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1 **Pulmonary and respiratory muscle function in response to 10 marathons in 10 days**

2

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8 Running Head: Respiratory responses to ultramarathon stage-racing

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16 **ABSTRACT**

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18 **Purpose:** Marathon and ultramarathon provoke respiratory muscle fatigue and pulmonary
19 dysfunction; nevertheless, it is unknown how the respiratory system responds to multiple, consecutive
20 days of endurance exercise. **Methods:** Nine trained individuals (6 male) contested 10 marathons in 10
21 consecutive days. Maximum static inspiratory and expiratory mouth-pressures (MIP and MEP),
22 pulmonary function (spirometry), perceptual ratings of respiratory muscle soreness (Visual Analogue
23 Scale), breathlessness (dyspnea, modified Borg CR10 scale), and symptoms of Upper-Respiratory
24 Tract Infection (URTI), were assessed before and after marathons on day 1, 4, 7 and 10. **Results:**
25 Group mean time for 10 marathons was 276±35 min. Relative to pre-challenge baseline (159±32
26 cmH₂O), MEP was reduced after day 1 (136±31 cmH₂O, $p=0.017$), day 7 (138±42 cmH₂O, $p=0.035$),
27 and day 10 (130±41 cmH₂O, $p=0.008$). There was no change in pre-marathon MEP across days 1, 4, 7,
28 or 10 ($p>0.05$). Pre-marathon forced vital capacity was significantly diminished at day 4 (4.74±1.09
29 vs. 4.56±1.09 L, $p=0.035$), remaining below baseline at day 7 ($p=0.045$) and day 10 ($p=0.015$). There
30 were no changes in FEV₁, FEV₁/FVC, PEF, MIP, or respiratory perceptions during the course of the
31 challenge ($p>0.05$). In the 15-d post-challenge period, 5/9 (56%) runners reported symptoms of URTI,
32 relative to 1/9 (11%) pre-challenge. **Conclusions:** Single-stage marathon provokes acute expiratory
33 muscle fatigue which may have implications for health and/or performance, but ten consecutive days
34 of marathon running does not elicit cumulative (chronic) changes in respiratory function or
35 perceptions of dyspnea. These data allude to the robustness of the healthy respiratory system.

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37 **Key words:** Ultramarathon, endurance, lung function, fatigue.

38 **ABBREVIATIONS**

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40 **FVC** forced vital capacity

41 **FEV₁** forced expiratory volume in 1 second

42 **PIF** peak inspiratory flow

43 **PEF** peak expiratory flow

44 **MVV** maximum voluntary ventilation

45 **MIP** maximum inspiratory mouth-pressure

46 **MEP** maximum expiratory mouth-pressure

47 **URTI** upper-respiratory tract infection

48 **VAS** visual analogue scale

49 **SD** standard deviation

50 **CV** coefficient of variation

51 **SEM** standard error of measurement

52 **CI** confidence interval

53 **ICC** intraclass correlation

54 **ANOVA** analysis of variance

55

56 **INTRODUCTION**

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58 Respiratory muscle fatigue is a phenomenon whereby the inspiratory and/or expiratory musculature
59 exhibit a [transient reduction in force-generating capacity](#), relative to baseline values (Romer and
60 Polkey. 2008). Respiratory muscle fatigue has been assessed objectively following high-intensity,
61 exhaustive cycling and running, manifesting in a 15 - 30% pre-to-post-exercise reduction in
62 transdiaphragmatic or gastric twitch-pressure in response to [nerve stimulation](#) (Johnson et al. 1993;
63 Taylor et al. 2006). [When respiratory muscle fatigue has been assessed indirectly using maximum
64 volitional mouth-pressure manoeuvres](#), similar pre-to-post-exercise reductions were observed
65 following rowing and swimming time-trials (Lomax and McConnell. 2003; Volianitis et al. 2001).
66 [Using a proportional assist ventilator to offload the respiratory muscles during exercise](#), Babcock et al.
67 (2002) found that the workload endured by the diaphragm was a critical determinant of exercise-
68 induced diaphragmatic fatigue. Moreover, using objective nerve stimulation techniques, we recently
69 observed expiratory, but not inspiratory, muscle fatigue following maximal upper-body exercise
70 (Tiller et al. 2017). Given that the exercise trial induced only a modest ventilatory demand, the data
71 support the notion that high minute ventilations are a prerequisite for diaphragm fatigue, where-as the
72 expiratory muscles may be less fatigue-resistant. Respiratory muscle fatigue is thought to be
73 underpinned by peripheral, rather than central, mechanisms (Jones. 1996; Wuthrich et al. 2015), and
74 contractile function typically returns to baseline within 1 - 2 h of exercise.

75 There is a growing body of work pertaining to respiratory muscle function following
76 [endurance and ultra-endurance running](#). Reductions in maximum inspiratory mouth-pressure in the
77 region of ~15% have been observed immediately following single-stage marathon (Chevrolet et al.
78 1993; Ross et al. 2008), although no evidence of expiratory muscle fatigue was reported. [Evidence of
79 post-marathon decreases in respiratory muscle endurance \(~27%\)](#) have been noted, when assessed via
80 [time-to-exhaustion \(Tlim\)](#) during sustained inspiratory pressure (Ker and Schultz. 1996), with similar
81 observations made following 24 h of treadmill running when respiratory muscle endurance was
82 assessed via maximum voluntary ventilation in 12 s (MVV₁₂) (Warren et al. 1989). The only study to
83 use [magnetic nerve-stimulation](#) to assess respiratory muscle fatigue [following ultramarathon \(defined](#)

84 as a race that exceeds the traditional marathon distance of 42.2 km; Millet and Millet. 2012) observed
85 a reduction in mouth twitch-pressure of ~19% immediately following a 110 km mountain race
86 (Wuthrich et al. 2015); such a response is indicative of low-frequency inspiratory muscle fatigue.

