

Effects of respiratory muscle training versus placebo on endurance exercise performance

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Accepted 15 May 2001

Abstract

We evaluated the effects of a 5 week (25 sessions); (30–35 min/day, 5 days/week), respiratory muscle training (RMT) program in nine competitive male cyclists. The experimental design included inspiratory resistance strength training (3–5 min/session) and hyperpnea endurance training (30 min/session), a placebo group which used a sham hypoxic trainer ($n = 8$), and three exercise performance tests, including a highly reproducible 8 km time trial test. RMT intensity, measured once a week in terms of accumulated inspiratory pressure and the level of sustainable hyperpnea increased significantly after 5 weeks (+64% and +19%, respectively). The RMT group showed a significant 8% increase in maximal inspiratory pressure ($P < 0.05$) while the placebo group showed only a 3.7% increase ($P > 0.10$). RMT and placebo groups both showed significant increases in the fixed work-rate endurance test performance time (+26% and +16%, respectively) and in the peak work-rate achieved during the incremental maximal oxygen consumption ($\dot{V}_{O_2\max}$) test (+9 and +6%). The 8 km time trial performance increased $1.8 \pm 1.2\%$ (or 15 ± 10 sec; $P < 0.01$) in the RMT group with 8 of 9 subjects increasing; the placebo group showed a variable non-significant change in 5 of 8 subjects ($-0.3 \pm 2.7\%$, $P = 0.07$). The changes observed in these three performance tests were not, however, significantly different between the RMT and placebo groups. Heart rate, ventilation, or venous blood lactate, at equal work-rates during the incremental exercise test or at equal times during the fixed work-rate endurance test were not changed significantly across these exercise trials in either group. We propose that the effect of RMT on exercise performance in highly trained cyclists does not exceed that in a placebo group. Significant placebo and test familiarization effects must be accounted for in experimental designs utilizing performance tests which are critically dependent on volitional effort. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Exercise, performance; Mammals, humans; Muscle, respiratory, training; Test, time trial performance

1. Introduction

The effects of respiratory muscle training (RMT) on exercise performance in healthy persons are controversial. While some studies report dramatic improvements ranging from 25 to 50%

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in endurance exercise performance (Boutellier and Piwko, 1992; Boutellier et al., 1992; Spengler et al., 1999), others have not found a significant effect (Morgan et al., 1987; Fairbairn et al., 1991; Kohl et al., 1997). Furthermore, some also report a substantial reduction of exercise ventilation (Boutellier and Piwko, 1992; Boutellier et al., 1992) and blood lactate (Boutellier and Piwko, 1992; Kohl et al., 1997; Spengler et al., 1999) after RMT; these changes are cited as further evidence of a 'training' effect of RMT.

Perhaps it is not unexpected that findings might differ among studies, given the subjective nature of performance tests and the wide variation among studies in the relative intensity of exercise used for testing, the fitness of test subjects and the inclusion and exclusion of control groups. We reasoned that two major confounders were: (a) the use of a fixed work-rate performance test, which has little relevance to the subject's competitive experience and does not usually yield reproducible results (Jeukendrup et al., 1996); and (b) the absence of a legitimate placebo group—a consideration which is especially critical when most of the performance outcomes tested are so critically dependent upon volitional effort and therefore on subject expectation and motivation.

Accordingly, our study design to address these questions of RMT effects on exercise performance employed a placebo group and, in addition to the more usual laboratory performance tests, utilized a time trial test of performance which we documented to be highly reproducible upon repeat testing. We also sought to enhance the effects of specific RMT by using both strength and endurance training regimens (Leith and Bradley, 1976) and to minimize the learning effect on the performance tests by using highly experienced competitive cyclists as subjects.

2. Methods

2.1. Subjects

Seventeen healthy, non-smoking competitive male cyclists with normal resting pulmonary function were recruited to participate in the study. All

subjects participated regularly in local races. Informed written consent was obtained from each subject and all procedures were approved by the Institutional Review Board of the University of Wisconsin-Madison. The physical characteristics of the subjects were as follows: age 24.2 ± 4.9 years (mean \pm S.D.), height 179.2 ± 6.4 cm, weight 74.1 ± 6.8 kg, and maximal oxygen consumption ($\dot{V}_{O_2\max}$) 54.9 ± 3.8 ml/kg/min. Before the start of testing, subjects were randomly assigned to either the RMT group or the placebo group.

2.2. Pulmonary function tests

Slow vital capacity (VC), 1 sec forced expiratory volume (FEV_{1.0}), forced vital capacity (FVC), and FEV_{1.0}/FVC were determined using a computerized spirometry system (model PFT 3000, Pulmonizer, St. Louis, MO) according to criteria published by the American Thoracic Society (ATS, 1995). Each test was repeated, after verbal feedback was given to the subject, until three acceptable results were obtained. The greatest value from each *set* of repeated measurements for each test was used for subsequent analysis.

2.3. Pressure, gas, flow, and volume measurements

We have previously described all measurements (McClaran et al., 1995; Johnson et al., 1992). Mouth pressure was measured with a Validyne transducer (model MP45-1, ± 300 cm H₂O, Northridge, CA). Flow rates were measured by heated pneumotachographs (model 3800, Hans Rudolph, Kansas City, MO) placed on the inspiratory and expiratory sides of the breathing circuit. Subjects breathed through the circuit via a low resistance one-way, non-rebreathing valve (model 2700, Hans Rudolph, Kansas City, MO). The flow resistance of the measurement circuit was 0.8 and 1.0 cmH₂O/L/sec at flow rates of 3 and 6 L/sec, respectively. Mixed expired and end-tidal gases were analyzed using a Perkin-Elmer mass spectrometer (model 1100, Pomona, CA). All signals were recorded on a Gould chart recorder (model TW11, Valley View, OH) and a

computer for subsequent analysis. Ventilation volumes were determined by computer integration of the flow signals. Oxygen consumption (\dot{V}_{O_2}) and carbon dioxide production (\dot{V}_{CO_2}) were computed from the inspired and expired minute ventilation \dot{V}_E and mixed expired CO_2 and O_2 .

