

# Hyperpnea training attenuates peripheral chemosensitivity and improves cycling endurance

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## Summary

Well-trained endurance athletes frequently have a lower peripheral chemoreceptor ( $pR_c$ ) sensitivity and a lower minute ventilation ( $\dot{V}_E$ ) during exercise compared to untrained individuals. We speculated that the decreased  $pR_c$  response may be specifically associated with repeated exposure to the high rates of ventilation occurring during exercise training. We therefore examined the effect of respiratory muscle training (RMT; 20×30 min sessions of voluntary normocapnic hyperpnea) on the  $pR_c$  sensitivity during exercise and on cycling performance. RMT was chosen to achieve a high  $\dot{V}_E$ , similar to that of heavy exercise, while avoiding the other accompanying effects of whole body exercise. 20 trained male cyclists were randomized into RMT ( $N=10$ ) or control ( $N=10$ ) groups. Subjects'  $pR_c$  response was assessed by a modified Dejours O<sub>2</sub> test (10–12 breaths of 100% O<sub>2</sub>, repeated 4–6 times) during cycling exercise at 40% of the maximal

work capacity ( $\dot{W}_{max}$ ). Cycling performance was measured during a cycling test to exhaustion (85%  $\dot{W}_{max}$ ). The RMT group exhibited a significantly reduced  $pR_c$  sensitivity (mean ± s.d.) compared to the control group ( $-5.8 \pm 6.0\%$  versus  $0.1 \pm 4.6\%$ ,  $P < 0.5$ ). Cycling endurance improved significantly after RMT in comparison to the control group ( $+3.26 \pm 4.98$  versus  $-1.46 \pm 3.67$  min,  $P < 0.05$ ). However, these changes in  $pR_c$  response were not significantly correlated with exercise ventilation or cycling endurance time. We conclude that the high levels of ventilation achieved during exercise, as simulated by RMT in this study, appear to be accompanied by a reduction in  $pR_c$  sensitivity; however, the role of the  $pR_c$  in the control of ventilation during exercise seems to be minor.

Key words: respiratory muscle endurance training, carotid body, control of breathing, hyperpnea, exercise, human.

## Introduction

Endurance athletes frequently have a lower peripheral chemosensitivity and a lower minute ventilation ( $\dot{V}_E$ ) during exercise than untrained individuals (reviewed by Weil and Swanson, 1991). The specific mechanism of the reduced peripheral chemoreceptor ( $pR_c$ ) response in endurance athletes remains unresolved. Following whole body endurance training, Benoit et al. (1992) and Levine et al. (1992) found no significant change in the resting response of  $pR_c$  to hypoxia, i.e. the hypoxic ventilatory response, favoring a genetic component previously proposed by Scoggin et al. (1978). However, Katayama et al. (1999) demonstrated a reduction in hypoxic ventilatory response after endurance training. This latter finding supports the involvement of a training component in the reduced  $pR_c$  sensitivity of endurance athletes. We wondered whether the reduced  $pR_c$  sensitivity associated with endurance training might result specifically from repeated exposure to the high levels of ventilation that occur during endurance exercise training.

Respiratory muscle training (RMT: 20×30 min sessions of voluntary normocapnic hyperpnea) was used to simulate the

high  $\dot{V}_E$  achieved during heavy exercise. RMT isolates the effect of high levels of ventilation on the  $pR_c$  sensitivity while minimizing other potentially confounding adaptations, e.g. adaptations of the cardiovascular system, that normally accompany whole-body exercise (Markov et al., 2001), although both types of training improve endurance performance (Boutellier et al., 1992; Boutellier and Piwko, 1992; Spengler et al., 1999).

Markov et al. (1996) investigated the effects of RMT on the resting hypoxic ventilatory response and found no significant change. However, it is known that the  $pR_c$  respond to stimuli other than hypoxia, e.g. CO<sub>2</sub>, [H<sup>+</sup>] and [K<sup>+</sup>] (reviewed by Nye, 1994). Furthermore, the hypoxic ventilatory response and thus the  $pR_c$  sensitivity may be increased during exercise (Weil et al., 1972). With these factors in mind, we reasoned that any changes resulting from an exercise or a respiratory training program would be more readily identifiable by examining the response of the  $pR_c$  to their full range of stimuli during exercise. Therefore, to assess the complete  $pR_c$  contribution to  $\dot{V}_E$  during exercise, we used a modified Dejours O<sub>2</sub> test (Dejours, 1963). The modified Dejours O<sub>2</sub> test assumes that

the  $pR_c$  drive to breathe is effectively eliminated by briefly breathing 100%  $O_2$ .