87 Notwithstanding the implications of respiratory muscle fatigue, marathon and ultramarathon
88 are also thought to negatively impact on pulmonary function. The first study to investigate this
89 phenomenon measured lung capacity in the first 22 finishers of the 1923 Boston Marathon, noting that
90 post-race values were significantly reduced by 0.8 L (17%) (Gordon et al. 1924). More recently, (Ross
91 et al. 2008) reported an acute decrease in peak inspiratory flow (PIF; 6.3 to 4.9 L·s⁻¹) and forced vital
92 capacity (FVC; 5.73 to 5.46 L) immediately following a marathon, but parameters had recovered
93 within 24 h. Races of extreme duration (330 km mountain ultramarathon) also elicited reductions in
94 peak inspiratory and expiratory flow, as well as forced expiratory volume in 1 second (FEV₁)
95 (Vernillo et al. 2015). Given the positive correlation between pulmonary function and marathon
96 performance (Salinero et al. 2016), and the negative correlation between the pre-to-post exercise
97 reduction in MVV₁₂ and ultramarathon finish time (Vernillo et al. 2015), it is reasonable to suppose
98 that a pulmonary dysfunction might negatively impact on exercise performance.

99 Despite the available literature on the respiratory responses to single-stage endurance running,
100 an important, as of yet undetermined, component of pulmonary and respiratory muscle function is the
101 impact of chronic endurance exercise that is performed on multiple, consecutive days. Multi-stage
102 endurance running presents an excellent model with which to study the limits of human physiological
103 function. Data on the respiratory responses to stage-racing would offer a novel insight into the
104 robustness or fallibility of the human respiratory system in responding to repeated exercise stimuli.
105 Furthermore, such data might influence endurance running training strategies, in addition to the best
106 practice of medics overseeing these events.

107 Accordingly, this study assessed respiratory muscle and pulmonary function in a group of
108 endurance runners who contested a pre-determined ultra-endurance exercise challenge comprising 10
109 marathons in 10 consecutive days. It was hypothesised that: i) there would be an acute (within-day)
110 reduction in respiratory muscle and pulmonary function following any given marathon; and ii) there
111 would be a chronic (between-day) reduction in baseline parameters as the challenge progressed.

112 **MATERIALS AND METHODS**

113

114 **Participants**

115 Eleven recreationally-active endurance runners (8 male, 3 female), volunteered to participate in data-
116 collection protocols. Two participants withdrew from the study due to injury at day six and eight,
117 respectively; therefore, statistical data are presented for $n = 9$ (6 male, 3 female) (mean \pm S.D. age =
118 48.6 ± 9.4 y; mass = 74.7 ± 14.2 kg; stature = 174.1 ± 10.8 cm). Participants had been training for 10
119 ± 4 y (range = 5 - 14 y), ran 47 ± 16 miles (7.7 ± 2.8 h) per week, and exhibited a group mean season's
120 best marathon time of 217 ± 22 min (3 h 37 min ± 22 min). Participants were free from known
121 cardiorespiratory diseases, with the exception of one participant who had previously been treated for
122 asthma (FEV₁/FVC, 0.65 [77% predicted]). There were three ex-smokers in the group, all with > 4 y
123 smoking cessation (mean = 9.0 ± 8.7 y). Procedures were approved by the institution Research Ethics
124 Committee, and performed in accordance with the 1964 Declaration of Helsinki. Prior to data
125 collection, participants were issued with a *Participant Information Document*, completed a pre-test
126 medical questionnaire, and provided written, informed consent.

127

128 **Experimental Overview**

129 Participants contested 10 marathons in 10 consecutive days on courses of varying terrain (The Great
130 Barrow Challenge '10-in-10'; Suffolk Academy, Suffolk, UK). The marathons began from the same
131 location at 08:00 each day, affording participants consistent recovery time between races. Mean
132 temperature and humidity throughout the challenge was 22.2 ± 1.5 °C and $69 \pm 4\%$, respectively.
133 Assessments of respiratory muscle strength, pulmonary function, and perceptual responses were made
134 before and within 10 min of finishing marathons on day 1, 4, 7 and 10. Prior to testing, participants
135 were familiarised with the respiratory manoeuvres, aided by demonstrations and tutorial videos.

136

137 **Respiratory Measures**

138 *Maximum Inspiratory and Expiratory Mouth-Pressure:* Maximum static inspiratory mouth-pressure
139 (MIP, from residual volume) and maximum static expiratory mouth-pressure (MEP, from total lung

140 capacity) were assessed as a simple, convenient, and non-invasive index of respiratory muscle
141 strength (Evans and Whitelaw. 2009). The merits and limitations of volitional manoeuvres for
142 assessing respiratory muscle function are discussed later (see *Technical Considerations*). Manoeuvres
143 were performed using a handheld device (MicroRPM; CareFusion, Hampshire, UK), attached to a
144 phlanged mouthpiece with a 1-mm leak to prevent glottic closure during the MIP manoeuvre and to
145 reduce the use of buccal muscles during the MEP manoeuvre (American Thoracic Society/European
146 Respiratory Society. 2002). Participants were seated, and given verbal encouragement to maintain a
147 maximal effort for ~2 - 3 s, with the largest of three values within 5% variability recorded (Wen et al.
148 1997).

149 *Spirometry*: Pulmonary volumes, capacities, and flows were assessed via spirometry, whereby
150 participants performed between three and eight FVC manoeuvres into a two-way disposable
151 mouthpiece connected to a portable pneumotachograph (Alpha Touch; Vitalograph Ltd., Buckingham,
152 England), with the nose occluded. Participants were seated, and verbal encouragement was given to
153 ensure consistent efforts. Spirometry was performed in accordance with ATS/ERS guidelines (Miller
154 et al. 2005).

156 **Within- and Between-Day Reliability of Respiratory Measures**

157 Six healthy participants, independent from the main study, were recruited in order to quantify the
158 reliability of maximum static mouth-maximum manoeuvres and spirometry. Within-day reliability
159 was determined by comparing baseline measurements to those made after ~4 h passive rest, and
160 between-day reliability was determined by re-assessing participants three days later. Tests were
161 performed following similar coaching and instructions to that used with the main-study participants.
162 Moreover, reliability data were collected under the same time-constraints, following a similar
163 schedule, and with identical apparatus to that applied in the field. Data on the reliability of maximum
164 static mouth-pressure manoeuvres and spirometry are shown in Table 1. There were no systematic
165 differences in measurements ($p > 0.05$), and the between-occasion reliability was excellent (all CV <
166 5%; low SEM; all ICC > 0.94).

