Acute Effects of a Respiratory Sprint-Interval Session on Muscle Contractility

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ABSTRACT

WÜTHRICH, T. U., J. MARTY, P. BENAGLIA, P. A. EICHENBERGER, and C. M. SPENGLER. Acute Effects of a Respiratory Sprint-Interval Session on Muscle Contractility. *Med. Sci. Sports Exerc.*, Vol. 47, No. 9, pp. 1979–1987, 2015. **Introduction**: Respiratory muscle training has been shown to improve physical performance in healthy individuals and patients. One training modality for both inspiratory and expiratory muscles is respiratory muscle endurance training (RMET), which consists of normocapnic hyperpnea at constant ventilation for 30 min. Here, a new training regimen, respiratory muscle sprint-interval training (RMSIT), is introduced and tested for its potential to fatigue respiratory muscles. In addition, effects of both modalities on airway properties are investigated. **Methods**: In 12 healthy subjects (six men and six women; 24 ± 3 yr; forced expiratory volume in 1 s, 115% ± 10%), changes in inspiratory transdiaphragmatic twitch pressure ($P_{di,tw}$) and expiratory gastric twitch pressure ($P_{ga,tw}$) were assessed during cervical magnetic stimulation or thoracic magnetic stimulation before and after a single bout of RMET and RMSIT. At similar time points, mechanical airway properties were assessed by impulse oscillometry. RMET was performed for 30 min at 60% of maximal voluntary ventilation, with constant tidal volume and breathing frequency. RMSIT consisted of six 30-s respiratory sprints (with 2-min breaks in between) at constant tidal volume, with the greatest possible breathing frequency and added resistance. **Results**: $P_{di,tw}$ and $P_{ga,tw}$ decreased significantly after RMET (−17.7% ± 9.0% and −22.4% ± 18.5%; $P < 0.01$) and RMSIT (−18.1% ± 12.8% and −21.2% ± 13.1%; $P < 0.01$), and changes did not differ between training modalities ($P = 0.50$ and $P = 0.12$), suggesting similar levels of fatigue. Work of breathing per minute was 2.4 ± 0.8-fold greater in RMSIT than in RMET, whereas total work of breathing was substantially smaller in RMSIT (3.4 ± 0.8 kJ) than in RMET (15.0 ± 0.42 kJ). No subject showed clinically relevant changes in mechanical airway properties. **Conclusions**: Despite different work history, RMSIT appears to place a metabolic load on respiratory muscles similarly to RMET and could therefore be considered a time-saving and safe training alternative. **Key Words:** HYPERPNEA, RESPIRATORY MUSCLE FATIGUE, RESPIRATORY MUSCLE TRAINING

Specific training of respiratory muscles was shown to have beneficial effects on exercise capacity in healthy individuals (8,12) and patients suffering from different diseases (4,6). Yet, the underlying mechanisms are not fully understood and may vary depending on the investigated population. For healthy individuals, however, improvements in whole-body exercise performance after a period of respiratory muscle training have been associated with reduced activation of the respiratory muscle metaboreflex (22,39) secondary to attenuated development of respiratory muscle fatigue (22,37).

One training modality is respiratory muscle endurance training (RMET), which consists of volitional normocapnic hyperpnea at high levels of ventilation sustained for 20–30 min (e.g., [36]). A single session of RMET can acutely impair respiratory muscle contractility (28), which is associated with the accumulation of a variety of metabolites within working muscles. In fact, metabolic disturbance has a dual role—it may not only impair muscle contractility but also trigger muscular adaptations through a variety of signaling pathways within muscle cells (11).

Endurance-type whole-body training regimens—or RMET for respiratory muscles—are time consuming and often perceived as monotonous. As a result, repeated bouts of maximal-intensity or near-maximal-intensity exercise interspersed with short breaks (named high-intensity or sprint-interval training) have become increasingly popular for whole-body training, as they are characterized by very low training volume (a total of 180–300 s) while being equally effective in improving whole-body exercise performance compared to traditional endurance-type training (e.g., [27]). However, to date, no such modality has been considered despite existing evidence that maximal voluntary ventilation (MVV) for as little as 120 s is sufficient to substantially reduce the contractility of inspiratory and expiratory muscles (9,17). In fact, there exists a considerable body of literature on the development of fatigue under different respiratory loading conditions (for review, see [13]); however, this mainly includes inspiratory resistive or static maneuvers, whereas high-intensity interval conditions have not yet been investigated.

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Thus, it is difficult to predict whether repeated, very short respiratory sprints (respiratory muscle sprint-interval training (RMSIT)) have the potential to load and thus fatigue respiratory muscles to the same extent as traditional RMET or 2 min of maximal unloaded breathing. If this load during RMSIT was indeed high enough to acutely cause a similar level of contractile fatigue, one could expect long-term adaptations to chronic exposure with clearly lower training volume than with RMET. In a first step, it is therefore important to investigate the acute effects of RMSIT on contractile function.

However, when considering a new type of respiratory muscle training modality aimed also at training of patients, potential side effects need to be considered. We observed, for instance, that the high levels of ventilation performed during RMET can acutely reduce measures of lung function, even in young healthy individuals (38). Apart from respiratory muscle fatigue (10), these changes could originate from altered airway resistance and/or reactance (subsequently referred to as mechanical airway properties) resulting from, for example, changes in airway wall compliance, secretions, cellular exudate, etc. In order to resolve this controversy, we need to consider measurement techniques that are independent of voluntary effort or respiratory muscle fatigue. Unpublished data from our laboratory using nonvoluntary assessments of mechanical airway properties by impulse oscillometry suggest that small, yet clinically irrelevant changes in airway resistance may occur during RMET, whereas the effects of RMSIT on mechanical airway properties are currently unknown and warrant further examination.

