person conducting the experimental sessions was blinded regarding the type of training that the subjects had performed.

2.3. Respiratory endurance test (RET)

The RET consisted of 8-min of normocapnic hyperpnoea followed by a 6-min pause, followed by a further 8-min of hyperpnoea, another 6-min pause, etc., until task failure, as previously described (Renggli et al., 2008). The test was performed with the SpiroTiger device connected to the metabolic cart. Task failure was defined as (i) subjective exhaustion and/or (ii) the subject's inability to maintain target ventilation ($\dot{V}_E$, V_T or f_R) despite three consecutive "warnings" by the experimenter. The test was stopped by the experimenter if the subject reached a total of 40 min of hyperpnoea, i.e. test duration of 64 min.

$\dot{V}_E$, V_T, f_R and end-tidal CO_2 partial pressure ($P_{ET}CO_2$) were recorded continuously during hyperpnoea. To assess P_{oes} and P_{ga}, conventional balloon-catheters (Milic-Emili et al., 1964) were connected to Validyne pressure transducers (DP45-34). Transdiaphragmatic pressure (P_{di}) was obtained by online subtraction of P_{oes} from P_{ga}. Analogue signals were amplified, digitized and recorded on a Macintosh computer.

Subjects were asked to rate their perception of respiratory sensations before the start of RET, during the last 30 s of each 8-min period of hyperpnoea, and at task failure. Breathlessness and respiratory exertion were assessed by means of a visual analogue scale (VAS) split post hoc into values between 0 and 10. They were labelled with the qualities "breathlessness" and "respiratory exertion" and ranged from "none" on the left-hand side to "maximal" on the right-hand side. Subjects were interviewed extensively prior to the test regarding their experience and understanding of different respiratory sensations. Subsequently, we discussed 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 (Harver et al., 2000; Lansing et al., 2000). The definitions were read to the subjects before each test and the following calibration terms were used as previously discussed with the subjects: "none" was defined as perceiving no breathlessness/respiratory exertion, similar to the sensation when sitting on a chair at rest; "maximal" was defined as the intensity at which the hyperpnoea task would have to be stopped immediately due to this particular sensation. Immediately after the rating, 20 μl of arterialized capillary blood was taken from an ear lobe for blood lactate analysis. Analysis was performed with a Biosen 5040-lactate analyzer (EKF Diagnostik, Barleben, Germany).

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P_{oes} and P_{ga} were recorded during cervical and thoracic magnetic nerve stimulation before the start of the RET, immediately after each 8-min period of hyperpnoea, at task failure, and after 30 and 60 min of recovery. Magnetic nerve stimulation was carried out using a MagStim 200 (MagStim, Sheffield, UK) equipped with a 90 mm circular coil. Cervical magnetic stimulation of the phrenic nerves was performed at the C_7 level while subjects were seated comfortably in a special chair (Similowski et al., 1989). Thoracic stimulation of the nerve roots innervating the abdominal muscles was performed at the T_{10} level while subjects lay prone on a bed (Kyroussis et al., 1996). To avoid the confounding effect of potentiation (Mador et al., 1994; Kyroussis et al., 1996), subjects performed three 5-s maximal inspiratory (before cervical stimulation) or expiratory (before thoracic stimulation) efforts against a closed airway prior to the first series of three stimulations. Prior to the following two sets of three stimulations, one 5-s maximal contraction was performed. Nine stimulations were delivered at functional residual capacity (FRC) with the airway occluded. To assure FRC, the experimenter checked on an oscilloscope (Tektronix, Beaverton, OR, USA) that P_{oes} before every stimulation stayed at a similar level over the entire protocol for each subject on each stimulation position (i.e. sitting and lying). Supramaximality of stimulation was checked by decreasing the stimulation intensities from 100 to 98, 94, 90, 80 and 70% of maximal stimulator output (six stimulations at each intensity) either with cervical ($n = 9$) or thoracic stimulation ($n = 10$) after RET. The order of cervical and thoracic stimulations was randomized between subjects but remained constant for a given subject during the entire RET session as well as during RETs before and after the respective training period.

The RET could not be completed by one subject in the RMET-group, three subjects in the IMT-group and three subjects in the SHAM-group, due to inability to swallow or tolerate balloon-catheters on the day of the first test.

2.4. Respiratory muscle training/sham-training

The RMET-group completed 20 training sessions lasting 30 min (within 30 days) with 1 day of rest following 2 consecutive days of training, according to previous studies (Boutellier et al., 1992; Boutellier and Piwko, 1992; McMahon et al., 2002; Holm et al., 2004; Leddy et al., 2007; Wylegala et al., 2007). Subjects performed voluntary normocapnic hyperpnoea using the SpiroTiger with a target V_T and f_R and a duty cycle of 0.5. Minute ventilation of the first training session was set at 60% of the individual MVV_{15}, with V_T set at 50–60% VC and f_R was adjusted accordingly. Subjects were required to maintain this $\dot{V}_E$ for 30 min. If subjects felt after 25 min of training that they would not be exhausted after 30 min of training, they were instructed to increase f_R by 5 breaths min^{-1} for the last 5 min of the training. In this case, the next training session started with an f_R that was 2 breaths min^{-1} higher than f_R at the start of the previous session. Otherwise, if subjects could not increase f_R after 25 min of training, the next training session started with f_R increased by 1 breath min^{-1}. If subjects felt after 25 min of training that they would not able to continue for another 5 min at the same target f_R, they were allowed to decrease f_R by 5 breaths min^{-1}. In this case the next training session started with identical settings to the previous training.

