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Contribution of respiratory acidosis to diaphragmatic fatigue at exercise

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ABSTRACT: The factors that may modulate ventilatory muscle fatigue during exercise are controversial. In this study the contribution of acidosis to exercise-induced diaphragmatic fatigue was investigated, using measurements of the twitch mouth pressure response (tw,P_{mo}) to cervical magnetic stimulation.

After learning sessions, 14 healthy subjects performed two cycling tests (at 60% of maximal aerobic power for 16 min), one while breathing spontaneously (mean minute ventilation (V'_E) 67.9 L·min^{-1}) and the other while hypoventilating voluntarily (mean V'_E 53.8 L·min^{-1}). Exercise was voluntarily set at a moderate power to avoid a fatiguing effect of exercise *per se*.

As compared with spontaneous breathing (SB), voluntary hypoventilation (VHV) significantly increased mean carbon dioxide tension in arterial blood (P_{a,CO_2}) (51 mmHg *versus* 41 mmHg) and significantly decreased arterial pH (7.28 *versus* 7.34). After 10 min of SB test, tw,P_{mo} was unchanged compared to the baseline value (19.1 *versus* 18.5 cmH_2O) whereas tw,P_{mo} fell significantly as compared to baseline (17.1 *versus* 18.5 cmH_2O) and to SB (17.1 *versus* 19.1 cmH_2O) after the VHV test.

The results of this study suggest that exposure to hypercapnia may impair respiratory muscle function. This impairment could be more clinically relevant in patients with chronic obstructive lung disease.

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Studies showing that the diaphragm is susceptible to fatigue [1–3] have led to a flurry of research into the factors that influence diaphragmatic function. COAST *et al.* [4] recently demonstrated that increased work of breathing is not sufficient to explain the respiratory muscle fatigue seen during exercise. Several factors linked to exercise have been suggested as causes of inspiratory muscle fatigue, including: 1) competition for blood flow between the motor skeletal muscles and the diaphragm; and 2) accumulation in the diaphragm and other inspiratory muscles of metabolites produced by motor skeletal muscles [5]. Acidosis is among the major extracellular modifications seen during exercise, and can be considered as a factor that contributes to muscular fatigue [6]. Whether hypercapnia impairs respiratory muscle function is a matter of debate. *In vivo* [7] and *in vitro* [8, 9] animal studies suggest that hypercapnia-induced acidosis may affect diaphragmatic contractility, whereas others do not [10]. Human studies are also controversial. JUAN *et al.* [11] found that hypercapnia was associated with accelerated diaphragmatic fatigue while MADOR *et al.* [12] refute this. Using hyperventilation, RAFFERTY *et al.* [13] showed that hypercapnia may reduce diaphragm contractility immediately after maximal voluntary ventilation but it did not intensify long-lasting fatigue in these conditions.

To the best of the authors' knowledge, the possible contribution of acidosis to diaphragmatic fatigue during exercise has never been evaluated in humans using cervical magnetic stimulation (CMS) of the phrenic nerves [14]. This method allows reliable and noninvasive measurement of respiratory muscle strength during nonvolitional contraction.

To determine whether respiratory acidosis may contribute to diaphragmatic fatigue during exercise, normal subjects were submitted to two exercise sessions, with an intensity of 60% of maximal aerobic power. One trial was performed during normocapnia produced by spontaneous breathing (SB), while in the other trial hypercapnia was produced by voluntary hypoventilation (VHV). Diaphragmatic fatigue was assessed using measurement of the twitch mouth pressure response (tw,P_{mo}) to CMS of the phrenic nerves. In an additional study, tw,P_{mo} was used concomitantly with twitch transdiaphragmatic pressure (tw,P_{di}) to insure the adequacy of tw,P_{mo} in the detection of diaphragmatic fatigue.

