Exercise-induced diaphragm fatigue in a Paralympic champion rower with spinal cord injury

TILLER, Nicholas <http://orcid.org/0000-0001-8429-658X>, AGGAR, Thomas R., WEST, Christopher R. and ROMER, Lee M.

Case Studies in Physiology: Exercise-induced diaphragm fatigue in a Paralympic champion rower with spinal cord injury

Nicholas B. Tiller[1], Thomas R. Aggar[2], Christopher R. West[4] & Lee M. Romer[2,3]

[1]Academy of Sport and Physical Activity, Sheffield Hallam University, UK

[2]Centre for Human Performance, Exercise and Rehabilitation, College of Health and Life Sciences, Brunel University London, Uxbridge, UK

[3]Division of Sport, Health and Exercise Sciences, Department of Life Sciences, College of Health and Life Sciences, Brunel University London, Uxbridge, UK

[4]ICORD, 818 West 10th Avenue, Vancouver, BC, Canada.

Running Head: Exercise-induced diaphragm fatigue in SCI

Correspondence:

Nicholas B. Tiller

Academy of Sport and Physical Activity

Sheffield Hallam University

S10 2BP

Email: n.tiller@shu.ac.uk

Conflict of interest: There are no competing financial interests in relation to the described research.

ABSTRACT

Introduction. The aim of this case report was to determine whether maximal upper-body exercise was sufficient to induce diaphragm fatigue in a Paralympic champion adaptive rower with low-lesion spinal cord injury (SCI). **Case Presentation.** An elite arms-only oarsman (age 28 y, stature 1.89 m, mass 90.4 kg) with motor-complete SCI (T_{12}) performed a 1000 m time-trial on an adapted rowing ergometer. Exercise measurements comprised pulmonary ventilation and gas exchange, diaphragm EMG-derived indices of neural respiratory drive and intrathoracic pressure-derived indices of respiratory mechanics. Diaphragm fatigue was assessed by measuring pre- to post-exercise changes in the twitch transdiaphragmatic pressure ($P_{di,tw}$) response to anterolateral magnetic stimulation of the phrenic nerves. The time-trial (248 ± 25 W, 3.9 min) elicited a peak O_2 uptake of 3.46 $L \cdot min^{-1}$ and a peak pulmonary ventilation of 150 $L \cdot min^{-1}$ (57% MVV). Breath-to-stroke ratio was 1:1 during the initial 400 m and 2:1 thereafter. The ratio of inspiratory transdiaphragmatic pressure to diaphragm EMG (neuromuscular efficiency) fell from rest to 600 m (16.0 vs. 3.0). Potentiated $P_{di,tw}$ was substantially reduced (−33%) at 15-20 min post-exercise, with only partial recovery (−12%) at 30-35 min. **Conclusions.** This is the first report of exercise-induced diaphragm fatigue in SCI. The decrease in diaphragm neuromuscular efficiency during exercise suggests that the fatigue was partly due to factors independent of ventilation (e.g., posture and locomotion).

Keywords: Paralympics, respiratory mechanics, rowing, upper-body exercise, wheelchair sport

41 **NEW & NOTEWORTHY**

42 This case report provides the first objective evidence of exercise-induced diaphragm fatigue in SCI
43 and, for that matter, in any population undertaking upper-body exercise. Our data support the notion
44 that high levels of exercise hyperpnea and factors other than ventilation (e.g., posture and locomotion)
45 are responsible for the fatigue noted after upper-body exercise. The findings extend our
46 understanding of the limits of physiological function in SCI.

47 **INTRODUCTION**

48 High-intensity, whole-body exercise is sufficient to induce contractile fatigue of the diaphragm in
49 healthy, able-bodied subjects. This exercise-induced diaphragm fatigue has been documented
50 following cycle ergometry and treadmill running, as demonstrated by 15-30% pre-to-post-exercise
51 reductions in the twitch transdiaphragmatic pressure ($P_{di,tw}$) response to bilateral phrenic nerve
52 stimulation (6, 18). More recently, we reported non-significant reductions in $P_{di,tw}$ following high-
53 intensity arm ergometry in healthy, able-bodied subjects (36), and in athletes with high-lesion
54 (cervical) spinal cord injury (SCI) (35). Since the severity of diaphragm fatigue after whole-body
55 exercise is critically dependent on the diaphragmatic workload endured (5), it is likely that upper-
56 body exercise imposes insufficient stress on the diaphragm to induce contractile fatigue, and is likely
57 a function of the subjects' low aerobic fitness and/or small active muscle (35, 36).

