

End-tidal pressure of CO₂ and exercise performance in healthy subjects

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Abstract High arterial CO₂ pressure ($P_a\text{CO}_2$) measured in athletes during exercise suggests inadequate hyperventilation. End-tidal CO₂ pressure ($P_{\text{ET}}\text{CO}_2$) is used to estimate $P_a\text{CO}_2$. However, $P_{\text{ET}}\text{CO}_2$ also depends on exercise intensity (CO₂ production, $\dot{V}\text{CO}_2$) and ventilation efficiency (being $P_{\text{ET}}\text{CO}_2$ function of respiratory rate). We evaluated $P_{\text{ET}}\text{CO}_2$ as a marker, which combines efficiency of ventilation and performance. A total of 45 well-trained volunteers underwent cardiopulmonary tests and were grouped according to $P_{\text{ET}}\text{CO}_2$ at respiratory compensation (RC): Group 1 ($P_{\text{ET}}\text{CO}_2$ 35.1–41.5 mmHg), Group 2 (41.6–45.7) and Group 3 (45.8–62.6). At anaerobic threshold, RC and peak exercise, ventilation ($\dot{V}\text{E}$) was similar, but in Group 3, a greater tidal volume (V_t) and lower respiratory rate (RR) were observed. Peak exercise workload and $\dot{V}\text{O}_2$ were lowest in Group 1 and similar between Group 2 and 3. Group 3 subjects also showed high peak $\dot{V}\text{CO}_2$ suggesting a greater glycolytic metabolism. In

conclusion, a high $P_{\text{ET}}\text{CO}_2$ during exercise is useful in identifying a specific respiratory pattern characterized by high tidal volume and low respiratory rate. This respiratory pattern may belong to subjects with potential high performance.

Keywords Athletes · End tidal of CO₂ · Ventilation · Exercise

Introduction

Many studies have gathered data suggesting ventilatory limitations of aerobic exercise in athletes. Excessive alveolar to arterial O₂ pressure ($\Delta P_{\text{A-a}}\text{O}_2$) difference, abnormal increases in arterial CO₂ pressure ($P_a\text{CO}_2$) and haemoglobin desaturation have been demonstrated (Dempsey and Wagner 1999; Durand et al. 2000; Rodman et al. 2002).

A high value of $P_a\text{CO}_2$ suggests an inadequate ventilation increase during exercise. This phenomenon may be due to mechanical respiratory constraint, on reaching the upper limit of expiratory flow rate and/or respiratory muscle force production (Johnson et al. 1992), or to a low chemoreceptor responsiveness (Harms and Stager 1995). However, a lower hyperventilation and the consequent higher $P_a\text{CO}_2$ can, *per se*, affect maximal exercise performance. Indeed, a reduced hyperventilation could determine lower respiratory muscles work allowing for a lower blood flow towards respiratory muscles and a gain of up to 10%, in leg blood flow (Harms et al. 1997, 1998, 2000). This mechanism delays the onset of leg fatigue and permits greater exercise performance. Furthermore, a higher $P_a\text{CO}_2$ is associated with greater tissue and blood acidosis, which through a rightward shift on the HbO₂ saturation curve allows greater O₂ delivery to muscles.

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End-tidal pressure of CO₂ ($P_{ET}CO_2$) is used for a non-invasive estimate of P_aCO_2 (Benallal and Busso 2000; Wasserman et al. 2005). During exercise, the difference between P_aCO_2 and $P_{ET}CO_2$ is mainly related to respiratory rate (RR) because expiratory CO₂ does not reach a plateau. Consequently, for a given alveolar CO₂, higher the $P_{ET}CO_2$ the lower is the RR. It is worthy to note that a high RR means low ventilation efficiency, since the higher the RR the greater is the percentage of dead space/tidal volume ventilation. Therefore, $P_{ET}CO_2$ derives from muscle metabolism (amount of CO₂ production), from the respiratory rate (RR) and CO₂ chemoreceptor set point. Accordingly, in normal subjects, high $P_{ET}CO_2$ may be due to high exercise performance and efficiency of ventilation. Consequently $P_{ET}CO_2$ can be proposed as a marker, which combines performance and efficiency of ventilation.