Methods

Subjects

Fourteen healthy males aged 23.9±1.7 yrs gave their informed consent for the study, which was approved

Table 1. – Main characteristics of the study subjects

Subject no.	Age yr	Height cm	Weight kg	$V'O_{2max}$ L·min^{-1}	MAP W	Load W
1	24	187	90	4.0	375	210
2	22	175	72	4.3	375	220
3	26	183	79	3.5	300	180
4	24	168	68	3.4	300	180
5	25	179	73	3.7	325	190
6	21	176	75	4.5	350	210
7	22	186	70	3.7	300	180
8	24	176	70	3.9	425	290
9	24	186	70	3.6	325	190
10	26	191	79	4.0	375	220
11	22	171	65	3.5	325	200
12	25	180	77	4.1	325	185
13	26	178	81	2.9	300	170
14	23	178	74	2.9	300	170
Mean±SD	23.9±1.7	179.6±6.4	74.5±6.4	3.7±0.5	336±39	200±31

$V'O_{2max}$: maximal oxygen intake; MAP: maximal aerobic power; Load: work load.

by the appropriate ethics committee. All 14 subjects denied a personal or familial history of epilepsy. None wore a pacemaker or an implanted electronic device that would have contraindicated CMS. Baseline characteristics of the study subjects are reported in table 1.

Preliminary exercise testing and voluntary hypoventilation

At the first visit, each subject underwent a physical examination and a 12-lead electrocardiogram (ECG), and then performed an incremental exercise test to allow maximal oxygen uptake ($V'O_{2max}$) determination as follows: the subjects exercised to exhaustion on an electronically-braked cycle ergometer (Bosch Erg 602; Dimeq, Berlin, Germany). After a 10-min warm-up at 75 W, the load was increased (25 W·min^{-1}) until the subject was unable to continue despite encouragement. The subject breathed through a facemask (Hans Rudolph, Kansas City, MO, USA), and expired gases were analysed breath-by-breath using an automated system (CPX, Medical Graphics, St Paul, MN, USA). Expired gas flow was measured using a pneumotachograph (Type 3; Hans Rudolph). Oxygen uptake ($V'O_2$), and carbon dioxide production ($V'CO_2$) were averaged over the last 15 s of each min. End-tidal pressures of oxygen (P_{ET,O_2}) and carbon dioxide (P_{ET,CO_2}), expiratory flow ($V'E$), tidal volume (VT), respiratory rate (RR), and inspiratory oxygen fraction (F_{I,O_2}) were monitored continuously. Criteria for $V'O_{2max}$ determination were: 1) stabilization of $V'O_2$ despite a further increase in workload, 2) attainment of the age-predicted maximal cardiac frequency (220-age), and 3) a respiratory exchange ratio >1.15. Cardiac frequency was recorded continuously by four ECG leads.

During the next 3 weeks (once or twice a week), the subjects participated in learning sessions, during which they were instructed to voluntarily decrease their $V'E$ while exercising at 60% of their predetermined maximal aerobic power (MAP) for 10 min. VHV was considered learned when the subject was able to voluntarily decrease $V'E$, mainly by decreasing VT, for at least 10 min. The subjects breathed through a face mask connected to a three-way valve. A pneumotachograph was connected to the inspiratory port of the circuit for breath-by-breath automated gas analysis (as described earlier). Inspired airflow was adjusted using a flow meter. Inspired air was humidified after entry into a 10-L balloon placed on the inspiratory breathing circuit. The subjects used the balloon as a target to control their VT.

Voluntary hypoventilation, spontaneous breathing

During experimental sessions, the subjects performed two standardized tests. Because it was important that exercise by itself did not induce fatigue, its intensity was chosen voluntarily moderate (60% of the MAP). This intensity was similar during VHV and during SB.

After a 12-min warm-up, power was increased to 60% MAP±10 W (fig. 1). After 3 min, the subjects

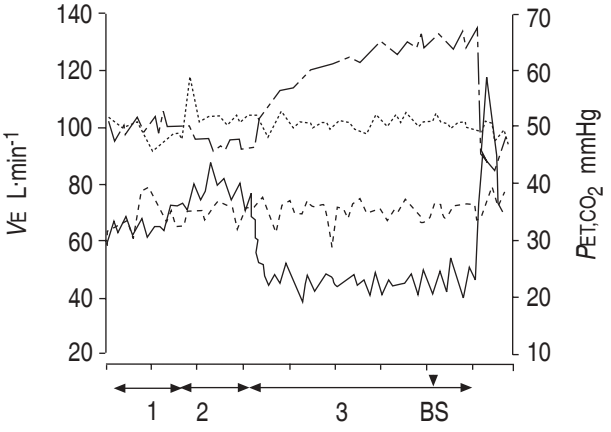

Fig. 1. – Ventilatory output ($V'E$) and end-tidal pressure of oxygen (P_{ET,CO_2}) during voluntary hypoventilation (VHV) and spontaneous breathing (SB) tests in one subject. 1: last 3 min of warm-up; 2: familiarization with the breathing circuit; 3: 10 min exercise with either VHV or SB; BS: blood sampling. - - -: VE during SB; —: VE during VHV; ·····: P_{ET,CO_2} during SB; – · –: P_{ET,CO_2} during VHV.