We hypothesized that RMT would decrease  $pR_c$  sensitivity, as whole-body endurance training has been shown to do, if the high levels of ventilation occurring during exercise were responsible for the change in  $pR_c$  sensitivity after whole-body training.

## Materials and methods

### Subjects

20 healthy male subjects (22–41 years old), who had normal lung function, were not taking any medication, and were trained, experienced cyclists (i.e. undertook a minimum of 3 h of physical exercise per week), participated in the study. They were randomly assigned to two groups, RMT and control, by a matched pairs design, based on their anthropometric data (means  $\pm$  S.D.) (RMT: age  $26\pm 4$  years, height  $179\pm 7$  cm, mass  $69\pm 6$  kg; control:  $28\pm 6$  years,  $180\pm 4$  cm,  $70\pm 9$  kg) and their hourly level of endurance training (RMT:  $7\pm 4$  h week<sup>-1</sup>; control:  $7\pm 3$  h week<sup>-1</sup>). There were no significant differences ( $P>0.05$ ) in these parameters between the two groups. The experimental group performed RMT (see below) and the other group served as a control. Subjects were instructed not to exercise the day of any test and to avoid intensive exercise the day before any test. Subjects did not drink caffeine the day of the test and they had their last meal at least 2 h prior to the test. The subjects were questioned on each test day to ensure these stipulations were fulfilled. In addition, they were requested to keep their individual training constant for at least 4 weeks prior to and throughout the course of the study. The subjects were required to keep a log of their physical activities in which they entered the type, duration, intensity (on a 5-point scale) and perceived exertion for all the exercises they participated in, including RMT. This log was checked regularly to ensure compliance.

Before obtaining written informed consent, the study requirements, the experimental protocol, and all risks associated with the study were outlined for each subject. However, the subjects were kept unaware of the purpose of the study. The study was approved by the Ethics Committee of Physiology and Pharmacology at the University of Zurich.

### Protocol

On a separate day, prior to any testing, subjects underwent at least one familiarization session, including familiarization with the respiratory training device. This familiarization was critical to ensure normocapnic conditions during hyperpnea, to remove any learning effect associated with the use of the respiratory training device, and to select an appropriate ventilatory level for the breathing endurance test (see below). After the familiarization session(s), both groups of subjects underwent four test sessions on four different days. The test sessions consisted of: (1) spirometric measurements followed by a pause of at least 15 min and then an incremental cycling test to exhaustion; (2) breathing endurance test; (3) modified

Dejours  $O_2$  test; (4) cycling endurance test to exhaustion. All four test sessions were performed on separate days with a minimum of 2 days between test sessions. The entire test period lasted approximately 14 days. A 4–6 week RMT or control period followed.

During the RMT period, subjects completed 20 voluntary normocapnic hyperpnea sessions of 30 min duration each, using a special device (see below). The  $\dot{V}_E$  of the first training session was approximately 60% of the individual maximum voluntary ventilation in 15 s. Afterwards, the intensity level was increased such that the subjects could hold the training- $\dot{V}_E$  constant for at least 30 min, but no longer than 35–40 min, i.e. subjects had to feel that they could have continued for a maximum of 5–10 min longer than the actual training time of 30 min. Increases in training intensity were made by increasing  $\dot{V}_E$ , primarily by increasing breathing frequency. The subjects performed their training at home. Every fifth RMT was performed in the laboratory where training logs were checked and subjects were connected to the metabolic cart during training to observe their training technique [constant tidal volume ( $V_T$ ) and respiratory frequency ( $f_R$ )] and to ensure normocapnia. Analysis of the four observed RMT training sessions performed in the laboratory showed the subjects maintained the end-tidal fractional concentration of carbon dioxide  $F_{ET}CO_2$  within the range 4.6–5.8%. After the RMT or control period, the four test sessions were repeated.