2.4. Tests of respiratory muscle performance

Respiratory muscle strength was assessed using maximal inspiratory pressure (MIP) maneuvers. To determine MIP, subjects inspired maximally from residual volume against an occluded airway; an oscilloscope (model 4111, Tektronix, Beaverton, OR) provided visual feedback of the pressure signal. The occlusion had a small hole (2 mm diameter) to prevent pressure generation by the cheeks when the subject's glottis was closed. Subjects sustained each inspiratory effort for at least 1 sec. In all, four efforts, separated by 20 sec, comprised one set of MIPs. The greatest effort from each set was used for subsequent analysis.

Tests for maximal volitional ventilation in 15 sec (MVV_{15}) were performed on a computerized spirometry system (model PFT 3000, Pulmonizer, St. Louis, MO) according to procedures published by the ATS (1995). The greatest value from each set of three repeated measurements was used for subsequent analysis. During all tests of respiratory muscle performance, subjects were seated upright.

Respiratory muscle endurance was determined using a sustained ventilation test based on the design described by Morgan et al. (1987). The first three subjects (2 RMT and 1 placebo) ventilated at 80% MVV_{15} —but this was deemed to be too low a level and all subsequent subjects were tested at 90% MVV_{15} . During the test, subjects inspired from a 13.5-L water-sealed spirometer (model P1300, Collins, Braintree, MA) via a low resistance one-way, non-rebreathing valve (model 2700, Hans Rudolph, Kansas City, MO) as compressed room-air was delivered into the spirometer at the target \dot{V}_E . The spirometer, therefore, served as a visual target during the test since the average displacement of the spirometer bell was constant only as long as the subject's \dot{V}_E prevented it from filling. Connected to the mouth-

piece port of the one-way, non-rebreathing valve was a 1.22 m long tube (diameter = 35 mm) that created a small rebreathing volume to humidify the inspired air and maintain end-tidal CO_2 . Additional CO_2 was added, if necessary, through a port in the non-rebreathing valve. One technically acceptable trial was completed on a test day.

2.5. Cycling performance tests

Incremental \dot{V}_{O_2} max and fixed work-rate endurance tests were conducted on an electronically braked cycle ergometer (Elema-Schönder, Stockholm-Solna, Sweden). At rest and during exercise, measurements were made of \dot{V}_{O_2} , \dot{V}_E , and heart rate (HR) (Polar, Oulu, Finland). Ratings of perceived exertion (RPE) (scale 0–10) of leg effect and dyspnea were taken every 2 min throughout each test using hand signal communication with the subject. A 10 min warm-up at 83 Watts was provided before the incremental \dot{V}_{O_2} max test and at 117 W for the fixed work-rate endurance test followed by a 2–3 min rest period during which subjects performed a set of MIP maneuvers. The incremental \dot{V}_{O_2} max test began at 167 W and every minute subsequent to the start the work-rate was increased by 17 W. The fixed work-rate endurance test began after the resistance was increased over 30 sec from the warm-up work-rate to a work-rate selected to elicit 80–85% of each subject's peak work-rate (W_{peak}) achieved during the incremental \dot{V}_{O_2} max test. Subjects were verbally encouraged to perform at their best during both tests. Each test continued until volitional fatigue, defined as failure to maintain cadence ≥ 60 rpm.

The 8 km time trial was done using each subject's personal bicycle connected to an indoor stationary resistance trainer (model TravelTrac3 with model HF300 resistance unit, Performance, Inc., Chapel Hill, NC). All subjects had considerable experience with these trainers and practiced on our laboratory trainer on days prior to the time trials. The distance and time (12–14 min) of this test was chosen for two reasons: (a) the results would be minimally effected by lack of motivation which might occur even in these athletic subjects during repeated laboratory tests

which lacked real-life competition; and (b) an 8 km time trial is commonly used for training purposes and in competition. Distance was measured using a cycling computer (model piccolo, VDO, Frankfurt, Germany) mounted to the rear tire. Subjects warmed-up for 10 min at a self-selected pace and then stopped exercising for 2–3 min to perform one set of MIP maneuvers. The elapsed time for the test was then started after 0.16 km had been ridden by the subject, a small distance allowed to reach full speed. Time splits were provided at 0.8 km intervals. During the test, subjects were required to remain seated to avoid slip between the tire and resistance unit; subjects used a gear combination of their choice with the option to change gears at any time. Subjects were not encumbered with a mouthpiece or nose clip during this test. The only variables measured were HR and RPE at 0.8 km intervals using verbal communication with the subjects. This test was completed twice on different days before the training intervention started and again twice afterwards by 7 RMT and seven placebo subjects so that within-subject reproducibility could be evaluated. The best finishing time from each repeated pair was used to determine the effects of RMT or placebo on performance.

2.6. Blood measurements

A 20 gauge plastic catheter was inserted into an antecubital or forearm vein before the fixed work-rate endurance test. Samples (3–5 ml) of venous blood were then drawn over 10–20 sec at rest and every 2–3 min during the test. Blood lactate concentration was determined using a lactate analyzer (model 1500 Sport, Yellow Springs Instrument, Yellow Springs, OH).

2.7. Training

Both RMT and placebo training were conducted five times a week for 5 weeks for a total of 25 sessions in all. Each week, four of the five training sessions were performed at home; the fifth training session was supervised at the lab. All subjects continued their regular exercise training programs and were required to keep a daily

record of all physical activity, including RMT or placebo, throughout the study.

For the hyperpnea endurance training the goal was to have the subject complete 30 min of dynamic respiratory muscle work in an all out effort and to increase the amount of work as the RMT progressed over the 5-week period. To this end, we had subjects first practice at a \dot{V}_E of approximately 50–60% of MVV_{15} using a breathing frequency (f_R) of 50–60 min^{-1} for 30 min. The subjects were then instructed to follow this fatiguing regimen in their daily training sessions, attempting to increase their depth of breathing from one session to the next. Over a 1-week period subjects paced their breathing frequency using a digital metronome. Increases in f_R were made once a week at the supervised session. Subjects ventilated through a 1.2–1.8 m-long, 35 mm-diameter tubing (dead space volume = 1–1.8 L). Based on weekly in-lab tests we found that these subjects were able to maintain end tidal CO_2 P_{ET,CO_2} within ± 2 mmHg of eupneic control values.