58 Individuals with cervical SCI often exhibit chronic respiratory dysfunction owing to weakness
59 of the respiratory muscles, reduced compliance of the lung and chest wall, and increased abdominal
60 compliance (8). The impact of SCI on respiratory function is usually less severe in those with lower
61 lesions (28, 31). Moreover, paraplegics with low-lesion SCI exhibit greater control of the upper-limbs
62 and trunk as well as supraspinal control over the major portion of the sympathetic chain, manifesting
63 in greater cardiac capacity and oxygen uptake relative to high-lesion paraplegics or tetraplegics (11).
64 It is not currently known whether a greater cardiorespiratory capacity predisposes individuals with
65 low-lesion SCI to exercise-induced diaphragm fatigue. Rowing is considered to be one of the most
66 physiologically demanding sports, with ventilatory requirements that are substantial relative to arm-
67 cranking (37). Exercise-induced diaphragm fatigue is most likely to occur in response to maximal
68 rowing because the diaphragm must contract to expand the ribcage during inspiration while also
69 opposing mechanical forces transmitted through the thorax (24, 32). An important, yet undetermined,
70 component of diaphragm fatigue relates to the measured inspiratory muscle ‘work’ which comprises
71 both the exercise hyperpnea and the additional mechanical demands imposed by upper-body
72 locomotor mechanics.

73 Accordingly, the aim of this study was to use phrenic nerve stimulation to assess diaphragm
74 fatigability in response to a simulated 1000 m arms-only rowing time-trial performed by an elite

75 Paralympic oarsman. This case study presented a unique opportunity to investigate the limits of
76 physiological function in low-lesion SCI; therefore, a further aim was to quantify the physiological
77 demands of adaptive rowing, with emphasis on the respiratory neuromechanical responses.

CASE PRESENTATION

Participant

The participant was a Paralympic, World and European champion oarsman with traumatic motor-complete SCI (T_{12}, ASIA Impairment Scale grade A) who competed for Great Britain in the "arms and shoulders" single sculls classification (1×AS). At the time of study, the participant was the reigning Paralympic champion and in a maintenance phase of aerobic training. The participant's characteristics were: age 28 y, stature 1.89 m, body mass 90.4 kg, and time post-injury 6.5 y. Before testing, the participant abstained from strenuous exercise for 48 h, caffeine and alcohol for 12 h and food for 3 h, and was not taking any drugs known to influence the exercise response. The study was approved by the institutional research ethics committee and the participant provided written informed consent.

Experimental Overview

The participant visited the laboratory on two occasions separated by 48 h. The first visit comprised pulmonary function testing and a thorough familiarisation with the nerve stimulation protocol. At the second visit, the participant completed a simulated 1000 m arms-only time-trial on an adapted rowing ergometer, with assessment of cardiorespiratory, metabolic and respiratory neuromechanical responses. Exercise-induced diaphragm fatigue was assessed via magnetic stimulation of the phrenic nerves.

Resting Pulmonary Function

Pulmonary volumes, capacities, flows, and resistance were assessed using whole-body plethysmography, and diffusion capacity via CO-rebreathe (Masterscreen Body, CareFusion, Hampshire, UK). Maximum inspiratory pressure at residual volume (P_{Imax}) and maximum expiratory pressure at total lung capacity (P_{Emax}) were measured using a handheld device (MicroRPM, CareFusion). All procedures were conducted in accordance with recommended standards (13, 22, 25, 38).

Time-trial

After a self-selected warm-up, the participant completed a simulated 1000 m rowing time-trial on an adapted rowing ergometer (Concept 2C, Nottingham, UK) fitted with a custom non-movable seat, and with the flywheel resistance (drag factor) adjusted to 140. The participant wore regulation strapping at chest-level to secure the upper-body to the seat. Stroke force and length were assessed using a bespoke transducer and potentiometer affixed to the ergometer handle. Pulmonary ventilation and gas exchange were assessed continuously using an online system (Oxycon Pro, CareFusion, Hampshire, UK) and averaged over the last 30 s of each 200 m split. A 20 µl capillary blood sample was collected from the earlobe immediately after exercise and every 2 min thereafter for the determination of peak blood lactate concentration [BLa] (Biosen C-Line Sport, EKF Diagnostics, Barleben, Germany). Locomotor-respiratory coupling (LRC) was calculated as the ratio of complete or partial respiratory cycles within a given stroke (7).