Therefore, the aims of the present study were to investigate the effects of RMSIT on respiratory muscle contractility and airway properties compared to RMET. We hypothesized that impairment of respiratory muscle contractility is of similar magnitude in RMSIT and RMET and that neither protocol negatively affects mechanical airway properties.

METHODS

Twelve healthy subjects (six men and six women; Table 1) with a wide range of fitness (weekly training, 7.9 ± 4.7 h·wk^{-1}) gave their written informed consent to participate in this study. Inclusion criteria were as follows: 18–35 yr old, normal lung function, normal body mass index (i.e.,18–25 kg·m^{-2}), nonsmoker, no chronic or acute disease, and no metallic implants. Subjects refrained from intensive physical exercise 2 d before the tests and completely refrained from physical exercise 24 h before the tests. Subjects were not allowed to consume any caffeinated products on test days, were asked to sleep at least 7 h the night before the test, and were asked to have their last meal 2 h before the tests. The study was approved by the local ethics committee.

TABLE 1. Subjects' characteristics.

Age (yr)	24 ± 3	FEV_1 (L)	4.45 ± 0.57
Height (m)	1.73 ± 0.10	FEV_1 (%pred)	115 ± 10
Body mass (kg)	66.9 ± 10.2	PEF (L·s^{-1})	9.1 ± 1.9
Body mass index (kg·m^{-2})	22.2 ± 1.8	PEF (%pred)	106 ± 10
Vital capacity (L)	5.82 ± 1.07	MVV (L·min^{-1})	178 ± 33
Vital capacity (%pred)	124 ± 15	MVV (%pred)	130 ± 17

Values are presented as mean ± SD.

Experimental protocol. Subjects reported to the laboratory on three different days. During the first visit, lung function was measured and subjects were familiarized with all testing equipment and techniques to be used during the second and third visits. Familiarization included insertion of balloon catheters, technique of magnetic nerve stimulation, and detailed procedures for and a test run of each training modality. During the second and third visits, subjects performed either a session of RMET or a session of RMSIT in a randomized and balanced order. Mechanical airway properties were assessed before and immediately after RMET and RMSIT. Respiratory muscle testing (volitional and nonvolitional respiratory muscle strength assessment) was performed before, immediately after, and 30 min after completion of the trial. All test sessions were scheduled at the same time of day to control for the confounding influence of circadian rhythm (31). A minimum of 48 h was mandatory between sessions to allow for full recovery.

Lung function assessment. Vital capacity, forced expiratory volume in 1 s (FEV_1), peak expiratory flow (PEF), and MVV were assessed according to current guidelines (23) using a metabolic cart with a calibrated turbine for volume measurements (Oxycon pro; Jaeger, Höchberg, Germany). Absolute and percent predicted values of pulmonary function variables are reported in Table 1 (25,26).

Assessment of mechanical airway properties. Respiratory resistance at 5 Hz (R5Hz), respiratory resistance at 20 Hz (R20Hz), and respiratory reactance at 5 Hz (X5Hz) were assessed according to current guidelines (24) using impulse oscillometry (MasterScreen IOS; Jaeger). The device was calibrated with a 3-L calibration syringe before each testing session. Subjects were instructed to sit in front of the device in an upright position with the head in a slightly extended position, to press their hands gently against their cheeks, and to support the floor of the mouth with their thumbs. Subjects wore a noseclip and breathed through a mouthpiece with an antibacterial filter (MicroGard® IIC and VIASYS®; CareFusion USA) for 45 to 60 s. At baseline and immediately after (before respiratory muscle testing) both RMET and RMSIT, three measurements were performed, and the average thereof was taken as the final value.

RMET consisted of continuous volitional normocapnic hyperpnea performed for 30 min with a commercially available training device using partial rebreathing (SpiroTiger®; idiag, Fehraltorf, Switzerland). Subjects were instructed to breathe at a target ventilation of 60% MVV with constant tidal volume (V_T; 55% vital capacity) and breathing frequency (f_B). During the familiarization session, subjects performed RMET for 25 min. If they felt that they would not be exhausted by 30 min, f_B was increased by 2 breaths per minute for the RMET testing session, as suggested by previous studies (e.g., [37]). In case subjects could sustain target ventilation for 25 min but felt that they would not have been able to go any longer, f_B remained unchanged on the RMET testing day. During the RMET session, subjects received auditory (metronome), visual (V_T on a screen in

front of the subject), and verbal (experimenter) feedback to keep their V_T and f_B at the target levels. A stopwatch in front of the participant gave feedback on elapsed time. Partial pressure of end-tidal CO_2 was constantly monitored and held within the normocapnic range.

For RMSIT, the same training device described above was used, but additional resistance was introduced by adding an orifice with reduced diameter between the mouthpiece and the device to maximize respiratory muscle work. For participants with MVV higher than 160 $L \cdot min^{-1}$, an orifice with a diameter of 11 mm was used (n = 8), whereas for those with MVV lower than 160 $L \cdot min^{-1}$, an orifice with a diameter of 8.5 mm was chosen (n = 4) in order to account for the nonlinear relationship between resistive work and flow. Participants were asked to maximally ventilate for 30 s at constant V_T (55% vital capacity) and with the highest possible f_B. A total of six 30-s bouts were performed, with a break of 2 min between bouts. Subjects received the same feedback as described above, and strong verbal encouragement was given throughout the sprints.