168 Perceptual Measures

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2 **169** *Symptoms of Upper-Respiratory Tract Infection (URTI)*: Following each bout of respiratory
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4 **170** assessment, participants were presented with four questions pertaining to symptoms commonly
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6 **171** associated with URTI, and asked to rate the severity of their symptoms by marking a line on a series
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8 **172** of 100 mm visual analogue scales. The questions posed were: 1) *Since waking this morning, have you*
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10 **173** *experienced any coughing?* (Anchored by "completely free of cough" and "worst cough I can
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12 **174** *imagine"); 2) Since waking this morning, have you experienced any wheezing?* (Anchored by
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14 **175** "completely free of wheeze" and "worst wheeze I can imagine"); 3) *Since waking this morning, have*
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16 **176** *you experienced any chest-tightness?* (Anchored by "completely free of chest-tightness" and "worst
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18 **177** *chest-tightness I can imagine"); 4) Since waking this morning, have you experienced any mucus*
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20 **178** *secretions?* (Anchored by "completely free of mucus" and "worst mucus I can imagine"). Following
21
22 **179** the final marathon, symptoms were monitored for a 15-d period using a daily online symptom log. An
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24 **180** individual was considered symptomatic of an URTI if ≥ 2 symptoms were present for at least 2-d in a
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26 **181** 3-d period (Robson-Ansley et al. 2012). As a control, participants were asked to report on the
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28 **182** prevalence of symptoms in another member of their household (adult, non-runner) using an identical
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30 **183** questionnaire. Prior to testing, participants completed the Allergy Questionnaire for athletes (AQUA),
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32 **184** with a score of ≥ 5 positively predicting allergy with a correlation coefficient of 0.94 (Bonini et al.
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34 **185** 2009).

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36 **186** *Respiratory Muscle Soreness*: In an effort to quantify the degree of respiratory muscle
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38 **187** damage, participants were asked to rate their perceived intensity of respiratory muscle soreness by
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40 **188** marking a line on a 100 mm Visual Analogue Scale (VAS) - anchored by "no pain" and "unbearable
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42 **189** pain", respectively - and to indicate the location of any muscle soreness by shading areas on a body
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44 **190** diagram (Mathur et al. 2010). These measures of respiratory muscle soreness were made immediately
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46 **191** following each set of MIP (MIP_{VAS}) and MEP (MEP_{VAS}) manoeuvres.

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48 **192** *Dyspnea*: Following baseline respiratory assessment, participants were asked to rate *the*
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50 **193** *intensity of their breathing discomfort* since waking, by circling a number on the modified Borg CR10
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52 **194** Scale (Mahler and Horowitz. 1994). Following post-race assessment, participants were asked the
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54 **195** same question in relation to the sensations experienced throughout the preceding marathon.
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Data Analysis

Descriptive and inferential statistics were calculated using SPSS 24 for Windows (IBM; Chicago, IL). Reliability of respiratory measures was assessed using coefficient of variation (CV), standard error of measurement (SEM), and intra-class correlation coefficients (ICC; mean of trials one & two vs. trial three). Two main comparisons were made on mouth-pressure, pulmonary function, and perceptual data: i) pre-challenge baseline to post-marathon values on day 1, 4, 7 and 10 (acute response); ii) pre-challenge baseline to pre-marathon baseline values on day 4, 7 and 10 (chronic response). Respiratory and perceptual responses were assessed for differences using repeated-measures ANOVA (eight time-points; pre-to-post day 1, 4, 7, and 10) and Fisher's LSD post-hoc comparisons. The assumption of equal variance was assessed via Mauchly's test of Sphericity and, if violated ($p < 0.05$), a Greenhouse-Geisser correction applied. Effect size (Cohen's d) was calculated to estimate the magnitude of the difference between group means, with $d = 0.2, 0.5,$ and 0.8 reflecting small, medium, and large effect size, respectively (Cohen. 1977). Alpha level was set at $p < 0.05$, and data were presented as mean \pm S.D., unless stated.

212 RESULTS

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214 Participants

215 Individual and group mean marathon times throughout the challenge are illustrated in Figure 1. Group
216 mean time across all 10 marathons was 276 ± 35 min (4 h 36 min \pm 35 min), with a mean range of
217 221 (3 h 41 min) to 319 min (5 h 19 min). Fifty six percent (5/9) runners exhibited a positive AQUA
218 score (≥ 5) for allergic diseases. The single asthmatic participant exhibited responses consistent with
219 the group-mean.

220

221 Respiratory Responses

222 *Maximum Inspiratory and Expiratory Mouth Pressure:* Group mean MIP and MEP responses are
223 illustrated in Figure 2. Relative to pre-challenge baseline, MEP was reduced after day 1 ($-14 \pm 14\%$, p
224 $= 0.017$, $d = 0.73$), day 7 ($-14 \pm 18\%$, $p = 0.035$, $d = 0.56$) and day 10 ($-19 \pm 18\%$, $p = 0.008$, $d =$
225 0.79), with a non-significant reduction after day 4 ($-9 \pm 18\%$, $p = 0.111$, $d = 0.52$). There was no
226 change in pre-marathon (baseline) MEP across days 1, 4, 7, or 10 ($p > 0.05$). Relative to pre-challenge
227 baseline, there were slight reductions in post-marathon MIP, but with no significant changes in the
228 group mean at any time point.

229 *Spirometry:* Group mean FVC, FEV₁, and PEF, are illustrated in Figure 3. Relative to pre-
230 challenge baseline, there were no differences in post-marathon FVC on day 1, 4, 7 or 10 ($p > 0.05$),
231 but there was a significant reduction in pre-marathon (baseline) FVC at day 4 ($p = 0.035$, $d = 0.17$),
232 which remained below baseline at day 7 ($p = 0.045$, $d = 0.17$) and day 10 ($p = 0.015$, $d = 0.19$). When
233 assessing FEV₁, relative to pre-challenge baseline, there were no differences in post-marathon values
234 on day 1, 4, 7, or 10, and no significant reduction in pre-marathon (baseline) FEV₁ across days 1, 4, 7,
235 or 10 ($p > 0.05$). There were significant pre-to-post marathon increases in FEV₁ on day 1 ($p = 0.012$, d
236 $= 0.51$), day 7 ($p = 0.039$, $d = 0.90$), and day 10 ($p = 0.038$, $d = 0.40$). Relative to pre-challenge
237 baseline, there were no significant changes in group mean PEF at any time point. When assessing the
238 FEV₁/FVC ratio, relative to pre-challenge baseline (0.70 ± 0.07), values had increased after day 1

239 (0.74 ± 0.06, $p = 0.047$, $d = 0.61$) and day 7 (0.74 ± 0.05, $p = 0.015$, $d = 0.66$), but there were no
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2 240 differences in pre-marathon (baseline) FEV₁/FVC at day 1, 4, 7 or 10 ($p > 0.05$).
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6 242 **Perceptual Responses**