The IMT-group trained twice a day every day for 30 days with an inspiratory resistance-training device (DeVilbiss RT-Trainer, Hounslow, UK), according to previous studies (Volianitis et al., 2001; Romer et al., 2002b). Before each training session, subjects performed three maximal inspiratory manoeuvres from residual volume to total lung capacity against the internal resistance (i.e. inspiring through a small hole). Subjects were requested to inspire as hard and fast as possible. The pressure–time curves were displayed on a computer screen. From the three breaths, the breath that achieved the highest area under the curve (AuC) was taken as the reference breath for the training session. The software then calculated a curve referring to 80% of this pressure at any time point which was displayed on the computer screen. This curve had to be reproduced 30 times by the subjects. Each inspiration lasted about 20 s. After each inspiration, a 10-s pause allowed normal breathing. Thus one training session lasted about 15 min. If a training breath did not achieve at least 95% of the target AuC, it was discarded by the system and the subject had to repeat it. The AuC of each training breath was recorded as an index of the work performed. This resulted in an average training load of 62% ± 5% MIP.

The SHAM-group trained twice a day every day during 30 days using an incentive spirometer (Voldyne 5000 R, Sherwood Medical, St. Louis, USA). The subjects were instructed to completely exhale slowly. Then they inspired slowly up to 70% of their VC, producing a constant flow controlled by feedback from the device. This procedure was repeated every 30 s (paced by a metronome) for 15 min, twice a day, resulting in a total of 60 inspirations per day. Subjects were told they were training their respiratory muscle coordination, which would have the potential to improve respiratory muscle efficiency and reduce muscle fatigue during hyperpnoea.

To verify compliance, heart rate (HR) was recorded during each session using a heart rate monitor (Polar Vantage, Polar Electro, Kempele, Finland). Training data of RMET and IMT were recorded by the training system and checked during each laboratory visit. In addition the settings of every training were recorded by the subjects in a diary. Training was performed at home, except for every fifth training session that was supervised in the laboratory to ensure correct performance. For the RMET-group, the SpiroTiger was connected to the metabolic cart to ensure that normocapnia was maintained and to adjust ventilatory settings if subjects felt uncomfortable with the f_R of their target $\dot{V}_E$ that they had reached in the past week. In this case, V_T was changed and f_R was adjusted accordingly. Once per training day, lung function [VC, forced inspiratory volume in 1 s (FIV_1), forced expiratory volume in 1 s (FEV_1), peak inspiratory flow rate (PIF), peak expiratory flow rate (PEF), MVV_{15}] was determined by the subject using a portable spirometer (Spirobank, Medical International Research, Rome, Italy). Measurements were performed before and directly after the training session for RMET- and IMT-groups while subjects in the SHAM-group only performed before-training measurements to avoid a muscular training effect provided by repeated MVV-manoeuvres. Lung function data were not available for one subject in the RMET-group, three subjects in the IMT-group and one subject in the SHAM-group due to technical problems. These subjects were not those who were unable to perform the RET.

2.5. Data analysis

As all subjects that performed the RET were able to complete at least two 8-min hyperpnoea periods, we analyzed (i) respiratory muscle twitch forces before RET, after the first and second 8-min periods of hyperpnoea, immediately after task failure, and after 30 and 60 min of recovery, and (ii) respiratory sensations and blood lactate concentrations measured before the RET, at the end of the first and second 8-min periods of hyperpnoea and at task failure.

Within each group, changes over the course of the RET and differences before *vs.* after the training period were assessed using a two-way analysis of variance (ANOVA) with repeated measures and Fisher's protected least-significant difference post hoc analysis (SPSS 11, Chicago, IL, USA). Changes in daily lung function variables were analyzed over the course of the training period by one-way ANOVA with repeated measures and Fisher's protected least-significant difference post hoc analysis. All results are given as means ± SD and $p < 0.05$ was considered as statistically significant.

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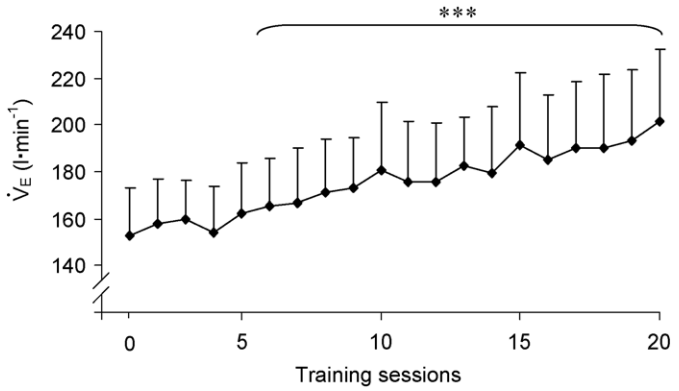

Fig. 1. Average minute ventilation ($\dot{V}_E$) during each respiratory muscle endurance training session over the 30-min training. ***Significantly different from the first session ($p < 0.001$).

3. Results

Training compliance was excellent. All of the subjects performed all training sessions. Mean $\dot{V}_E$ during each RMET-session is shown in Fig. 1. A significant increase in $\dot{V}_E$ was observed over the training period. AuC during the IMT-sessions increased significantly over the 1-month period (Fig. 2). Average HR during training sessions of the first and last quarters of the training period were 93 ± 13 bpm and 101 ± 12 bpm in the RMET-group, 80 ± 15 bpm and 86 ± 17 bpm in the IMT-group, 69 ± 11 bpm and 69 ± 13 bpm in the SHAM-group, respectively ($p < 0.05$ between groups).

3.1. Effect of training on lung function

Mean daily lung function data measured before and after each training session throughout the training periods are shown in Table 1. After RMET-sessions, VC, FIV_1, FEV_1, PEF and MVV_{15} were significantly reduced. After IMT-sessions, only PEF was significantly reduced.

VC, FEV_1 and PIF measured before each training session throughout the training periods are shown in Fig. 3. Over the course of the RMET-period, VC increased significantly. Over the course of the IMT-period, VC and FEV_1 increased significantly while PIF decreased significantly. Over the course of the SHAM-period no change in VC, FEV_1 and PIF were observed. PEF, however, increased slightly but significantly over the course of the SHAM-period (from 8.6 ± 1.0 l s^{-1} in the first training session to 9.1 ± 1.1 l s^{-1} in the last training session, $p < 0.05$), while there was no significant change over the course of the RMET- and IMT-periods (results not shown, $p > 0.05$).