Ventilation and partial pressure of end-tidal CO_2 were measured breath by breath via the metabolic cart comprising a calibrated volume sensor and a calibrated infrared absorption gas sensor for CO_2 analysis. Heart rate was obtained with a portable heart rate monitor (Polar s610i; Polar Electro, Kempele, Finland). Before and immediately after stopping RMET and RMSIT, 20 μL of capillary blood was taken from the earlobe to measure blood lactate concentration enzymatically (Biosen C-Line Sports; EKF-diagnostic, Barleben, Germany). Subjects were asked to rate their perception of breathlessness and respiratory effort using a visual analog scale. Data were collected at the end of each 30-s sprint (i.e., at 0.5, 3, 5.5, 8, 10.5, and 13 min after the start of RMSIT), at identical time points after the start of RMET, and additionally at 15, 20, 25, and 30 min during the remainder of RMET. End points of the visual analog scale were marked with "no breathlessness" and "no respiratory effort" and with "maximal breathlessness" and "maximal respiratory effort." For proper understanding of the terms "breathlessness" and "respiratory effort," these two terms were extensively discussed with the subjects before the tests and, finally, definitions of breathlessness (sensation of "not getting enough air") and respiratory exertion ("work/effort that is required by breathing") were given (19).

Pressure measurements and respiratory muscle testing. Esophageal pressure (P_{es}) and gastric pressure (P_{ga}) were measured by conventional balloon catheters (Cooper Surgical, Trumbull, CT, USA). Transdiaphragmatic pressure (P_{di}) was calculated by online subtraction of P_{es} from P_{ga}. Balloon catheters were inserted through the nose and placed in the middle third of the esophagus and in the stomach according to current guidelines (2). The esophageal balloon contained 1 mL whereas the gastric balloon contained 2 mL of air to prevent collapse under high pressure. Both catheters were connected separately to pressure transducers (DPT-100; Utah Medical Products Ltd., Athlone, Republic of Ireland). Pressure signals were amplified (Quad Bridge Amp; ADInstruments, Bella Vista, Australia), A/D converted (PowerLab 3516 Interface; ADInstruments), and recorded on a computer (LabChart Software; ADInstruments). For the insertion of balloon catheters, subjects received no more than 0.4 mL of lidocaine gel to anesthesize the airways.

To assess nonvolitional respiratory muscle strength, we stimulated phrenic nerves (around the seventh cervical vertebra) or nerve roots innervating the abdominal muscles (around the 10th thoracic vertebra) with a MagStim 200 stimulator (maximum, 2 T; 1-ms rectangular pulses; MagStim, Whitland, UK) equipped with a 90-mm circular coil. For respiratory muscle strength testing, subjects were comfortably seated on a chair, with a noseclip in place and breathing through a system that included a flow head (Pneumotach 3813; Hans Rudolph Inc., Shawnee, KS, USA) connected to a spirometer (FE141; ADInstruments) to measure respiratory flow. This system included a shutter for short airway occlusions during stimulations (Zan, Oberthulba, Germany). Before each stimulation, participants were instructed to passively expire to functional residual capacity (FRC). As soon as the point of zero flow was reached (i.e., FRC), the shutter closed and a single stimulation was automatically delivered. For inspiratory muscle contractility, inspiratory twitch P_{di} ($P_{di,tw}$) was used, whereas expiratory muscle contractility was assessed by expiratory twitch P_{ga} ($P_{ga,tw}$). To ensure that end-expiratory lung volumes stayed at FRC before all stimulations, a second investigator continuously monitored P_{es}, which was maintained within ± 1 cm H_2O of the P_{es} obtained at FRC during resting breathing.

The stimulation protocol was identical for inspiratory and expiratory muscle strength measurements. Cervical stimulation was performed first for six subjects, whereas thoracic stimulation was performed first for six subjects. Nine potentiated twitch responses were assessed after three maximal voluntary efforts (lasting 5 s) at FRC. After the third and sixth stimulation, another maximal effort followed to maintain the potentiated state. Only potentiated muscle twitches were evoked as they are known to be more sensitive to changes occurring within a fatigued muscle (16).

To test for supramaximal nerve stimulation before and after each training modality, we performed three additional twitches at 98%, 94%, and 90% of stimulator output (each preceded by a 5-s maximal volitional maneuver).

Data analysis. For twitch pressures, the average amplitude from baseline to peak was calculated. Recordings where P_{es} before stimulations were not within the defined range were rejected *post hoc*. For maximal volitional P_{di} ($P_{di,max}$) during inspiration and maximal volitional P_{ga} ($P_{ga,max}$) during expiration, the average of the two best maneuvers was analyzed. Voluntary activation for the diaphragm and expiratory muscles was calculated with the following formula:

$$\text{voluntary activation (\%)} = \left(1 - A\,\frac{\text{superimposed twitch amplitude}}{\text{amplitude of potential twitch}}\right) \times 100.$$

A correction term A was included in order to account for superimposed stimulations that were not delivered at the highest volitionally produced pressure:

$$A = \left(\frac{\text{volitional pressure just before superimposed twitch}}{\text{highest volitional pressure during maneuver}}\right).$$