The aim of this paper is to evaluate, in healthy well-trained subjects, if during exercise a relationship between physical performance/efficiency of ventilation and $P_{ET}CO_2$ exists.

Methods

A total of 45 healthy, physically well-trained volunteers participated in the study. We defined “well-trained” subjects as those who had been performing aerobic exercise on a regular basis for at least 1 year. Immediately before exercise testing, all subjects underwent standard lung function measurements (Vmax 29C, SensorMedics, USA).

A maximal symptom-limited cardiopulmonary exercise test was performed on an electronically braked cycloergometer (Ergometrics-800, SensorMedics, USA), with the subject wearing a nose clip and breathing through a mass flow sensor (Vmax 29C, SensorMedics, USA) connected to a saliva trap. A personalized ramp exercise protocol was chosen, aiming at a test duration of ≈ 10 min. The exercise was preceded by 5 min of resting breath-by-breath gas exchange monitoring (rest) and by a 3 min unloaded warm-up. A 12-lead ECG, blood pressure and heart rate were also recorded.

Tests were evaluated by two expert readers. The anaerobic threshold (AT) was identified by V -slope analysis of consumption of O₂ ($\dot{V}O_2$) and production of CO₂

($\dot{V}CO_2$) increase and confirmed by specific behaviour of O₂ ($\dot{V}E/\dot{V}O_2$) and CO₂ ($\dot{V}E/\dot{V}CO_2$) ventilatory equivalents and end-tidal pressure of O₂ ($P_{ET}O_2$) and $P_{ET}CO_2$ (Beaver et al. 1986). The end of respiratory compensation (RC) was identified when $\dot{V}E/\dot{V}CO_2$ increased and $P_{ET}CO_2$ decreased (Beaver et al. 1986; Wasserman 1978). $\dot{V}E/\dot{V}CO_2$ is reported both as the slope of the relationship, and measured from the beginning of loaded exercise to RC, and at each exercise workload, as the actual $\dot{V}E/\dot{V}CO_2$ ratio. The $\Delta\dot{V}O_2/\Delta\text{WorkRate}$ (WR) slope was measured throughout the entire exercise (Wasserman et al. 2005).

We divided our study population into three groups according to $P_{ET}CO_2$ values at RC: Group 1 (1st tertile: from 35.1 to 41.5 mmHg), Group 2 (2nd tertile: from 41.6 to 45.7 mmHg), Group 3 (3rd tertile: from 45.8 to 62.6 mmHg).

The investigation was approved by the local ethics committee and subjects signed a written informed consent before participating in the study.

Statistical analysis

Data are reported as mean \pm sd. Mean values of the cardiopulmonary exercise tests are results of 20 s averages. All data were evaluated with SPSS-PC + 13.0 statistical software (SPSS-PC + Inc, Chicago, Illinois). We compared all cardiopulmonary data of three groups at Rest, AT, RC and at peak exercise (Peak). The same data were also analysed at iso-workloads (50, 100, 150 and 200 W), where 200 W was the highest workload reached by all subjects. All comparisons were made by one-way ANOVA followed by a paired t -test as appropriated (Bonferroni post hoc analysis). A P value of <0.05 was considered to indicate statistical significance.

Results

All three groups were well matched with respect to age, gender and BMI (Table 1). The forced expiratory volume in the first second (FEV₁) (107 ± 13 , 105 ± 8 and $111 \pm 9\%$ of predicted in Group 1, 2 and 3, respectively, $P = \text{NS}$) and the forced vital capacity (FVC) (113 ± 14 , 113 ± 9 and $112 \pm 7\%$ of predicted in

Table 1 Demographics parameters of the study population

Groups	Gender (male/female)	Age (years)	BMI (kg/m ²)	Weight (kg)	Height (cm)
1	12/2 $P = 0.330$	39 \pm 10 $P = 0.275$	22.6 \pm 2.0 $P = 0.180$	69.7 \pm 8.5 $P = 0.071$	175.6 \pm 7.9 $P = 0.399$
2	12/3	38 \pm 8	23.1 \pm 3.3	70.2 \pm 10.5	174.4 \pm 5.5
3	16/0	33 \pm 11	24.3 \pm 2.3	76.7 \pm 8.2	177.7 \pm 6.8