MVV_{15} increased significantly only after the RMET-period (from 122.4 ± 8.9 l min^{-1} in the first training session to 130.2 ± 16.8 l min^{-1} in the last training session, $p < 0.05$).

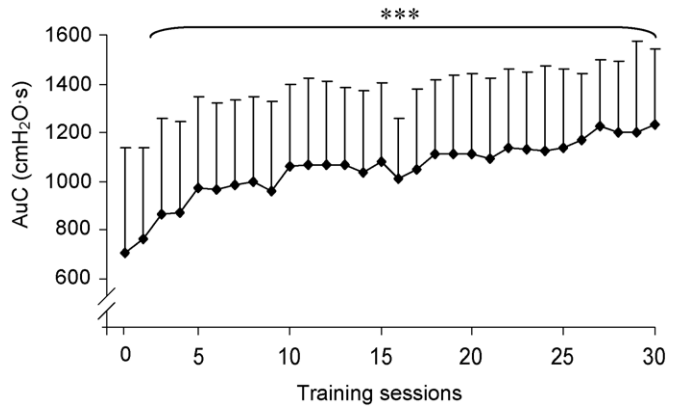

Fig. 2. Average mouth pressure production [area under the pressure–time curve (AuC) during each inspiration] during each inspiratory resistive training session (mean of 30 inspirations twice a day). ***Significantly different from the first session ($p < 0.001$).

3.2. Effect of training on respiratory muscle force and endurance

Respiratory endurance and maximal mouth pressures before and after the training periods are shown in Table 2. Respiratory endurance increased significantly after both the RMET- and IMT-period. However, while all of the subjects in the RMET-group reached the maximum 40-min RET-duration after the training period, only 70% of the subjects in the IMT-group and none in the SHAM-group reached this limit after the training period. Exclusively after the IMT-period, MIP increased and MEP decreased significantly. No other changes were observed after the training periods.

3.3. Effect of training on hyperpnoea-induced respiratory muscle fatigue

Supramaximality of magnetic stimulation was confirmed by reaching maximal levels of $P_{di,tw}$ during cervical stimulation and $P_{ga,tw}$ during thoracic stimulation at submaximal outputs of the stimulator (Mador et al., 1996). Inspiratory $P_{oes,tw}$, $P_{di,tw}$ and expiratory $P_{ga,tw}$ significantly decreased during and following the RET, as previously described (Renggli et al., 2008), both before and after the training period in all groups (Fig. 4). The hyperpnoea-induced decrease in inspiratory $P_{oes,tw}$ was, however, significantly less after the RMET-period. No other significant changes in twitch pressures were observed after the training period in any group compared to before training.

3.4. Effect of training on adverse respiratory sensations and blood lactate concentration during the RET

Respiratory exertion, breathlessness and blood lactate concentration significantly increased in the course of the RET both before and after training in all groups (Fig. 5). Increases in respiratory exertion and blood lactate concentration were only significantly reduced after the RMET-period.

4. Discussion

The present study aimed to compare the effects of RMET and IMT on different aspects of respiratory muscle performance. While only RMET-sessions acutely reduced most measures of lung function, after the 30-day training period both RMET and IMT resulted in a significant increase in VC. Although RMET specifically increased MVV_{15} and IMT specifically improved MIP after training, both RMET and IMT significantly increased respiratory endurance, with a more pronounced improvement after RMET (all subjects reached the 40-min time limit after RMET compared to only 70% of the subjects in the IMT-group). However, during hyperpnoea, only RMET reduced the development of inspiratory muscle fatigue, the increase in blood lactate concentration and the perception of adverse respiratory sensations.

4.1. Specific effects of the two training regimes on respiratory muscle function

While single 30-min RMET-sessions resulted in significant reductions in lung function variables (VC, FIV_1, FEV_1, PEF and

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Table 1
Mean daily lung function before and after RMET- and IMT-sessions.

	RMET-session		IMT-session	
	Before	After	Before	After
VC (l)	5.5 (0.8)	5.3* (0.8)	5.3 (0.4)	5.4 (0.5)
FIV_1 (l)	4.8 (0.4)	4.6* (0.4)	4.7 (0.9)	4.7 (0.8)
FEV_1 (l)	4.4 (0.4)	4.2* (0.3)	4.6 (0.6)	4.5 (0.6)
PIF ($l\,s^{-1}$)	6.9 (1.6)	6.4 (1.6)	6.0 (1.5)	5.8 (1.2)
PEF ($l\,s^{-1}$)	9.3 (1.4)	8.8* (1.3)	9.5 (1.3)	9.1* (1.2)
MVV_{15} ($l\,min^{-1}$)	126 (13)	121* (11)	134 (20)	133 (19)

Values are mean (SD) of the individual average lung function variables measured before and after each training session; VC, vital capacity; FIV_1, forced inspiratory volume in 1 s; FEV_1, forced expiratory volume in 1 s; PIF, peak inspiratory flow; PEF, peak expiratory flow; MVV_{15}, maximum voluntary ventilation.
* Significantly different compared to before ($p < 0.05$).