Diaphragm Function

Neuromuscular activation of the diaphragm (EMG_{di}) was assessed using a bespoke multi-pair oesophageal electrode catheter (Gaeltec Devices Ltd., Dunvegan, Isle of Sky, UK) that was inserted pernasally and positioned using standard procedures (21). Inspiratory tidal EMG_{di} was normalised against the highest root mean square (RMS) recorded during a maximal Müller manoeuvre. Oesophageal pressure (P_{es}) and gastric pressure (P_{ga}) were measured using two independent pressure transducers that were attached to the catheter proximally and distally to the electrodes (33). Transdiaphragmatic pressure (P_{di}) was obtained by online subtraction of P_{es} from P_{ga}. Tidal inspiratory P_{di} (ΔP_{di}) was calculated as the change in P_{di} between points of zero flow. To quantify the extent to which the diaphragm was recruited for non-respiratory tasks, diaphragm neuromuscular efficiency was calculated as the ratio of ΔP_{di} (cmH_2O) to EMG_{di} ($\%RMS_{max}$) (1).

Phrenic Nerve Stimulation

Two magnetic stimulators (Magstim 200, The Magstim Company Ltd., Whitland, Wales), each connected to a 25 mm figure-of-eight coil, were used to stimulate the phrenic nerves for the

134 determination of twitch transdiaphragmatic pressure ($P_{di,tw}$) at baseline and at 15 - 20 and 30 - 35 min
135 after exercise. The procedure was identical to that used in our previous study of athletes with cervical
136 SCI (35). A pre-exercise incremental stimulation protocol was performed to determine whether
137 depolarisation of the phrenic nerves was maximal. All subsequent stimulations discharged at 100%
138 stimulator power when the participant was relaxed at functional residual capacity (FRC) with the
139 glottis closed. Membrane excitability was determined by measuring the peak-to-peak amplitude and
140 duration of magnetically evoked M-waves. We have previously discussed the potential sources of
141 error associated with nerve stimulation protocols (35, 36).
142
143 **Data Processing**
144 Handle force and displacement, in addition to respiratory pressure and airflow signals, were passed
145 through an amplifier (1902, Cambridge Electronic Design, Cambridge, UK) and digitised at a
146 sampling frequency of 150 Hz using an analogue-to-digital converter (micro 1401 mkII, Cambridge
147 Electronic Design). EMG signals were sampled at 4 kHz, high-pass filtered at 100 Hz, and notch-
148 filtered at 50 Hz (20). ECG artefact was removed from the EMG waveforms using a custom script
149 procedure (3).

RESULTS

Pulmonary Function

Baseline pulmonary function generally exceeded predicted values for healthy, able-bodied individuals (Table 1), with no evidence of any pre-existing respiratory disorder.

Time-trial

Cardiorespiratory responses to the simulated 1000 m time-trial are shown in Table 2. The time-trial was completed in 3.89 min at a power output of 248 ± 25 W (mean ± SD). Power output peaked during the initial 200 m and then stabilised for the remainder of the trial, maintained by small increases in stroke rate and length. Oxygen uptake ($\dot{V}O_2$) and minute ventilation ($\dot{V}_E$) increased sharply over the initial 200 - 400 m and increased at a more gradual rate thereafter, reaching peak values of 3.46 $L \cdot min^{-1}$ (38.3 $ml \cdot kg^{-1} \cdot min^{-1}$) and 150 $L \cdot min^{-1}$ (57% of measured maximum voluntary ventilation, MVV_{12}), respectively. Minute ventilation over the initial 400 m was achieved primarily via increases in tidal volume (V_T), with respiratory frequency (f_R) entrained with stroke rate at a breath-to-stroke ratio of 1:1, switching to 2:1 after 400 m (Fig. 1). The change in respiratory pattern was accompanied by reductions in breath timing (T_I, T_E, T_{TOT}) and increases in ventilatory drive (V_T/T_I, V_T/T_E). Blood lactate concentration was 0.7 $mmol \cdot L^{-1}$ at baseline, peaking at 15.8 $mmol \cdot L^{-1}$ at 8 min post-exercise. Inspiratory transdiaphragmatic pressure swings decreased after 200 m whereas EMG_{di} tended to increase, resulting in a fall in ΔP_{di} / EMG_{di} (i.e., a reduction in diaphragm neuromuscular efficiency) (Fig. 2). Immediately following the cessation of exercise, absolute ventilation during five respiratory cycles increased substantially (13.6 to 18.7 L), primarily the result of an increased tidal volume (2.7 to 3.1 L), whereas transdiaphragmatic pressure swings and diaphragm EMG decreased (ΔP_{di}, 133 to 53 cmH_2O; EMG_{di}, 91 to 58%max RMS) (Fig. 3).