For technical reasons, the cardiorespiratory data pertaining to the cycling endurance test of two subjects, one from each group, was not available for the final analysis. Another two subjects, one from each group but different from the two above, were unable to successfully complete the modified Dejours  $O_2$  test.

### Tests and equipment

#### Test session 1

Spirometric variables, i.e. vital capacity, forced expiratory vital capacity, forced expiratory volume in 1 s, peak expiratory flow and maximum voluntary ventilation, were measured according to ATS criteria (American Thoracic Society, 1991, 1995) with an ergospirometric device (Oxycon Beta, Jaeger, Höchberg, Germany) using a calibrated turbine for volume measurements.

The incremental exercise test was performed on an electromagnetically braked cycle ergometer (Ergometrics 800S, Ergoline, Bitz, Germany) to determine peak oxygen consumption ( $\dot{V}_{O_{2peak}}$ ) and maximal work capacity ( $\dot{W}_{max}$ ). The test began at 100 W and the intensity was increased by 30 W every 2 min until the subjects could no longer continue. The subjects selected their preferred pedaling frequency and maintained this cadence  $\pm 5$  revs min<sup>-1</sup> throughout the test. Ventilatory variables and gas exchange were measured breath by breath with the Oxycon Beta metabolic cart, using fast-responding gas analyzers (paramagnetic for  $O_2$ , infrared for  $CO_2$ ). Cardiac frequency ( $f_c$ ) was recorded every 5 s (PE 4000, Polar Electro, Kempele, Finland). Blood samples (20  $\mu$ l), from an earlobe, were collected at the end of each workload step and

at the end of the test and the whole blood samples were analyzed enzymatically for blood lactate concentration with a Biosen 5040 apparatus (EKF Industrie, Barleben, Germany).

### Test session 2

The breathing endurance test was conducted at a  $\dot{V}_E$  corresponding to  $74 \pm 10\%$  of the pre-RMT maximum voluntary ventilation, i.e.  $\dot{V}_E$ ,  $V_T$  and  $f_R$  were similar for breathing endurance tests before and after the RMT/control period ( $\dot{V}_E$ , RMT:  $142 \pm 25$  versus  $144 \pm 24$   $\text{min}^{-1}$ , control:  $141 \pm 25$  versus  $140 \pm 24$   $\text{min}^{-1}$ ;  $V_T$ , RMT:  $3.0 \pm 0.6$  versus  $3.1 \pm 0.6$  l, control:  $2.9 \pm 0.6$  versus  $2.9 \pm 0.6$  l;  $f_R$ , RMT:  $47 \pm 5$  versus  $47 \pm 4$  breaths  $\text{min}^{-1}$ , control:  $49 \pm 5$  versus  $49 \pm 4$  breaths  $\text{min}^{-1}$ ). During the breathing endurance test, the RMT device (see below) was connected to the metabolic cart. During familiarization sessions (see below), a level of ventilation was chosen by the investigators that ensured the subjects could continue for a minimum of 6 min but not longer than 15 min. Subjects were required to maintain this pre-selected  $\dot{V}_E$  while holding  $V_T$  and  $f_R$ , paced by a metronome (DM-20, Seiko, Tokyo, Japan), constant. If necessary, the test administrator corrected subjects'  $V_T$  or  $f_R$  (which he supervised on the metabolic cart) and he ensured normocapnia was maintained. The test ended when the subject reached volitional exhaustion, when the experimenter stopped the test because the subject could not maintain the  $V_T$ - or  $f_R$ -target any longer (i.e. the experimenter observed  $\dot{V}_E$  and if it fell, he told the subject to increase either  $V_T$  or  $f_R$ ; if the subject was not able to reach the target after a 3<sup>rd</sup> 'warning', the test was stopped) or when 40 min were reached. Otherwise, subjects were not encouraged during this test. The 40 min cut-off time was reached by five subjects in the RMT group during the post-training breathing endurance test. If subjects continued for more than 15 min in the pre-test or if normocapnia was not maintained, the test was considered to be an additional 'training session', the training device was adjusted and the test was repeated on another day (this occurred once). The end-time was used as an estimate of respiratory muscle endurance. Ventilatory variables and gas exchange were measured breath by breath and heart rate was sampled every 5 s.

