

# Expiratory muscle fatigue impairs exercise performance

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Accepted: 4 May 2007 / Published online: 2 June 2007  
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**Abstract** High-intensity, exhaustive exercise may lead to inspiratory as well as expiratory muscle fatigue (EMF). Induction of inspiratory muscle fatigue (IMF) before exercise has been shown to impair subsequent exercise performance. The purpose of the present study was to determine whether induction of EMF also affects subsequent exercise performance. Twelve healthy young men performed five 12-min running tests on a 400-m track on separate days: a preliminary trial, two trials after induction of EMF, and two trials without prior muscle fatigue. Tests with and without prior EMF were performed in an alternate order, randomly starting with either type. EMF was defined as a  $\geq 20\%$  drop in maximal expiratory mouth pressure achieved during expiratory resistive breathing against 50% maximal expiratory mouth pressure. The average distance covered in 12 min was significantly smaller during exercise with prior EMF compared to control exercise ( $2872 \pm 256$  vs.  $2957 \pm 325$  m;  $P = 0.002$ ). Running speed was consistently lower ( $0.13 \text{ m s}^{-1}$ ) throughout the entire 12 min of exercise with prior EMF. A significant correlation was observed between the level of EMF (decrement in maximal expiratory mouth pressure after resistive breathing) and the reduction in running distance ( $r^2 = 0.528$ ,  $P = 0.007$ ). Perceived respiratory exertion was higher during the first 800 m and heart rate was lower throughout the entire test of running

with prior EMF compared to control exercise ( $5.3 \pm 1.6$  vs.  $4.5 \pm 1.7$  points,  $P = 0.002$ ;  $173 \pm 10$  vs.  $178 \pm 7$  beats  $\text{min}^{-1}$ ,  $P = 0.005$ ). We conclude that EMF impairs exercise performance as previously reported for IMF.

**Keywords** Respiratory muscle · Resistive breathing · Running · Endurance

## Introduction

At rest, the work of breathing is essentially performed by the inspiratory muscles while the expiratory muscles remain largely passive. Hyperpnoea, however, also requires active expiration in addition to increased inspiratory muscle activity (Abraham et al. 2002; Henke et al. 1988; Strohl et al. 1981). Active expiration not only contributes to a higher breathing frequency by increasing expiratory flow rates, but also facilitates inspiration by decreasing the end-expiratory lung volume. On the one hand, a smaller end-expiratory lung volume (below functional residual volume) increases the proportion of “passive” inspiration due to elastic recoil of the chest wall. On the other hand, it extends the diaphragm, thereby optimizing its ability to generate inspiratory flow (Henke et al. 1988; Martin and De Troyer 1982; Verges et al. 2006a).

In the course of exhaustive high-intensity exercise ( $\geq 85\%$  of maximal oxygen consumption), inspiratory muscles are known to fatigue (Johnson et al. 1993; Mador et al. 1993; Perret et al. 1999, 2000) but also, expiratory muscle fatigue (EMF) was recently shown to develop under similar conditions (Taylor et al. 2006; Verges et al. 2006b). Expiratory muscles may be even more prone to fatigue than inspiratory muscles as several studies have shown that expiratory muscles are in general less oxidative than

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inspiratory muscles (Lieberman et al. 1973; Uribe et al. 1992) and are therefore expected to be less fatigue resistant.

Respiratory muscle fatigue, in turn, may affect exercise performance. Mador and Acevedo (1991), for example, showed that cycling time to exhaustion at high intensities was significantly reduced when subjects exercised with their inspiratory muscles already fatigued prior to the start of exercise. Increased sensation of respiratory effort (Gandevia et al. 1981) as well as increased leg muscle sympathetic nerve activity (St Croix et al. 2000) and reduced leg blood flow (Sheel et al. 2001) are associated with inspiratory muscle fatigue (IMF). All of these factors may contribute to this decrease in exercise performance. Because expiratory muscles have been shown to critically contribute to the perception of respiratory exertion (Kayser et al. 1997) and because EMF has been shown to increase muscle sympathetic nerve activity (Derchak et al. 2002) similar to IMF, we hypothesized that EMF, like IMF, affects exercise performance.

To test this hypothesis, we measured the maximal distance covered in a 12-min running test with and without prior induction of EMF. A shorter running distance after induction of fatigue would support the hypothesis of an adverse effect of EMF on exercise performance.