Diaphragm Fatigue. Potentiated $P_{di,tw}$ was substantially reduced below baseline at 15 - 20 min after exercise (41 vs. 61 cmH_2O), with only partial recovery at 30 - 35 min (50 cmH_2O). Moreover, maximum inspiratory P_{di} and maximum inspiratory P_{es} were markedly reduced at 15 - 20 min after exercise ($P_{di,max}$, 200 vs. 233 cmH_2O; $P_{es,max}$, 157 vs. 183 cmH_2O). Nerve stimulation during the pre-

exercise incremental stimulation protocol was not deemed to be supramaximal, as indicated by a small increase in $P_{di,tw}$ (40 to 45 cmH_2O) when stimulator intensity was increased from 95 - 100%. Evoked diaphragm M-waves were similar at baseline, 15 - 20 min, and 30 - 35 min after exercise (amplitude 8.5, 8.4 vs. 8.2 mV; duration 1.5, 1.4 vs. 1.3 ms).

DISCUSSION

This study provides the first objective evidence of exercise-induced diaphragm fatigue following upper-body exercise. In a Paralympic Champion oarsman with low-lesion SCI, we noted a substantial (33%) reduction in evoked transdiaphragmatic pressure at 15 - 20 min after a simulated 1000 m time-trial, with only partial recovery by 30 - 35 min. The ratio of inspiratory transdiaphragmatic pressure to diaphragm EMG (diaphragm neuromuscular efficiency) fell substantially during the early phase of exercise. Furthermore, tidal transdiaphragmatic pressure fell immediately on exercise cessation despite maintained pulmonary ventilation. These data suggest that diaphragm fatigue was partly due to work derived from non-respiratory loading.

Muscle fatigue is defined as *a condition in which there is a loss in the capacity for developing force and/or velocity of a muscle, resulting from muscle activity under load, and which is reversible with rest* (26). Moreover, respiratory muscle fatigue is considered present if there is a ≥10 - 15% reduction in $P_{di,tw}$ relative to baseline (15), i.e., a change that is two- to threefold the typical variation in resting $P_{di,tw}$. Based on these criteria, we are confident that the fatigue observed was physiologically meaningful. The magnitude of the post-exercise reduction in $P_{di,tw}$ was similar to that noted in able-bodied subjects following high-intensity lower-limb cycle ergometry and treadmill running (6, 18).

When interpreting our findings, there are several technical considerations that warrant discussion. Using identical stimulation procedures, we have previously obtained a within-day, between-occasion coefficient of variation for potentiated $P_{di,tw}$ of ~3% in athletes with cervical SCI (35), and we are confident that a similar level of reliability was achieved presently. It is important to note, however, that some recovery of diaphragm function likely occurred during the delay between end-exercise and the post-exercise evaluation of neuromuscular function. The delay was necessary to enable lung volumes (and muscle length) to return to baseline, but the severity of fatigue was likely underestimated as a consequence (9). A second factor that may have contributed to an underestimation of diaphragm fatigue is that supramaximal stimulation of the phrenic nerves was not achieved. Supramaximal stimulation can be difficult to achieve in subjects with short, thick necks (23), and it is plausible that supramaximal stimulation is less frequently achieved in subjects with a

large body mass due to larger respiratory muscles. Importantly, there were no substantial changes in diaphragm muscle M-wave characteristics (amplitude and duration) when baseline stimulations were compared to those delivered at 15 - 20 min and 30 - 35 min after exercise. This strongly suggests that the reductions in evoked pressure were attributable to contractile fatigue rather than transmission failure or de-recruitment of muscle fibres.

The present observation of exercise-induced diaphragm fatigue in a highly-trained athlete with low-lesion (thoracic) SCI extends our understanding of how SCI impacts on cardiorespiratory function. In the current study, ventilatory demands were substantial (peak ventilation of 150 $L \cdot min^{-1}$; 57% MVV). These findings, along with those of previous studies in which we failed to observe diaphragm fatigue during upper-body exercise at lower ventilations (35, 36), support the notion that high ventilation might be a prerequisite for exercise-induced diaphragm fatigue. However, since upper-body tasks place additional mechanical loads on the thoracic complex for stiffening the spine (16, 17) and maintaining torso stabilisation (10), it is possible that the fatigue observed presently was not attributable exclusively to the exercise hyperpnea. In an effort to quantify the diaphragmatic contribution to postural stability during maximal arms-only rowing, we compared the data from five respiratory cycles immediately before the cessation of the time-trial (peak-exercise) to five respiratory cycles performed immediately after the abrupt cessation of exercise when ventilation was still high (2). When the high thoracic loads of exercise were relinquished, there was an abrupt increase in tidal volume (2.7 to 3.1 L), suggesting that arm-exercise imposes a degree of constraint on the ribcage. Despite an increase in ventilation immediately post-exercise (13.6 to 18.7 L), there was a substantial and instantaneous decrease in inspiratory transdiaphragmatic pressure and diaphragm EMG (see Fig. 3). Furthermore, *during* exercise, the ratio between inspiratory transdiaphragmatic pressure and diaphragm EMG (i.e., diaphragm neuromuscular efficiency) tended to decrease as the time-trial progressed (see Fig. 2). Thus, it appears that a large portion of diaphragm activity during the time-trial was a result of postural and/or locomotor tasks.

