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Effects of two types of training on pulmonary and cardiac responses to moderate exercise in patients with COPD

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ABSTRACT: The effects of two 8-week programmes of exercise reconditioning on the time constants (τ) of the pulmonary gas exchange, ventilatory and heart rate responses to moderate intensity exercise in patients with chronic obstructive pulmonary disease (COPD) were studied.

Thirty-five subjects (mean±SD 64±5 yrs; forced expiratory volume in one second (FEV_1) 1.09±0.17 L; 41±6.2% predicted) were randomly assigned either to supervised (s) training on a treadmill, 4 days·week^{-1} (group S; n=21) or self-monitored (SM) walking 3 or 4 km in 1 h 4 days·week^{-1} (group SM; n=20). The different levels of supervision resulted in a different estimated intensity of training (35±10 W in the SM group and 70±22 W in the S group). The kinetics were evaluated with a constant-load exercise test on a cycle-ergometer at a work rate corresponding to 80% the highest oxygen consumption ($V'O_2$) that can be achieved without blood lactic acidosis ($V'O_2$,LAT) or 50% of $V'O_2$,max, if maximum oxygen consumption $V'O_2$,LAT was not found.

Mean endurance time at a work rate equivalent to 70% of the pretraining $V'O_2$,max increased by 493±281 s in the S group and 254±283 s in the SM group (p<0.001). Mean $\tau V'O_2$ decreased from 83±17 s to 67±11 s (p<0.0001) in the S group and from 84±12 to 79±16 (p=0.04) in the SM group. Mean τ for carbon dioxide output minute ventilation and heart rate were also speeded after training, again more markedly in the S group. In the S group there was a significant correlation between the decrease in $\tau V'O_2$ and the increase in endurance time (r=-0.56, SEM=0.21).

It is concluded that training speeds the kinetic response of oxygen consumption, carbon dioxide production, minute ventilation and heart rate to moderate exercise and that the effect is greater after supervised, more intense training.

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The ability to sustain high intensity exercise is mainly dependent on the subject's capacity to transport and utilize oxygen at rates commensurate with the energy demands. This ability may be characterized by four aerobic parameters: 1) the upper limit for oxygen utilization ($V'O_2$,max) [1]; 2) the highest oxygen consumption ($V'O_2$) that can be achieved without sustained blood lactic acidosis ($V'O_2$,LAT) [2]; 3) the rate at which $V'O_2$ increases towards its steady state requirement, characterized by the time constant (τ) of the response kinetics [3]; and 4) work efficiency [3].

Patients with chronic obstructive pulmonary disease (COPD) show reduced $V'O_2$,max [4, 5] and $V'O_2$,LAT [6] and slower $V'O_2$ kinetics [7, 8]. Work efficiency, however, has been shown to be similar to that of normal subjects [7, 9]. While some studies have shown that $V'O_2$,max [6] and $V'O_2$,LAT [10] can be increased by intense leg muscle training in COPD patients, others have pointed out that the increase in $V'O_2$,max is not always demonstrable [11, 12]. The kinetics of the $V'O_2$ response, however, has the potential to detect beneficial physiological changes even at submaximal work rates (WR) that do not generate lactic acidosis and hence are better tolerated.

The purpose of the present study, therefore, was to determine the effects of two different training programmes on the dynamic ventilatory, pulmonary gas exchange and heart rate (HR) responses to constant WR exercise of moderate intensity (*i.e.* below the lactic acidosis threshold): one treadmill based, supervised (S) by a physiotherapist at the hospital and the other self-monitored (SM; by means of a pedometer) level walking.

Materials and methods

The study was designed as a randomized, controlled, parallel study. Patients were selected if they were currently nonsmoking males, diagnosed with stable COPD as defined by the American Thoracic Society [13] with: post-bronchodilator forced expiratory volume in one second (FEV_1) <50% of predicted; <15% increase in FEV_1 after bronchodilator inhalation; <3% of carboxyhaemoglobin; and no other significant lung or extrapulmonary diseases or any physical disability that could hinder the exercise testing. All patients signed an informed consent and the protocol was approved by the Institutional Committee for

Ethics in Human Research of the authors' tertiary, university hospital.