$P = \text{ANOVA test result}$

Table 2 Cardiopulmonary data at metabolic steps in the three study groups divided according to $P_{ET}CO_2$ values

Groups	HR (bpm)	Work (Watt)	$\dot{V}E$ (l/min)	RR (breath/min)	V_t (l)	$\dot{V}O_2/kg$ (ml/kg/min)	$\dot{V}CO_2/kg$ (ml/kg/min)	Pet CO_2 (mmHg)
Rest								
1	68 ± 4	0.140	12.7 ± 3.8	16 ± 5	0.88 ± 0.49	5.1 ± 1.1	4.7 ± 1.9	33.8 ± 3.4
2	72 ± 6	-	10.6 ± 1.1	16 ± 3	0.70 ± 0.12	4.8 ± 0.7	3.8 ± 0.5	35.6 ± 2.4
3	67 ± 5	-	13.1 ± 4.2	15 ± 2	0.88 ± 0.21	5.3 ± 1.4	4.7 ± 1.6	37.6 ± 3.1*
AT								
1	129 ± 14	0.163	50.3 ± 13.1	28 ± 8	1.89 ± 0.53	28.2 ± 7.8	21.6 ± 5.4	40.1 ± 2.3
2	141 ± 14	0.154	48.5 ± 13.0	25 ± 5	1.96 ± 0.40	32.2 ± 7.2	18.2 ± 3.3	43.9 ± 1.9 [§]
3	138 ± 19	0.140	49.1 ± 11.8	22 ± 5*	2.38 ± 0.71	31.3 ± 6.7	19.4 ± 10.1	49.6 ± 3.8 [‡] &
RC								
1	154 ± 15	0.022	82.8 ± 18.8	33 ± 7	2.58 ± 0.50	37.3 ± 5.9	35.4 ± 6.4	38.8 ± 1.9
2	165 ± 11	0.027	75.2 ± 16.8	31 ± 5	2.47 ± 0.48	42.7 ± 7.0	27.8 ± 4.8	43.9 ± 1.4 [§]
3	168 ± 15*	0.025	82.0 ± 19.2	28 ± 7	3.00 ± 0.63 [†]	43.4 ± 7.1*	32.7 ± 18.5	50.2 ± 4.5 [‡] &
Peak								
1	165 ± 14	0.006	104.4 ± 21.5	41 ± 9	2.59 ± 0.54	41.8 ± 6.6	46.7 ± 8.3	36.5 ± 2.5
2	178 ± 9 [§]	0.0025	112.6 ± 26.6	44 ± 8	2.59 ± 0.45	48.8 ± 6.5 [§]	52.0 ± 6.4	39.0 ± 3.3
3	181 ± 15*	0.025	115.0 ± 22.5	39 ± 11	3.12 ± 0.51 ^{†*}	48.0 ± 7.1*	59.4 ± 10.0 ^{†*}	45.2 ± 5.3 [‡] &

$P =$ ANOVA test result; * $P < 0.05$ Group 3 vs. Group 1; † $P < 0.05$ Group 2 vs. Group 1; ‡ $P < 0.001$ Group 3 vs. Group 1; § $P < 0.001$ Group 2 vs. Group 1; ¶ $P < 0.001$ Group 3 vs. Group 2; * $P < 0.001$ Group 2 vs. Group 1

Group 1, 2 and 3 respectively, $P =$ NS) between groups were similar.

At Rest, a significant difference between groups was found only for $P_{ET}CO_2$ (Table 2, Figure 1). Figure 1 reports the behaviour of $\dot{V}O_2$ versus $P_{ET}CO_2$ at Rest, AT, RC and Peak: Group 3 showed a significantly higher $P_{ET}CO_2$ at all stages of exercise. Workload, heart rate (HR) and ventilatory parameters at all stages of exercise under examination are reported in Table 2.

AT was reached by all subjects under similar workload and metabolic conditions (Table 2). At this step, we observed similar $\dot{V}E$ with, however, different ventilatory patterns: indeed V_t progressively increased and RR reduced from Group 1 to Group 3.

RC was reached at a progressively higher workload from Group 1 to 3 (Table 2). At this stage, the difference in HR, workload, V_t and $\dot{V}O_2$ became significant.