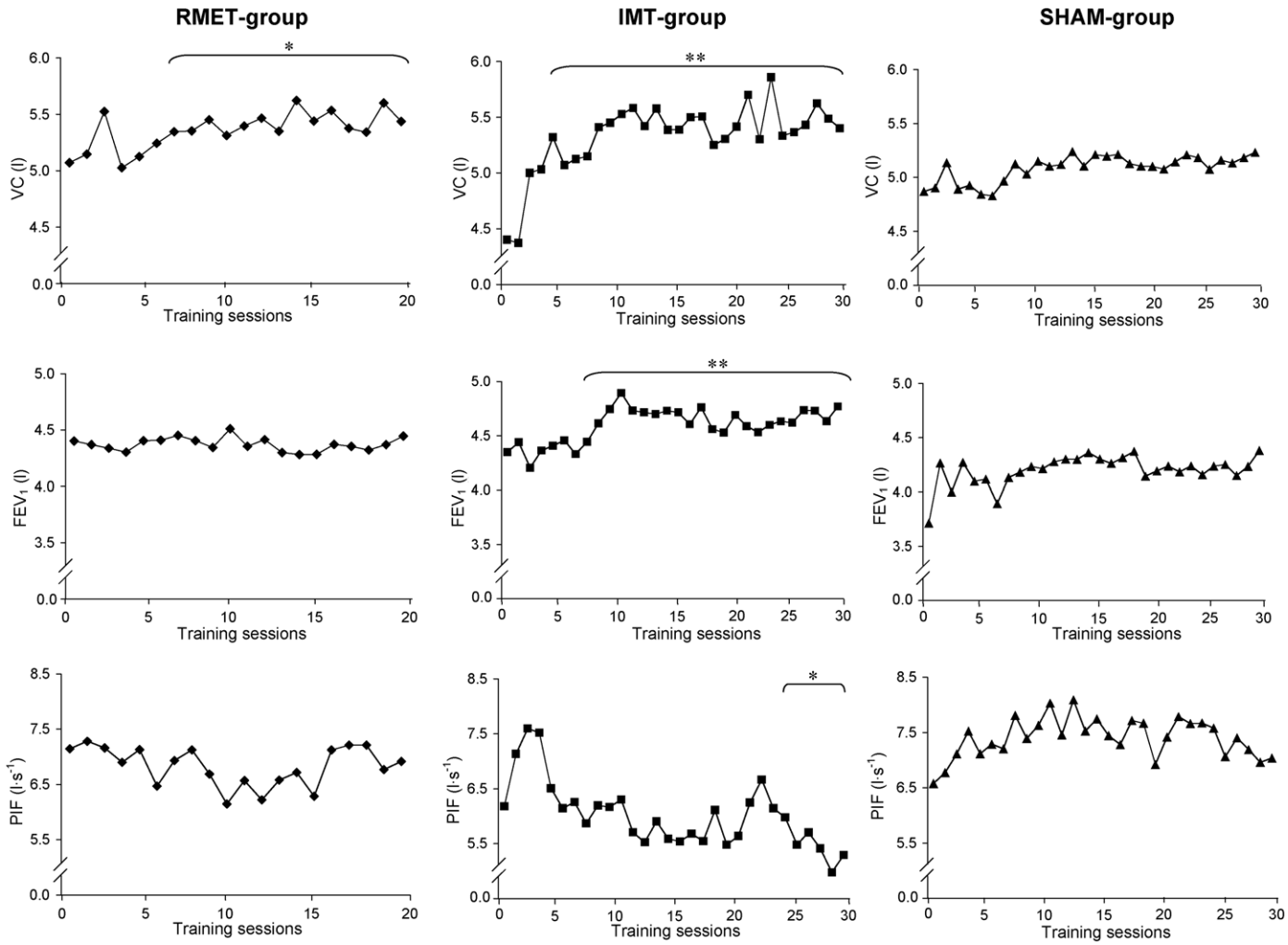

Fig. 3. Vital capacity (VC), FIV_1 (forced inspiratory volume in 1 s), FEV_1 (forced expiratory volume in 1 s), PIF (peak inspiratory flow), PEF (peak expiratory flow) and maximal voluntary ventilation (MVV_{15}) measured before each training sessions throughout the respiratory muscle endurance training (RMET), inspiratory resistive training (IMT) and sham-training (SHAM) periods. Significantly different from the first training session (*$p < 0.05$, **$p < 0.01$).

Table 2
Respiratory endurance and maximal mouth pressures before and after the training periods.

	RMET-period		IMT-period		SHAM-period	
	Before	After	Before	After	Before	After
Breathing duration (min)	24.65 (7.11)	40.00* (0)	26.19 (5.45)	36.17* (6.67)	25.81 (3.35)	28.29 (7.56)
MIP (cmH_2O)	134 (32)	128 (45)	119 (29)	157* (26)	112 (23)	118 (29)
MEP (cmH_2O)	168 (53)	171 (60)	148 (35)	122* (31)	159 (42)	156 (38)

Values are mean (SD); RMET, respiratory muscle endurance training; IMT, inspiratory resistive training; SHAM, sham-training; MIP, maximal inspiratory mouth pressure; MEP, maximal expiratory mouth pressure.
* Significantly different compared to before ($p < 0.05$).