Inspiratory resistive strength training required subjects to repeatedly inspire against a resistive threshold load, set initially to $\sim 50\%$ MIP, until task failure. Typically, this took approximately 40 inspirations or 3–5 min. The inspiratory threshold load was generated using an adjustable pop-it valve (POWERbreathe, IMT Technologies Ltd., Birmingham, England). For each breath, subjects inspired quickly and forcefully from residual volume and then expired slowly over 4–6 sec to prevent hyperinflation and hyperventilation. Subjects attempted to increase this training load every 1 or 2 days by increasing the number of inspiratory efforts. The threshold load was increased once a week at the supervised training session. Performances on the resistance trainer and during hyperpnea were evaluated weekly in the laboratory. Subjects completed their resistive and hyperpneic training sessions at different times on each training day, separated by 6–8 h.

Placebo subjects were instructed to use a placebo breathing device for 30 min/day, 5 days/week for 5 weeks). The device was similar in appearance to the resistance training device but contained small amounts of loosely packed aquar-

ium gravel. Subjects were told the material reduced the oxygen content of each breath, mimicking the effects of high altitude. Placebo subjects were instructed to breathe normally and not to increase their normal, 'breathing effort', while using the training device. \dot{V}_E and P_{ET,CO_2} during placebo training were measured prior to the outset of the placebo trial and once weekly in the laboratory; they did not differ more than $\pm 10\%$ from spontaneous breathing.

2.8. Experimental protocol

Prior to beginning placebo or RMT, each subject initially performed the cycling exercise performance tests on separate days separated by 24–48 h, in the following order: incremental \dot{V}_{O_2} max, time trial # 1, fixed work-rate endurance test, and time trial # 2. On days when the incremental \dot{V}_{O_2} max test or time trials were scheduled, pulmonary function, was measured before the whole body exercise tests. MIP was measured before every cycling performance test. Sustained ventilation tests were conducted before each time trial. The entire test protocol, exclusive of practice days, took 8–10 days and the order of testing was identical prior to beginning and following RMT or placebo.

Nine subjects underwent RMT, while the other eight used the placebo device. After the third week of training, subjects completed a mid-study 8 km time trial. Each week, RMT intensity was increased, as previously described, after an in-lab training session. The 'oxygen absorbent' material (white fish tank gravel) in the placebo breathing device was replaced weekly. Beginning 24–48 h after the final RMT or placebo session, each subject repeated all of the initial cycling performance tests and respiratory muscle strength and endurance tests according to the pre-testing schedule (see above). Pulmonary function testing, however, was only repeated on the first day of post-testing. Subjects underwent no placebo or RMT sessions the day before or on the day of their testing. The intensities used for measuring fixed work-rate endurance and breathing endurance were identical to pre-test values.

2.9. Statistics

A two-way analysis of variance for repeated measures over the 5-week placebo and RMT periods was used to determine the probability of differences in mean values within and between placebo and RMT groups. Tukey's post-hoc analysis was used to determine where statistically significant differences existed between pairs of mean values. Specifically, this statistical analysis assessed the changes in mean values over time in: (a) each of the three exercise performance tests, using peak work-rate and \dot{V}_{O_2} max for the incremental test, time to exhaustion for the fixed work-rate test and time to complete 8 km for the time trial test; (b) changes in cardiorespiratory responses to incremental exercise at each of several fixed work-rates and at peak work-rate; and (c) changes in cardiorespiratory responses, perceived exertion and plasma lactate concentration at each of several fixed time intervals during the constant work-rate endurance test. Test reproducibility for repeated trials of the time trial test was determined prior to and following RMT or placebo using the intra-class correlation coefficient (Portney and Watkins, 1993).

3. Results

3.1. Respiratory muscle training load

Significant increases occurred in the inspiratory resistive load per breath, the number of inspiratory efforts per training session, and the accumulated inspiratory pressure per training session over the course of RMT ($P < 0.05$; Table 1). For hyperpnea endurance training sessions, f_R and \dot{V}_E increased significantly with RMT ($P < 0.05$). Based on the daily diaries, we observed no significant departures from the subject's routine training regimens for the RMT or placebo periods.

3.2. Pulmonary function (PF), respiratory muscle strength and endurance (Table 2)

Placebo and RMT groups did not differ in age (24.6 and 23.9 years), height (180 and 179 cm),

weight (76 and 72 kg). PF, MIP and the duration of sustained \dot{V}_E were also similar between groups. The only significant change in PF appeared after RMT as a $4 \pm 3\%$ increase in FVC ($P < 0.05$) which exceeded that in the placebo group. MIP increased significantly from 168.5 ± 39.8 to 181.4 ± 40.4 cmH₂O after RMT and this increase exceeded that in the placebo group ($P < 0.05$). No significant changes were observed in the placebo group.

Endurance breathing pre-tests measured at 90% of each subject's best pre-test MVV₁₅ results were highly variable between trials conducted on different days ($CV \pm 163\%$). Post-testing after RMT or placebo showed no further significant change in this test in either group. Increases in the endurance breathing test occurred in four of six subjects in the RMT group and in all seven in the placebo group but these changes were highly variable. One RMT subject is absent from these results because a lingering cough was especially aggravated by this test, preventing him from performing at his true ability. In three subjects (2 RMT and 1 placebo), endurance breathing performance measured at 80% MVV₁₅ increased significantly from 3.4 ± 3.2 to 59.5 ± 12.9 min ($P < 0.05$) by the end of the study (+72 and 41 min in the 2 RMT subjects and +55 min in the placebo subject). MVV₁₅ increased significantly by

7–10% in both RMT and placebo subject groups over 3 pre-testing control days ($P < 0.01$) and did not change further after 5 weeks of RMT or placebo.

3.3. Cycling performance

Placebo and RMT groups did not differ in any of the performance tests during the initial test period (Table 3). Incremental exercise tests showed no significant change in $\dot{V}_{O_2\max}$ after RMT or placebo (Table 3). Eight of nine subjects in the RMT group and five of eight subjects in the placebo group reached a higher peak work-rate during post-testing. The improvement in peak work-rate was significant in both the RMT group ($+8.6 \pm 5.3\%$, $P < 0.01$) and the placebo group ($+6.3 \pm 8.9\%$, $P < 0.05$). These improvements did not differ between RMT and placebo groups.