## Materials and methods

### Subjects

Twelve healthy, non-smoking male subjects gave their written informed consent to participate in the study. The mean age was  $25.7 \pm 2.9$  years, the mean height was  $178.9 \pm 6.8$  cm, and the mean weight was  $73.6 \pm 5.8$  kg. The subjects were physically active (mean exercise activity:  $3.8 \pm 2.8$  h/week) and free from any diagnosed acute or chronic disease. Subjects were allowed to only perform light physical exercise on the second day prior to the test day and they were not allowed to perform any physical exercise on the day before the test day as well as on the test day prior to the test. Also subjects were not allowed to eat or drink any caffeinated products on the day of the test prior to the test. They had to keep their training activity constant during the 2 weeks before testing as well as during the testing period itself, and they received a high-carbohydrate meal at least 2 h prior to each test in order to load their carbohydrate stores. The study was approved by the local ethics committee and performed according to the Declaration of Helsinki.

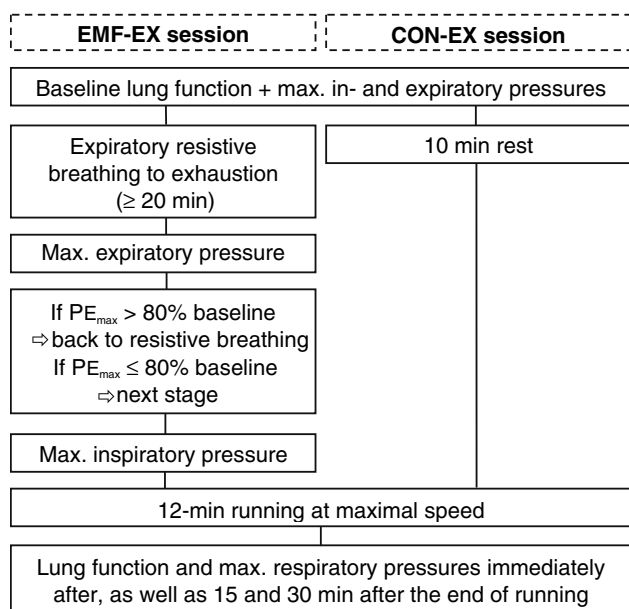
### Pulmonary function and maximal pressure measurements

Pulmonary function (American Thoracic Society 1995) and maximal pressure (American Thoracic Society/European

Respiratory Society 2002) measurements were performed according to standard procedures. Forced vital capacity (FVC) and forced expiratory volume in 1 s ( $FEV_1$ ) were measured with a portable turbine spirometer (Micro Medical Spirometer, Micro Medical, Rochester, UK). The highest value of three measurements varying by less than 0.2 l was recorded. Maximal inspiratory pressure ( $PI_{max}$ ) and maximal expiratory pressure ( $PE_{max}$ ) were measured at residual volume and total lung capacity, respectively, using a portable device (MicroMPM; Micro Medical, Rochester, UK) with a built-in small air leak to prevent glottis closure. Subjects pressed their cheeks with their hands during  $PE_{max}$  measurements to avoid air leakage. Pressure measurements were repeated at least ten times until the three highest values sustained for  $\geq 1$  s varied by  $<5\%$ . The reported  $PI_{max}$  and  $PE_{max}$  represent the mean of the three highest values.

### Resistive breathing

During resistive breathing, subjects inspired freely through the nose and expired through a mouthpiece (nose occluded by hand) connected to a resistance consisting of a closed perspex tube with three holes of 0.5–1 mm diameter. Subjects had to expire through this device achieving a target pressure corresponding to at least 50% of their individual  $PE_{max}$  similar to previous studies (Derchak et al. 2002; Haverkamp et al. 2001; Suzuki et al. 1992). The target expiratory pressure was displayed to the subjects on a mercury column and had to be maintained as a square wave. The expiratory duty cycle was 0.8 and the breathing frequency was set to 12 breaths  $min^{-1}$ , corresponding to a spontaneous breathing pattern during expiratory resistive breathing (Suzuki et al. 1991). Subjects used a “mask” developed in our laboratory to prevent leaks at the mouthpiece and puffing up of the cheeks during forced expiration. This “mask” consisted of a large latex band covering both cheeks, being tightly fixed around the head and containing an opening for the mouthpiece. When the subjects were unable to overcome the expiratory resistance for two successive expirations despite encouragement by the experimenters or after a maximum of 20 min,  $PE_{max}$  was assessed again (Fig. 1). If the reduction of  $PE_{max}$  was still less than 20%, the subjects were asked to continue breathing against the expiratory resistance, and  $PE_{max}$  was assessed again after exhaustion or after another 20 min. When either a  $\geq 20\%$  decrease in  $PE_{max}$  was observed or a maximum time of 90 min had elapsed,  $PI_{max}$  was also measured again. A 20% threshold was chosen in order to induce a degree of fatigue similar to that in Mador and Acevedo’s study (1991). During resistive breathing, the subjects were asked to rate their perception of air hunger (the sensation of an uncomfortable urge to breathe) on a 10-point scale by holding up 0–10 fingers when asked to do so every minute