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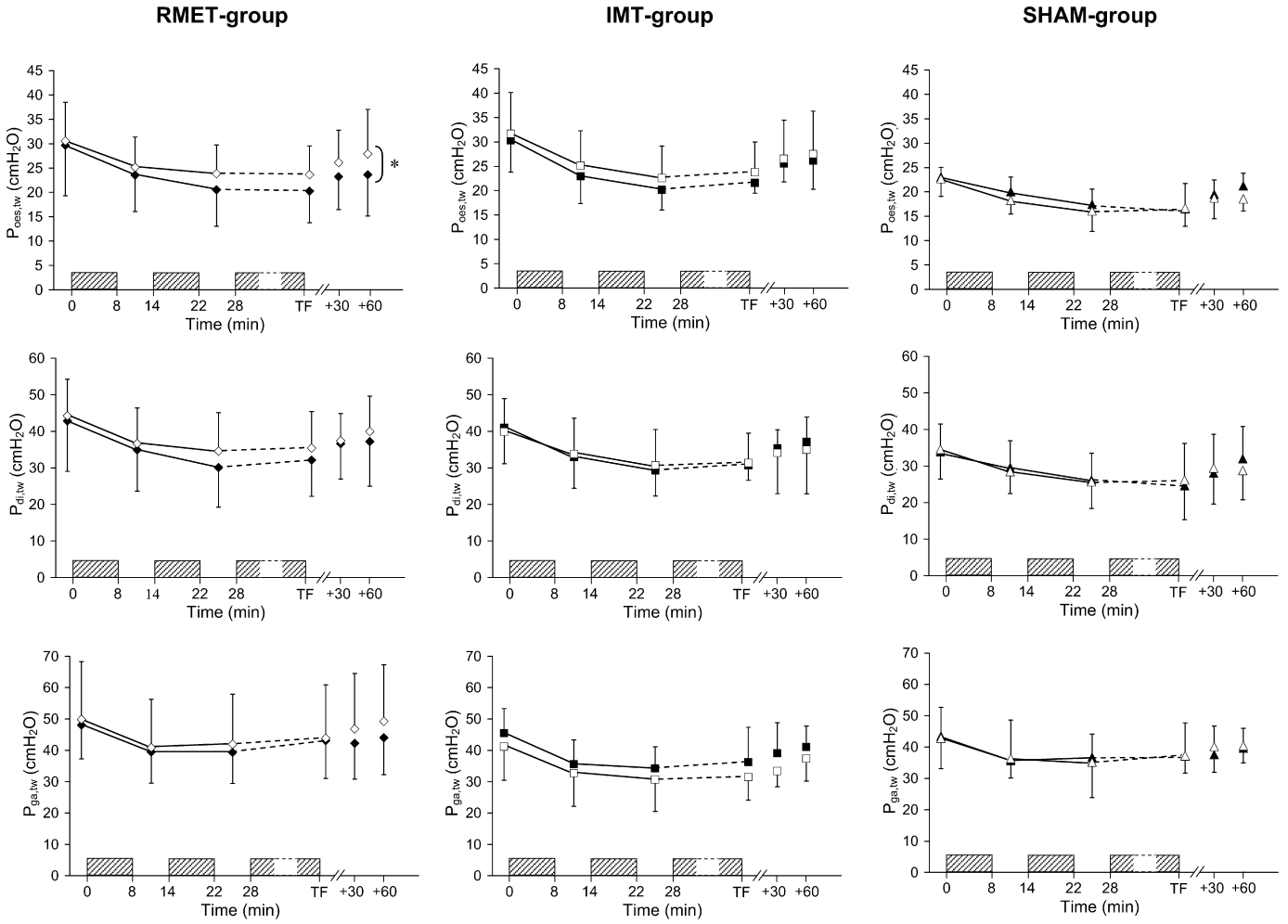

Fig. 4. Changes in twitch inspiratory oesophageal ($P_{oes,tw}$) and transdiaphragmatic ($P_{di,tw}$) pressures and in twitch expiratory gastric pressure ($P_{ga,tw}$) during and after task failure (TF, +30 and +60 min) the respiratory endurance tests performed before (black symbols) and after (white symbols) the respiratory muscle endurance training (RMET), inspiratory resistive training (IMT) and sham-training (SHAM) periods. *Significant difference between before and after training ($p < 0.05$). Before as well as after training, twitch pressures during and after the hyperpnoea were significantly reduced compared to rest.

MVV_{15}), 15-min of IMT only significantly reduced PEF, suggesting a higher training load for RMET compared to IMT. This is supported by the higher HR during RMET-sessions compared to IMT and SHAM sessions. One would therefore expect the training stimulus and associated improvements to be greater after the RMET- than after the IMT-period. However, despite training-specific improvements (RMET improved MVV_{15} while IMT improved MIP), both of these training regimes improved VC, a fact previously reported (Enright et al., 2006; Verges et al., 2008). Regarding the reduction in PIF over the course of the IMT-period, two potential mechanisms might be responsible: (i) an 'overtraining'-like phenomenon of inspiratory and/or airway dilating muscles (Verges et al., 2006) occurring due to insufficient recovery between respiratory training sessions, and/or (ii) training-specific adaptations of inspiratory muscles to IMT leading to improved performance during slow and forceful inspirations only, i.e. improved MIP, thereby compromising high speed manoeuvres such as forced, fast inspirations. Together these results suggest, on the one hand, that acute changes resulting from single training sessions cannot predict chronic effects of respiratory muscle training and, on the other hand, that RMET and IMT are able to induce significant and, at least partially, distinct changes in several lung function variables, even in healthy subjects with normal lung function.

While increases in MVV_{15} after the RMET-period and in MIP after the IMT-period are expected and well-known functional improvements related to specific respiratory muscle training (Leith and Bradley, 1976; Boutellier et al., 1992; Boutellier and Piwko, 1992; Suzuki et al., 1993; Spengler et al., 1999; Volianitis et al., 2001; McMahon et al., 2002; Romer et al., 2002a; Gething et al., 2004; Holm et al., 2004; Leddy et al., 2007; Wylegala et al., 2007), the reduction in MEP following the IMT-period has not previously been described. We believe we observed a genuine physiological change since abdominal muscle contractility, reflected in expiratory $P_{ga,tw}$, tended to be lower before and during the RET after the IMT-period (Fig. 4). Possibly, the increase in inspiratory muscle strength after IMT might have affected respiratory mechanics (e.g. increased chest wall stiffness) and/or agonist/antagonist respiratory muscle balance which may be disadvantageous for maximal expiratory pressure production. However, this effect, as well as its potential underlying mechanisms, await further investigation.

4.2. Effects of the two respiratory muscle training regimes on respiratory muscle fatigue, metabolic changes and perception of adverse respiratory sensations during volitional hyperpnoea

During volitional hyperpnoea, RMET improved global inspiratory muscle fatigue (as reflected by a smaller decrease in $P_{oes,tw}$ during cervical stimulation) while it did not affect specific diaphragm fatigue or the development of abdominal muscle fatigue. This differs from our previous findings (Verges et al., 2007)