Group mean work-rate during the fixed work-rate endurance test was 304 ± 39 W (range 250–367 W) for the RMT group and 320 ± 36 W (range 292–367 W) for the placebo group, which averaged $83 \pm 3\%$ of W_{peak} . Time to volitional fatigue during the fixed work-rate endurance test increased significantly following both RMT and placebo ($+26.4 \pm 18.2\%$ and $+16.4 \pm 13.1\%$, respectively, $P < 0.05$; Table 3). Only 1 of 17 subjects failed to improve his performance (Fig. 1).

Table 1
Respiratory muscle training loads in RMT group

	Training weeks				
	1	2	3	4	5
<i>Inspiratory resistance strength training</i>					
P_{insp} , (cmH ₂ O/breath)	79.0 ± 20.0	87.7 ± 21.5	$92.5 \pm 22.9^*$	$98.8 \pm 24.9^{*\dagger}$	$100.9 \pm 20.0^{*\dagger}$
# of efforts	44.4 ± 8.7	47.1 ± 11.4	43.4 ± 4.1	47.9 ± 10.9	$55.4 \pm 14.9^{*\ddagger}$
T_{ses} (min)	4.51 ± 1.63	4.55 ± 1.46	4.26 ± 0.99	5.12 ± 2.55	5.21 ± 2.18
P_{tot} , (cmH ₂ O $\times 10^2$)	36.0 ± 14.7	40.9 ± 12.5	40.3 ± 11.1	$46.9 \pm 15.5^*$	$55.9 \pm 19.2^{*\dagger}$
<i>30 min hyperpnea endurance training</i>					
\dot{V}_E (L/min)	128.5 ± 9.2	145.2 ± 15.1	141.9 ± 19.3	143.3 ± 22.4	$149.1 \pm 33.9^*$
f_R (breaths/min)	57.6 ± 1.8	62.9 ± 5.5	67.0 ± 6.1	66.2 ± 6.9	$68.5 \pm 8.4^*$
VT (L)	2.25 ± 0.14	2.33 ± 0.29	2.13 ± 0.27	2.17 ± 0.24	2.15 ± 0.32

Values are means \pm S.D.; $n=9$ inspiratory resistance strength training, $n=6$ hyperpnea endurance training. P_{insp} , average inspiratory resistive load per breath; T_{ses} , time of training session; P_{tot} , total inspiratory pressure per session, calculated as the product of P_{insp} and the number of inspiratory efforts; \dot{V}_E , minute ventilation; f_R , respiration frequency; VT, tidal volume. *Significantly different from week 1, † significantly different from week 2, ‡ significantly different from week 3, $P < 0.05$.

Table 2
Pulmonary function and respiratory performance

	RMT group		Placebo group	
	Pre	Post	Pre	Post
VC (L)	5.61 ± 0.72	5.84 ± 0.87	5.77 ± 0.66	5.77 ± 0.70
FEV _{1.0} (L/s)	4.76 ± 0.44	4.78 ± 0.53	4.98 ± 0.53	4.89 ± 0.49
FVC (L)	5.62 ± 0.78	5.82 ± 0.93*	5.95 ± 0.49	5.86 ± 0.49
FEV _{1.0} /FVC (%)	86.2 ± 4.6	84.0 ± 4.9	85.2 ± 5.0	84.2 ± 5.2
MIP (cmH ₂ O)	168.5 ± 39.8	181.4 ± 40.4*	154.4 ± 31.5	159.2 ± 27.2
MVV ₁₅ (L/min)	213.0 ± 23.0	214.6 ± 22.4	217.1 ± 34.5	214.9 ± 31.7
SVT _{90%} ^a (min)	0.66 ± 0.33	1.15 ± 0.94	2.00 ± 2.93	3.55 ± 4.39

Values are means ± S.D.; *n* = 9 RMT group, *n* = 8 placebo group.

^a *n* = 6 RMT group, *n* = 7 placebo group. VC, vital capacity; FEV_{1.0}, forced expiratory volume in 1 sec; FVC, forced vital capacity; MIP, maximal inspiratory pressure; MVV₁₅, maximal voluntary ventilation in 15 sec; SVT_{90%}, endurance breathing test at 90% of MVV. *Significantly different from pre.

The change in endurance performance time between the placebo versus RMT groups was not significantly different.

One placebo subject increased his fixed work-rate performance time more than twofold but showed changes similar to those of the group in the other two tests of exercise performance, forcing us to exclude his data for the fixed work-rate test from all analyses. We attribute the subject's relatively poor performance on the initial test to a lack of enthusiasm and effort throughout the fixed work-rate endurance test caused by repeated, failed attempts of venous catheterization beforehand. This was not the case for the second endurance test for which no catheterization was attempted.

Repeat time trial tests were conducted within both the pre- and post-RMT and placebo periods in seven subjects in each group (see Table 3). We observed no significant systematic effect of these repeat time trial tests on group mean values for performance time in either RMT or placebo groups. Random variability of performance times between these repeat tests was also very small, as shown by a CV of ± 0.9–1.1% and an intraclass correlation coefficient of 0.97.

Time to complete the 8 km time trial was unchanged after 3 weeks of RMT but decreased significantly following 5 weeks (−1.8 ± 1.2% or −14.8 ± 10.0 sec, *P* < 0.05, range −3.1% to +0.7%; Table 3). The placebo group time trial

performance remained unchanged from control at 3 (*P* > 0.10) and 5 weeks (*P* = 0.07). The increase in mean time trial performance in the RMT group did not exceed that in the placebo group. By week 3, five of nine RMT subjects had improved compared to only one of eight in the placebo group; by week 5, improved performance was seen in eight of the nine RMT subjects and five of the eight placebo subjects (Fig. 2A, B).

3.4. Responses to exercise

After RMT, \dot{V}_{O_2} and \dot{V}_{CO_2} were unaltered from control during the incremental \dot{V}_{O_2} max test (at fixed work-rates) and at all time points during the fixed work-rate endurance test (*P* > 0.10). After placebo \dot{V}_{O_2} was also unchanged during the incremental \dot{V}_{O_2} max test and during the fixed work-rate endurance test for all but two time points (min 6 and 8), at which \dot{V}_{O_2} was reduced by 5 and 7% below control (*P* < 0.05). \dot{V}_{O_2} data from three subjects (1 RMT and 2 placebo) were not included in these calculations due to technical problems with gas analysis.