**Fig. 1** Flow chart of experimental sessions with (EMF-EX) and without (CON-EX) induction of expiratory muscle fatigue prior to the 12-min run

(0 corresponded to “no air hunger at all” and 10 corresponded to “maximal air hunger”, i.e. meaning the subject would need to stop the test latest within the coming 30 s due to this sensation). Before the test, we extensively discussed the difference between the sensations of air hunger and respiratory exertion (how hard it is to breathe). This ensured that subjects could distinguish between air hunger and respiratory exertion (Lansing et al. 2000). If subjects started to experience air hunger during resistive breathing, they were allowed to take a few deep breaths and expire without resistance (through the nose) in order to avoid hypercapnia.

#### Exercise test

The exercise test was performed outdoor on a 400 m track. Subjects had to run for 12 min with the aim to cover the greatest possible distance. At the end of each 400-m lap, respiratory exertion was assessed, i.e. the experimenter shouted to the subject “Respiratory exertion?” and the subject shouted out a number between 0 and 10 (0 means no respiratory exertion at all and 10 means maximal respiratory exertion, i.e. the subject would have to slow down immediately to avoid having to stop exercise due to this sensation; these meanings were explained prior to each test). Immediately upon the elapse of the 12-min period, as well as 15 and 30 min later, FVC, FEV<sub>1</sub>, PI<sub>max</sub> and PE<sub>max</sub> were measured as described above. Heart rate (HR) was recorded every 5 s throughout the entire running test (PE 4000, Polar Electro, Kempele, Finland).

#### Experimental protocol

The experiment involved six test sessions on separate days with at least 72 h between test days. Each subject performed all his tests at the same time of day. The first two sessions were used to familiarize the subjects with all test procedures. During the first session, subjects were trained in proper spirometric and maximal pressure measurement techniques and performed a 12-min running test. During the second session, the subjects were familiarized with expiratory resistive breathing. The next four sessions (Fig. 1) consisted of four 12-min running tests, two with EMF (EMF-EX) and two without (CON-EX). EMF-EX sessions included baseline lung function, maximal inspiratory and expiratory pressure measurements and expiratory resistive breathing, followed by 200 m of slow running (warm-up) to reach the start of the 400 m track where the 12-min running test started immediately. CON-EX sessions consisted of baseline lung function, maximal inspiratory and expiratory pressure measurements, a 10-min resting period, followed by 200 m of slow running (warm-up) to reach the start of the 400 m track where the 12-min running test started immediately. The two EMF-EX and two CON-EX were performed in an alternate order, randomized such that six subjects performed EMF-EX first and six performed CON-EX first. While the first 12-min test was performed as a group, the subsequent four tests were carried out individually. Weather conditions [temperature, sun/rain (rated 0, 1, 2) and wind (rated 0, 1, 2)] did not differ significantly between EMF-EX (temperature  $17 \pm 6^\circ\text{C}$ ; sun/rain  $0.8 \pm 0.7$ ; wind  $0.7 \pm 0.9$ ) and CON-EX (temperature  $17.7 \pm 7^\circ\text{C}$ ; sun/rain  $0.7 \pm 0.8$ ; wind  $0.8 \pm 0.8$ ).

#### Statistical analysis

First, each subject’s two EMF-EX and CON-EX, respectively, were compared using Wilcoxon’s signed rank test. As there was no significant difference, the results of the same test modality were averaged for each subject. Next, EMF-EX and CON-EX results were compared with the Friedman test in order to assess differences in running distance, speed, HR and respiratory exertion between tests as well as spirometric and pressure changes within one test. If  $P$  was  $<0.05$ , Wilcoxon’s signed rank test was used to identify the differences. Pearson’s product-moment correlation was used to assess correlations of changes in distance, HR and respiratory exertion between EMF-EX and CON-EX. Fisher’s  $R$ -to- $Z$  test was used to determine the statistical significance of the correlation. All statistical calculations were performed on standard statistics software (Statview 5.0, SAS Institute, Cary, NC, USA). The coefficient of variation was calculated as the standard deviation (SD) relative to the mean multiplied by 100. All data are presented as

means  $\pm$  SD, and  $P < 0.05$  was considered as statistically significant.