Patients were randomly assigned to one of the following 8 week training programmes: 1) the subjects in the SM group were supplied with a pedometer and asked to walk 3 km in ≤1 h on level, unobstructed ground, 4 days per week. In addition, they were asked to walk at a pace brisk enough to elicit "moderate" dyspnoea for at least 10 min each day. Patients came to the clinic once a week to have the records checked; and 2) the S group was trained on a treadmill, under the supervision of a physiotherapist. The training began with speed of 3 km·h^{-1} and a slope chosen to provide an $V'O_2$ equivalent to 70% of $V'O_{2,max}$ in the incremental test (see below). The WR was subsequently increased on an individualized basis. Patients trained for 60 min per day, 4 days per week. Sessions could be split into as many as three periods.

Spirometry was performed using a Neumoscreen II (Jaeger, Hochberg, Germany) spirometer according to international guidelines [14]. Ventilation and pulmonary gas exchange was measured breath by breath by an Oxycon α (Jaeger). The gas analysers of this system (infrared for carbon dioxide and differential paramagnetic for O_2) were calibrated immediately prior to each test. The Oxycon α system (Jaeger) measures flow with a turbine that was calibrated with a 2 L syringe at 14, 21 and 28 strokes per min was measured from the electrocardiogram recorded from a standard three lead configuration. The exercise consisted of an incremental test on a treadmill (Laufergometer Junior; Jaeger) following a protocol modified from BALKE and WARE [15] to a symptom limited maximum. All subjects, however, performed a preliminary trial for familiarization with the procedure. Arm support was only allowed in those instances necessary to re-establish equilibrium. The lactic acidosis threshold (LAT) was estimated by the V-Slope method [16]. On a subsequent day, a constant WR test at 3 km·h^{-1} was performed at a slope corresponding to ~70% of the $V'O_{2,max}$ in the pretraining incremental test. The patient started with the slope preset and a speed of 1.5 km·h^{-1} for 1 min. The speed was then increased to 3 km·h^{-1} for the remainder of the test. This was terminated at 20 min or when, after standardized encouragement, the patient was unable to continue because of symptoms. The exercise tests used for the kinetic analyses were performed on an electromagnetically-braked cyclo-ergometer ER-900 (Jaeger). The seat was adjusted for the legs to be almost fully extended when the pedal was in the lowest position. The patient wore a face-mask with a dead space of ~100 mL. The room was conditioned to 25°C. A radial artery was cannulated for the first of the two separated trials. The sequence of the test was: 3 min resting, 3 min of unloaded pedalling, then the computer controlled WR was abruptly instituted to a WR corresponding to 80% $V'O_{2,LAT}$ or 50% of $V'O_{2,max}$ of the pretraining test, depending on whether the $V'O_{2,LAT}$ was discriminable, for 10 min.

To calculate WR the formula: WR (watts) = ($V'O_2$ (mL·min^{-1}) - 5.8 × body weight (kg) - 151) /10.1 was used [17]. Blood was drawn anaerobically from the cannulated radial artery before, immediately after the test and also at 2 min after the exercise test for immediate blood gas and pH analysis with an electrode analyser IL 1306 (Instrumentation Laboratory, Lexington, MA, USA). The syringes containing blood samples for lactate analysis were put in iced water and were analysed within 15 min by enzymatic methods. An identical constant WR test was repeated after 2 h without the radial artery cannula.

The kinetics of $V'O_2$, carbon dioxide production ($V'CO_2$), minute ventilation ($V'E$) and HR were analysed on the average of the two curves in an attempt to establish a "characteristic" time constant and gain for the response. To do this the breath-by-breath measurements of each curve were averaged in 10 s bins and the two curves aligned at the point at which the work-load was started. The following first order exponential model was adjusted by means of the graphic software Origin@ version 3.71 (Microcal Software Inc., Northampton, MA, USA), using iterative techniques:

$$y_t = y_b + y_{am} \times (1 - e^{-(t-d)/\tau})$$

where y_t is the variable at time t, y_b is the mean value of the last minute of the reference value (unloaded pedalling), y_{am} is the response amplitude, d the response delay and τ the time constant. To estimate the training WR and total work performed on the treadmill the formulas developed by GIVONI and GOLDMAN [18] were used.