No change in HR was observed after RMT or placebo at equal \dot{V}_{O_2} values during the incremental \dot{V}_{O_2} max test (Fig. 3A), at equal times during the fixed work-rate endurance test (Fig. 4A), or at equal distances throughout the time trial (data not shown). HR rose to within 2.6 ± 2.3% of max by the end-point of the fixed work-rate endurance

Table 3
Cycling performance variables

	Initial		Midpoint		End	
	RMT	Placebo	RMT	Placebo	RMT	Placebo
<i>Incremental \dot{V}_{O_2max} test</i>						
W_{peak} (W)	372 ± 43	396 ± 36			391 ± 41*	413 ± 48*
$\dot{V}_{O_2max}^a$ (ml/kg/min)	55.0 ± 5.0	54.2 ± 2.5			56.5 ± 7.3	54.1 ± 4.0
<i>Fixed work-rate endurance test</i>						
t_{lim}^b (min)	16.63 ± 6.19	17.18 ± 7.59			20.84 ± 7.47*	19.88 ± 8.71*
<i>Time trial</i>						
Test 1 ^c (min)	13.43 ± 0.64	13.13 ± 0.67			13.26 ± 0.52	12.92 ± 0.64
Test 2 ^c (min)	13.34 ± 0.72	12.93 ± 0.59			13.10 ± 0.55	12.84 ± 0.62
Best ^d (min)	13.33 ± 0.55	13.01 ± 0.52	13.24 ± 0.47	13.05 ± 0.56	13.08 ± 0.50*	12.96 ± 0.59

Values are mean ± S.D.; $n = 9$ RMT, $n = 8$ placebo.

^a $n = 8$ RMT, $n = 6$ placebo.

^b $n = 9$ RMT, $n = 7$ placebo.

^c $n = 7$ RMT and placebo d. $N = 9$ RMT, $N = 8$ placebo. Initial, testing prior to RMT or placebo; Midpoint, testing after week 3 of RMT or placebo; End, testing after 5 weeks of RMT or placebo; W_{peak} , peak work-rate; \dot{V}_{O_2max} , maximal oxygen consumption; t_{lim} , time to fatigue; Test 1, first pre- or post-time trial; Test 2, second pre- or post-time trial; Best, fastest of test 1 and test 2. *Significantly different from initial ($P < 0.05$).

test and to within $0.7 \pm 2.9\%$ of max at the end of the 8 km time trial.

With few exceptions, the ventilatory response to exercise also did not change significantly after RMT or placebo. During the incremental \dot{V}_{O_2max} test, \dot{V}_E was increased significantly following RMT at the two lowest intensities and at max ($P < 0.05$; Fig. 3B); no changes were observed after placebo. During prolonged, constant exercise of the fixed work-rate endurance test, \dot{V}_E was increased after RMT only during the initial 2 min of exercise ($P < 0.05$; Fig. 4B, C); \dot{V}_E was reduced significantly after placebo only at minute 8 ($P < 0.05$).

Blood lactic acid concentration rose progressively with time during the fixed work-rate endurance test in all subjects, plateauing at levels five to six times resting levels after 9 min of exercise. Neither group showed a significant change in lactate concentration at any exercise time point after 5 weeks of RMT or placebo ($P > 0.10$). Group mean lactate concentrations, however, tended to be lower than control and reduced by an average of 0.9–1.8 mmol/L in both RMT and placebo groups from the ninth minute to exhaustion (Fig. 4D).

Dyspnea ratings rose progressively with time throughout both the fixed work-rate and 8 km time trial exercise performance tests (Fig. 5A, B). No significant changes were recorded in dyspnea ratings in either the RMT or placebo group during the time trial and at only one time point

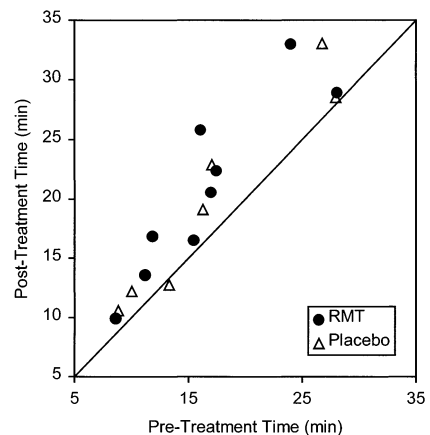


Fig. 1. Comparison of fixed work-rate endurance test times to exhaustion in individual subjects before (pre) and after (post) 5 weeks of RMT or placebo. Points lying above the line of identity (diagonal line, slope = 1) indicate improvement from initial test.

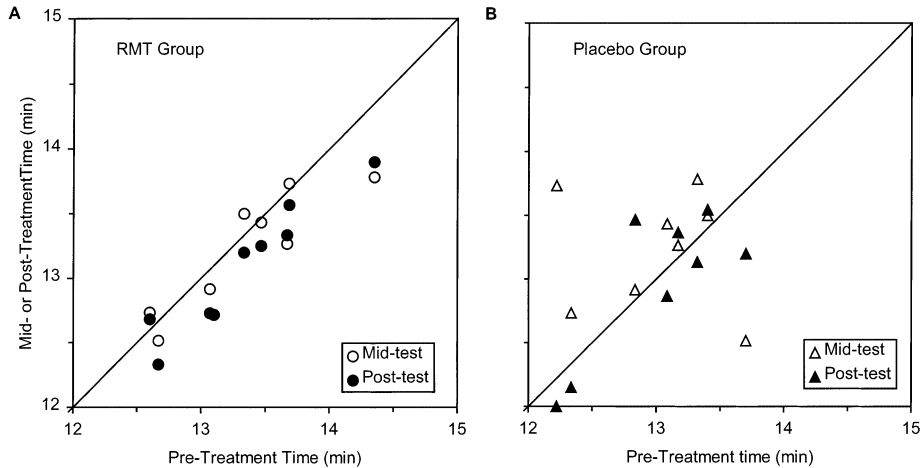


Fig. 2. Effects of 3 and 5 weeks of RMT (A) or placebo (B) on 8 km time trial finishing times. Points lying below the line of identity (diagonal line) indicate improvement from initial test.

during the fixed work-rate test (in the placebo group). No significant changes in perceived exertion of the legs were recorded in either group during the fixed work-rate endurance test or the time trial (data not shown).