were connected to the breathing circuit for 13 min. For the SB test, they were given no instructions about breathing, whereas for the VHV test they were asked to hypoventilate after breathing spontaneously through the system for 3 min. Blood samples were drawn during the last minute of the SB and VHV periods. Each test was followed by a 2-min active postexercise period.

The following were required for study inclusion: 1) >15% difference in V'_E between VHV and SB; 2) >10% difference in V_T between VHV and SB; 3) similar pedalling frequency and RR values during VHV and SB; 4) >4-point difference in pH between VHV and SB; 5) normoxia during VHV as well as during SB. F_{I,O_2} was maintained close to 23% during VHV and at 21.5% during SB, in order to avoid hypoxia and possible hypoxia-induced metabolic acidosis.

To determine blood gases a radial artery blood sample was obtained from nine subjects during the last minute of exercise, under local anaesthesia (Emla 5%; Astra, France). In the five other subjects, arterialized blood was taken from the earlobe previously warmed by application of ointment (Finalgon; Boehringer, Germany).

Measurement of the twitch mouth pressure response

Cervical magnetic stimulation. Five acceptable stimulations were used for each set of pressure measurement. Mouth pressure was measured using a differential pressure transducer (Validyne ±150 cmH_2O; Northridge, UK). The signal was acquired at 20,000 Hz for 260 ms after stimulation (MP100 Manager V3.2.6; Biopac systems Inc., Santa Barbara, CA, USA).

The subjects were seated comfortably in a quiet room and were asked to relax and to breathe freely. Throughout the stimulation session, they wore a nose clip and were connected to a mouthpiece with a small leak to prevent glottis closure. Airflow was measured using a pneumotachograph (Labmanager V4.34a; Masterscreen IOS; E. Jaeger GmbH, Höchberg, Germany). Lung volumes were continuously monitored and plotted on a screen. An automatic nonresistant flow interrupter (type 6519; Bürkert, Germany) was placed between the pneumotachograph and the mouthpiece. This occlusion device (response time 50 ms) was activated manually. The stimulation was triggered by the occlusion device at the functional residual capacity (FRC) by means of electronic synchronization. CMS was achieved using a Magstim 200 stimulator with a circular 90-mm coil (maximum output 2 Teslas, pulse duration 0.05 ms; Magstim, Whiteland, Dyfed, UK). The optimal position between fifth and seventh cervical vertebra for the coil was determined based on the pressure response at 60% of the maximum power output [14]. Stimulation was considered supramaximal when the tw,P_{mo} response reached a plateau and the electromyogram amplitude failed to increase further as the stimulation power increased [15]. Otherwise, power was set at 100%.

Electromyograms

Surface recordings of the electromyograms (EMGs) of the right and left costal diaphragm were obtained using two pairs of disposable silver-cup electrodes. The electrodes were taped to the skin along the anterior axillary line in the seventh right and left intercostal spaces. Acquisition of the diaphragmatic EMG signals was performed as for tw,P_{mo}. The amplitude of the motor evoked potential (M-wave) was the parameter used in statistical analyses.

Additional studies

Study 1: in an additional set of experiments tw,P_{mo} and tw,P_{di} in response to CMS were recorded in four subjects before and 10 min after cycling at 85% V'_{O_2max} for 15 min. The purpose of this study was to assess the amplitude of the fall in tw,P_{mo} following exercise, confirmed as fatiguing by tw,P_{di} variations. Recordings of tw,P_{di} were obtained by pressure transducers mounted on a gastro-oesophageal catheter (CTO-2; Gaeltec Ltd, Scotland, UK).

Study 2: it was determined whether differences in ventilatory output could lead to different degrees of potentiation. The tw,P_{mo} obtained before, and 10 and 30 min after two exercises soliciting spontaneously ventilation to levels similar to SB and VHV were compared. Three subjects underwent both the exercise sessions following the same timing as the experimental sessions, *i.e.* warm up, habituation to the load, and 13 min of exercise while breathing into the circuit either at 60%, or at 45% of MAP.