The RMT-device allowed partial rebreathing of  $\text{CO}_2$  to maintain normocapnia. The device consisted of a mouthpiece connected by a tube to a rebreathing bag. The size of the bag was adjusted to be 50–60% of the subjects' vital capacity. Subjects were instructed to fill and empty the bag completely while additional inspiratory and expiratory flow passed through a small hole in the tube to avoid an increase in arterial  $\text{CO}_2$  partial pressure and a fall in  $\text{O}_2$  saturation, i.e.  $V_T$  was slightly larger than the bag itself. Breathing frequency was adjusted to reach the target  $\dot{V}_E$ . Correct performance, i.e. the maintenance of normocapnia, was checked with the training device connected to the Oxycon Beta. If normocapnia was not maintained during training sessions, the hole was adjusted in size and/or the combination of  $V_T$  and  $f_R$  was changed.

### Test session 3

A modified Dejours  $\text{O}_2$  test (Dejours, 1963) was completed

while the subjects were cycling at 40%  $\dot{W}_{\text{max}}$ . First, the subjects rested for 10–15 min while sitting in a chair and listening to relaxing music. Next, the subjects moved to the ergometer and cycled for 5 min breathing room air, followed by another 5 min of breathing compressed air. The subjects' mouthpiece was connected to a three-way valve, out of sight such that they could not see or hear when inspired gases were changed. Then, during an exhalation, the compressed air was surreptitiously switched to 100% oxygen for 10–14 breaths (20–30 s) while the periods of breathing compressed air lasted for 3 min each. Every subject completed 4–6 hyperoxic trials. Dejours's (1963) one- or two-breath  $\text{O}_2$  test was slightly modified as preliminary trials showed the most consistent responses during cycling at 40%  $\dot{W}_{\text{max}}$  occurred while breathing 100% oxygen for approximately 12 breaths, which resulted in a decrease in ventilation to an eventual nadir within 30 s. This decrease reflects the  $pR_c$  contribution to the ventilatory drive and can be expressed as a percentage of the pre-oxygen breathing ventilation. Blood samples were taken prior to and at the end of the test to measure lactate concentration.

### Test session 4

The cycling endurance test at 85% of pre-RMT  $\dot{W}_{\text{max}}$  was performed to exhaustion. This test began with 4 min of sitting quietly on the cycle ergometer, followed by 2 min of unloaded pedaling, 2 min at 40%  $\dot{W}_{\text{max}}$ , 3 min at 60%  $\dot{W}_{\text{max}}$  and, finally, 85%  $\dot{W}_{\text{max}}$  for the remainder of the test. Subjects chose their preferred cadence, and this was maintained throughout all cycling endurance tests ( $\pm 5$  revs  $\text{min}^{-1}$ ). The time at which the subject was unable to maintain the cadence within the proper range or reached volitional exhaustion was used as the end-time. This time, excluding rest and unloaded pedaling, was used as the measure of cycling endurance. Ventilatory variables and gas exchange were recorded breath by breath (Oxycon Beta) and  $f_C$  was sampled every 5 s. Blood samples were taken every 2 min and at the end of the test to measure lactate concentration. The subjects never received verbal encouragement throughout any of the tests. The last two meals before this test were supplemented by 0.5 l of a 15.8% carbohydrate drink (Wander isostar long energy; Novartis Consumer Health Schweiz AG, Bern, Switzerland) to replenish glycogen stores.

### Data analysis

The  $\dot{W}_{\text{max}}$  was defined as the highest workload sustained for a minimum of 90 s during the incremental test.  $\dot{V}_{\text{O}_2\text{peak}}$  was obtained from the highest  $\dot{V}_{\text{O}_2}$  reached over a 30 s period during this test.

Each modified Dejours  $\text{O}_2$  test was analyzed using breath-by-breath measurements. The steady-state  $\dot{V}_E$  was obtained from the mean value during the 30 s period preceding the switching to hyperoxia. The magnitude of the following decrement in  $\dot{V}_E$  was determined using a two-breath moving average. The lowest two-breath average was compared to the steady-state  $\dot{V}_E$  obtained prior to the switching to hyperoxia and the reduction was expressed as percentage of the baseline

ventilation. Equipment errors, sighs or swallows (single breaths that deviated by more than  $\pm 2$  s.d. from the mean  $\dot{V}_E$  of the prior and following breaths) were not included in the analysis. 4–6 hyperoxic episodes were completed by each subject. The average of these trials was taken as the subject's  $pR_c$  response.