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9 243 Group mean symptoms of URTI, perceptions of respiratory muscle soreness, and perceptions of
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11 244 dyspnea, are summarised in Table 2. The four symptoms of Upper Respiratory Tract Infection (URTI)

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13 245 (i.e., cough, wheeze, chest-tightness, mucus secretions) were assessed independently, with no
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15 246 significant changes in group mean values at any time point ($p > 0.05$). In the 15-d post-challenge
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17 247 period, 56% (5/9) runners reported symptoms of URTI (i.e., cough, watery eyes, blocked or runny
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19 248 nose, sneezing, sore throat), relative to 11% (1/9) pre-challenge, and 11% (1/9) of non-running
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21 249 controls. Respiratory muscle soreness was assessed following MIP and MEP manoeuvres before
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23 250 marathons on day 1, 4, 7 and 10. Relative to pre-challenge baseline, there were no significant changes
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25 251 in group mean values, for either MIP or MEP, at any time point ($p > 0.05$). Dyspnea (subjective
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27 252 ratings of *the intensity of breathing discomfort*) was first compared among the pre-marathon
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29 253 (baseline) scores, and then among the post-marathon scores, with no significant changes in group
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31 254 mean values at any time point ($p > 0.05$).
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255 **DISCUSSION**

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4 257 This study assessed respiratory muscle and pulmonary function in a group of endurance runners who
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6 258 contested 10 marathons in 10 consecutive days. The principal findings were: i) there was evidence of
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8 259 acute pre-to-post-marathon expiratory muscle fatigue as demonstrated by reductions in maximum
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10 260 static expiratory mouth-pressure, but no cumulative (chronic) changes in baseline respiratory muscle
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12 261 strength; ii) despite a fall in baseline forced vital capacity at day 4, other indices of pulmonary
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14 262 function were maintained; iii) changes in respiratory function were not associated with changes in
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16 263 perceptual responses during the challenge, although 56% of runners exhibited symptoms of URTI
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18 264 within 15-d of the final marathon. [These novel data speak to the robustness of the healthy respiratory](#)
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20 265 [system to maintain baseline pulmonary and respiratory muscle function during multiple, consecutive](#)
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22 266 [days of endurance exercise.](#)

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27 268 **Technical Considerations**

28
29 269 There are certain technical considerations that should predicate a discussion of our findings. First,
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31 270 maximum static pressure manoeuvres are considered a global measure of respiratory muscle strength
32
33 271 (Polkey et al. 1995). The techniques are widely used in the assessment of respiratory muscle fatigue
34
35 272 (44% of 77 studies; Janssens et al. 2013), and the manoeuvres [show strong test/re-test reliability](#)
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37 273 [\(Dimitriadis et al. 2011\)](#). These techniques are non-invasive, easily applied in the field, and can be
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39 274 reported alongside well-established normative data. Nevertheless, a common limitation is that
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41 275 manoeuvres are volitional, dependent on participant motivation, and might be subject to a practice
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43 276 effect. To increase the likelihood that maximal efforts were achieved, we followed standard guidelines
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45 277 by recording a minimum of three manoeuvres within 5% variability (American Thoracic
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47 278 Society/European Respiratory Society. 2002; Wen et al. 1997). Participants were familiarised with
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49 279 respiratory manoeuvres prior to data-collection, and our [reliability](#) data show strong between-occasion
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51 280 reliability (Table 1), congruent with previously-reported test/re-test reliability coefficients for these
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53 281 techniques (Dimitriadis et al. 2011). Moreover, the finding that MEP was acutely diminished
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55 282 following a given marathon while maximum indices of pulmonary function (e.g., PEF) were well
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283 maintained, suggests a mechanism that was independent of motivation and/or a practice effect.

284 Although objective measures (i.e., nerve-stimulation) are preferable in the assessment of respiratory

285 muscle fatigue, the invasive nature of such protocols, coupled with the ecological nature of our

286 experimental design, made nerve stimulation inappropriate for this study.

287 Second, in order to evaluate the carry-over effects of the previous day's marathon, we would

288 have preferred to have collected additional data before each of the 10 marathons. Respiratory and

289 perceptual assessments can be time-consuming, and it was not logistically feasible to take daily

290 measurements from our cohort. Our measures, therefore, strike a balance between obtaining sufficient

291 data to address our research questions, while not overly inconveniencing our participants. Should

292 respiratory muscle strength have not recovered following an overnight rest, we reasoned that function

293 would have steadily fallen on subsequent days, manifesting in lower baseline values. Accordingly, it

294 was deemed appropriate to test baseline function at four time points throughout the challenge. Finally,

295 it is likely that our participants implemented pacing strategies which allowed them to exhibit

296 consistent marathon times throughout the 10-day challenge (Fig. 1). This would preclude any

297 concerns that participants did not sufficiently recover between marathons; accordingly, a general

298 whole-body fatigue and/or insufficient recovery are less likely to have influenced our data.

299

300 **Respiratory Muscle Fatigue**

301 Throughout the challenge, the magnitude of the post-marathon fall in maximum expiratory muscle

302 strength ranged from 15 – 20%, and is in accordance with earlier reports of diminished respiratory

303 muscle strength following single-stage marathon (Chevrolet et al. 1993; Loke et al. 1982; Ross et al.

304 2008), and ultramarathon (Wuthrich et al. 2015). Nevertheless, this is the first study to assess these

305 parameters in response to multiple, consecutive days of endurance exercise. Respiratory muscle

306 fatigue is defined as *a condition in which there is a loss in the capacity for developing force and/or*

307 *velocity of a muscle, resulting from muscle activity under load, and which is reversible with rest*

308 (NHLBI 1990). Moreover, respiratory muscle fatigue is considered to be detectable if the measured

309 reduction in pressure-generating capacity (relative to baseline) is two- to threefold the typical pressure

310 variation (Guenette et al. 2010). The mean decrease in MEP was at least fivefold greater than the CV,