Comparisons of means before and after training were performed by paired t-tests after checking for normal distribution of the differences. Comparisons of means between groups were performed with unpaired t-tests. In this case it was checked by appropriate normality and equality-of-variance tests that the assumptions of the test

Table 1. – Statistical description of the two groups

		Self-monitored n=17		Supervised n=18	
Variable	Units	Mean	SD	Mean	SD
Age	yrs	63.4	4.8	65.8	5.7
Height	cm	163.3	4.8	164.9	5.7
Body mass	Kg	69.0	8.1	68.5	12.6
FEV1	L	1.09	0.17	1.09	0.19
FEV1 % pred	%	41.0	7.1	40.4	7.5
FEV1/VCIN	%	45.0	8.3	47.0	8.7
FVC	L	2.60	0.52	2.56	0.69
P_{a,O_2}	mmHg	67.5	5.4	62.8	8.5
P_{a,CO_2}	mmHg	37.9	2.6	37.7	3.3
$T_{L,CO}$	mmol·min^{-1}·kPa^{-1}	4.8	1.6	5.2	1.7
$T_{L,CO}$ % pred	%	62.2	19.7	66.7	21.5
K_{CO}	mmol·min^{-1}·kPa^{-1}·L^{-1}	1.2	0.4	1.1	0.4
K_{CO} % pred	%	77.6	33.9	77.7	29.0
$V'O_{2,max}$	L·min^{-1}	1.20	0.26	1.20	0.35
$V'O_{2,max}$ % pred	%	59.1	11.6	61.0	18.1
Work-rate	W	35.1*	10.4	69.8*	22.3
Work	kJ	4044*	1205	8047*	2882

In the table it can be appreciated that the characteristics of the two groups are similar except for the estimated training intensity. FEV1: forced expiratory volume in one second; FEV1 % pred: FEV1 as per cent of predicted; FEV1/VCIN: FEV1 divided by inspiratory vital capacity; FVC: forced vital capacity; P_{a,O_2}: partial pressure of oxygen in arterial blood; P_{a,CO_2}: partial pressure of carbon dioxide in arterial blood; $T_{L,CO}$: transfer factor of the lung for carbon monoxide; $T_{L,CO}$ % pred: $T_{L,CO}$ as per cent of predicted; K_{CO}: $T_{L,CO}$ divided by alveolar volume; K_{CO} % pred: K_{CO} as per cent of predicted; $V'O_{2,max}$: maximal oxygen uptake; $V'O_{2,max}$ % pred: $V'O_{2,max}$ as per cent of predicted. *: p<0.0001.