Ventilatory variables were averaged over six intervals of 5 min duration for RMET and over the entire sprint for RMSIT. Work of breathing (WOB) was calculated by multiplying the mean inspiratory and expiratory P_{es} with the corresponding inspiratory and expiratory V_T and then converted into joules. For P_{es} pressure–time product (PTP_{es}), P_{ga} pressure–time product (PTP_{ga}), and P_{di} pressure–time product (PTP_{di}), mean pressure was multiplied with the corresponding expiratory and inspiratory times. WOB and pressure–time products were analyzed every 5 min over 10 consecutive breaths for RMET and for each breath during the 30-s sprints in RMSIT. R5Hz, R20Hz, and X5Hz assessed after RMET and RMSIT sessions and relative changes from prior assessments were compared to "reference" values obtained by Guan et al. (7) and Rundell et al. (30) in order to detect clinically relevant effects on mechanical airway properties.

Twitch amplitudes were compared between protocols using a mixed-effects model with type of protocol (RMET vs RMSIT) and time point (before, after, and 30 min into recovery) as main factors. To account for differences among participants, we included a random intercept for each subject. For significant main effects, pairwise comparison was conducted *post hoc*. The same model was chosen for R5Hz, R20Hz, and X5Hz with only two time points (before vs after). Physiological response data (i.e., ventilation, WOB, pressure–time product, gas exchange, and heart rate) were analyzed using a mixed-effects model with protocol as main factor. Again, a random intercept for each subject was included. To investigate the time course of physiological response data within RMET or RMSIT, we used a separate mixed-effects model with time point as main factor and a random intercept for each participant. Differences in blood lactate concentration and perception of respiratory sensations at the end of both protocols were compared by paired *t*-tests. SPSS Statistics 21 (IBM Company, New York, NY, USA) was used for statistical analyses. All results are given as mean ± SD. $P < 0.05$ was accepted for significance.

RESULTS

Fatigue After RMET and RMSIT

Diaphragm and expiratory muscle contractility. Inspiratory $P_{di,tw}$ was similarly reduced after both RMET (−17.9% ± 9.0%) and RMSIT (−18.2% ± 12.2%), as indicated by a significant main effect of time point ($P < 0.01$) without an effect of protocol or time point–protocol interaction (Fig. 1). Also, expiratory $P_{ga,tw}$ was similarly reduced after RMET (−22.4% ± 18.5%) and RMSIT (−21.2% ± 13.1%) with a significant main effect of time point ($P < 0.01$) without an effect of protocol or time point–protocol interaction (Fig. 1). After 30 min of recovery, both inspiratory $P_{di,tw}$ and expiratory $P_{ga,tw}$ were still significantly reduced compared to values before RMET and RMSIT (both $P < 0.01$) and had not recovered compared to values immediately after exercise ($P = 0.13$ and $P = 0.48$, respectively).

Within-day coefficients of variation (CV) for potentiated $P_{di,tw}$ were similar at rest (RMET, 6.9% ± 2.4%; RMSIT, 7.2% ± 3.8%) and after the protocols (RMET, 7.9% ± 4.7%; RMSIT, 8.6% ± 4.7%). For $P_{ga,tw}$, CV at rest (RMET, 8.9% ± 4.5%; RMSIT, 9.9% ± 4.1%) and after the protocols (RMET, 10.2% ± 3.8%; RMSIT, 9.9% ± 3.3%) were slightly higher but did not differ significantly. The average between-day CV of potentiated $P_{di,tw}$ and $P_{ga,tw}$ were 7.2% ± 5.5% and 9.9% ± 9.6%, respectively. The average P_{es} − baseline immediately preceding each twitch was constant for all measurements and measurement time points, thereby confirming identical lung volumes before stimulations at all times.

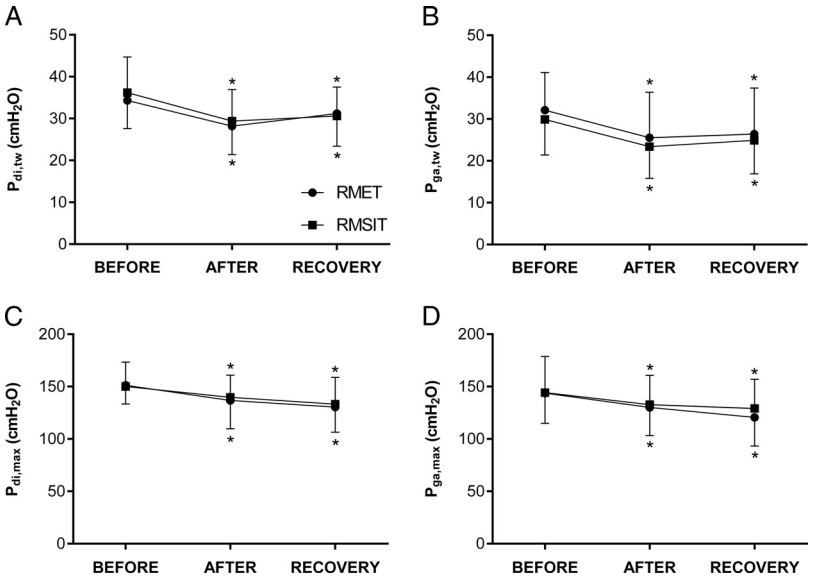

FIGURE 1—Respiratory muscle strength before, directly after, and 30 min after (recovery) a single session of RMET or RMSIT. Values are presented as mean ± SD (n = 12). A, $P_{di,tw}$ in response to cervical magnetic stimulation. B, $P_{ga,tw}$ in response to thoracic magnetic stimulation. C, Maximal volitional inspiratory transdiaphragmatic pressure ($P_{di,max}$). D, Maximal volitional expiratory gastric pressure ($P_{ga,max}$). *Significantly different from baseline, $P < 0.05$.