311 and at any given point of measurement, between 5 and 7 participants exhibited post-race decreases in
312 MEP >10% (i.e., >threefold the CV). Based on these criteria, our strong reliability coefficients (Table
313 1), and the observation of a moderate-to-large effect size with respect to acute reductions in MEP
314 (0.56 – 0.79), we are confident that our participants exhibited a fatigue that was underpinned by a
315 physiological mechanism. The acute post-marathon fall in expiratory muscle strength is indicative of
316 low-frequency fatigue, which is underpinned by two potential mechanisms: reduced Ca²⁺ release from
317 the sarcoplasmic reticulum and/or damaged sarcomeres caused by overextension of muscle fibres
318 (Jones. 1996). Given the time-course for the recovery of expiratory muscle strength (i.e., there was no
319 systematic decay in pre-marathon values), we suppose that the transient post-marathon fatigue was
320 due to reduced Ca²⁺ availability in the sarcolemma, rather than damaged sarcomeres, although neither
321 were assessed directly. Furthermore, perceptions of respiratory muscle soreness following MIP and
322 MEP manoeuvres did not rise above baseline at any time-point (Table 2) and we can, therefore,
323 discount any cumulative mechanical contribution to fatigue. These observations support the notion
324 that respiratory muscle contractility generally recovers within a few hours of exercise (for review, see
325 (Romer and Polkey. 2008).

326 The abdominal muscles have an important role in regulating the ventilatory response to
327 exercise (Abraham et al. 2002); however, it is unlikely that the post-race decreases in expiratory
328 muscle strength were exclusively the result of high ventilation rates. The group mean marathon time
329 over the 10-day challenge was ~20% slower than the season's best single-stage marathon, and
330 individual performance times throughout the challenge were relatively consistent (Figure 1). It is
331 likely, therefore, that participants implemented strategies of self-regulation (Barkley. 2001) to
332 prioritise performance on consecutive days over any individual day, and work rate was tempered as a
333 result. This notion of *preservation* is reflected in the modest ratings of post-marathon dyspnea (Borg
334 CR10 scale; 2.0 ± 0.3), which are lower than that reported elsewhere during single-stage marathon
335 (Borg 6 - 20 scale; 12 [Ross et al. 2008]). Expiratory muscle fatigue was more likely attributable to
336 the additional non-ventilatory functions that these muscles assume during exercise (e.g., forced
337 expiration and postural support [Hodges et al. 2005]), which render them more susceptible to fatigue
338 during relatively low ventilation ultra-endurance activities.

339 By contrast, although we observed small decreases in post-marathon inspiratory muscle
1
2 340 strength relative to baseline (Figure 2), the extent of the absolute reduction did not reach statistical
3
4 341 significance. The magnitude and prevalence of diaphragmatic fatigue is significantly correlated with
5
6 342 the ventilatory demands of exercise (Babcock et al. 2002; Johnson et al. 1993), and it may simply be
7
8 343 that the multi-day challenge did not impose a sufficient ventilatory stimulus to significantly fatigue
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10
11 344 the inspiratory muscles. The diaphragm also has a postural role, but this is only coordinated with its
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13 345 respiratory functions during transient, intermittent disturbances to trunk stability (e.g., brief arm
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15 346 movements) (Hodges and Gandevia. 2000). Indeed, when ventilation is mediated by humoral factors
16
17 347 (e.g., during sustained exercise), postural drive to the phrenic motoneurons is withdrawn, and
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19 348 respiratory input is prioritised (Hodges, Heijnen et al. 2001). A diminished postural drive to the
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21 349 diaphragm, coupled with a modest ventilatory demand, might explain the lack of inspiratory muscle
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23 350 fatigue noted in this study.
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28 352 **Pulmonary Function**

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31 353 Relative to pre-challenge baseline, there was a fall in FVC at day 4, which remained below baseline
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33 354 for the remainder of the event (Figure 3). It was first suspected that these baseline reductions in FVC
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35 355 may have been due, at least in part, to modest (non-significant) reductions in expiratory muscle
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37 356 strength; however, others report no change in pulmonary function when the expiratory muscles are
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39 357 pre-fatigued via expiratory threshold loading (Haverkamp et al. 2001). As such, a more likely
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41 358 explanation for the observed pulmonary dysfunction is a modest degree of lower-airway obstruction,
42
43 359 which manifested in a fall in the baseline FEV₁/FVC ratio at day 7 (0.65 ± 0.08) and at day 10 ($0.68 \pm$
44
45 360 0.08). Upper-airway obstruction can be discounted, since this is typically characterised by discordance
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47 361 between FEV₁ and PEF (Miller et al. 1990), and the baseline ratio of these parameters was maintained
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49 362 throughout the challenge (day 1 = 6.9 ± 1.2 ; day 4 = 6.8 ± 1.2 ; day 7 = 6.3 ± 2.1 ; day 10 = 6.7 ± 1.4).
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51 363 Despite these observations, lower airway obstruction as a causative factor in reduced lung function is
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53 364 difficult to assert because others have observed post-race reductions in pulmonary function both with
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55 365 (Maron et al. 1979) and without (Vernillo et al. 2015) the presence of airway obstruction. Additional
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57 366 lung volume data collected via whole-body plethysmography, in addition to measures of airway
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367 resistance, would further elucidate the mechanisms underpinning our observations. Worthy of note is
1
2 368 that we also observed acute pre-to-post marathon increases in FEV₁ (Figure 3), which was likely
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4 369 attributable to exercise-induced bronchodilation (Freedman. 1991).
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8 9 371 **Upper-respiratory tract infection (URTI)**

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11 372 Finally, in the 15-d post-challenge period, 56% (5/9) runners reported symptoms of Upper-
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13 373 Respiratory Tract Infection (URTI) (i.e., cough, watery eyes, blocked or runny nose, sneezing, sore
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15 374 throat), relative to 11% (1/9) pre-challenge, and 11% (1/9) of non-running controls. [Symptoms of](#)
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17 375 [URTI are a common complaint among endurance runners; for example](#), there are reports of URTI in
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19 376 47% of 208 runners who completed a single-stage marathon, relative to 19% of non-running controls
20
21 377 (Robson-Ansley et al. 2012). Moreover, URTI occurred in 33% of runners who completed a 56 km
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23 378 single-stage race, relative to 15% of non-running controls (Peters and Bateman. 1983). It has been
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25 379 postulated that symptoms of URTI are the manifestation of an allergic or pro-inflammatory response,
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27 380 coupled with a transient suppression of cellular immune functions; although, neither were assessed in
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29 381 the present study. Worthy of note, is that 56% (5/9) runners exhibited a positive AQUA outcome,
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31 382 suggesting the presence of allergy, which is consistent with 60% prevalence in elite marathoners,
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33 383 whose reported symptoms were predominantly related to the upper-respiratory tract (Teixeira et al.
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35 384 2014). Consequently, both single-stage and multi-stage endurance competition appear sufficient to
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37 385 cause symptoms of URTI and, in light of the present findings, the development of URTI appears to be
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39 386 mechanistically unrelated to changes in pulmonary function.
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45 46 388 **Implications for Health and Endurance Performance**