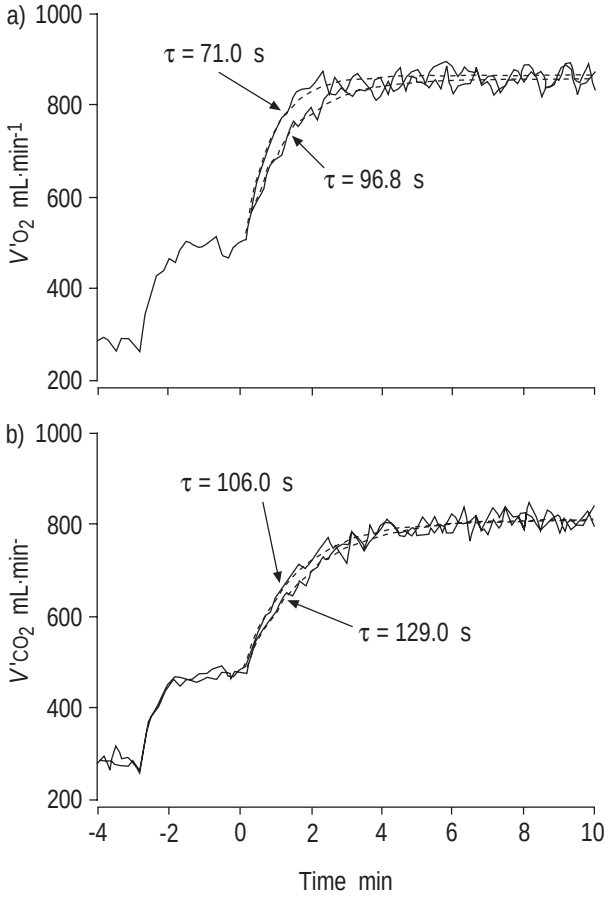

Fig. 1. – Figure showing the averaged trace of oxygen consumption ($V'O_2$) and carbon dioxide production ($V'CO_2$), and the corresponding exponential fitting of the four measured variables for a representative subject of supervised group. It can be seen that the data are well fitted by the monoexponential function (– – –). The traces with greater time constants (τ) correspond to the pretraining trials.

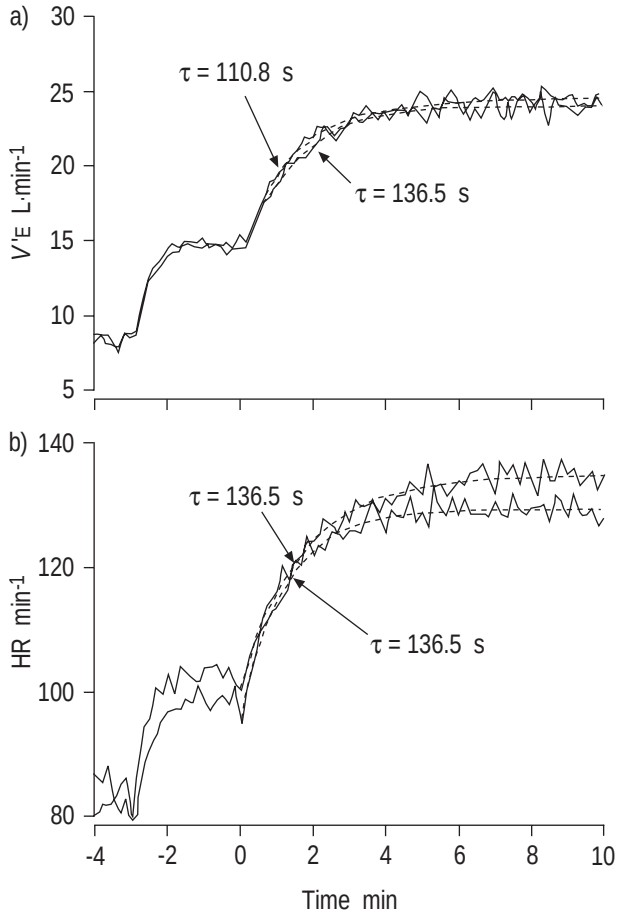

Fig. 2. – Figure showing the averaged trace heart rate (HR) and the corresponding exponential fitting of the four measured variables for a representative subject of the supervised group. It can be seen that the data are well fitted by the monoexponential function (– – –). The traces with greater time constants (τ) correspond to the pretraining trials.

were not violated. If the equality-of-variances could not be assumed, the proper correction was applied [19]. Means were considered to be different when the probability of a two-tailed type I error was <0.05. Correlation was considered with respect to the Pearson correlation coefficient. Statistics were performed with a statistical package (SPSS 7.5; Hispanoportuguesa SPSS, SL, Madrid, Spain) on a personal computer.

Results

Twenty-one subjects in the SM group and 20 in the S group were included. Four subjects of the SM group and two of the S group did not produce breath-by-breath signals of sufficient quality to study the kinetics. Exercise tests were well tolerated and none had to be suspended before 10 min. None of the patients developed significant oxyhaemoglobin desaturation (*i.e.* >3% from baseline) during the exercise test.