Analysis

The three median values of each set of five valid stimulations were used and averaged. Any aberrant values were excluded from the analysis. Measurements were considered invalid (and therefore were excluded) if any of the following occurred: 1) stimulation was not initiated at the FRC as determined based on the V_T plot or presence of an early decrease in mouth pressure or presence of a slight positive shift in mouth pressure before the decrease; 2) closure of the glottis was suspected based on abnormal pressure trace or a very low pressure value; 3) M-wave amplitude on the diaphragmatic EMG was not similar to the previous ones.

Data for tw,P_{mo} are reported as the means of the three median values±SD and p-values <0.05 were considered statistically significant.

The pressure, EMG amplitude, and ventilatory parameters changes over time and the effect of the exercise condition (VHV *versus* SB) were assessed using two-way analysis of variance (ANOVA) for repeated measures. *Post-hoc* comparisons were made with the Newman-Keuls test.

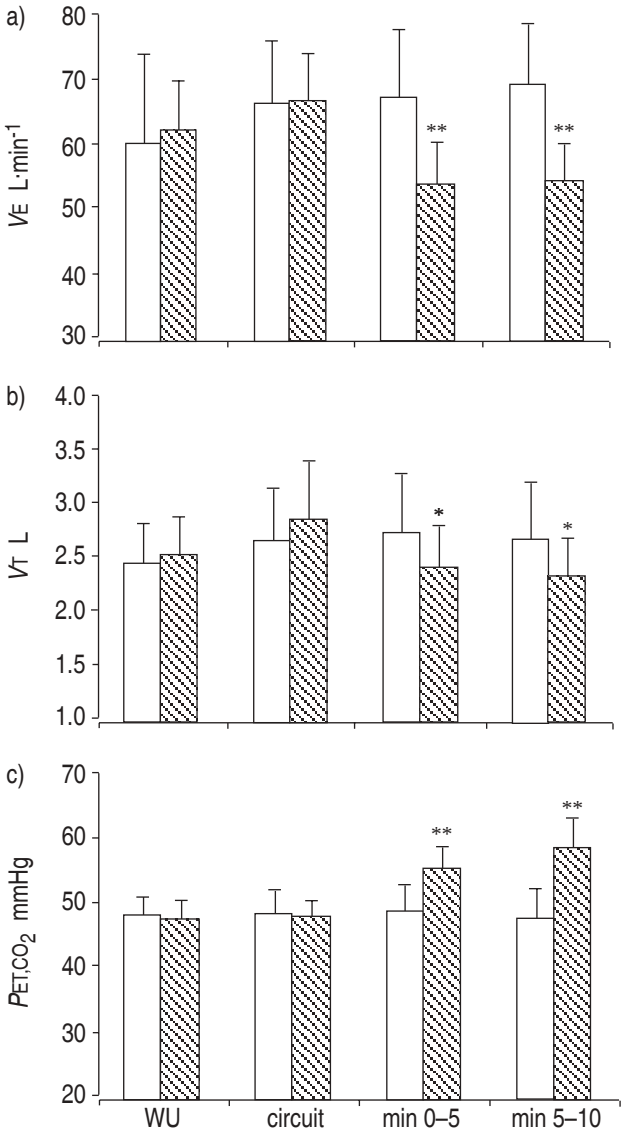

Fig. 2. – a) Ventilatory output ($\dot{V}_E$), b) tidal volume (V_T) and c) end-tidal pressure of oxygen (P_{ET,CO_2}) during the last 3 min of warm-up (WU), 3 min of familiarization with the breathing circuit (circuit), min 0–5 and 5–10 of spontaneous breathing (SB) (□) or voluntary hypoventilation (VHV) (▨) during the exercise tests. Data are presented as mean±SD. *: $p<0.05$ between VHV and SB; **: $p<0.01$ difference between VHV and SB.

Results

Subjects exercised at 200±31 W. During exercise, oxygen uptake was 75.7±6.5 and 75.5±7.7% $\dot{V}'_{O_2max}$ during VHV and SB, respectively.