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49 389 There may be several means by which our findings might impact on health and/or endurance
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51 390 performance. First, the respiratory muscles have a critical role in maintaining torso stabilisation
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53 391 during exercise (Celli et al. 1988). The major expiratory muscles contract to increase intra-abdominal
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55 392 pressure which, in turn, increases stiffness and stability of the lumbar spine (Hodges, Cresswell et al.
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57 393 2001; Hodges et al. 2005). This likely helps to protect spinal structures during periods of postural
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59 394 disturbance. As a consequence, exercise that induces expiratory muscle fatigue might place the runner
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395 at a greater risk of injury, and render them less able to sustain the rigours of competition. Moreover,
1 396 given that the limb-locomotor muscles exhibit substantial neuromuscular fatigue following prolonged
2 397 running (Millet and Lepers. 2004), it is plausible that a simultaneous respiratory and locomotor
3 398 muscle fatigue may further increase the risk of fall and/or injury when traversing challenging terrain.
4 399 Accordingly, we propose that marathon and ultramarathon runners investigate strategies that attenuate
5 400 the degree of expiratory muscle fatigue that manifests during competition.
6 401

13 401 Second, respiratory muscle fatigue results in reflex effects of breathing on vascular function
14 402 (Dempsey et al. 2008). This metaboreflex causes sympathoexcitation and vasoconstriction of
15 403 exercising limb vasculature, thereby eliciting a fall in limb blood flow and vascular conductance
16 404 (Harms et al. 1998). Diminished blood flow to working muscles would be expected to accelerate
17 405 locomotor muscle fatigue. Indeed, a fatigue-induced reduction in respiratory muscle work capacity
18 406 has been modelled to significantly predict ultramarathon performance (Vernillo et al. 2015), although
19 407 further studies are needed to investigate the presence of a metaboreflex in response to ultra-endurance
20 408 exercise.
21 409

31 409 Third, it is possible that the development of respiratory dysfunction might impact on
32 410 endurance performance. In a sample of 110 marathon runners (Salinero et al. 2016), there existed a
33 411 significant negative correlation between indices of pulmonary function and marathon finish time; i.e.,
34 412 faster marathon runners exhibited better metrics of lung function ($FVC = r = -0.41, p < 0.001$; $FEV_1 =$
35 413 $r = -0.40, p < 0.001$; $PEF = r = -0.50, p = 0.005$). Moreover, in an earlier study, (Warren et al. 1989)
36 414 assessed the predictive power of lung function on ultramarathon performance by testing runners every
37 415 3 h throughout a 24 h footrace. The authors reported a significant reduction in MVV_{12} after 24 h, and
38 416 modelled the variance in MVV_{12} to predict 39% of the variance in running speed. Although the
39 417 mechanisms that underpin these relationships require further scrutiny, these studies do provide an
40 418 insight into lung function and its potential predictive power on endurance running performance.
41 419

53 419 Finally, a pertinent question is whether the observed changes in pulmonary function were
54 420 clinically meaningful. Given that the majority of values remained within the predicted range (i.e.,
55 421 above the lower-limit of normal), it is reasonable to suppose that - with adequate rest between stimuli
56 422 - the respiratory systems of trained runners are sufficiently robust to recover from multiple,
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423 consecutive days of endurance exercise, providing that athletes begin the race with a healthy baseline
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2 424 function. Although speculative, the same responses in individuals with underdeveloped baseline
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4 425 parameters or a pre-existing respiratory disorder (e.g., asthma), may result in manifestations of
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6 426 clinical significance.
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11 428 In conclusion, we present novel data to suggest that the expiratory muscles are prone to acute
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13 429 contractile fatigue during ultramarathon stage-racing; however, we found limited evidence of a
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15 430 cumulative baseline-drift in respiratory muscle strength. Moreover, relatively well-maintained
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17 431 pulmonary and perceptual responses throughout the challenge suggest that the respiratory systems of
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19 432 trained runners are sufficiently robust to recover from multiple, consecutive days of endurance
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21 433 exercise. Nevertheless, acute fatigue of the expiratory muscles, combined with that of the locomotor
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23 434 muscles during marathon/ultramarathon, might impact on exercise performance and expose the
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25 435 individual to an increased risk of running-related injury. Further studies should aim to assess the
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27 436 pulmonary and respiratory muscle response to stage-races of a greater ventilatory demand and/or
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29 437 duration.
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34
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36
37 440 kind hospitality and cooperation, and the runners who gave their time to participate in data-collection
38
39 441 protocols. *Conflict of Interest.* There are no conflicts of interest associated with the production of this
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41 442 study. Data are presented clearly, honestly, and without fabrication, falsification, or inappropriate data
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43 443 manipulation.
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552 **FIGURE/TABLE CAPTIONS**

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4 554 **Figure 1.** Individual and group-mean marathon times throughout the 10-day challenge.

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8 556 **Figure 2.** Maximum static expiratory (panel A) and inspiratory (panel B) mouth-pressure, before and
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11 557 after marathons on day 1, 4, 7 and 10. *significantly different versus pre-challenge baseline, $p < 0.05$.

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15 559 **Figure 3.** Forced vital capacity (panel A), forced expiratory volume in 1 second (panel B), and peak
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17 560 expiratory flow (panel C), before and after marathons on day 1, 4, 7 and 10. *significantly different
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19 561 versus pre-challenge baseline, $p < 0.05$; †significantly different versus pre-marathon, $p < 0.05$.