The general characteristics of the two groups are described in table 1. This shows that there were no significant differences between the two groups except that the WR and total work of the training programme as estimated by the formula of GIVONI and GOLDMAN [18], were significantly higher in the group S (p<0.001). After training there was a modest, but significant, improvement in FEV1 of (mean±SD) 70±113 mL, but without differences between groups. For $V'O_{2,max}$ the increase was 110±101.2

Table 2. – Mean response time of the supervised training patients

	$V'O_2$		$V'CO_2$		$V'E$		HR	
	Before	After	Before	After	Before	After	Before	After
Mean	83.4	67.4	114.4	101.9	118.4	107.9	125.1	111.6
SD	17.6	10.5	16.9	12.5	17.4	13.5	17.6	11.5
p-value	0.0000		0.0005		0.0084		0.0002	

Time constant, expressed in seconds, of the exponential fittings of the average of the two traces obtained in each subject. The p-values refer to the mean difference between the values obtained before and after training. $V'O_2$: oxygen consumption; $V'CO_2$: carbon dioxide output; $V'E$: minute ventilation; HR: heart rate.

Table 3. – Mean response time of the self-monitored training patients

	$V'O_2$		$V'CO_2$		$V'E$		HR	
	Before	After	Before	After	Before	After	Before	After
Mean	84.5	79.2	116.4	111.1	124.1	118.3	128.2	122.0
SD	11.6	15.6	12.3	18.2	12.1	18.3	12.1	16.9
p-value	0.0380		0.0621		0.0699		0.0138	

Time constant, expressed in seconds, of the exponential fittings of the average of the two traces obtained in each subject. Significance refers to the mean difference between the values obtained before and after training. $V'O_2$: oxygen consumption; $V'CO_2$: carbon dioxide output; $V'E$: minute ventilation; HR: heart rate.

mL·min^{-1} ($p<0.001$) and 5±176.6 mL·min^{-1} ($p=0.9$) in groups S and SM respectively.

Figures 1 and 2 show the averaged trace and the corresponding exponential fitting of the four measured variables for a representative subject of the S group. The data were well fitted by the monoexponential function. The mean τ values were not significantly different prior to training between the two groups (tables 2 and 3); after the training, however, they became significantly different ($p<0.05$). After the two training programmes τ decreased significantly in both groups. The change was more pronounced, however for the S group.

In 12 of 18 (67%) subjects from group S and 7 of 17 (41%) from group SM, the τ of $V'O_2$ decreased by >8.5 s ($p=0.059$). Using the one tail cut-off point (7.5 s) the resulting proportions were 13/18 (72%) and 7/17 (41%) respectively ($p<0.026$). Thus, intense training not only improved this index, but also improved it in a larger number of the patients.

The mean endurance time for the 70% of pretraining $V'O_{2,max}$ exercise test (estimated WR 50±17 W), improved in both groups: 493±281 s in the S group and 254±283 s in the SM group ($p<0.01$ for between groups comparison) as can be seen in figure 3. There was a significant inverse correlation between improvement in endurance time and $\tau V'O_2$ (r= -0.56. SEM 0.207), but only in the S group (fig. 4).

Analysis of the ventilatory pattern during the constant load exercise test also demonstrated changes after training in the S group, but not in the SM group (table 4). This was evidenced by a deeper, slower breathing pattern and resulted in a decreased dead space (V_D) tidal volume (table 4); this, combined with a slight decrease in $V'CO_2$ (table 5), yielded a reduction in $V'E$, although there were