Breath-by-breath data from the cycling endurance test was averaged into 15 s segments. For comparison of cardiorespiratory variables, these 15 s segments were organized into two categories, steady state and end-time. The 2 min samples of blood lactate concentration were grouped into similar categories. The steady-state included data from the 85% level, less the first 1 min 45 s and the last 2 min of the shorter of the pre- or post-tests. An identical time period was chosen for the longer of the two tests. Thus, the steady-state of the cycling endurance test was a comparison of identical times for the pre- and post-test of each subject. The end-time category included the last complete 60 s of each test.

Values are reported as means  $\pm$  s.d. Between group comparisons of pre/post changes, i.e. changes within the subjects pre- to post-RMT or control period, were performed using unpaired *t*-tests with the exception of the breathing endurance test. Since this was stopped at 40 min in 5 subjects, the non-parametric Mann–Whitney *U*-test was employed. The Pearson product–moment correlation coefficients were used for calculating correlations between selected variables. Fisher's *R* to *Z* test was used for detecting statistical significance. For all tests statistical significance was defined as a value of  $P < 0.05$ . Statistical analyses were completed with StatView 4.53 (Abacus Concepts, Berkeley, CA, USA).

## Results

### Modified Dejours $O_2$ test

RMT significantly reduced the  $pR_c$  response in the RMT

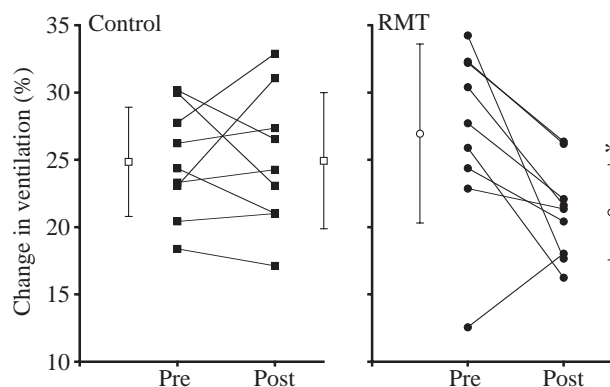


Fig. 1. Percentage decline in ventilation during brief hyperoxia (10–14 breaths) while cycling at 40% of maximal power output for individuals of the control group (■,  $N=9$ ) and the respiratory muscle training (RMT) group (●,  $N=9$ ) before (Pre) and after (Post) the RMT or control period. Open symbols show means  $\pm$  s.d. \*Significantly different for between-group difference of the pre/post-changes in the response,  $P < 0.05$ .

group ( $-5.8 \pm 6.0\%$ ) compared to controls ( $0.1 \pm 4.6\%$ ; Fig. 1). Baseline  $\dot{V}_E$  during exercise before  $O_2$  breathing did not significantly change after the RMT or control period in either group (RMT, pre:  $53.0 \pm 3.91 \text{ min}^{-1}$  versus post:  $54.4 \pm 6.51 \text{ min}^{-1}$ ; control, pre:  $52.6 \pm 3.01 \text{ min}^{-1}$  versus post:  $52.9 \pm 4.01 \text{ min}^{-1}$ ). The changes in  $pR_c$  response did not correlate with changes in baseline  $\dot{V}_E$  (RMT:  $r=0.01$ ,  $P=0.97$ ; control:  $r=-0.37$ ,  $P=0.35$ ). Also, end lactate concentration was not significantly changed in the RMT (pre:  $0.84 \pm 0.26 \text{ mmol l}^{-1}$  versus post:  $1.17 \pm 0.37 \text{ mmol l}^{-1}$ ) nor in the control group (pre:  $0.78 \pm 0.12 \text{ mmol l}^{-1}$  versus post:  $1.06 \pm 0.29 \text{ mmol l}^{-1}$ ). There were no significant correlations between the changes in lactate concentration and  $pR_c$  response (RMT:  $r=-0.10$ ,  $P=0.80$ ; control:  $r=0.02$ ,  $P=0.96$ ).