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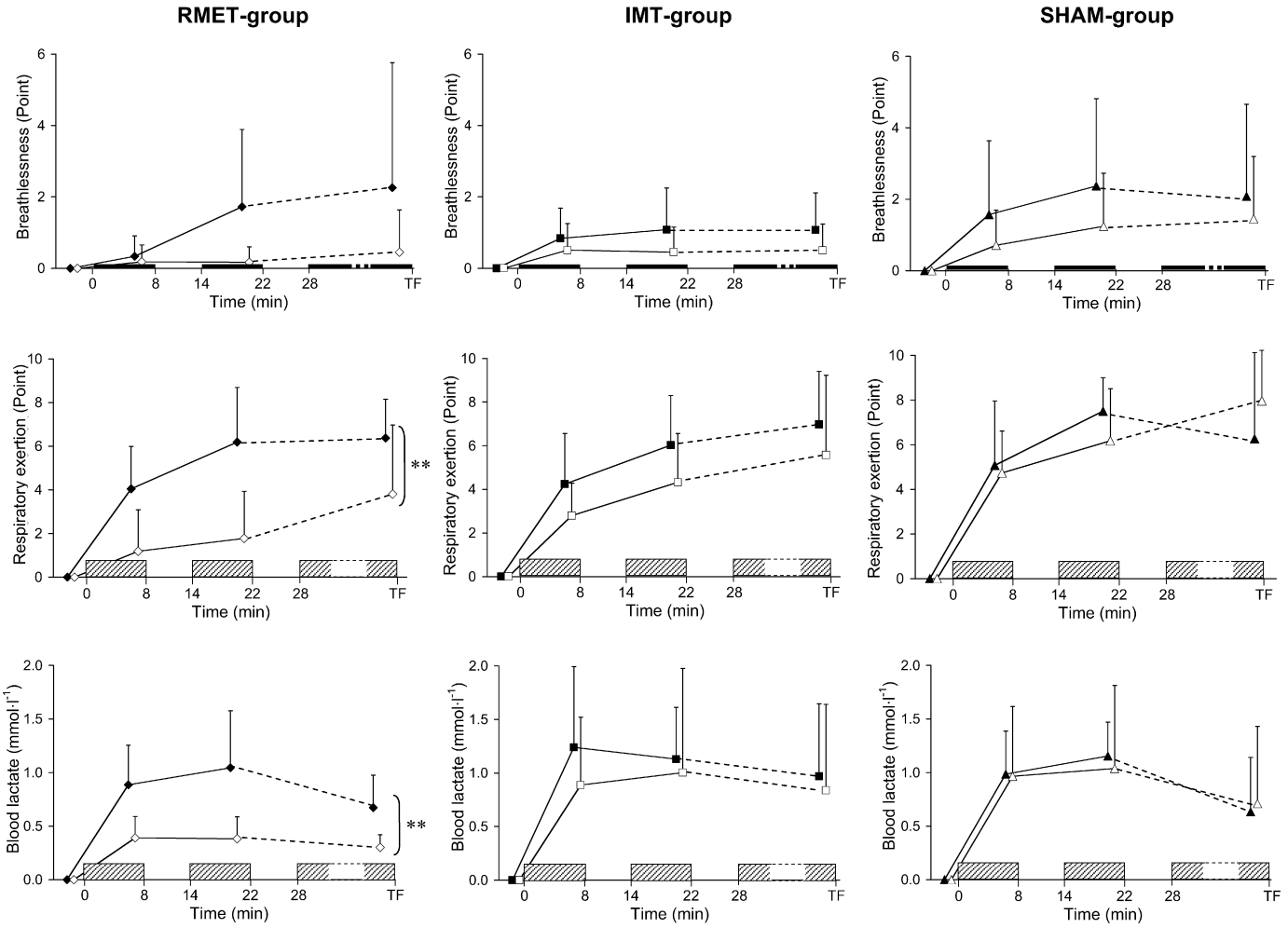

Fig. 5. Breathlessness, respiratory exertion and blood lactate concentration during the respiratory endurance tests performed before (black symbols) and after (white symbols) the respiratory muscle endurance training (RMET), inspiratory resistive training (IMT) and sham-training (SHAM) periods. TF, task failure. **Significant difference between before and after training ($p < 0.01$). Before as well as after training, all parameters were significantly increased during hyperpnoea compared to rest, except for breathlessness that was significantly increased from the second bout of hyperpnoea only.

that show a reduction in the development of both diaphragm and abdominal muscle fatigue during constant load cycling after RMET. The discrepancy between these findings might result from different characteristics of the hyperpnoeic task, i.e. discontinuous hyperpnoea with 6-min breaks between 8-min bouts of hyperpnoea at 71% MVV_{15} in the present study, allowing for some recovery or at least washout of metabolites, *versus* continuous hyperpnoea at an average of 54% MVV_{15} during exercise lasting 16 min on average (Verges et al., 2007). Moreover, the interaction between functional/metabolic changes in respiratory and leg muscles specific to whole-body exercise (Dempsey et al., 2006) might have enhanced the positive effect of respiratory muscle training in our previous exercise study (Verges et al., 2007).

In contrast to our hypothesis, IMT did not improve hyperpnoea-induced inspiratory muscle fatigue, despite an increase in MIP. This indicates that improving the capacity for maximal inspiratory muscle pressure generation, resulting in inspiratory muscles working at a lower percentage of their maximal strength, does not necessarily affect the development of inspiratory muscle fatigue during a respiratory endurance-type task. However, as IMT improved respiratory endurance, we suggest that other factors than those related to respiratory muscle fatigue itself contribute to task performance during volitional hyperpnoea.

The greater effect of RMET than of IMT on respiratory muscles is also shown by the significant reduction of [La] and perception of adverse respiratory sensations during volitional hyperpnoea after RMET, as shown previously (Verges et al., 2008), while no significant changes were observed after IMT. The latter, however, contrasts with recent results of Brown et al. (2008), who found a significant reduction in [La] during volitional hyperpnoea after IMT. Differences in respiratory muscle loading (80% MVV_{10} in Brown's study versus 70% MVV_{15} in the present study), training duration (6 weeks vs. 4 weeks) and modality (subjects of the present study trained over the entire VC at 80% of the maximal pressure registered at every lung volume while Brown's subjects trained at ≥50% MIP assessed at RV, possibly not covering the entire VC) may explain this difference. A reduction in anaerobic metabolism and/or an increase in lactate consumption within the respiratory muscles may be responsible for the reduction in [La] after RMET and may represent specific adaptations to endurance training as known for whole-body endurance training (Jones and Carter, 2000). The reduced perception of adverse respiratory sensations that was present only during hyperpnoea after RMET suggests that mechanisms associated with the reduced development of respiratory muscle fatigue are more likely to contribute to the perception of respiratory exertion than the relative force at which muscles contract, also suggested (Killian et al., 1982; Redline et al., 1991).