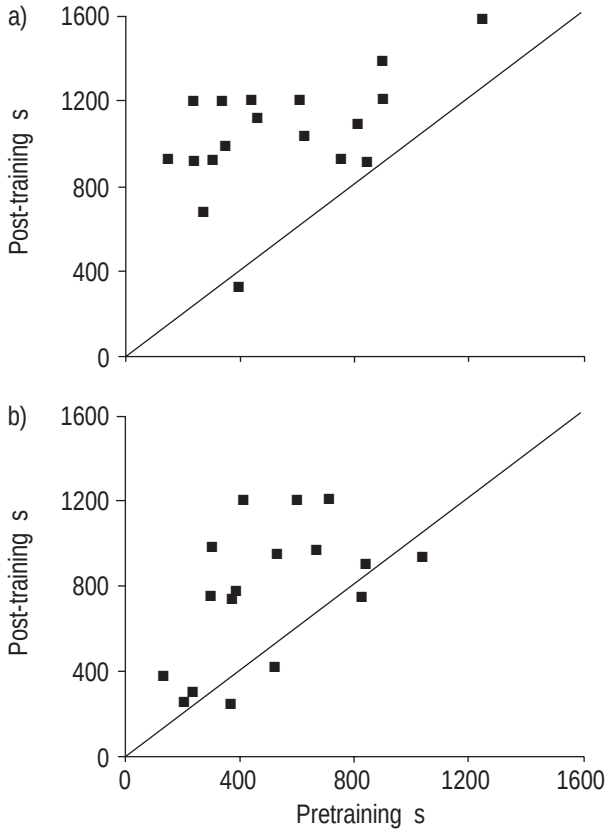

Fig. 3. – In this figure the pretraining endurance times of the constant tests above lactate threshold at 70% of maximal oxygen consumption are plotted against the post-training values for both groups: supervised (a) and self-monitored (b). The points represent individual patients. Identity lines are shown.

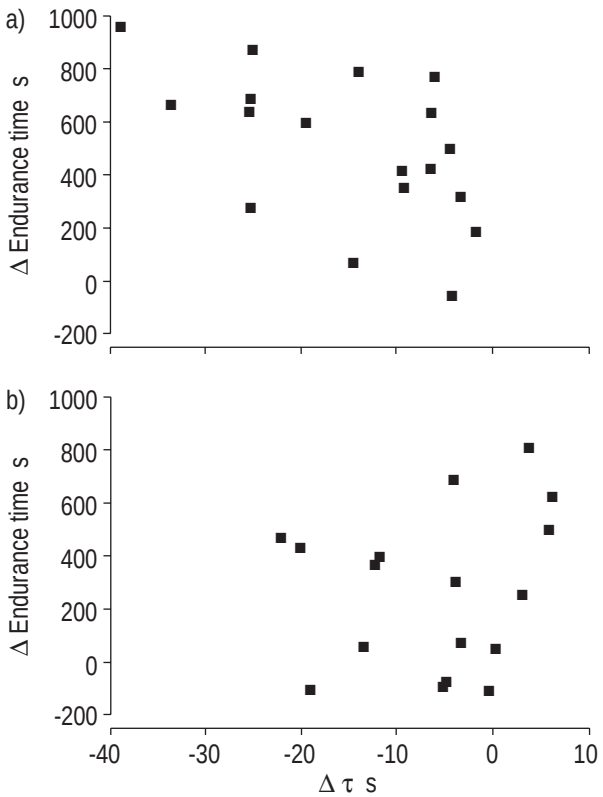

Fig. 4. – Scatter plots of the changes (Δ) in time constant (τ) against changes in endurance time of the constant tests above lactate threshold at 70% of maximal oxygen consumption. The points represent individual patients. a: supervised group; b: self-monitored group.

Table 4. – Effects of training on ventilation during constant, moderate intensity exercise

	Training		
	Before	After	p-value
Supervised			
V'_E L·min^{-1}	29.4±5.7	27.5±5.8	0.0246
V'_E/MVV %	65.4±11.8	60.7±9.2	0.0204
BR min^{-1}	27.2±4.0	24.1±4.3	0.0005
V_T mL	1090.2±211	1156.7±204	0.0212
V_D/V_T	0.37±0.10	0.34±0.10	0.0120
P_{a,CO_2} mmHg	40.2±2.5	39.1±3.5	0.3660
La mmol·L^{-1}	2.17±0.27	2.18±0.28	0.9376
Self-monitored			
V'_E L·min^{-1}	27.4±6.2	26.5±6.5	0.4532
V'_E/MVV %	65.3±14.5	61.9±11.2	0.2262
BR min^{-1}	25.8±4.2	26.1±7.8	0.8764
V_T mL	1077±237	1062±313	0.7852
V_D/V_T	0.36±0.09	0.37±0.12	0.7726
P_{a,CO_2} mmHg	40.4±3.0	41.8±4.7	0.2019
La mmol·L^{-1}	2.23±0.40	2.29±0.38	0.6312

Data are presented as mean±SD. Values obtained at the end of the constant exercise test. V'_E: minute ventilation at the end of the test; V'_E/MVV: minute ventilation divided by maximal voluntary ventilation; BR: breath rate; V_T: tidal volume; V_D/V_T: relative dead space calculated from partial pressure of carbon dioxide in arterial blood (P_{a,CO_2}); La: blood lactic acid.

no differences either in the blood lactate level (table 4) or respiratory exchange ratio (table 5). HR showed a significant decrease after S training and a trend to do so after the SM training (table 5).