4. Discussion

We evaluated the effects of a 5-week RMT program in competitive male cyclists with an experimental design that included: (a) both strength and endurance RMT; (b) a true placebo group; and (c) three different types of exercise performance tests. The RMT group alone showed significant increases in MIP and in inspiratory pressures and breathing frequency during training sessions. RMT caused significant increases of $8.6 \pm 5.3\%$ in peak work-rate achieved, and $26.4 \pm 18.2\%$ in time to exhaustion at a fixed work-rate. Similar improvements, however, were also seen in the placebo group ($6.3 \pm 8.9\%$ and $16.4 \pm 13.1\%$, respectively). RMT caused a small but significant $1.8 \pm 1.2\%$ increase in the 8 km time trial performance test which did not occur in the placebo group; however, the improvement in the RMT group was not significantly greater than that in the placebo group. Other indices of a physiological ‘training’ effect such as reductions

in heart rate, $\dot{V}E$, blood lactate or perception of limb and respiratory effort measured at a fixed work-rate and/or exercise time showed no consistent changes with RMT or placebo.

4.1. Placebo effects

To quantify the portion of the observed effects due to the special attention and subject expectations associated with RMT, our experimental design included a placebo group. To be considered a true placebo, Ojaunen (1994) suggests the following two criteria: (1) the placebo needs to be inert; and (2) it should generate expectations, involvement, subjective utility, and be meaningful to the subjects. Our sham ‘altitude breather’ satisfied both of these requirements. Breathing through the device had little or no effect on overall $\dot{V}E$, flow resistance, or PET_{CO_2} ; our placebo subjects trained five times weekly on the sham device, as did our RMT subjects; and subjects in both groups had equal amounts of contact time with the investigators in the laboratory. Additionally, the principle of increasing the oxygen carrying capacity of the blood, either by living at altitude or by using synthetic erythropoetin, is a widely known means of increasing exercise performance in the cycling community. More recently, even the supposed benefits of only intermittent hypoxic exposure

(during sleep) has been marketed to athletes (Farand, 1996).

It is possible that our placebo group underwent neuromuscular improvement as a result of daily use of their sham breathing device. This seems highly unlikely because our subjects followed no specific breathing regimen while on the sham device and almost always were distracted from the task by reading. We also found no evidence for an increased muscular efficiency of breathing because \dot{V}_{O_2} remained unchanged at any given \dot{V}_E during incremental or fixed work-rate exercise.

Previous studies exploring the effects of RMT on exercise performance have not included a true placebo group. Fairbarn et al. (1991) and Morgan et al. (1987), included ‘control’ groups who participated in pre- and post-testing. This level of involvement, however, was much less than that of a true placebo group and consequently cannot accu-

rately document the influence of the special attention and subject expectations have on performance. Most recently, Inbar et al. (2000) employed a placebo group that ‘trained’ with negligible resistance. Such a ‘minimal exercise’ placebo, however, may not be sufficient to activate important placebo factors, such as expectations (Ojaunen, 1994).

4.2. Placebo versus familiarization effects

For all tests where the end point is based on volitional effort, it is important to distinguish between the effects of placebo and the effects of test familiarization (or learning) with repeat trials. Ideally, given sufficient time, resources, and subject tolerance, we should have tested for this ‘familiarization’ effect by either having several repeat tests for all measures or, ideally, a third control group tested over the same time span. Even though we did not employ this ideal design, we did complete a substantial amount of between-day repeat testing on the criterion time trial performance test and found no systematic changes and even a barely discernable random variation ($CV < \pm 2\%$ and intra-class correlation coefficient = 0.97) (see Table 3). Furthermore, these levels of reproducibility were documented by repeat testing both within the pre-treatment and within the post-treatment periods. The latter data showed that RMT or extra time trial tests (as conducted at the 3-week period) or the subjects’ routine cycling training regimen over the 5-week training period did not further influence test reliability. Other groups have also reported excellent test–retest reproducibility of time trial type performance tests (Hickey et al., 1992). Given these data, we feel secure in proposing that any changes in the time trial performance in the placebo group truly represented a ‘placebo’ (i.e. expectations) influence rather than one of test familiarization. Interestingly, even though our placebo group did not improve their best time trial performance significantly, times were reduced measurably in five of eight subjects and the P value for the mean values ($P = 0.07$) was quite close to the 95% probability criteria for significance. So even with this highly reproducible time trial performance test

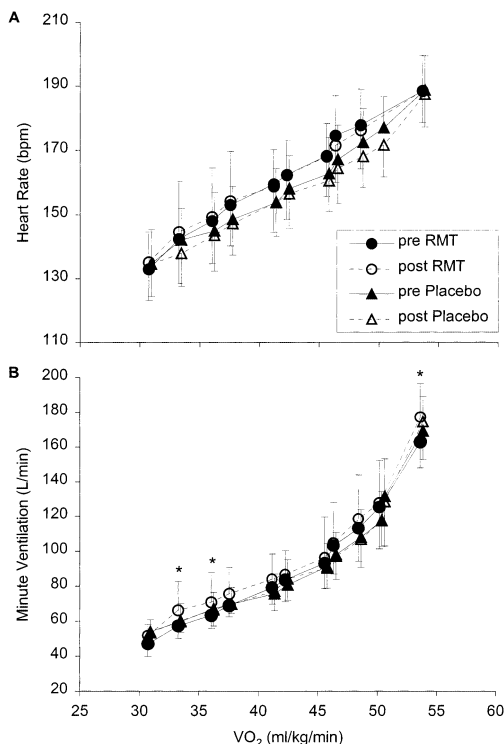


Fig. 3. Effects of 5 weeks of RMT ($n = 9$) or placebo ($n = 8$) on heart rate (A) and minute ventilation (B) during the incremental \dot{V}_{O_2} max test. Values are mean \pm S.D. *Significantly different from pre-test ($P < 0.05$).