Breathing control and blood gases

Two subjects were unable to hypoventilate by decreasing their V_T. This left twelve subjects for analysis. During the VHV test in these twelve subjects, mean V_T was 2.3±0.3 L and mean $\dot{V}_E$ 53.8±5.6 L·min^{-1}, as compared to 2.7±0.5 L and 67.9±9.9 L·min^{-1} during the SB test (fig. 2).

Table 2. – Individual values of carbon dioxide tension in arterial blood (P_{a,CO_2}) and pH from arterial blood end-tidal pressure of oxygen sampled during the last 2 min of exercise with spontaneous breathing (SB) and voluntary hypoventilation (VHV)

Subject no.	P_{a,CO_2} mmHg		PH	
	VHV	SB	VHV	SB
1#	48		7.28	
2	56	42	7.25	7.35
3#		40		7.34
4#	53	37	7.26	7.32
5#	53	36	7.25	7.33
6		41	7.33	7.39
7	52	44	7.32	7.36
8	47	42	7.28	7.32
9#	50	42	7.27	7.31
10#	53	45	7.29	7.35
11#	50	43	7.26	7.33
12#	52	39	7.26	7.40
Mean±SD	51±3	41±3	7.28	7.34

#: from arterialized blood.

Pronounced hypercapnia was seen following VHV as compared to SB (P_{a,CO_2} 51.3 and 41.3 mmHg, respectively; P_{ET,CO_2} 56.1 and 47.7 mmHg, respectively) and was associated with a decrease in pH (7.28 during VHV and 7.34 during SB, table 2).

Diaphragmatic response to magnetic stimulation after exercise

Because the total EMG activity differed between the left and right hemidiaphragms, the signals for each were interpreted separately. For both the left and right hemidiaphragms, signal amplitude was similar at all measurement time points, indicating similar supramaximal stimulation intensity (fig. 3).

Ten minutes after the end of exercise, the VHV-SB difference in tw,P_{mo} was 2.0 cmH_2O. In contrast, this difference was nonexistent at rest, and nonsignificant (p=0.09) 30 min after the end of exercise (fig. 4).

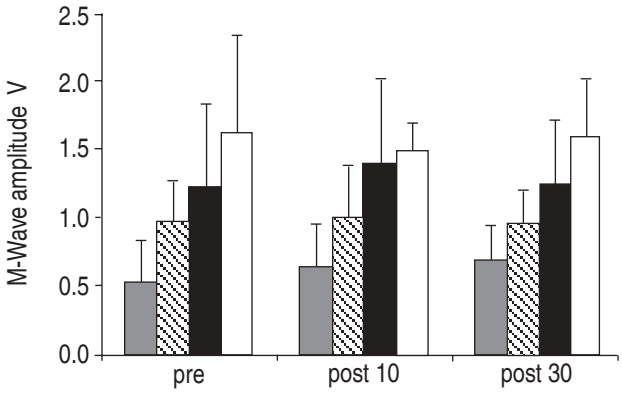

Fig. 3. – Diaphragmatic electromyogram amplitude for the right or left hemidiaphragm before and 10 min and 30 min after the end of exercise with spontaneous breathing (SB) or voluntary hypoventilation (VHV). Data are presented as mean±SD. ■: right SB; ▨: left SB; ■: right VHV; □: left VHV.

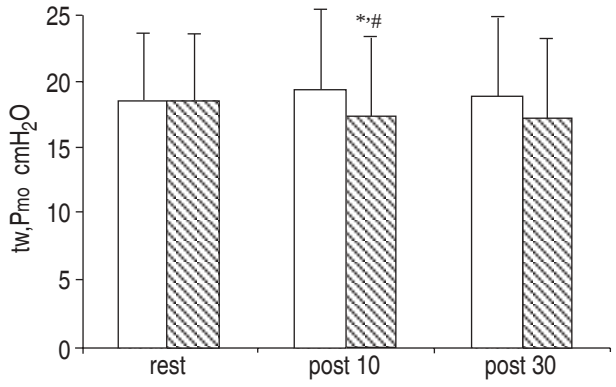

Fig. 4. – Twitch mouth pressure response (tw,P_{mo}) measured at rest, 10 and 30 min after the end of spontaneous breathing (SB) (□) or voluntary hypoventilation (VHV) (▨) exercise test. *: $p<0.05$ between VHV and SB; #: $p<0.05$ compared to baseline.