The metabolic changes associated with the reduced [La] during hyperpnoea after RMET may be critical regarding the expected impact of hyperpnoea-induced respiratory muscle fatigue during

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exercise through the "respiratory muscle metaboreflex" (Dempsey et al., 2006). Moreover, the significant reduction in adverse respiratory sensations during hyperpnoea following RMET also suggests that this type of training may be particularly adapted to improve exercise tolerance in patients limited by the perception of dyspnoea. However, the similarity of the primary outcomes associated with voluntary hyperpnoea during the RET with the training modality of RMET may have biased the results in favour of RMET. In addition, because volitional and exercise-induced hyperpnoea are not entirely identical, results from the present study cannot directly be translated to exercise conditions. Hence, further studies are needed to compare the effects of RMET and IMT on exercise-induced hyperpnoea and exercise performance.

4.3. Methodological limitations

In order to follow the time course of potential changes in lung function measures over the course of the training periods as well as to assess acute changes resulting from single training sessions, subjects performed daily lung function measurements before and after home-training sessions using a portable spirometer. Although subjects were trained repeatedly during laboratory sessions to perform lung function manoeuvres properly, we cannot exclude that some learning effects might have influenced lung function measurements over the trainings period, as suggested by the increase in PEF over the SHAM-period. However, as most of the modifications in lung function parameters were observed in the RMET- and IMT-groups only, they likely represent effects specific to these training regimes.

Although lung function measurements gave insight regarding the acute effect of the training sessions, assessment of respiratory muscle strength by measurement of maximal mouth pressure would have given additional insight with respect to the development of respiratory muscle fatigue during a training session. Unfortunately, we were unable to provide the subjects with a portable device for home-assessment of MIP and MEP, thus we had to rely on forced spirometric manoeuvres as a surrogate for loss of performance after a training session.

It should also be acknowledged that, in the present study, respiratory muscle fatigue was assessed during the first minutes directly after stopping the hyperpnoea bouts, while recent results suggest that these measurements may not reflect muscle fatigue *during* loading (Kabitz et al., 2007, 2008). In addition, the number of subjects in the present study might have been too small to detect changes in diaphragmatic or abdominal muscle fatigue after training due to type 2 error. The results did not differ, however, when performing the statistical analysis by doubling the sample size.

In conclusion, the present study suggests that RMET and IMT induced distinct changes in lung function measurements, except for VC that increased after both types of training. In addition to the expected improvement in respiratory muscle endurance after RMET and in MIP after IMT, our results revealed that IMT also increases respiratory muscle endurance at high levels of volitional hyperpnoea, although to a lesser extent than RMET. The greater improvement in respiratory endurance after RMET is likely be attributed to a reduced development of inspiratory muscle fatigue associated with improved respiratory muscle metabolism and to a reduced perception of adverse respiratory sensations during hyperpnoea. As mechanisms associated with hyperpnoea-induced respiratory muscle fatigue may be critical regarding whole-body endurance performance, these results suggest that RMET may be particularly effective in improving respiratory muscle performance during hyperpnoea and subsequently exercise performance. Further studies are needed, however, to compare the effects of RMET and IMT on exercise performance.