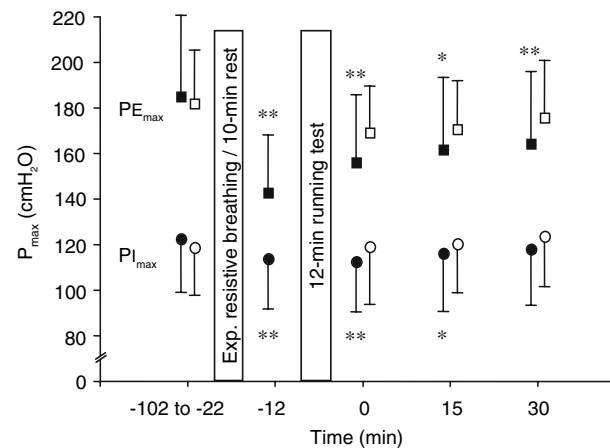
## Results

The pulmonary function values are shown in Table 1.  $PI_{\max}$  and  $PE_{\max}$  were  $122.7 \pm 23.6$  cm H<sub>2</sub>O ( $116 \pm 3\%$  predicted) and  $185.0 \pm 35.7$  cm H<sub>2</sub>O ( $157 \pm 3\%$  predicted), respectively. The average duration of expiratory resistive breathing was  $38 \pm 25$  min (range 10–90 min). All but one subject showed a  $\geq 20\%$  decrease in  $PE_{\max}$  at the end of resistive breathing. One subject showed only an 11% decrease in  $PE_{\max}$  after 90 min of expiratory resistive breathing before his first EMF-EX.

$PI_{\max}$  and  $PE_{\max}$  were significantly reduced compared to baseline before, immediately after, and 15 min after EMF-EX (Fig. 2). Thirty minutes after EMF-EX,  $PE_{\max}$  but not  $PI_{\max}$  was significantly decreased compared to baseline. The mean change in  $PI_{\max}$  was significantly smaller than the change in  $PE_{\max}$  at the end of expiratory resistive breathing [ $\Delta PI_{\max} = -7.0 \pm 8.4\%$  ( $-8.7 \pm 22.0$  cmH<sub>2</sub>O) and  $\Delta PE_{\max} = -22.6 \pm 4.2\%$  ( $-42.2 \pm 13.0$  cmH<sub>2</sub>O);  $P = 0.002$ ]. No significant changes in  $PI_{\max}$  and  $PE_{\max}$  were observed after CON-EX (Fig. 2).

FVC and  $FEV_1$  were significantly reduced compared to baseline immediately after and 15 min after both EMF-EX and CON-EX, while after 30 min of recovery the differences had disappeared (Table 1).  $FEV_1/FVC$  was not significantly modified after either EMF-EX or CON-EX (Table 1). Changes in pressures did not correlate with changes in spirometric variables (results not shown, all  $P > 0.05$ ).

Mean distances covered during the two EMF-EX and the two CON-EX tests are shown in Fig. 3. Individual examination of the running distances showed that 12 out of 12 subjects achieved a shorter distance in the first EMF-EX compared to the average of the two CON-EX, and 10 out of 12 subjects did so in the second EMF-EX. The average distance covered in 12 min was significantly smaller during EMF-EX than during CON-EX ( $2872 \pm 256$  vs.



**Fig. 2** Mean (SD) of individual subjects' average maximal inspiratory ( $PI_{\max}$ , circles) and expiratory ( $PE_{\max}$ , squares) pressures during EMF-EX sessions (closed symbols) and CON-EX sessions (open symbols) ( $n = 12$ ). Measurements were taken at baseline (102–22 min before the start of the 12-min run), after expiratory resistive breathing (–12 min, EMF-EX only) and during recovery (0, 15 and 30 min). Significant difference compared to baseline: \* $P < 0.05$ , \*\* $P < 0.01$  (for abbreviations see Fig. 1)