During VHV, mean tw,P_{mo} decreased significantly from 18.5 before VHV to 17.1 cmH_2O 10 min after the end of VHV, while no changes were seen in tw,P_{mo} during SB.

Additional studies

Study 1: Mean cycling time was 16 min. The subjects reached 88% $V'_{O_2}max$ during the last 5 min of exercise. Therefore, the conditions previously described [16] to observe exercise-induced diaphragmatic fatigue were fulfilled. At rest, oesophageal and mouth pressures were 21.5±3.5 and 21.8±3.1 cmH_2O, respectively and fell to 18.7±2.6 and 19.5±2.5 cmH_2O 10 min after the end of exercise. The decrease of 17.0% in tw,P_{di} (from 30.4±5.4 to 25.2±3.4 cmH_2O) was due partially to a fall in twitch oesophageal pressure. Mouth pressure reflecting the osophageal component of the pressure generated by the respiratory muscles contraction, the decrease in tw,P_{mo} was only 2.3 cmH_2O (10.5%). Averaged individual measurements are shown in figure 5.

Study 2: mean ventilation was 73.2 and 51.5 $L \cdot min^{-1}$ during the cycling test performed at 180 and 135 W, respectively. Ten min after the end of the lower exercise, tw,P_{mo} was 19.9±5.0 cmH_2O compared to 19.7±4.3 cmH_2O at baseline. For the exercise reproducing the ventilation reached during SB, tw,P_{mo} was 17.0±3.5 cmH_2O at baseline and 17.6±5.1 cmH_2O 10 min after the end of exercise. The individual variations in tw,P_{mo} from baseline to 10 min after one or the other exercise were narrow. No common trend could be identified because these variations were not constant in direction, and were probably due to variability of the measurement than to potentiation itself.

Discussion

The main findings of this study were as follows: 1) most subjects (12 of 14) were able to decrease their ventilation voluntarily, on average from 68 to 54 $L \cdot min^{-1}$, thereby producing pronounced hypercapnia (51 mmHg instead of 41 mmHg P_{a,CO_2}) and