Discussion

Prior to the exercise training, the COPD patients had time constants for V'_{O_2}, V'_{CO_2}, V'_E and HR ~50% longer that expected from sedentary subjects of this age [20]. While the kinetics were speeded by both training regimens, the mean change in τ and the proportion of patients in which τ improved was significantly larger in the S group than in the SM group. After S training the ventilatory pattern changed towards a deeper, slower, more efficient pattern; this was achieved spontaneously *i.e.* without "coaching" from the supervisor. Both types of training also reduced the HR response.

Table 5. – Effects of training on gas exchange and heart rate

	Mean	SD	Mean	SD	p-value
Supervised					
V'_{O_2} mL·min^{-1}	920	193.3	869	223	0.1283
V'_{CO_2} mL·min^{-1}	872	252	820	226	0.0560$^{\#}$
R	0.94	0.11	0.95	0.07	0.9383
HRb min^{-1}	90	15	89	12	0.5942
HRm min^{-1}	131	16	124	12	0.0066*
HRm %	83	9	80	8	0.0255*
Self-monitored					
V'_{O_2} mL·min^{-1}	903	248.3	892	214.1	0.7712
V'_{CO_2} mL·min^{-1}	829	242	817	213.0	0.6405
R	0.91	0.06	0.92	0.07	0.8828
HRb min^{-1}	94	15.6	87	13.2	0.1814
HRm min^{-1}	131	13.7	126	10.4	0.0586$^{\#}$
HRm %	84	9.3	80	7.3	0.0526$^{\#}$

V'_{O_2}: oxygen consumption; V'_{CO_2}: carbon dioxide production; R: gas exchange quotient; HRb: basal heart rate; HRm: maximal heart rate reached; *: two-tailed $p<0.05$; $^{\#}$: one-tailed $p<0.05$.

CASABURI *et al.* [21] have also studied V'_{O_2}, V'_{CO_2}, V'_E and HR, before and after S training in a rehabilitation clinic in COPD patients. They also found an acceleration of the response kinetics. However, the current work is original, in that it is a randomized trial comparing two kinds of training programmes with different levels of supervision. This in practical terms translated into two different intensities. The current study used different devices for training (treadmill or walk) than for the tests (cycle-ergometer), showing that when similar muscle groups are trained, resulting improvements are not task specific.

The reduction of the time constant following exercise training may be considered to be beneficial in the sense that it reduces the reliance on the mechanisms which account for the O_2 deficit accumulated during transient (*i.e.* utilization of local creatine phosphate stores, O_2 stores and possibly some lactate production). The factors on which the rate of change of V'_{O_2} ($\delta V'_{O_2}/\delta t$) depend can be obtained by derivation of Fick's equation with respect to time. Accordingly:

$$\delta V'_{O_2}/\delta t = \delta \overline{Q}'/\delta t \times (C_{a,O_2} - C_{v,O_2}(t)) + \overline{Q}'(t) \times \delta(C_a - C_{v,O_2})/\delta t$$

where $\overline{Q}'$ is cardiac output, C_{a,O_2} the arterial oxygen content and C_{v,O_2} the venous oxygen content.