At Peak, HR, workload, V_t , $\dot{V}O_2$ and $\dot{V}CO_2$ differences were maintained (Table 2), but no differences in peak HR, workload and $\dot{V}O_2$ were observed between Group 2 and 3. Peak exercise respiratory exchange ratio (RER) is reported in Fig. 2; RER is higher in Group 3 with respect to the other two groups (1.12 ± 0.11 , 1.10 ± 0.07 and 1.23 ± 0.15 in Group 1, 2 and 3, respectively; $P = 0.005$). Peak $\dot{V}O_2$, expressed as percentage of $\dot{V}O_{2MAX}$ predicted by height, age and sex was: 113 ± 20 , 132 ± 16 and $127 \pm 16\%$ in Group 1, 2 and 3, respectively ($P = 0.013$), showing a lower exercise performance in Group 1 and similar performances in Group 2 and 3.

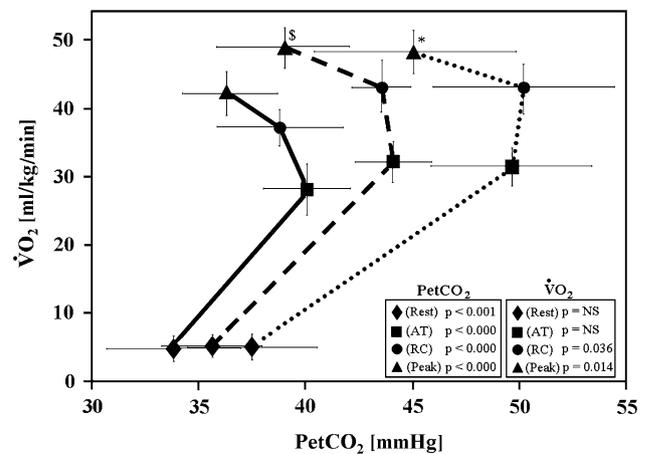


Fig. 1 O_2 consumption ($\dot{V}O_2$) and end-tidal pressure of CO_2 ($P_{ET}CO_2$) behaviour at Rest, at anaerobic threshold (AT), at end of respiratory compensation (RC) and at Peak in the three study groups. The standard deviation and ANOVA for $\dot{V}O_2$ and $P_{ET}CO_2$ between groups are given in the table inset. Continuous line, long dashed line and short dashed line identify respectively Group 1, 2 and 3. * $P < 0.05$ $\dot{V}O_2$ values of Group 3 vs. $\dot{V}O_2$ values of Group 1. § $P < 0.05$ $\dot{V}O_2$ values of Group 2 vs. $\dot{V}O_2$ values of Group 1

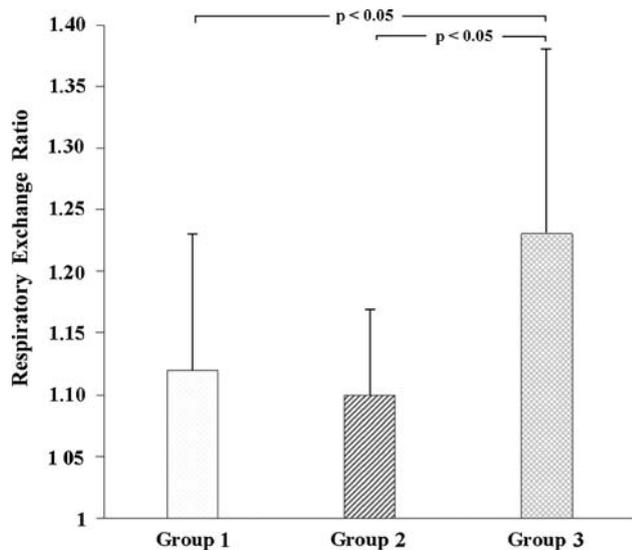


Fig. 2 Respiratory exchange ratio (RER) values and standard deviation at peak exercise in the three study groups

Data at iso-workloads are reported in Table 3. Differences in ventilatory pattern were observed at all stages. To evaluate the respiratory pattern throughout the exercise we also averaged all data obtained every 50 W (from 50 to 200 where data from all subjects were obtained). Mean $\dot{V}E$ was 39.3 ± 16.3 , $32.5 \pm 11.7^{\S}$ and $33.0 \pm 12.2^{* \dagger}$ l/min, mean V_t was 1.56 ± 0.46 , 1.54 ± 0.47 and $1.78 \pm 0.61^{* \dagger \ddagger}$ l/min, mean RR was 25.1 ± 7.0 , $21.7 \pm 5.0^{\S}$ and $19.0 \pm 5.2^{\ddagger \dagger}$ bpm in Group 1, 2 and 3 respectively.