### Spirometry

RMT significantly improved vital capacity and maximum voluntary ventilation compared to the control group (Table 1). Other spirometric variables, i.e. forced expiratory vital capacity, forced expiratory volume in 1 s, and peak expiratory flow, were not changed significantly.

### Breathing endurance test

Following the RMT period, the time to exhaustion during the breathing endurance test was significantly improved by more than 250% in the RMT group compared to the control group (Table 1). After the RMT period, the breathing endurance test was stopped at 40 min for 5 of the 10 subjects in the RMT group. None of the 10 subjects in the control group reached the 40 min cut-off time.

Table 1. Ventilatory parameters pre and post respiratory muscle training (RMT) or control period

Parameter	Treatment	Pre	Post
VC (l)	Control	6.1 $\pm$ 1.0	6.0 $\pm$ 1.0
	RMT	5.9 $\pm$ 0.6	6.1 $\pm$ 0.6*
FEVC (l)	Control	5.8 $\pm$ 0.9	5.8 $\pm$ 0.5
	RMT	5.8 $\pm$ 1.0	5.9 $\pm$ 0.6
FEV <sub>1</sub> (l)	Control	4.7 $\pm$ 0.6	4.6 $\pm$ 0.8
	RMT	4.7 $\pm$ 0.6	4.7 $\pm$ 0.5
PEF (l s <sup>-1</sup> )	Control	10.4 $\pm$ 2.0	10.4 $\pm$ 3.1
	RMT	10.2 $\pm$ 1.2	10.7 $\pm$ 1.7
MVV (l min <sup>-1</sup> )	Control	203 $\pm$ 31	200 $\pm$ 34
	RMT	182 $\pm$ 31	202 $\pm$ 29**
BET (min)	Control	11.12 $\pm$ 2.86	11.61 $\pm$ 4.40
	RMT	8.30 $\pm$ 2.00	29.80 $\pm$ 13.60**

Values are means  $\pm$  s.d. ( $N=10$  in each group).

VC, vital capacity; FEVC, forced expiratory vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 s; PEF, peak expiratory flow; MVV, maximum voluntary ventilation in 15 s; BET, breathing endurance test.

\* $P < 0.05$ ; \*\* $P < 0.01$  for between group differences of the pre/post-changes.

Table 2. Incremental cycling test results pre and post respiratory muscle training (RMT) or control period

Variable	Treatment	Pre	Post
$\dot{V}_{O_{2peak}}$ (ml min <sup>-1</sup> kg <sup>-1</sup> )	Control	70.1±12.6	69.4±10.2
	RMT	73.6±15.0	73.2±13.1
$f_c$ (beats min <sup>-1</sup> )	Control	186.3±11.7	183.8±10.3
	RMT	187.1±5.6	184.1±6.3
[Lactate] (mmol l <sup>-1</sup> )	Control	11.74±2.45	10.66±1.88
	RMT	11.65±1.88	11.26±1.79
$\dot{W}_{max}$ (W)	Control	360±38	350±47
	RMT	368±36	371±31

Values are means ± s.d. ( $N=10$  in each group).

$\dot{V}_{O_{2peak}}$ , peak oxygen consumption;  $f_c$ , cardiac frequency; [Lactate], blood lactate concentration;  $\dot{W}_{max}$ , maximum work capacity.

No significant differences for comparison of between-group differences of pre/post-changes.

#### Incremental test

The respiratory, cardiovascular and metabolic indicators of aerobic fitness (i.e.  $\dot{V}_{O_2}$ ,  $f_c$ , lactate concentration and  $\dot{W}_{max}$ ), measured during the incremental test, did not change significantly following the RMT or control period for either group, as shown in Table 2.