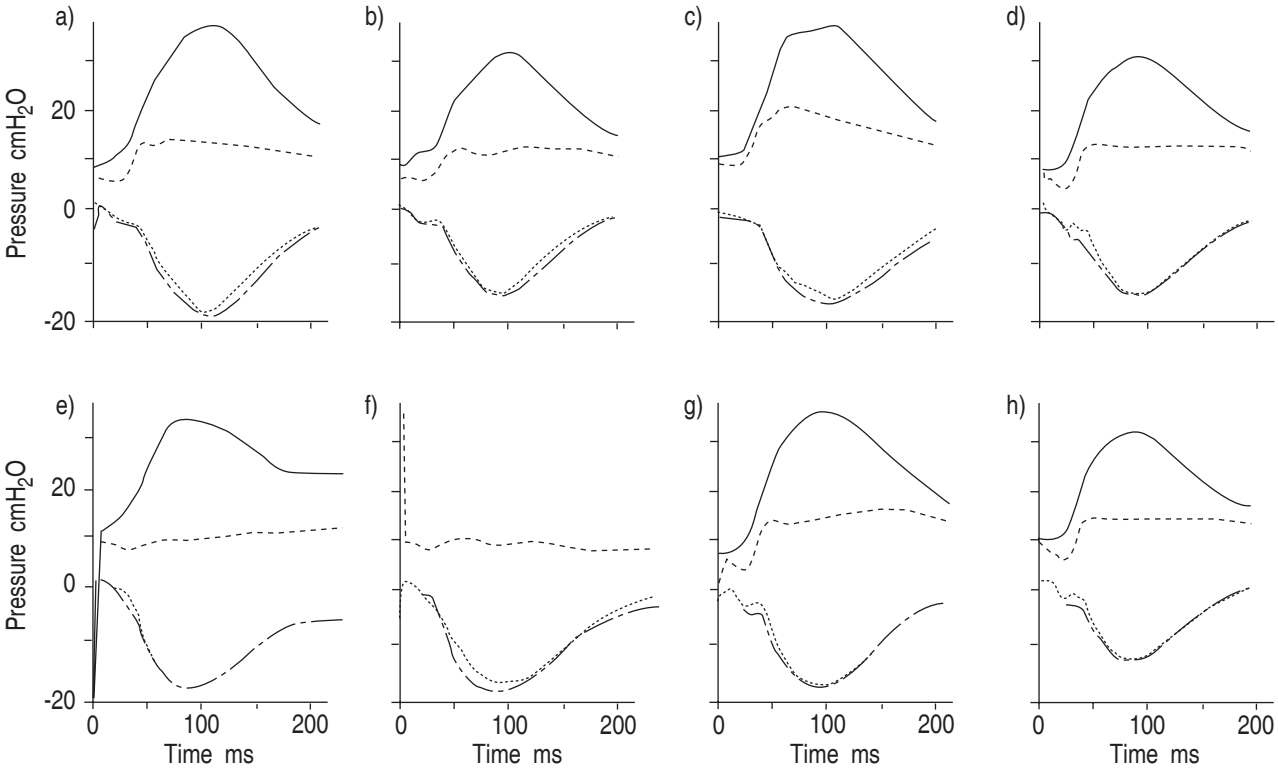

Fig. 5. – Individual mean transdiaphragmatic (P_{di}), gastric (P_{ga}), oesophageal (P_{oes}) and mouth (P_{mo}) pressures recorded a), c), e), g) before and b), d), f), h) 10 min after the end of exercise in four subjects. –: P_{di}; - - -: P_{ga}; – · –: P_{oes}; ·····: P_{mo}.

acidosis; 2) Ten minutes after the end of exercise, an effect of acidosis on diaphragmatic strength was observed, assessed by a significant decrease of tw,P_{mo}.

Ventilatory work

While the respiratory load the subjects had to sustain was different during both exercise sessions, the mechanical ventilatory work was carefully standardized, thus ensuring that the effects of acidosis were isolated from those of other factors contributing to diaphragmatic fatigue. Duty cycle and breathing frequency were similar during the VHV and SB tests. The inspiratory-time over total-time ratio was kept constant during all tests. VHV was achieved primarily by a reduction in V_T. It is likely that this reduction in V_T lightened the work of the respiratory muscles but the pressure-time product was not quantified. However, as the SB exercise was performed at the same intensity as VHV but with a lower F_{I,O_2} and larger V_T, it can be concluded that it was as demanding or even more demanding for the respiratory muscles as VHV. Furthermore, to maintain constant breathing-motor coordination, the pedalling rate was the same during all tests.

Hypercapnia, pH

As expected, based on the pronounced ($p<0.05$) hypercapnia observed during VHV, pH fell during the VHV tests (table 2), thus showing that VHV can effectively induce acidosis without a basic change in mechanical work of ventilation.

Methodological considerations

The main factors that affect tw,P_{mo} are magnitude of stimulation, quality of electrical input transmission, initial length of diaphragmatic fibres, and ability to generate a force in response to a stimulus. To minimize variations in the magnitude of stimulation, great care was taken to ensure optimal positioning of the coil on the neck. SIMILOWSKI *et al.* [15] suggested that the EMG should be used to determine whether CMS is supramaximal. Consequently, the site was marked and the power output of the stimulator where the tw,P_{mo} and M-wave responses were maximal was noted, and then this site and this power was used for subsequent stimulations. Careful attention was given to standardization of the posture of the subjects. Since there is general agreement that transmission fatigue does not occur during exercise in normal humans [16] and given the constancy of the EMG data during each test, it can be assumed that CMS was maximal and constant.

Evaluation of diaphragm strength by measurement of tw,P_{mo} previously provided conflicting results [17–20]. In aggregate, it is suggested that a decrease in tw,P_{mo} indicates inspiratory muscle fatigue. Discrepancies were based on diaphragmatic fibre length (in association with lung volume) at the moment of magnetic stimulation and possible glottis closure, which governs pressure transmission to the mouth. HAMNEGÅRD *et al.* [18] argued that tw,P_{mo} is useful, based on correlation and limits of agreement between mouth and oesophageal pressures. LAGHI and TOBIN [19] reported that the correlation between tw,P_{mo} and tw,P_{di} were relatively weak ($r=0.61$, $p<0.001$) in subjects relaxing at FRC. However, two of their subjects showed a close relationship between tw,P_{mo} and tw,P_{di} under the same conditions of stimulation ($r=0.87$). The results of the first additional study here, supports the use of tw,P_{mo} as an index of fatigue. It was observed that fatiguing exercise caused a decrease in tw,P_{mo} ranging from 2.0–2.5 cmH_2O and a concomitant decrease in tw,P_{di} of 5.2 cmH_2O. The methodological conditions were as follows: 1) all stimulations were performed at the same lung volume (*i.e.* passive FRC) and 2) a small leak was included at the mouthpiece to avoid glottis closure. So it is highly likely that the changes in tw,P_{mo} seen in this study reflect changes in the ability to generate force in response to the stimulus. It is also acknowledged that the magnitude of the fall in tw,P_{mo} is unlikely to exceed 2 cmH_2O within the type of exercise model used in this study. It is further acknowledged that functional consequences of a fall in tw,P_{mo} of this magnitude (~10%) remain uncertain.