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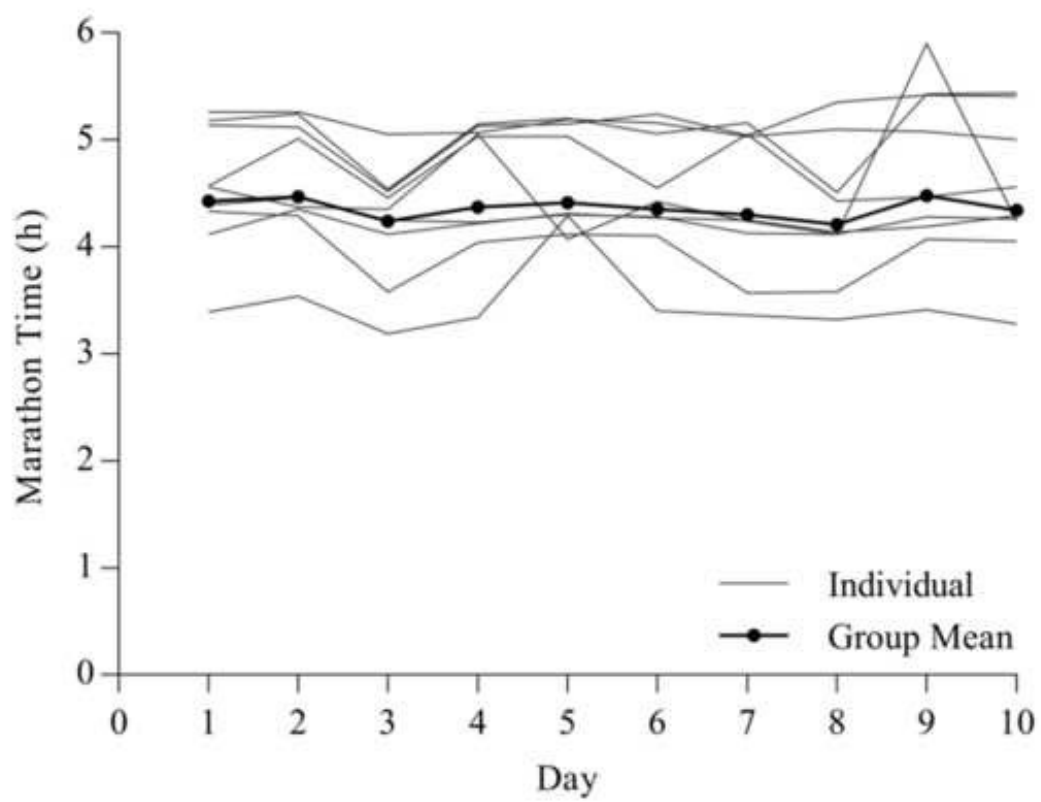
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24 563 **Table 1.** Within- and between-day reliability of respiratory measures.

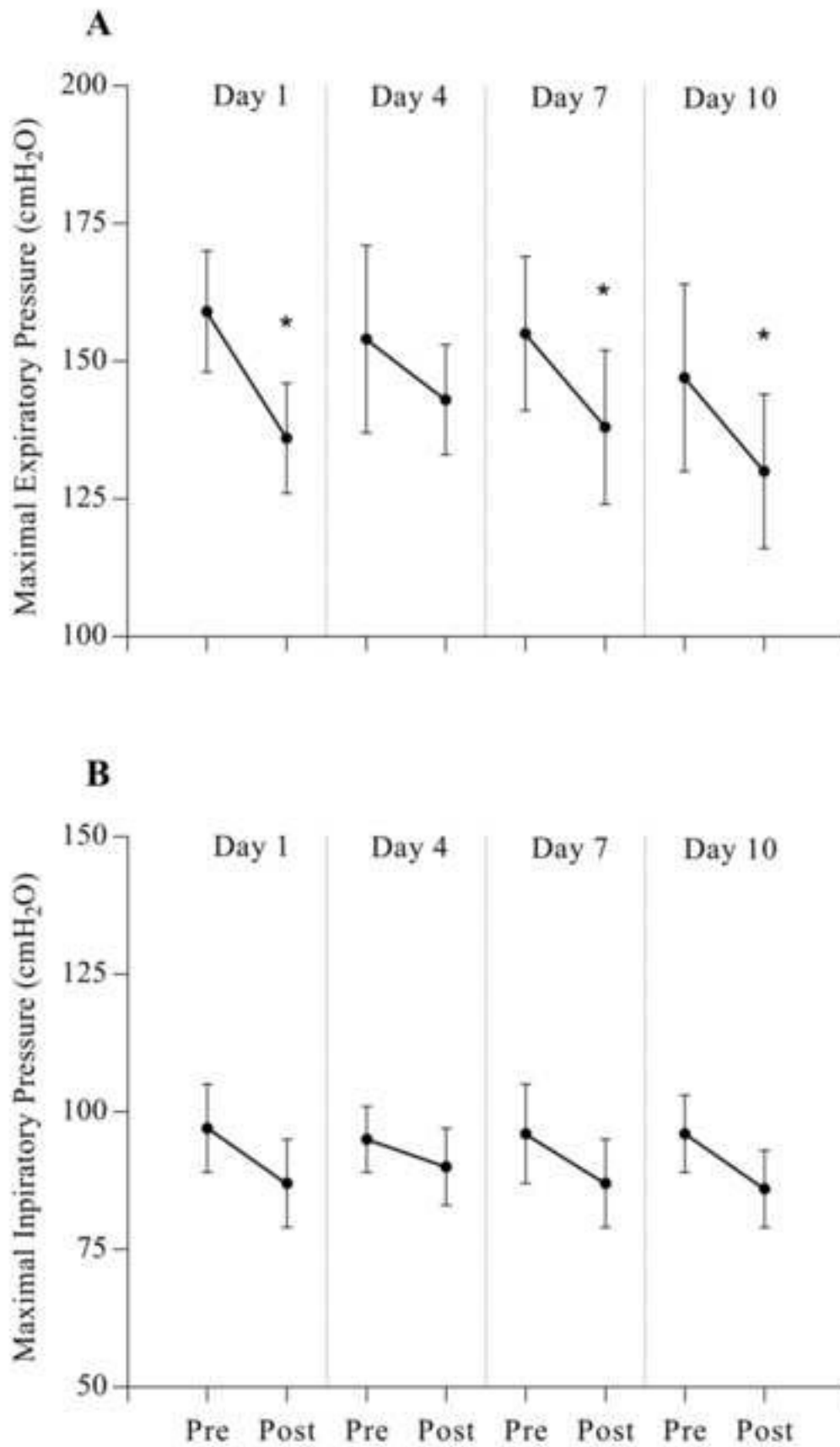
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28 564 **Table 2.** Perceptual responses before and after marathons on day 1, 4, 7, and 10.