As apparent from the formula the $\delta V'_{O_2}/\delta t$ increase can be expressed as being directly proportional to the rate of increase of cardiac output ($\delta \overline{Q}'/\delta t$) and to the rate of decrease in C_{v,O_2} ($\delta C_{v,O_2}/\delta t$). This formulation presupposes that the rate of change of V'_{O_2} is, in fact, dependent of the rate of change of $\overline{Q}'$; this has been shown not to be the case in normal subjects [22, 23]. In these $\delta V'_{O_2}/\delta t$ is dependent on other control features (*e.g.* the muscle phosphorylation potential, the free energy of adenosine triphosphate (ATP) splitting, *etc.*) such that different rate of change of $\overline{Q}'$ result in dependent changes of C_{a,O_2}-C_{v,O_2}. However, it may well not be the same in subjects with long kinetics such as those studied in the present investigation [24, 25]. An inadequate $\delta \overline{Q}'/\delta t$ can be the result of primary myocardial dysfunction [26] increased intrathoracic pressure swings during breathing or a consequence of high resistance with reduced compliance of the pulmonary vascular bed [26, 27]. After training, not only were the HR response dynamics substantially faster (tables 2 and 3), but there was also a decreased magnitude of the response *i.e.* the O_2 pulse was increased. At these subthreshold WRs this is likely to reflect a higher stroke volume. A slow $\delta C_{vO_2}/\delta t$ may be the result of decreased muscle capillary density [28], impaired O_2 diffusion to mitochondria or reduced oxidative capacity [29]. It has been shown that training increases the content of oxidative enzymes in muscle fibres in such patients [30]. The effects of muscle reconditioning on muscle O_2 extraction at submaximal WR have been studied recently in COPD. A slight increase in the O_2 extraction ratio was seen with training, its magnitude was related to the WR, being very small at low WR [31].

Despite the improvement after training, the τ for V'_{O_2} remained higher than in healthy age matched subjects (*i.e.*

~67 and 80 s in the S and SM groups respectively) compared with 46±17 s in the study of CHILIBECK *et al*. [20]. This indicates either that some of the circulatory or dysfunction is not reversible, or that the training strategy was not optimal. The authors believe that with regard to the intensity and frequency of the sessions, not much more could be done by the patients, but perhaps 8 weeks of training could be insufficient to obtain a maximal adaptive response. In fact, in normal subjects oxidative capacity and capillarization steadily increases in the first 12 month of training [32].

$V'CO_2$ kinetics during constant work load exercise are slower than those of $V'O_2$ kinetics because of the larger muscle capacitance for CO_2 than O_2. The speeding of the $V'CO_2$ kinetics can be explained by the faster $V'O_2$ kinetics as it is unlikely that training would reduce the tissue CO_2 capacitance. As previously reported ventilatory dynamics closely follow those of $V'CO_2$ [33], this was the case in this study.

A striking finding of the study is that the more intense training reduced ventilatory needs at a subLAT WR, *i.e.* where lactic acidosis does not play a role as a ventilatory stimulus. A similar finding has been found by WOOLF and SUERO [34] and CASABURI *et al*. [21]. Both studies have high intensity training in common. This reduction was due to a small reduction in $V'CO_2$ (table 4) and to a reduced V_D fraction of the breath (table 4), resulting at least in part from the improved pattern of breathing. The effect is not task specific: patients were trained on a treadmill and tested on a bicycle, although it does appear to depend on the training intensity.

CASABURI *et al*. [21] found that gas exchange data from 12 of 25 patients were not analysable with respect to gas exchange kinetics. In the current study most of the patients (35/41) did produce records good enough for analysis. This difference could be due to the fact that the confidence of the exponential fit depends on the steady-state amplitude or "gain" of response [35] and the patients of CASABURI *et al*. [21] were older, had a slightly worse lung function and had to be tested at a lower WR.

Another interesting finding of this study is the relationship that exists between improvement in the speed of the $V'O_2$ kinetics and the endurance time for heavy exercise. But while the faster τ for $V'O_2$ was associated with improved endurance time for constant-load exercise in the group S as a whole, individual relationships were highly disparate. This is likely to reflect the fact that the $V'O_2$ kinetics is only one of the contributors to exercise tolerance. Further research is needed on this proportional contributory influence (fig. 4).

In conclusion it has been shown that training can speed the kinetic responses of oxygen consumption, carbon dioxide production, minute ventilation and heart rate in patients with severe chronic obstructive pulmonary disease. Supervized, more intense training, produced greater improvement, suggesting a "dose dependent" effect. Intense training, such as was employed here, also had the effect of reducing ventilatory demands of sublactic acidosis threshold exercise and inducing a more efficient breathing pattern. The results also demonstrate that a low intensity exercise test on a cycle-ergometer may be used effectively to evaluate interventions such as rehabilitation. It can detect a variety of physiological changes which are unaffected by the motivation of the subject and such tests are not associated with significant risk.

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