With increasing stimulator intensity, a plateau or near-plateau was reached in a majority of all subjects before and after trials for both inspiratory $P_{di,tw}$ and expiratory $P_{ga,tw}$. The occurrence of a plateau in $P_{di,tw}$ with increasing stimulator output was confirmed by no statistical difference between 98% and 100% stimulator output in the fatigue state, whereas for expiratory $P_{ga,tw}$, no significant difference was detected between 94%, 98%, and 100% stimulator output. During baseline measurements however, even for the highest submaximal stimulator intensity (i.e., 98%), we found significantly lower values compared to 100% due to a large variation caused by a few subjects (see "Methodological Considerations").

Volitional respiratory muscle strength. For both $P_{di,max}$ and $P_{ga,max}$, a significant main effect was found for time point ($P = 0.01$) without an effect for protocol and time point–protocol interaction (Fig. 1). The magnitude of reduction in $P_{di,max}$ after RMET (−10.1% ± 11.9%) and RMSIT (−6.6% ± 7.0%) and the magnitude of reduction in $P_{ga,tw}$ after RMET (−8.5% ± 14.1%) and RMSIT (−6.7% ± 12.3%) were not statistically different. After 30 min of recovery, both $P_{di,max}$ and $P_{ga,max}$ did not recover compared to values immediately after RMET and RMSIT (both $P = 0.06$) and were still significantly reduced compared to values before RMET and RMSIT (both $P < 0.01$).

Voluntary activation. Voluntary activation for the diaphragm was not significantly different after RMET (before, 95.7% ± 5.5%; after, 92.0% ± 7.4%), whereas it was significantly reduced after RMSIT (before, 97.4% ± 4.0%; after, 94.8% ± 4.2%; $P = 0.02$). Voluntary activation of the expiratory muscles was not significantly altered after both RMET (before, 75.9% ± 11.9%; after, 72.5% ± 11.6%) and RMSIT (before, 78.1% ± 10.2%; after, 73.0% ± 13.6%).

Mechanical Airway Properties After RMET and RMSIT

For R5Hz, R20Hz, and X5Hz, full data sets could only be obtained in seven subjects (two women and five men) because, in some cases, the 2 min between end of RMSIT/RMET and start of magnetic stimulations did not allow for the required three or more measurements within quality requirements. Individual data and changes after RMET and RMSIT, compared to changes before RMET and RMSIT, are given in Figure 2. A significant effect of time point was observed for R5Hz ($P = 0.01$) and R20Hz ($P < 0.05$), but not for X5Hz ($P = 0.81$).

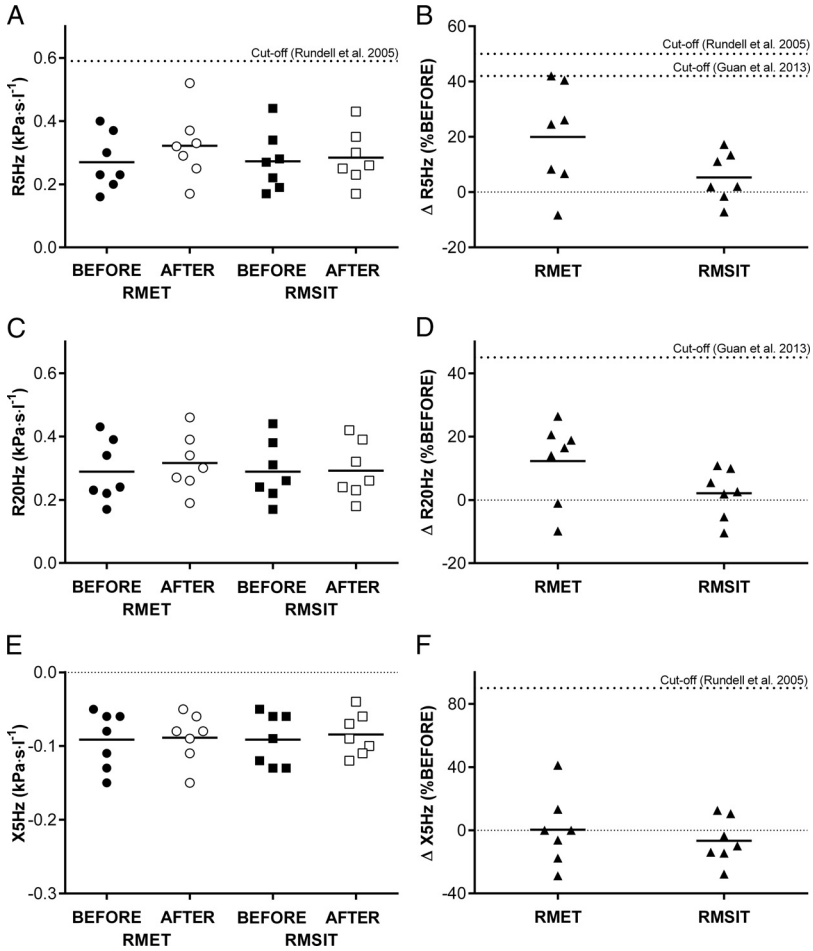

FIGURE 2—Mechanical airway properties before and after a single bout of RMET and RMSIT. A, R5Hz. B, Percent change in R5Hz. C, R20Hz. D, Percent change in R20Hz. E, X5Hz. F, Percent change in X5Hz. The straight line represents group average ($n = 7$). Dotted lines represent clinically relevant changes according to Guan et al. (7) and Rundell et al. (30). Both R5Hz ($P = 0.01$) and R20Hz ($P < 0.05$) showed a significant effect of time point and a tendency for a significant time point–protocol interaction (both $P < 0.1$).