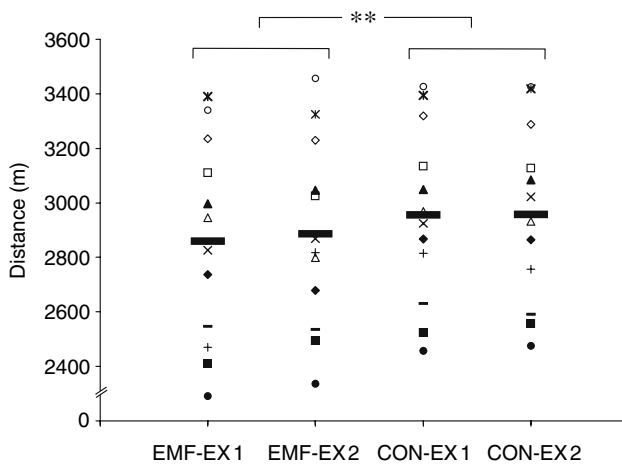
$2957 \pm 325$  m;  $P = 0.002$ ). The average reduction in distance was  $-85.1 \pm 45.3$  m (range  $-17$  to  $-153$  m), i.e.  $-3.0 \pm 1.8\%$ . Running speed was equally reduced in all 400-m laps of EMF-EX compared to CON-EX (mean decrease  $0.13$  m s<sup>-1</sup>). Changes in distance between EMF-EX and CON-EX correlated significantly with changes in  $PE_{\max}$  ( $r^2 = 0.528$ ,  $P = 0.007$ ) (Fig. 4) but they did not correlate with the duration of resistive breathing ( $r^2 = 0.025$ ,  $P = 0.625$ ) nor with subjects' weekly amount of training ( $r^2 = 0.051$ ,  $P = 0.482$ ). Coefficients of variation (CV) for the distances covered during the two EMF-EX and the two CON-EX tests were 2.26 and 0.96%, respectively. No sequence effect was observed with respect to running performance: The average running distances during the four successive 12-min tests taken in chronological order (i.e. six subjects performing EMF-EX and six subjects performing CON-EX at each time) were not significantly different from each other ( $2,902 \pm 345$  vs.  $2,912 \pm 362$  vs.  $2,945 \pm 318$  vs.  $2,899 \pm 361$  m;  $P = 0.473$ ).

**Table 1** Lung function before and after exercise with (EMF-EX) and without (CON-EX) induction of expiratory muscle fatigue prior to the 12-min run (means and SD,  $n = 12$ )

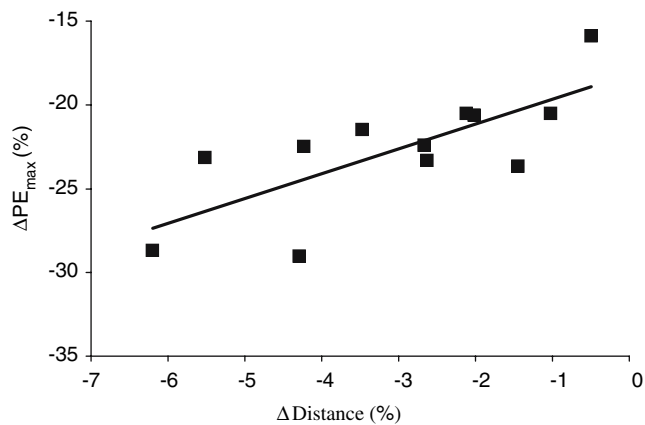
|                                | Baseline    |             | $t_0$        |              | $t_{15}$     |              | $t_{30}$    |             |
|--------------------------------|-------------|-------------|--------------|--------------|--------------|--------------|-------------|-------------|
|                                | EMF-EX      | CON-EX      | EMF-EX       | CON-EX       | EMF-EX       | CON-EX       | EMF-EX      | CON-EX      |
| FVC (l)                        | 5.51 (0.79) | 5.50 (0.78) | 5.10* (0.94) | 5.20* (0.94) | 5.39* (0.91) | 5.31* (0.88) | 5.42 (0.89) | 5.41 (0.91) |
| $FEV_1$ (l min <sup>-1</sup> ) | 4.41 (0.71) | 4.33 (0.75) | 4.01* (0.79) | 4.08* (0.71) | 4.26* (0.77) | 4.18* (0.76) | 4.30 (0.77) | 4.23 (0.76) |
| $FEV_1/FVC$ (%)                | 79.9 (5.5)  | 78.5 (6.2)  | 78.9 (9.0)   | 79.0 (8.1)   | 79.2 (6.0)   | 78.7 (6.5)   | 79.3 (7.0)  | 78.2 (6.8)  |

FVC forced vital capacity,  $FEV_1$  forced expiratory volume in 1 s,  $t_0$  end of exercise,  $t_{15}$  after 15 min of recovery,  $t_{30}$  after 30 min of recovery