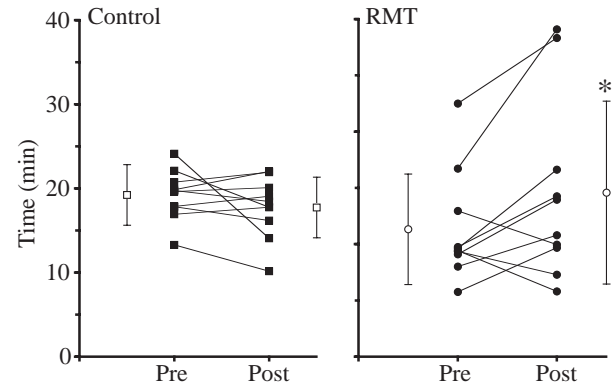


Fig. 2. Cycling endurance times at 85% of maximal power output for individuals of the control group (■,  $N=10$ ) and the respiratory muscle training (RMT) group (●,  $N=10$ ) before (Pre) and after (Post) the RMT or control period. Open symbols show means ± s.d. \*Significantly different for between-group difference of the pre/post-changes in end-time,  $P<0.05$ .

#### Cycling endurance test

RMT increased cycling endurance significantly in the RMT group compared to the control group (Fig. 2). Ventilatory and cardiovascular parameters of the cycling endurance test in both the steady-state and end-time categories are shown in Table 3. The change in end-time of the cycling endurance test did not correlate significantly with the change in the  $pR_c$  response in

Table 3. Cycling endurance test results pre and post respiratory muscle training (RMT) or control period

Variable	Treatment	Steady-state		End-time	
		Pre	Post	Pre	Post
$\dot{V}_E$ (l min <sup>-1</sup> )	Control	121.9±12.6	121.6±12.8	147.1±25.0	143.8±19.8
	RMT	119.3±20.9	124.2±24.4	147.5±23.8	156.2±32.6
$f_R$ (breaths min <sup>-1</sup> )	Control	41.1±8.8	42.6±9.4	53.0±13.7	53.5±14.4
	RMT	36.6±4.0	36.7±4.1	47.3±6.1	48.8±6.7
$V_T$ (l)	Control	3.1±0.6	3.0±0.7	2.9±0.6	2.8±0.8
	RMT	3.3±0.4	3.4±0.4	3.1±0.4	3.2±0.4
$P_{ETCO_2}$ (mmHg)	Control	39.5±3.4	39.0±3.7	32.4±4.2	33.8±3.8
	RMT	41.8±5.0	40.2±4.5	34.8±3.6	32.7±4.1
$\dot{V}_{O_2}$ (l min <sup>-1</sup> )	Control	4.2±0.4	4.2±0.5	4.4±0.6	4.4±0.7
	RMT	4.5±0.5	4.3±0.6	4.8±0.6	4.6±0.7
$\dot{V}_{CO_2}$ (l min <sup>-1</sup> )	Control	4.6±0.5	4.5±0.6	4.7±0.7	4.7±0.7
	RMT	4.7±0.5	4.7±0.6	5.0±0.7	4.9±0.6
$f_c$ (beats min <sup>-1</sup> )	Control	170.2±14.8	172.8±14.0	177.1±15.1	178.1±14.2
	RMT	175.8±7.9	174.8±9.4	183.5±8.7	182.6±10.2
[Lactate] (mmol l <sup>-1</sup> )	Control	7.54±1.58	7.70±2.22	11.71±3.30	10.97±3.00
	RMT	8.58±1.75	7.85±1.37	11.48±2.21	10.42±4.15

Values are means ± s.d. ( $N=9$  in each group).  $\dot{V}_E$ , expired minute ventilation;  $f_R$ , respiratory frequency;  $V_T$ , tidal volume;  $P_{ETCO_2}$ , end-tidal partial pressure of carbon dioxide;  $\dot{V}_{O_2}$ , oxygen consumption;  $\dot{V}_{CO_2}$ , carbon dioxide production;  $f_c$ , cardiac frequency; [Lactate], blood lactate concentration.

For definitions of Steady-state and End-time, please see text.

either group (RMT:  $r=0.11$ ,  $P=0.79$ ; control:  $r=0.13$ ,  $P=0.74$ ) nor was the correlation between changes in the steady-state  $\dot{V}_E$  of the cycling endurance test and the change in the  $pR_c$  response significant (RMT:  $N=8$ ,  $r=0.43$ ,  $P=0.09$ ; control:  $N=8$ ,  $r=0.64$ ,  $P=0.31$ ).

### Discussion

In the present study, we show that simulating the high levels of exercise ventilation with isolated normocapnic hyperpnea (RMT), caused a significant decrease in the  $pR_c$  sensitivity without changing  $\dot{V}_E$  during cycling exercise.