There was no effect of protocol ($P = 0.13$, $P = 0.10$, and $P = 0.48$ for R5Hz, R20Hz, and X5Hz, respectively) or time point–protocol interaction ($P = 0.08$, $P = 0.10$, and $P = 0.70$ for R5Hz, R20Hz, and X5Hz, respectively).

Physiological Responses and Respiratory Sensations During RMET and RMSIT

The average exercise response of RMET and RMSIT is given in Table 2. Minute ventilation ($\dot{V}_E$) was significantly higher in RMSIT (+8.5% ± 11.8%, $P = 0.03$) than in RMET. This resulted from higher f_B (+10.1% ± 11.1%, $P = 0.01$), whereas V_T (−1.4% ± 4.6%, $P = 0.30$) was not different between protocols. Mean absolute inspiratory P_{di} and expiratory P_{ga} were significantly lower in RMET (14.9 ± 4.4 and 20.5 ± 6.1 cm H_2O, respectively) than in RMSIT (27.1 ± 7.1 and 50.7 ± 7.7 cm H_2O, respectively).

The higher $\dot{V}_E$, together with the added resistance during RMSIT, increased inspiratory WOB per minute, compared to RMET, by a factor 2.0 ± 0.4 and expiratory WOB per minute by a factor 2.8 ± 0.9. Inspiratory PTP_{di} and PTP_{es} were 2.0 ± 0.4 and 2.0 ± 0.4 times larger in RMSIT, whereas expiratory PTP_{ga} and PTP_{es} were 2.6 ± 0.6 and 2.6 ± 0.7 times larger than in RMET. Total work in RMET was 15.0 ± 0.42 kJ (resulting from ~1013 breaths) and significantly higher than total work in RMSIT (3.4 ± 0.8 kJ, resulting from ~111 breaths). Time courses of ventilatory variables and indices of respiratory muscle work during RMET and RMSIT are depicted in Figure 3.

Average heart rate, blood lactate concentration, perception of breathlessness, and respiratory exertion are presented in Table 2.

DISCUSSION

The present study compared the impact of a single session of a novel respiratory muscle training regimen using six short bouts of maximal hyperpnea with added resistance interspaced by short breaks (i.e., RMSIT) with traditional RMET on the level of contractile fatigue of respiratory muscles and potential negative changes in airway properties. Present results suggest that a similar amount of diaphragm and expiratory muscle fatigue develops after both regimens despite clearly different work history. Airway resistance was slightly increased after the breathing tasks, whereas reactance remained unchanged. None of these changes in airway resistance appear to be clinically relevant.

TABLE 2. Physiological responses.

	RMET	RMSIT
$\dot{V}_E$ (L·min^{-1})	105 ± 15	114 ± 22[a]
$\dot{V}_E$ (% MVV)	59.3 ± 5.0	64.2 ± 7.5[a]
f_B (breaths·min^{-1})	33.7 ± 4.0	36.9 ± 4.0[a]
V_T (L)	3.14 ± 0.55	3.10 ± 0.54
$V_{T,ex}$ (% vital capacity)	54.1 ± 2.5	53.3 ± 2.1
Mean inspiratory P_{es} (% max)	21.2 ± 5.0	39.4 ± 8.7[a]
Mean expiratory P_{es} (% max)	21.5 ± 8.8	53.2 ± 12.8[a,b]
Breathlessness (%)	12 ± 5	15 ± 3
End breathlessness (%)	22 ± 22	18 ± 30
Respiratory effort (%)	52 ± 15	62 ± 10[a]
End respiratory effort (%)	74 ± 18	76 ± 21
Heart rate (bpm)	110 ± 22	124 ± 19[a]
End blood lactate (mmol·L^{-1})	1.27 ± 0.27	2.76 ± 0.91[a]

Values are presented as mean ± SD.
[a]Significantly different from RMET, $P < 0.05$.
[b]Significantly different from inspiratory P_{es}.

Effects of Different Respiratory Training Regimens on Respiratory Muscle Strength

Volitional respiratory muscle strength (i.e., $P_{di,max}$ and $P_{ga,max}$) was significantly reduced after both respiratory protocols most likely due to peripheral fatigue mechanisms, as indicated by significant reductions in twitch pressure responses to magnetic stimulation. The minor changes in voluntary activation suggest that fatigue at the spinal or supraspinal level (i.e., central fatigue) was likely of less importance. The significant reductions in both inspiratory $P_{di,tw}$ ($\Delta P_{di,tw}$) and expiratory $P_{ga,tw}$ ($\Delta P_{ga,tw}$) after RMSIT are within the range of other studies investigating contractile muscle fatigue in the diaphragm and expiratory muscles after volitional exhaustive hyperpnea (9,15,17,21,28,35,38). Compared to a previous study by Renggli et al. (28) where the development of diaphragm and expiratory muscle fatigue was investigated during exhaustive RMET, the level of fatigue that subjects developed in the present study during RMET was slightly lower for inspiratory muscles ($\Delta P_{di,tw}$, −18% vs −22%), whereas the level of expiratory muscle fatigue was of similar magnitude ($\Delta P_{ga,tw}$, −22% vs −20%), despite the fact that RMET was not exhaustive in the present study. This is consistent with the observation that diaphragm and expiratory muscle fatigue develop early during exhaustive volitional breathing rather than shortly before task failure (15,18,28,29). Therefore, we mainly attribute the small differences between present and existing studies to the large interindividual fatigue response rather than to differences in the protocol.