The $\dot{V}E/\dot{V}CO_2$ slope was 30.1 ± 2.8 , $25.4 \pm 2.3^{\S}$ and $22.0 \pm 3.6^{\ddagger \dagger}$ in Group 1, 2 and 3, respectively ($P < 0.0001$). The $\Delta\dot{V}O_2/\Delta\text{WorkRate}$ slope was 9.1 ± 0.9 , 9.3 ± 1.8 and 9.5 ± 1.0 ml/W/min in Group 1, 2 and 3, respectively ($P = 0.614$) ($* P < 0.05$ Group 3 vs. Group 1; $^{\S} P < 0.05$ Group 2 vs. Group 1; $^{\dagger} P < 0.05$ Group 3 vs. Group 2; $^{\ddagger} P < 0.001$ Group 3 vs. Group 1; $^{\dagger \ddagger} P < 0.05$ Group 3 vs. Group 2; $^{\S} P < 0.001$ Group 2 vs. Group 1).

Discussion

The main finding of our study is that in a group of healthy physically well-trained subjects, those with the lowest values of $P_{ET}CO_2$ during exercise have a low exercise performance, as demonstrated by lower workload and $\dot{V}O_2$ reached. Interestingly these subjects showed a specific ventilatory pattern, featuring high $\dot{V}E$ due to a high RR. Group 2 and 3 subjects have the same exercise capacity, but subjects with the highest $P_{ET}CO_2$ have also the highest $\dot{V}CO_2$ at peak exercise.

Table 3 Iso-watt cardiopulmonary data in the three study groups divided according to $P_{ET}CO_2$ values

Work (Watt)	Groups	$\dot{V}E$ (l/min)	RR (breath/min)	V_t (l)	$\dot{V}O_2/\text{kg}$ (ml/kg/min)	$\dot{V}CO_2/\text{kg}$ (ml/kg/min)	$\dot{V}E/\dot{V}CO_2$
50	1	21.5 ± 5.4	20 ± 5	1.09 ± 0.33	11.2 ± 1.5	9.0 ± 2.0	34.4 ± 3.7
	2	18.9 ± 3.8	19 ± 4	1.08 ± 0.38	11.3 ± 1.6	8.5 ± 1.5	32.2 ± 2.7
	3	20.4 ± 4.2	$16 \pm 3^*$	1.33 ± 0.35	10.6 ± 1.3	9.4 ± 1.7	$28.6 \pm 3.5^{\ddagger \dagger}$
100	1	30.9 ± 5.9	23 ± 5	1.40 ± 0.28	17.9 ± 2.2	14.6 ± 2.7	30.7 ± 2.3
	2	27.0 ± 3.6	20 ± 5	1.47 ± 0.43	18.7 ± 2.6	13.5 ± 3.0	29.2 ± 2.0
	3	$26.5 \pm 3.1^*$	$18 \pm 4^*$	1.60 ± 0.62	16.8 ± 2.7	13.7 ± 2.7	$25.7 \pm 2.6^{\ddagger \&}$
150	1	44.4 ± 7.4	27 ± 8	1.69 ± 0.29	24.5 ± 3.6	22.1 ± 4.7	29.4 ± 2.9
	2	$35.9 \pm 3.3^{\S}$	23 ± 4	1.63 ± 0.27	25.0 ± 4.1	19.1 ± 3.6	27.5 ± 2.2
	3	$36.0 \pm 5.9^{\ddagger}$	$20 \pm 5^*$	1.90 ± 0.41	23.4 ± 3.7	20.4 ± 6.7	$23.5 \pm 1.8^{\ddagger \&}$
200	1	60.2 ± 9.7	30 ± 6	2.04 ± 0.33	30.9 ± 4.0	30.2 ± 5.9	29.1 ± 2.2
	2	$48.3 \pm 5.4^{\S}$	25 ± 5	1.97 ± 0.30	31.0 ± 3.7	26.6 ± 5.5	$26.5 \pm 1.1^{\S}$
	3	$49.3 \pm 7.4^{\ddagger}$	$22 \pm 6^{\ddagger}$	2.31 ± 0.55	31.0 ± 4.3	28.7 ± 5.4	$22.7 \pm 2.2^{\ddagger \&}$