Changes in the tw,P_{mo} response to electrical stimulation (ES) of the phrenic nerves reflect changes in diaphragmatic contraction alone. This is not the case with CMS [21]. The magnetic field stimulates not only the phrenic nerves (not their roots [22]), but also the brachial plexus and the intercostal nerves, whose activation has non-negligible effects on oesophageal pressure. LAGHI *et al.* [23] reported that contraction of the accessory inspiratory muscles may account for the larger transdiaphragmatic pressure change following CMS as compared to ES, but found that the transdiaphragmatic pressure variation in response to CMS was nevertheless as accurate as ES for detecting diaphragmatic fatigue. A limitation of this study is the absence of gastric and oesophageal pressure measurements. These pressures are difficult to obtain under the exercise conditions used in the study. Consequently, it can not be confirmed that any tw,P_{mo} change was only due to diaphragmatic fatigue, *i.e.* would have been uninfluenced by fatigue of accessory inspiratory muscles.

MADOR *et al.* [24] demonstrated that potentiation takes place after maximal and submaximal voluntary contractions of the diaphragm. This phenomenon fades during recovery, but may mask fatigue for some minutes. Whatever the amplitude of the voluntary contractions, tw,P_{di} had recovered to control value in 8 min. This recovery occurred in 2 min for the lowest level of contraction. WRAGG *et al.* [25] demonstrated that for sustained diaphragm contractions the intensity is the major determinant of the degree of potentiation rather than duration. They considered that 20 min of rest before any measurement guarantees the absence of potentiation. Given the timing of the measurement and the amplitude of expiratory flow in SB as well as in VHV, tw,P_{mo} must have been only minimally affected by potentiation. Nevertheless, the

authors agree that 10 min after exercise, both potentiation and fatigue process were still likely to coexist.

Effect of exercise and of acidosis on twitch mouth pressure response

The level of exercise used in this study was well under 85% $V'O_2max$, which is considered as a threshold that can induce diaphragmatic fatigue [26, 27]. Accordingly, the level of exercise used in this study had no effect on tw,P_{mo} when the subjects breathed normally. From the results of the additional studies and from the few rare data about exercise and potentiation, it is hardly arguable that these measurements are affected differently by potentiation. Hence, the 2.0 cmH_2O difference in tw,P_{mo} between VHV and SB observed 10 min after exercise represents the effect of acidosis. It is congruous with the $\geqslant 20\%$ decrease in tw,P_{di} reported after exercise that leads to exhaustion [26], and hence gathers all the factors that contribute to muscle fatigue. Moreover, the first additional study shows that the expected variations in tw,P_{mo} should not be wide. The decrease in strength, observed in nonpathological subjects, without and with acidosis strongly suggests that acidosis is of physiological relevance.

To conclude, it was investigated whether exercise-induced acidosis affects diaphragmatic contractility by measuring the mouth pressure response to cervical magnetic stimulation. Voluntary hypoventilation during exercise induced a significant pH decrease, thus proving effective as a means of inducing acidosis without significantly changing mechanical ventilatory work. A significant decrease in mean twitch mouth pressure response was seen after exercise with voluntary hypoventilation, while exercise with normal breathing had no effect on twitch mouth pressure response. This result may help to understand how ventilatory failure occurs in patients with chronic obstructive lung disease. Recently, inspiratory pressure support has been shown to prolong exercise-induced lactataemia in patients with severe chronic obstructive lung disease [28]. This study similarly suggests that exposure to hypercapnia may contribute to impaired respiratory muscle function.

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