Peripheral muscle fatigue may originate from either reduced membrane excitability (i.e., a decrease in action potential propagation and/or transmission) or changes within the contractile apparatus. Membrane excitability can be assessed by measuring compound muscle action potential, which was not obtained in this study. Hence, both mechanisms may have contributed; however, altered characteristics of compound muscle action potential have not been reported for fatigued respiratory muscles in our laboratory and in those of others (14,34,37). Therefore, it appears likely that the observed reductions in twitch amplitudes can mainly be attributed to altered processes within the contractile apparatus of the muscles.

Comparison of Contractile Impairments and Work History

In accordance with our hypothesis, both RMET and RMSIT induced similar levels of diaphragm and expiratory muscle fatigue, as judged by similar reductions in voluntarily produced and stimulation-induced pressure responses. To our knowledge, this is the first study to compare diaphragm and expiratory muscle fatigue after two types of volitional hyperpnea training regimens with very different characteristics (i.e., 30 min of continuous ventilation at an average of 59% MVV without added resistance vs 3 min of maximal breathing at an average of

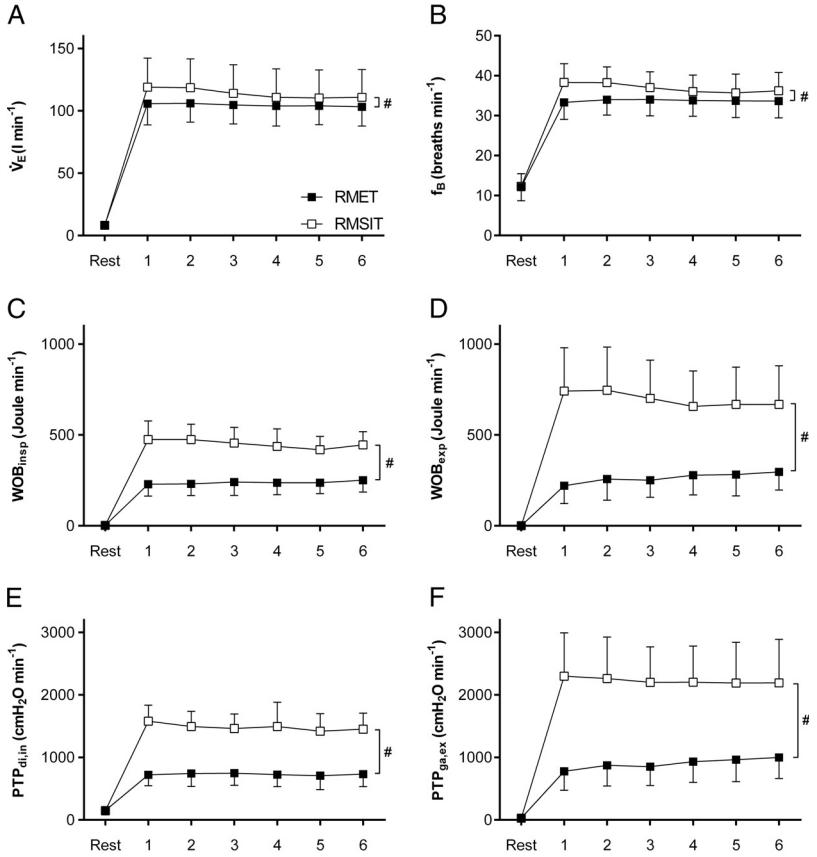

FIGURE 3—Ventilation and measures of respiratory muscle work during a session of RMET and RMSIT. Values are presented as mean ± SD (n = 12). RMET, averages of 10 breaths every 5 min; RMSIT, averages of each 30-s sprint. A, $\dot{V}_E$. B, f_B. C, Inspiratory WOB (WOBinsp). D, Expiratory WOB (WOBexp). E, Inspiratory transdiaphragmatic pressure–time product ($PTP_{di,in}$). F, Expiratory gastric pressure–time product ($PTP_{ga,ex}$). #Significant difference over the entire duration of RMET and RMSIT, $P < 0.05$.

64% MVV with added resistance). The all-out character of RMSIT resulted in WOB that was approximately doubled for inspiratory muscles and increased nearly threefold for expiratory muscles (Table 2) compared to RMET. In order to achieve this maximal respiratory power output, all available energy pathways needed to be fully activated. Although we did not measure respiratory oxygen consumption as an estimate of aerobic energy metabolism, we observed substantially higher blood lactate concentrations at the end of RMSIT (2.7 mmol·L^{-1}) compared to RMET (1.3 mmol·L^{-1}), which is suggestive of increased anaerobic energy supply in RMSIT. Moreover, we found that the difference in WOB between the two training modalities originated primarily from higher pressures achieved in RMSIT (+18% and 22% for inspiratory and expiratory P_{es}) compared to RMET, whereas ventilation was only modestly increased (+9%). The observed high pressures in RMSIT resulted in tension-time indices for the diaphragm (0.14) and expiratory muscles (0.26) within the range of those considered to be fatiguing (3,5). For RMET, on the other hand, these values were well below the suggested threshold of 0.15 (diaphragm, 0.07; expiratory muscles, 0.11). With tension-time indices above this threshold, blood supply (i.e., oxygen delivery and metabolite removal) to the working (respiratory) muscles is thought to be impeded, a fact that likely contributes to the development of contractile fatigue (3,5). Present data suggest that this was only the case in RMSIT.