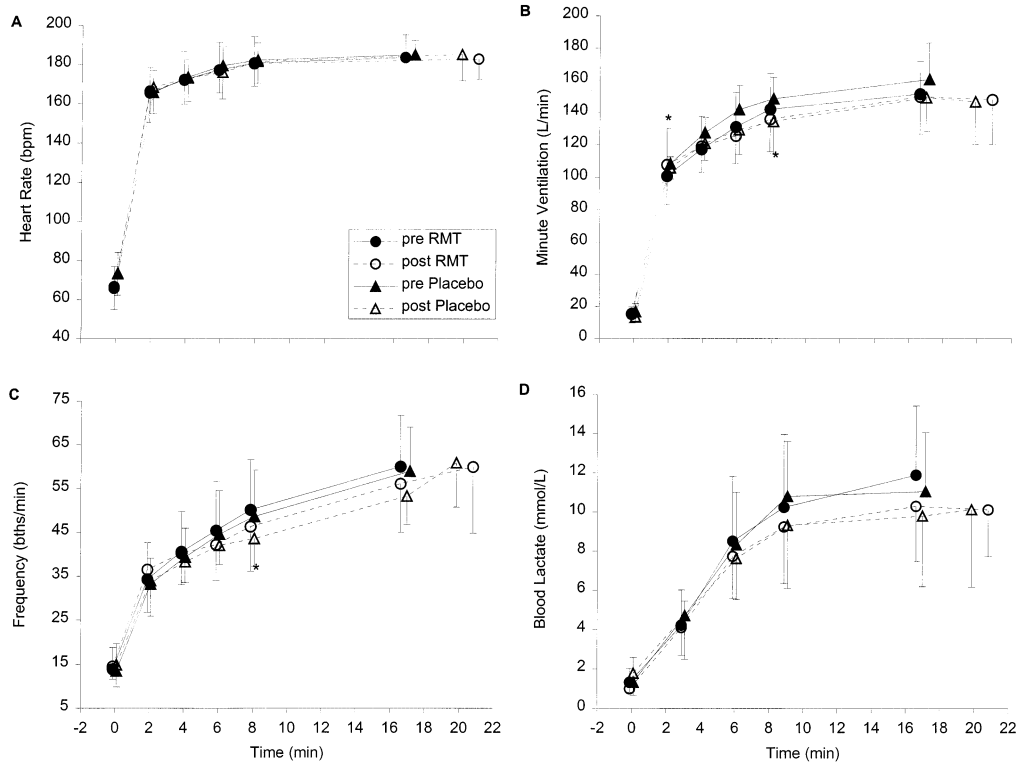


Fig. 4. Effects of five weeks of RMT ($n = 9$) or placebo ($n = 7$) on heart rate (A), minute ventilation (B), respiratory frequency (C), and blood lactate ($n = 6$ placebo) (D) during the fixed work-rate endurance test. Values are mean \pm S.D. *Significantly different from pre-test ($P < 0.05$).

there is a hint of a placebo effect which was apparently sufficient to prevent the small but systematic RMT effect from significantly exceeding that in the placebo group.

It is less certain that all of the significant effects in the placebo group observed for the incremental \dot{V}_{O_2} max test and fixed work-rate endurance test were true placebo effects, i.e. beyond those of test familiarization, per se. Others have shown low reproducibility with fixed work-rate tests at $< 80\%$ \dot{V}_{O_2} max (Krebs and Powers, 1989; Jeukendrup et al., 1996), this reproducibility was substantially less than with time trial type tests. In highly fit subjects working at a high fixed work-rate $> 85\%$ \dot{V}_{O_2} max, we did not see systematic variation in performance times upon repeat testing over 3 (control) test days. However, the random variation was significant (intra-class correlation coefficient = 0.47) (Harms et al.,

2000), and was almost twice that presently found for the time trial test. The relatively low reliability in these tests may not be surprising considering how unusual the task of riding to exhaustion at a fixed work-rate is in the field of competitive sports. The winner of a race is seldom defined as the last person standing on the course and yet this is how such an 'open-ended' test measures performance. A fixed distance exercise time trial type test, on the other hand, is not complicated to the same degree by these problems, probably because experienced cyclists know what to expect and how to push themselves when asked to ride a familiar distance as quickly as possible. In the case of peak work-rate, achieved via incremental type tests, day-to-day systematic and random variation are both quite small (Michelsen, 1990; Kuipers et al., 1985) and substantially less than with the fixed work-rate endurance test—at least in highly fit subjects.

In summary, while our own experimental design does not permit adequate assessment of familiarization effects on peak work-rate and fixed work-rate performance tests, previous data using repeat testing has shown that these effects are quite small for the former and substantial for the latter type of tests. Accordingly, we interpret the significant systematic effects presently observed in these performance tests in our placebo group to be a combination of test familiarization and placebo effect for the fixed work-rate test and primarily placebo effects for the peak performance test.

4.3. RMT, placebo and familiarization effects on respiratory muscle performance

In contrast to the time trial and peak performance exercise tests, test familiarity or learning effects clearly have substantial influences on tests of sustainable ventilation, as shown by the large random and systematic changes upon repeat testing prior to beginning either RMT or placebo periods. Eastwood et al., (1998) recently demonstrated the critical need for several repeat trials of ventilatory endurance tests to overcome ‘learning’ effects and especially the changes in effort perception that occur with repeat testing. We also emphasize that some other investigators report much better reproducibility with endurance breathing tests than we observed, which may question our

specific choice of tests or our ability to carry them out (Eastwood et al., 1998; Spengler et al., 1999). Nevertheless, given our current problems with these tests we were dependent primarily upon other evidence from the weekly in-lab training sessions to demonstrate a specific training effect in our RMT group which included significant increases in the sustainable f_R and the total resistive training load achieved after 5 weeks of RMT. These increases in training load were greater than or equal to values reported in other studies that have observed positive effects of RMT on exercise performance (Boutellier et al., 1992; Spengler et al., 1999). Furthermore, we also showed that MIP increased significantly in the RMT group despite a very high initial ‘control’ MIP value in these athletes and this increase with RMT exceeded the non-significant change in the placebo group.