\*  $P < 0.05$  significant difference compared to baseline



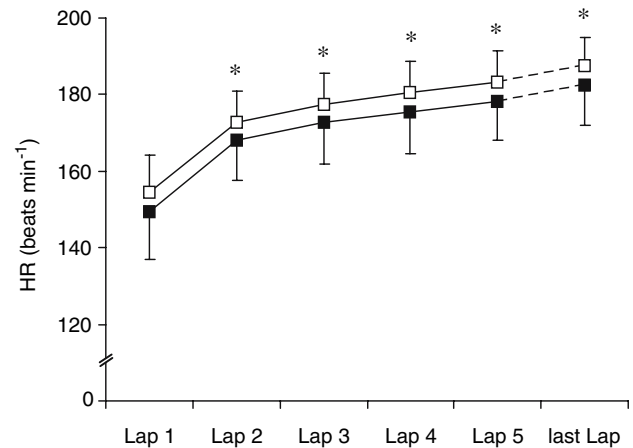
**Fig. 3** Mean (large thick line) and individual running distances during the two EMF-EX and the two CON-EX sessions ( $n = 12$ ). Significant difference between EMF-EX and CON-EX distances:  $**P < 0.01$  (for abbreviations see Fig. 1)



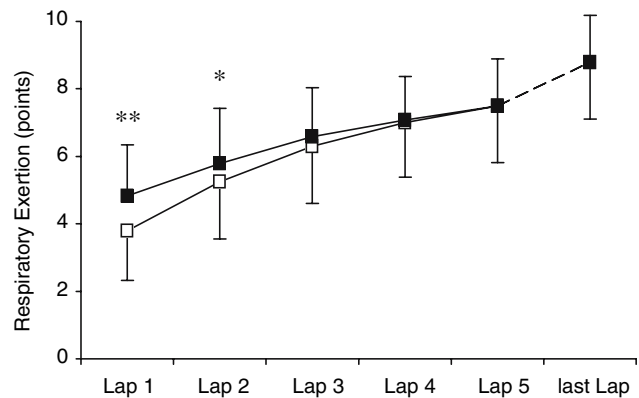
**Fig. 4** Correlation between individual subjects' change in maximal expiratory pressure ( $\Delta PE_{max}$ ) after expiratory resistive breathing (% change from baseline) and the difference in running distance between average EMF-EX and average CON-EX distances (% of CON-EX distance;  $r^2 = 0.528$ ,  $P = 0.007$ ;  $n = 12$ ) (for abbreviations see Fig. 1)

Beginning with the second 400-m lap, HR was significantly lower during EMF-EX compared to CON-EX (Fig. 5). Mean HR was  $173 \pm 10$  beats  $min^{-1}$  during EMF-EX and  $178 \pm 7$  beats  $min^{-1}$  during CON-EX ( $P = 0.005$ ). When HR was expressed as a function of speed (i.e. HR divided by speed on each lap), no significant difference was observed between EMF-EX and CON-EX (all  $P > 0.05$ ). The change in HR between EMF-EX and CON-EX did not correlate significantly with the change in distance ( $r^2 = 0.162$ ,  $P = 0.201$ ) or  $PE_{max}$  ( $r^2 = 0.002$ ,  $P = 0.959$ ).

Perceived respiratory exertion was higher in EMF-EX compared to CON-EX only during the first 800 m (Fig. 6). Similarly, when respiratory exertion was expressed as a



**Fig. 5** Mean (SD) of individual subjects' heart rate (HR) during the first five laps and the last lap of EMF-EX (filled square) and CON-EX (open square) ( $n = 12$ ). Significant difference between average EMF-EX and average CON-EX data:  $*P < 0.05$  (for abbreviations see Fig. 1)



**Fig. 6** Mean (SD) of individual subjects' perceived respiratory exertion (10-point scale) during the first five laps and the last lap of EMF-EX (filled square) and CON-EX (open square) ( $n = 12$ ). Significant difference between EMF-EX and CON-EX:  $*P < 0.05$ ,  $**P < 0.01$  (for abbreviations see Fig. 1)

function of speed (i.e. respiratory exertion divided by speed on each lap), a significant difference between EMF-EX and CON-EX was observed only during the first 800 m ( $P = 0.002$  and  $0.005$  for the first and second laps, respectively). The change in respiratory exertion between EMF-EX and CON-EX did not correlate significantly with the change in distance ( $r^2 = 0.011$ ,  $P = 0.730$ ), HR ( $r^2 = 0.246$ ,  $P = 0.103$ ) or  $PE_{max}$  ( $r^2 = 0.021$ ,  $P = 0.658$ ).

**Discussion**

In the present study, we found that exercise with EMF significantly decreased the maximal running distance covered during a 12-min period. The extent of expiratory muscle

fatigue ( $PE_{\max}$  decrease after expiratory resistive breathing) correlated significantly with the reduction in running distance. Furthermore, subjects running with EMF had a lower HR throughout the running test and perceived greater respiratory exertion during the first 800 m.