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Figure 1

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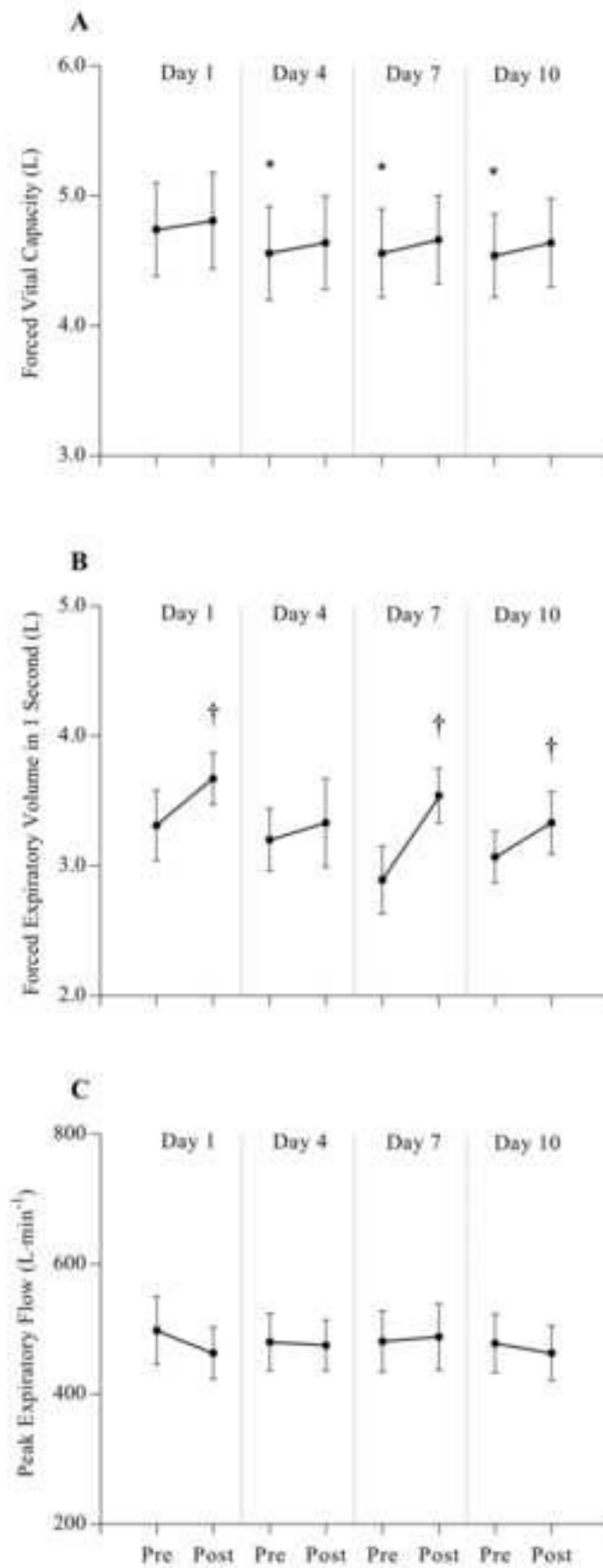


Table 1. Within- and between-day reliability of respiratory measures.

	Trial 1	Trial 2	Trial 3	CV (%)	SEM	ICC
FVC (L)	5.07 ± 0.75	5.02 ± 0.76	5.06 ± 0.74	0.7	0.075	0.999 (0.996-1.000)
FEV ₁ (L)	3.89 ± 0.71	3.84 ± 0.79	3.78 ± 0.69	2.6	0.103	0.994 (0.975-0.999)
FEV ₁ /FVC	0.77 ± 0.05	0.76 ± 0.06	0.75 ± 0.03	2.5	0.016	0.943 (0.760-0.991)
PEF (L·min ⁻¹)	607 ± 96	612 ± 135	615 ± 102	4.6	31.4	0.963 (0.842-0.994)
MIP (cmH ₂ O)	124 ± 30	126 ± 32	124 ± 30	4.0	6.16	0.988 (0.950-0.998)
MEP (cmH ₂ O)	200 ± 53	194 ± 51	193 ± 51	2.9	7.32	0.996 (0.983-0.999)

FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 second; PEF, peak expiratory flow; MIP, maximal static inspiratory pressure; MEP, maximal static expiratory pressure; CV, coefficient of variation; SEM, standard error of measurement; ICC, intra-class correlation coefficient. Data are means ± SD.

Table 2

Table 2. Perceptual responses before and after marathons on day 1, 4, 7, and 10.

	Day 1		Day 4		Day 7		Day 10	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
MIP _{VAS} (mm)	2.4 ± 4.3	0.3 ± 0.7	0.2 ± 0.4	0.4 ± 1.0	0.1 ± 0.3	0.2 ± 0.4	0.2 ± 0.4	0.3 ± 1.0
MEP _{VAS} (mm)	0.2 ± 0.7	0.0 ± 0.0	0.0 ± 0.0	0.2 ± 0.7	0.0 ± 0.0	0.1 ± 0.3	0.4 ± 1.0	0.3 ± 0.7
Dyspnea (CR10)	0.0 ± 0.0	1.7 ± 0.9	0.1 ± 0.3	2.3 ± 0.7	0.2 ± 0.4	2.0 ± 1.3	0.3 ± 1.0	2.0 ± 1.2
URTI (VAS):								
Cough (mm)	1.2 ± 2.4	0.7 ± 0.9	2.1 ± 5.6	2.8 ± 6.9	3.9 ± 10.6	2.0 ± 5.3	1.3 ± 2.6	3.3 ± 5.3
Wheeze (mm)	1.4 ± 4.3	0.9 ± 1.7	1.2 ± 2.6	3.1 ± 5.9	0.8 ± 2.0	0.6 ± 1.7	0.7 ± 2.0	2.1 ± 4.4
Chest (mm)	0.2 ± 0.7	1.8 ± 4.0	1.6 ± 3.1	5.9 ± 8.5	3.9 ± 7.6	3.3 ± 6.4	3.7 ± 8.4	3.4 ± 7.2
Mucus (mm)	9.2 ± 17.2	10.1 ± 17.2	3.3 ± 5.4	11.6 ± 18.0	9.1 ± 14.6	13.0 ± 24.0	13.0 ± 24.4	13.7 ± 22.1

MIP, maximal static inspiratory pressure; MEP, maximal static expiratory pressure; VAS, visual analogue scale; URTI, upper-respiratory tract infection; Cough, current experience of cough; Wheeze, current experience of wheeze; Chest, current experience of chest-tightness; Mucus, current experience of mucus secretions.