$P =$ ANOVA test result; $*$ $P < 0.05$ Group 3 vs. Group 1; $^{\dagger} P < 0.05$ Group 3 vs. Group 2; $^{\ddagger} P < 0.001$ Group 3 vs. Group 1; $^{\S} P < 0.001$ Group 2 vs. Group 1; $^{\&} P < 0.001$ Group 1, $^{\ddagger \&} P < 0.001$ Group 2 vs. Group 1

We evaluated if the algorithm used to measure $\dot{V}CO_2$ could be affected by the respiratory pattern and therefore our results could be influenced by the $\dot{V}CO_2$ calculation technique. $\dot{V}CO_2$ in the Sensor Medics Vmax 29C is measured according to the following formula: $\dot{V}CO_2 = STP \times (F_eCO_2 - F_iCO_2) \times RR / (1 - F_eCO_2 + F_iCO_2 / RER)$. The RR appears in the numerator of the formula so that subjects with higher RR (Group 2) should have, if anything, a higher measured $\dot{V}CO_2$. However, our results were the opposite, so that the algorithm used was not the cause of the observed $\dot{V}CO_2$ differences.

The decision to subdivide our study population into three different groups, using $P_{ET}CO_2$ values obtained at RC, was taken to evaluate the role of ventilatory patterns on exercise performance. Indeed, RC is the exercise stage featuring the highest $P_{ET}CO_2$ and is also the exercise stage less influenced by the volitional component of exercise ventilatory regulation and exercise performance (Wasserman et al. 2005). It should be stressed that $P_{ET}CO_2$ is a marker, which combines exercise performance and efficiency of ventilation and by no means can be considered an independent physiological variable (see “Introduction”).

$P_{ET}CO_2$ is used as a non-invasive measure of P_aCO_2 (Johnson et al. 1992; Wasserman 1978) in subjects with no evidence of cardiac and lung diseases and is most useful and indicative of P_aCO_2 when phase 3 of expiration is virtually flat, a situation that may not pertain to heavy exercise (Jones et al. 1979; Wasserman 1978). A high P_aCO_2 is considered a sign of inadequate hyperventilation (Dempsey and Wagner 1999; Martin et al. 1979) and of exercise limitation due to the respiratory system if a subject is near his maximal voluntary ventilation. However, and apparently in contradiction with the previous statement, subjects belonging to the lowest tertile of $P_{ET}CO_2$ and therefore to the lowest value of P_aCO_2 , achieved the lowest peak workload and $\dot{V}O_2$ during exercise.

Subjects with the lowest $P_{ET}CO_2$, and probably lowest P_aCO_2 , are likely to have the greatest exercise-induced acidosis, which explains the reduced exercise capacity. Why Group 2 and 3 have a different ventilatory pattern is much less clear but, in our opinion, very interesting. Group 2 and 3 reached the same exercise performance (same $\dot{V}O_2$ and workload) but in Group 3, $P_{ET}CO_2$, by definition, and $\dot{V}CO_2$, unexpectedly, were both higher at peak exercise. Several explanations for these results are possible. The ventilatory pattern of subjects with higher $P_{ET}CO_2$ at RC is peculiar and featured high V_t and low RR throughout exercise, albeit a similar $\dot{V}E$ was registered between Group 2 and 3. This ventilatory pattern, well described in endurance athletes, offers less expenditure of ventilation in dead space and, therefore, minor work of respiratory muscles (Clark et al. 1983; Johnson et al. 1992). This pattern could be related to a reduced chemoreceptor sensitivity

associated with a lower dyspnoea feeling (Rodman et al. 2002; Takano et al. 1997). Harms et al. showed that minor tiredness in respiratory muscles, which can be experimentally obtained by mechanical unloading of these muscles, allows for a reduction of respiratory muscles $\dot{V}O_2$ and blood flow and that this phenomenon is associated with more than 10% leg blood flow increase (Harms et al. 1995; Harms et al. 1997). Moreover, the same Authors suggested that the reduction of respiratory muscles workload and the increase in peripheral muscles flow, delays the feeling of dyspnoea, allowing a more advanced exercise load (Harms et al. 1998).