The effectiveness of the RMT program was demonstrated by the significant increases in maximum voluntary ventilation and breathing endurance time. These results are in agreement with previous studies in which subjects trained the respiratory muscles in a similar fashion (Boutellier et al., 1992; Boutellier and Piwko, 1992; Leith and Bradley, 1976; Spengler et al., 1999). The lack of significant changes of cardiovascular and metabolic indicators of aerobic fitness, e.g.  $f_c$ , lactate concentration,  $\dot{V}_E$ , during the incremental test (Table 2) and the cycling endurance test (Table 3) indicated that the general fitness of the subjects had not changed during the study. This was validated by examining the subjects' training logs, which confirmed that they kept their level of activity constant during the course of this study. Therefore, RMT was effective and it was likely responsible for the improved cycling endurance and the decreased  $pR_c$  sensitivity.

With respect to the modified Dejours  $O_2$  test that was used to determine  $pR_c$  sensitivity during exercise, it is important to note that a false reduction in  $pR_c$  sensitivity could be detected after RMT if  $pR_c$ -stimulation *per se* were smaller after RMT than before, i.e. if  $[H^+]$  or any other  $pR_c$ -stimulating factor were smaller. This, however, was unlikely to be the case as ventilation, gas exchange and blood lactate concentrations were similar during exercise before and after RMT. Also, the strength of the  $pR_c$  drive might have been underestimated because, on the one hand, some uncertainty exists as to whether the  $pR_c$  input is completely eliminated by hyperoxia and, on the other hand, secondary effects may stimulate ventilation after the initial drop, masking any further hyperoxia-mediated decrease (e.g. Ward, 1994). However, we investigated the ventilatory decline in response to 100% oxygen under the same conditions before and after the RMT/control period and found no difference in the control group, so we believe that, after RMT, we observed a true reduction in  $pR_c$  sensitivity, at least with respect to the  $O_2$  drive mediated by the  $pR_c$ .

This 5.8% reduction in  $pR_c$  sensitivity after RMT supports the hypothesis that RMT, which simulated the high rates of ventilation occurring during endurance exercise, can – by itself – cause a reduction in the  $pR_c$  response. As the  $pR_c$  are generally believed to contribute to augment  $\dot{V}_E$  during exercise (reviewed by Weil and Swanson, 1991), we expected to find a reduction in the exercise  $\dot{V}_E$  of the RMT group, given the attenuated  $pR_c$  sensitivity following RMT. However, exercise  $\dot{V}_E$  was not significantly changed following the RMT period

and there was no significant relationship between any change in the steady-state  $\dot{V}_E$  of the cycling endurance test and the change in  $pR_c$  response in the RMT group. Considering those endurance athletes that have a lower peripheral chemosensitivity and a lower exercise ventilatory response (e.g. Weil and Swanson, 1991), our findings suggest that the lower  $\dot{V}_E$  during exercise is not a direct result of the lower peripheral chemosensitivity. Results of the present study indicate that the  $pR_c$  contributed minimally to the regulation of ventilation during aerobic exercise. This is consistent with the theory that the  $pR_c$  only serve to 'fine tune' the ventilatory response to exercise (Dempsey et al., 1995), and other inputs to the medullary respiratory center may play a more prominent role in the control of breathing during exercise.

In conclusion, the high levels of ventilation achieved during exercise, as simulated by RMT in this study, significantly reduced the  $pR_c$  sensitivity during moderate-intensity exercise and extended the time to exhaustion during high-intensity constant-load cycling exercise. Nevertheless, the lack of a significant correlation between the decrease in  $pR_c$  sensitivity and exercise  $\dot{V}_E$  suggests that the role of the  $pR_c$  in the control of ventilation during normoxic exercise is minimal.

### List of symbols

$F_{ETCO_2}$	end-tidal fractional $CO_2$ concentration
$f_c$	cardiac frequency
$f_R$	respiratory frequency
$pR_c$	peripheral chemoreceptor
RMT	respiratory muscle training
$\dot{V}_E$	minute ventilation
$\dot{V}_{O_2}$	rate of oxygen consumption
$\dot{V}_{O_2peak}$	peak rate of oxygen consumption
$V_T$	tidal volume
$\dot{W}_{max}$	maximum work capacity

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