4.4. RMT effects on exercise responses

The small gains observed in exercise performance with RMT occurred without parallel changes in the usual physiologic markers for gains in whole body physical fitness. Specifically, no consistent reductions in HR, \dot{V}_E , or blood lactate, three commonly reported effects of whole body physical training (Gladden, 1996; Rowell et al., 1996), were observed following RMT during either the incremental or fixed work-rate tests (Figs. 3 and 4). As detailed in Section 3, there was

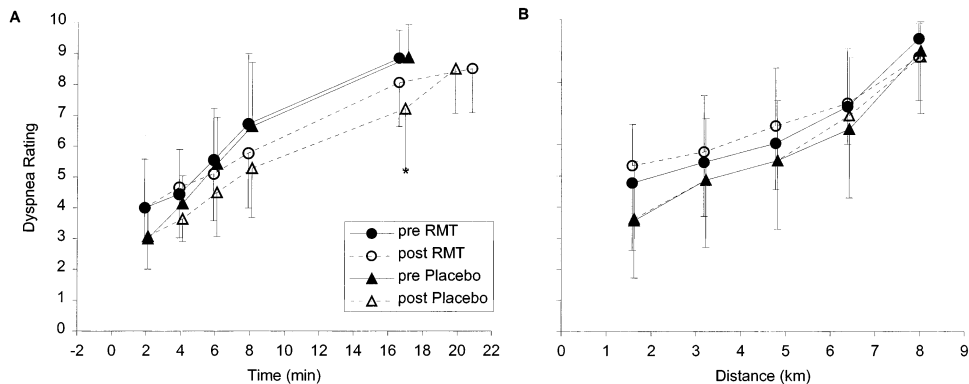


Fig. 5. Comparison of dyspnea ratings during the fixed work-rate endurance test (A) and the 8 km time trial (B) before and after 5 weeks of RMT or placebo. Values are mean \pm S.D. Experimental $n = 9$, placebo $n = 7$ for A, $n = 8$ for B. *Significantly different from pre-test ($P < 0.05$).

a tendency toward a 0.5–1.5 mmol/L reduction in plasma lactic acid concentration following RMT during the later portions of the fixed work-rate test but these changes were not significant and were observed in both RMT and placebo groups. We also observed no significant changes in perception of limb or respiratory effort during incremental fixed work-rate or time trial tests following RMT or placebo periods. Nor was an increase in \dot{V}_{O_2} max observed in either group (Table 3), as \dot{V}_{O_2} tended to plateau at a similar high work-rate following (as before) RMT and therefore \dot{V}_{O_2} remained unchanged even though peak work-rate increased.

Although these findings are in agreement with many previous studies of RMT, there are some exceptions. Boutellier and Piwko (1992) and Boutellier et al. (1992) report reductions in \dot{V}_E during their fixed work-rate endurance test after RMT, a trend that was not, however, reproduced in their most recent RMT studies (Kohl et al., 1997; Spengler et al., 1999). Additionally, modest but significant decreases in blood lactate at a fixed submaximal work-rate following RMT have been reported by other investigators (Boutellier and Piwko, 1992; Kohl et al., 1997; Spengler et al., 1999). We emphasize that the use of venous sampling from an arm vein by us and others may mean that the effect of exercise on lactate concentration may reflect the effect of a changing production and/or uptake from the arm in addition to the leg locomotor musculature (Gladden, 1996).

4.5. Is there a physiologic rationale for RMT effects on exercise performance?

First, it is reasonable to presume that the increased strength and endurance performance of the respiratory muscles due to specific RMT would also increase resistance to respiratory muscle fatigue and prevent (or delay) the diaphragmatic fatigue which is known to occur during sustained, high intensity exercise (Johnson et al., 1993; Babcock et al., 1995). In turn, preventing diaphragm fatigue may mean less recruitment of accessory respiratory muscles and therefore increased efficiency and reduced blood flow require-

ments of respiratory muscles during exercise. In addition, the diaphragmatic fatigue associated with prolonged heavy exercise may reflexly precipitate sympathetically mediated vasoconstriction (Hill, 2000; St. Croix et al., 2000) and decrease blood flow to limb locomotor muscles during exercise (Harms et al., 1997). This flow redistribution might be delayed with a fatigue-resistant diaphragm. Theoretically, then, RMT could result in a greater blood flow to, and therefore delayed fatigue of exercising locomotor muscles. These effects on locomotor and respiratory muscle fatigue might also be expected to decrease effort perception at any given exercise time. However, to what extent should exercise performance be affected?

When the respiratory muscles are mechanically unloaded by over 50% of their total inspiratory and expiratory work during heavy exercise and diaphragm fatigue is prevented (Babcock et al., 1995), blood flow is increased by 5–7% to locomotor muscles (Harms et al., 1997) and endurance exercise performance is increased in highly trained cyclists by $15 \pm 4\%$ (Harms et al., 2000). Respiratory muscle unloading caused no change in circulating lactate, a reduction in \dot{V}_{O_2} , cardiac output and dyspneic perception and had variable effects on \dot{V}_E (Harms et al., 1997, 1998, 2000). Other studies of respiratory muscle unloading in less fit subjects showed no significant effects on endurance exercise performance (Marciniuk et al., 1994); although these studies were conducted at lower relative exercise intensities and the respiratory muscle unloading did not effect \dot{V}_{O_2} . Although some recent RMT studies have reported huge improvements (+25–50%) in endurance performance (Boutellier and Piwko, 1992; Boutellier et al., 1992), it seems inconceivable that the effects of RMT, by itself, could surpass those seen with substantial mechanical unloading—unless, of course, RMT imparts some additional influences on locomotor muscles, which are not realized via substantial respiratory muscle unloading and the prevention of diaphragm fatigue. We do not suspect this to be the case since we presently observed a similarly large endurance performance improvement which was due, not to RMT, but primarily to a significant placebo plus familiariza-

tion effect for this type of fixed work-rate exercise test.

Based on the present findings in the time trial tests, we propose that specific respiratory muscle training in highly fit, competitive subjects may influence endurance exercise performance at most to a very limited extent and that most of this small influence can be explained by a placebo effect. On the other hand, RMT may have quite different effects under other circumstances, such as in patients with chronic heart failure who have very ill trained respiratory and locomotor muscles and who commonly experience marked hyperventilation, dyspnea and fatigue during even moderate exercise (O'Donnell et al., 1999; Mancini et al., 1995). In these patients, respiratory muscle unloading has very substantial effects on exercise performance (O'Donnell et al., 1999), theoretically then, RMT may well have substantial effects on exercise performance. These improvements with RMT have, in fact, been observed (Mancini et al., 1995). Unfortunately, a placebo group of patients was not used simultaneously to confirm a true training effect in this group. The rationale is clear for conducting such a controlled study in these patient populations and perhaps even in those with COPD.

Acknowledgements

This research was supported by the National Heart, Lung, and Blood Institute (NHLBI), and a grant sponsored jointly by the US Veterans Administration and the Department of Defense. David Sonetti was supported in part by a grant from the College of Letters and Science at the University of Wisconsin-Madison. Thomas Wetter was supported by an NHLBI training grant.

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