According to this theory, Group 3 subjects should have registered a greater exercise performance than Group 1 and 2, but we observed that Group 2 and 3 have the same exercise capacity. We assume that Group 3 subjects were less fit subjects compared to those of Group 2. Indeed, subjects in the third tertile of $P_{ET}CO_2$ had greater RER and peak $\dot{V}CO_2$, suggesting an increased glycolytic metabolism during exercise. Moreover, albeit not statistically different, anaerobic threshold showed a trend of lower work rates in Group 3 vs. Group 2. However, our hypothesis needs to be verified by a study on the effects of respiratory pattern as a guide to exercise training.

Our hypothesis that subjects with high $P_{ET}CO_2$ present a reduced ventilation response to exercise-induced CO_2 accumulation is strengthened by the iso-watt analysis of ventilatory pattern during exercise. Indeed, starting from 100 W, subjects with higher $P_{ET}CO_2$ at RC showed lower values of $\dot{V}E$ and of RR compared to Group 1 and a trend toward a higher V_t and lower RR compared to Group 2. Furthermore, if all data, all RR, V_t and $\dot{V}E$ of each of the iso-watt analysis are averaged, the ventilatory pattern difference between groups is clear, with lower RR and higher V_t in Group 3, even if there is a similar $\dot{V}E$ in Group 2 and 3.

A few study limitations should be recognized. Firstly, our research suffers an absence of blood gas analysis and plasmatic lactate concentration values. Indeed, differences between blood and end-tidal CO_2 data are likely not to be the same in comparing slow and fast breathing subjects. Blood gas data, which certainly would have been useful to support our findings, were not collected. However, Wasserman et al. (1978) reported a difference between P_aCO_2 and $P_{ET}CO_2$ values of approximately +2.5 mmHg at rest to -4 mmHg during heavy work, which is below the difference in $P_{ET}CO_2$ that we observed. Moreover, Jones et al. (1979) formulated an equation to predict P_aCO_2 directly from $P_{ET}CO_2$ values. All these works support a good reliability of $P_{ET}CO_2$ as an indirect measure of P_aCO_2 in healthy subjects (Benallal and Busso 2000). However, our study was aimed at investigating the relationship between physical performance and $P_{ET}CO_2$

considered as a marker, which combines efficiency of ventilation and exercise performance and not simply as an indicator of $P_a\text{CO}_2$.

Secondly, we used a cycloergometer. Therefore, we do not know if the observed respiratory pattern is also present in exercise performed with other ergometers e.g. a treadmill.

Thirdly, the cardiopulmonary tests were performed in our laboratory randomly during the year, without taking the subjects' training period into consideration. This could be an important point of remark, because training modifies the respiratory pattern through an alteration of chemo and muscular receptors responsiveness.

Fourthly, the population we analysed was a mixed population of physically well-trained subjects who practised varied sports and were therefore not athletes in a specific area. So our data needs to be confirmed for each specific sport.

Finally, because specific $\dot{V}E$ behaviour occurs through the entire exercise and is present even at rest (see differences in resting $P_{\text{ET}}\text{CO}_2$), it is possible, but totally unproven, that in the well-trained subjects, the ventilatory pattern pertains to regular life activity and not only to maximal exercise performance.

In conclusion, in a healthy physically well-trained population, $P_{\text{ET}}\text{CO}_2$ values during exercise could be useful in identifying particular respiratory patterns and their underlying physiological mechanisms. This parameter, which is easily and non-invasively detectable with a cardiopulmonary exercise test, could represent a tool in future studies on the relationship between ventilation and exercise performance. Indeed, it might be that subjects with the highest $P_{\text{ET}}\text{CO}_2$ could, with training, improve their exercise performance more than the participants in Group 2. Consequently, our study raises more questions than it provided answers. Further studies are certainly required to evaluate if and how training affects the respiratory pattern during exercise and whether $P_{\text{ET}}\text{CO}_2$ analysis during exercise can drive training methodologies.

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