#### Methodological aspects

It might be objected that respiratory muscle fatigue was assessed by a volitional test, i.e. measurement of maximal static inspiratory and expiratory mouth pressures, and that the result may therefore have been influenced by subjects' motivation. It is true that this technique is clearly less objective than the gold standard for assessing diaphragmatic fatigue, i.e. phrenic nerve stimulation and measurement of transdiaphragmatic pressure. For expiratory muscles, however, the gold standard is less well established. Moreover, the assessment of mouth pressures is widely used (American Thoracic Society/European Respiratory Society 2002) as this is the only technique to assess global inspiratory and expiratory muscle strength and fatigue. To minimize the influence of motivational factors on our measurements, only highly motivated subjects were recruited and maximal pressure maneuvers were repeated at least ten times until the three highest values varied by less than 5%. We also need to consider that maximal mouth pressure measurements may be influenced by changes in lung volumes, i.e. a change in residual volume may affect  $PI_{\max}$  and a change in total lung capacity may affect  $PE_{\max}$ . However, in previous studies no change in lung volume has been observed after expiratory resistive breathing (Haverkamp et al. 2001; Suzuki et al. 1991). Also, in the present study, FVC was reduced to the same extent after EMF-EX and CON-EX, making it unlikely that differences in  $PI_{\max}$  and  $PE_{\max}$  between EMF-EX and CON-EX resulted from changes in lung volumes.

Another possible objection is that resistive breathing did not elicit EMF at all. However, to induce EMF we applied a similar method as Suzuki et al. (1991). These authors observed a significant decrease in  $PE_{\max}$  persisting for 1 h following expiratory resistive breathing, and abdominal muscle fatigue was confirmed by a decrease of the H/L ratio in the electromyogram recorded from the M. rectus abdominis. These results suggest that this type of expiratory resistive breathing induces low frequency fatigue of abdominal muscles (Suzuki et al. 1991). As in the present study the decrease in  $PE_{\max}$  after expiratory resistive breathing was similar or even larger than that observed by Suzuki et al. (1991), we are confident that also our subjects fatigued their expiratory, likely abdominal, muscles and exercised in the presence of EMF during the two EMF-EX trials. Additionally, knowing that subjects might stop resistive breathing due to hypercapnia-induced perception of air

hunger prior to the development of muscular fatigue, our subjects were permitted to take deep breaths and expire several times without resistance when they felt uncomfortable due to air hunger. This prevented subjects from stopping the task due to air hunger rather than EMF and it reduced the chance of the subsequent exercise being impaired by changes in acid–base homeostasis.

Moreover, it may be argued that subjects' expectation with respect to the effect of resistive breathing on subsequent exercise performance may have influenced running speed during EMF-EX trials. Although we cannot completely rule out that subjects' expectation may explain part of the decreased performance during EMF-EX, we are confident that we assessed a true effect of EMF on exercise performance. Our reasoning is threefold: first, we selected highly motivated subjects only; second, we told subjects we would not know whether EMF would affect exercise performance or not; third, 53% of the variance in running distance were accounted for by changes in  $PE_{\max}$ .

Lastly, one could argue that a 12-min all-out field test, subject to different environmental conditions, would be less well suited to assess performance than a laboratory based test. We aimed, however, to assess performance under conditions approximating actual competition (except that subjects ran alone to avoid that subjects' interaction, being different between tests, would influence performance). We used a 12-min all-out test rather than a fixed-distance (e.g. 3 km) test as our subjects were experienced with this particular test such that very good reproducibility could be expected (CV was 0.96% for the two CON-EX tests). As EMF-EX and CON-EX were performed in an alternating order (half of the subjects starting with EMF-EX, the other half with CON-EX), it is unlikely that the differences in running distance represent a learning or training effect or result from changes in ambient conditions. First, all subjects performed a preliminary trial prior to the four experimental sessions to familiarize with the testing environment; second, considering the running distances of the four successive 12-min tests in chronological order, we did not observe any time-dependent effects; third, the weather conditions were the same on average on the four experimental days.

#### Potential mechanisms for impaired exercise performance with EMF

Recent experiments suggest that fatigue of inspiratory and expiratory muscles may activate a metabolic reflex resulting in increased sympathetic nerve activity (Derchak et al. 2002; St Croix et al. 2000) and thereby compromising blood flow to the legs at rest (Sheel et al. 2001). Even during exercise, when local vasodilation in the working limbs occurs, an additional load on inspiratory muscles

may compromise leg blood flow (Harms et al. 1997). Hence, it may be hypothesized that the induction of EMF in the present study caused limb vasoconstriction by a similar mechanism, leading to compromised muscle perfusion during EMF-EX and thus to reduced performance.