Although WOB and tension-time indices were clearly greater in RMSIT, total work performed during the entire protocol was considerably larger in RMET. Taken together, it is evident that both breathing tasks seem to load the respiratory muscles to an extent that leads to similar impairments in contractile function, irrespective of work history, potentially different energy pathways, and fatiguing mechanisms.

Effects of Different Respiratory Training Regimens on Mechanical Airway Properties

We recently observed consistent acute reductions in FEV_1 and PEF after single RMET training sessions, which could have been caused either by an increase in airway resistance due to a reduction in airway caliber and/or by respiratory muscle fatigue that may have compromised the capacity to generate maximal flow (38). Although the latter may seem unlikely in light of findings by Haverkamp et al. (10), where expiratory muscle fatigue did not affect FEV_1, we decided to further investigate potential mechanisms by using a nonvolitional measurement of mechanical airway properties (impulse oscillometry), thereby avoiding any potential effect of respiratory muscle fatigue or motivation.

In the present study, a significant increase in R5Hz and R20Hz was observed, whereas X5Hz remained unaffected. Visual inspection of individual data in Figure 2 suggests larger increases in airway resistance after RMET than after RMSIT, yet the time point–protocol interaction for both R5Hz and R20Hz only tended to be significant ($P = 0.08$ and $P = 0.10$), possibly due to the small sample. The change in airway resistance likely occurred within peripheral airways rather than central airways, as indicated by a more pronounced increase in R5Hz than in R20Hz (33). However, we would like to emphasize that these very small changes in airway resistance are likely not clinically relevant because i) absolute values of airway resistance were all well below reported cutoff values for clinically relevant effects (7,30) and ii) changes in only one single measurement of one person at R5Hz reached the cutoff level suggested by Guan et al. (7), indicating the potential presence of minor peripheral airway obstruction. Moreover, there is clear evidence that chronic application of RMET does not impair mechanical airway properties because FEV_1 was shown to remain unchanged after a 4-wk intervention even though RMET acutely induced an ~5% reduction in FEV_1 (38). The present results suggest that, despite higher ventilation in RMSIT, acute effects on airway resistance and/or reactance are similar or smaller than those after RMET. Therefore, we suggest that chronic use of RMSIT is unlikely to induce clinically relevant negative effects on mechanical airway properties in healthy subjects.

Methodological Considerations

Supramaximal magnetic nerve stimulation. A plateau in $P_{di,tw}$ and $P_{ga,tw}$ was found less frequently before RMSIT and RMET than thereafter. Extreme care was taken to perform all measurements in a standardized posture. Therefore, we are convinced that, together with the low CV for twitch pressure responses in the present study, $\Delta P_{di,tw}$ and $\Delta P_{ga,tw}$ actually represent contractile muscle fatigue of the diaphragm and expiratory muscles. If anything, we believe that the lack of supramaximal stimulation during measurements before RMSIT and RMET could have led to a slight underestimation, rather than overestimation, of respiratory muscle fatigue.

Implications of Similar Levels of Contractile Fatigue for Chronic Application of RMSIT

Although not measured in the present study, it is likely that contractile fatigue after RMET and RMSIT is caused by the interplay of numerous metabolic factors, including local reduction in ATP availability, increase in ADP concentration, accumulation of inorganic phosphate, production of reactive oxygen species, and/or glycogen depletion (1). In fact, metabolic disturbance as a consequence of muscle contractions may not only cause an acute reduction in contractility but also trigger signaling pathways known to elicit adaptations with chronic exposure (11). Furthermore, it is important to consider the fact that RMSIT combines both high flow rates and high peak respiratory pressures (~45% of $P_{di,max}$ and ~70% of $P_{ga,max}$; data not shown). In fact, these pressures are within the range of those reported for respiratory muscle strength training (32) and suggest that RMSIT has the potential to simultaneously improve endurance- and strength-related parameters of respiratory muscles. The latter might further improve effectiveness of RMSIT, as functional adaptations to respiratory muscle training have been shown to be very specific for the training modality used, that is, endurance training improves flow-related parameters such as MVV and strength training elevates pressure related variables such as maximal respiratory pressures (e.g., [20,38]). Further investigations on the effects of chronic application of RMSIT are therefore required.

CONCLUSIONS

The present findings revealed that the new respiratory muscle training regimen RMSIT, consisting of six short maximal respiratory sprints with additional resistance, reduces respiratory muscle contractility to the same extent as RMET (i.e., endurance-type hyperpnea training). RMSIT is characterized by very high respiratory muscle power output and tension-time indices but considerably lower total work compared to RMET. Neither protocol induced clinically relevant adverse changes in mechanical airway properties. Thus, we conclude that RMSIT is a safe and time-saving potential alternative to RMET. Further studies are warranted to confirm whether chronic use of RMSIT translates into enhanced respiratory muscle function and improved whole-body exercise performance.

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The authors declare no conflicts of interest.

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