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References

American Thoracic Society/European Respiratory Society, 2002. ATS/ERS Statement on respiratory muscle testing. Am. J. Respir. Crit. Care Med. 166, 518–624.
Belman, M.J., Botnick, W.C., Nathan, S.D., Chon, K.H., 1994. Ventilatory load characteristics during ventilatory muscle training. Am. J. Respir. Crit. Care Med. 149, 925–929.
Boutellier, U., Buchel, R., Kundert, A., Spengler, C., 1992. The respiratory system as an exercise limiting factor in normal trained subjects. Eur. J. Appl. Physiol. Occup. Physiol. 65, 347–353.
Boutellier, U., Piwko, P., 1992. The respiratory system as an exercise limiting factor in normal sedentary subjects. Eur. J. Appl. Physiol. Occup. Physiol. 64, 145–152.
Brown, P.I., Sharpe, G.R., Johnson, M.A., 2008. Inspiratory muscle training reduces blood lactate concentration during volitional hyperpnoea. Eur. J. Appl. Physiol. 104, 111–117.
Dempsey, J.A., Romer, L., Rodman, J., Miller, J., Smith, C., 2006. Consequences of exercise-induced respiratory muscle work. Respir. Physiol. Neurobiol. 151, 242–250.
Enright, S.J., Unnithan, V.B., Heward, C., Withnall, L., Davies, D.H., 2006. Effect of high-intensity inspiratory muscle training on lung volumes, diaphragm thickness, and exercise capacity in subjects who are healthy. Phys. Ther. 86, 345–354.
Faulkner, J.A., 1984. Structural and functional adaptations of skeletal muscle. In: Roussos, C., Macklem, P.T. (Eds.), The Thorax. Dekker, M., New York, pp. 1329–1352.
Geddes, E.L., Reid, W.D., Crowe, J., O'Brien, K., Brooks, D., 2005. Inspiratory muscle training in adults with chronic obstructive pulmonary disease: a systematic review. Respir. Med. 99, 1440–1458.
Gething, A.D., Williams, M., Davies, B., 2004. Inspiratory resistive loading improves cycling capacity: a placebo controlled trial. Br. J. Sports Med. 38, 730–736.
Harver, A., Mahler, D.A., Schwartzstein, R.M., Baird, J.C., 2000. Descriptors of breathlessness in healthy individuals: distinct and separable constructs. Chest 118, 679–690.
Holm, P., Sattler, A., Fregosi, R.F., 2004. Endurance training of respiratory muscles improves cycling performance in fit young cyclists. BMC Physiol. 4, 9.
Jones, A.M., Carter, H., 2000. The effect of endurance training on parameters of aerobic fitness. Sports Med. 29, 373–386.
Kabitz, H.J., Walker, D., Schwoerer, A., Sonntag, F., Walterspacher, S., Roecker, K., Windisch, W., 2007. New physiological insights into exercise-induced diaphragmatic fatigue. Respir. Physiol. Neurobiol. 158, 88–96.
Kabitz, H.J., Walker, D., Sonntag, F., Walterspacher, S., Kirchberger, A., Burgardt, V., Roecker, K., Windisch, W., 2008. Post-exercise diaphragm shielding: a novel approach to exercise-induced diaphragmatic fatigue. Respir. Physiol. Neurobiol. 162, 230–237.
Killian, K.J., Bucens, D.D., Campbell, E.J., 1982. Effect of breathing patterns on the perceived magnitude of added loads to breathing. J. Appl. Physiol. 52, 578–584.
Kyroussis, D., Mills, G.H., Polkey, M.I., Hamnegard, C.H., Koulouris, N., Green, M., Moxham, J., 1996. Abdominal muscle fatigue after maximal ventilation in humans. J. Appl. Physiol. 81, 1477–1483.
Lansing, R.W., Im, B.S., Thwing, J.I., Legedza, A.T., Banzett, R.B., 2000. The perception of respiratory work and effort can be independent of the perception of air hunger. Am. J. Respir. Crit. Care Med. 162, 1690–1696.
Leddy, J.J., Limprasertkul, A., Patel, S., Modlich, F., Buyea, C., Pendergast, D.R., Lundgren, C.E., 2007. Isocapnic hyperpnea training improves performance in competitive male runners. Eur. J. Appl. Physiol. 99, 665–676.
Leith, D.E., Bradley, M., 1976. Ventilatory muscle strength and endurance training. J. Appl. Physiol. 41, 508–516.
Mador, M.J., Magalang, U.J., Kufel, T.J., 1994. Twitch potentiation following voluntary diaphragmatic contraction. Am. J. Respir. Crit. Care Med. 149, 739–743.
Mador, M.J., Rodis, A., Magalang, U.J., Ameen, K., 1996. Comparison of cervical magnetic and transcutaneous phrenic nerve stimulation before and after threshold loading. Am. J. Respir. Crit. Care Med. 154, 448–453.
McMahon, M.E., Boutellier, U., Smith, R.M., Spengler, C.M., 2002. Hyperpnea training attenuates peripheral chemosensitivity and improves cycling endurance. J. Exp. Biol. 205, 3937–3943.
Milic-Emili, J., Mead, J., Turner, J.M., Glauser, E.M., 1964. Improved technique for estimating pleural pressure from esophageal balloons. J. Appl. Physiol. 19, 207–211.
Padula, C.A., Yeaw, E., 2007. Inspiratory muscle training: integrative review of use in conditions other than COPD. Res. Theory Nurs. Pract. 21, 98–118.
Redline, S., Gottfried, S.B., Altose, M.D., 1991. Effects of changes in inspiratory muscle strength on the sensation of respiratory force. J. Appl. Physiol. 70, 240–245.
Renggli, A.S., Verges, S., Notter, D.A., Spengler, C.M., 2008. Development of respiratory muscle contractile fatigue in the course of hyperpnoea. Respir. Physiol. Neurobiol. 164, 366–372.

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Romer, L.M., McConnell, A.K., Jones, D.A., 2002a. Effects of inspiratory muscle training upon recovery time during high intensity, repetitive sprint activity. Int. J. Sports Med. 23, 353–360.
Romer, L.M., McConnell, A.K., Jones, D.A., 2002b. Inspiratory muscle fatigue in trained cyclists: effects of inspiratory muscle training. Med. Sci. Sports Exerc. 34, 785–792.
Sheel, A.W., 2002. Respiratory muscle training in healthy individuals: physiological rationale and implications for exercise performance. Sports Med. 32, 567–581.
Similowski, T., Fleury, B., Launois, S., Cathala, H.P., Bouche, P., Derenne, J.P., 1989. Cervical magnetic stimulation: a new painless method for bilateral phrenic nerve stimulation in conscious humans. J. Appl. Physiol. 67, 1311–1318.
Spengler, C.M., Roos, M., Laube, S.M., Boutellier, U., 1999. Decreased exercise blood lactate concentrations after respiratory endurance training in humans. Eur. J. Appl. Physiol. Occup. Physiol. 79, 299–305.
Suzuki, S., Yoshiike, Y., Suzuki, M., Akahori, T., Hasegawa, A., Okubo, T., 1993. Inspiratory muscle training and respiratory sensation during treadmill exercise. Chest 104, 197–202.
Verges, S., Boutellier, U., Spengler, C.M., 2008. Effect of respiratory muscle endurance training on respiratory sensations, respiratory control and exercise performance: a 15-year experience. Respir. Physiol. Neurobiol. 161, 16–22.
Verges, S., Lenherr, O., Haner, A.C., Schulz, C., Spengler, C.M., 2007. Increased fatigue resistance of respiratory muscles during exercise after respiratory muscle endurance training. Am. J. Physiol. Regul. Integr. Comp. Physiol. 292, R1246–1253.
Verges, S., Notter, D., Spengler, C.M., 2006. Influence of diaphragm and rib cage muscle fatigue on breathing during endurance exercise. Respir. Physiol. Neurobiol. 154, 431–442.
Volianitis, S., McConnell, A.K., Koutedakis, Y., McNaughton, L., Backx, K., Jones, D.A., 2001. Inspiratory muscle training improves rowing performance. Med. Sci. Sports Exerc. 33, 803–809.
Wylegala, J.A., Pendergast, D.R., Gosselin, L.E., Warkander, D.E., Lundgren, C.E., 2007. Respiratory muscle training improves swimming endurance in divers. Eur. J. Appl. Physiol. 99, 393–404.

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