Similar to previous studies (O’Kroy et al. 1992; Perret et al. 1999), intensive exercise per se did not induce a significant change in  $PI_{\max}$  (CON-EX). However,  $PI_{\max}$  was reduced by 7% after expiratory resistive breathing. This reduction of  $PI_{\max}$  may indicate the development of either IMF [potentially due to reduced inspiratory time and subsequently increased inspiratory flow (Suzuki et al. 1991)] and/or central fatigue during expiratory resistive breathing, two factors possibly affecting subsequent exercise performance. If expiratory resistive breathing had induced only central fatigue rather than specific EMF, we would expect both  $PI_{\max}$  and  $PE_{\max}$  to be reduced to a similar extent. However, the mean decrease in  $PE_{\max}$  exceeded the decrease in  $PI_{\max}$  after resistive breathing by a factor of >3. Furthermore, the decrease in  $PE_{\max}$  (but not in  $PI_{\max}$ ) after resistive breathing, but not the duration of resistive breathing per se, correlated significantly with the decrease in running distance. These results strongly suggest that EMF, rather than central fatigue or IMF, was the major determinant of the exercise performance decrease during EMF-EX.

Mador and Acevedo (1991) proposed that an increased perception of respiratory effort might be responsible for the impairment of exercise performance after IMF induction. Expiratory muscles have been shown to play a critical role in the perception of respiratory exertion (Kayser et al. 1997). Therefore, the greater perceived respiratory exertion during EMF-EX suggested that EMF was responsible for an increased level of perceived respiratory exertion during running, which may have contributed to the performance reduction. After the second lap, however, these differences were no longer significant, and changes in respiratory exertion did not correlate with changes in running distance. It follows that other factors than a change in respiratory exertion are likely to account for the change in exercise performance with EMF.

Some studies suggested that intense exercise with one muscle group (e.g. arm cranking) may affect muscle lactate and pH levels during subsequent exercise with another muscle group (e.g. leg exercise) via an increase in blood lactate (up to 10 mmol  $l^{-1}$ ), resulting in reduced performance (Bangsbo et al. 1996; Hogan and Welch 1984; Jacobs et al. 1993). However, recent studies have shown that muscle performance is enhanced rather than impaired by higher lactate concentrations (Nielsen et al. 2001; Pedersen et al. 2004). Moreover, in a previous study we did not observe a significant increase in blood lactate concentration as a result of inspiratory resistive breathing at 70%  $PI_{\max}$  to exhaustion (Rohrbach et al. 2003). Hence, it is unlikely that

the decreased performance during EMF-EX was caused by increased blood lactate concentration resulting from expiratory resistive breathing.

$FEV_1$  and FVC were similarly decreased after EMF-EX and CON-EX. Because  $PE_{\max}$  was significantly altered only after EMF-EX, our findings confirm that exercise affects pulmonary function independently of respiratory muscle fatigue (Coast et al. 1999; Haverkamp et al. 2001). Furthermore, the transient decrease in FVC following intense exercise similar to previous observations (Coast et al. 1998; Maron et al. 1979) was likely the cause of the decreased  $FEV_1$  since  $FEV_1/FVC$  was unchanged. However, since these changes were similar during EMF-EX and CON-EX, it is improbable that they are responsible for the reduced performance with EMF.

Finally, the lower HR during EMF-EX (Fig. 5) is more likely a consequence, rather than a cause, of the reduced speed throughout the entire EMF-EX. Indeed, HR relative to speed did not differ between EMF-EX and CON-EX, and previous studies have shown that induction of IMF did not modify HR during subsequent exercise at a given power output (Mador and Acevedo 1991; Sliwinski et al. 1996).

In conclusion, induction of EMF prior to exercise significantly decreased the distance covered during a 12-min running test. The present study is therefore the first to show that EMF, like IMF (Mador and Acevedo 1991), may impair exercise performance. EMF increased respiratory exertion only during the first 800 m, while HR and speed were lower during the entire course of EMF-EX compared to CON-EX. Since EMF was shown to develop during high-intensity exhaustive exercise both in healthy subjects (Taylor et al. 2006; Verges et al. 2006b) and in patients (Hopkinson et al. 2006), EMF may contribute to exercise limitation in these instances.

**Acknowledgments** We thank the subjects for their time and effort dedicated to this study. Financial support was provided by the Swiss National Science Foundation (grant no. 31-54071.98). Samuel Vergès was supported by the Scientific Council of AGIRàdom, Grenoble, France.

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