The participant exhibited a breath-to-stroke ratio of 1:1 during the initial 400 m, after which he assumed a ratio of 2:1 with a concomitant reduction in tidal volume (2.8 to 1.9 L; see Fig. 1). Able-bodied rowers entrain ventilation at integer multiples of stroke rate (1:1, 2:1 or 3:1), with a 2:1

entrainment pattern most common during a 2000 m time-trial (30), and this appears congruent with our observations for arms-only rowing. The sharp and dramatic increase in respiratory frequency at 400 m is in accordance with previous studies noting that ventilation during upper-body exercise is achieved primarily via increases in respiratory frequency (34). During lower-body exercise, tidal volume tends to plateau at 50 - 60% of vital capacity (4), and yet, our participant exhibited an increase in respiratory frequency at 400 m when tidal volume was only 38% of vital capacity. It is likely that the two-fold increase in respiratory frequency resulted from a necessity to coordinate respiratory rhythm with the frequency of the power stroke, and these data reinforce the notion that, during rowing, ventilation is subordinate to locomotor drive (30).

The present findings have potential implications for individuals with SCI. Exercise-induced diaphragm fatigue may limit endurance performance via reflex effects of breathing on vascular function (12). A fatigue-induced metaboreflex would be expected to cause sympathoexcitation and vasoconstriction of exercising limb vasculature, thereby reducing limb blood flow and accelerating locomotor muscle fatigue. This, in turn, may limit endurance performance via alterations in effort perceptions and central motor output to the upper-limbs. A further consideration is that a reduction in neuromuscular efficiency of the diaphragm during exercise (i.e., increased ratio of ΔP_{di}-to-EMG_{di}) may impact negatively on exertional breathlessness and endurance performance. In healthy, able-bodied subjects, neuromuscular uncoupling of the diaphragm during exercise is unlikely to contribute to exertional breathlessness (1). In clinical populations with diaphragm weakness/dysfunction, however, neuromuscular uncoupling of the diaphragm has been mechanistically linked to exertional breathlessness (19). This may be pertinent for individuals with cervical or high-thoracic SCI, who often exhibit chronic symptoms resulting from pulmonary dysfunction (8). Moreover, in addition to lung volume restriction, many individuals with tetraplegia exhibit airway obstruction resulting from overriding cholinergic airway tone (29). The present findings, therefore, provide a physiological rationale for the further exploration of exercise-induced inspiratory muscle fatigue and neuromuscular uncoupling in SCI.

In conclusion, this case report provides the first objective evidence of exercise-induced diaphragm fatigue in SCI. In combination with other recent findings (35, 36), our data support the

notion that the work incurred by the diaphragm during high-intensity upper-body exercise is a significant determinant of exercise-induced diaphragm fatigue. Moreover, the decrease in diaphragm neuromuscular efficiency noted during upper-body exercise suggests that factors other than ventilation (e.g., posture and locomotion) must also contribute to the fatigue. These findings extend our understanding of the limits of physiological function in SCI and may have important implications for individuals who exercise using the upper-limbs.

Acknowledgements

Technical assistance was provided by the English Institute of Sport.

REFERENCES

1. Abdallah SJ, Chan DS, Glicksman R, Mendonca CT, Luo Y, Bourbeau J, et al. Abdominal binding improves neuromuscular efficiency of the human diaphragm during exercise. *Front Physiol* 8: 345, 2017.

2. Abraham KA, Feingold H, Fuller DD, Jenkins M, Mateika JH, Fregosi RF. Respiratory-related activation of human abdominal muscles during exercise. *J Physiol* 541(2): 653 - 663, 2002.

3. Alty SR, Man WD, Moxham J, Lee KC. *Denoising of diaphragmatic electromyogram signals for respiratory control and diagnostic purposes.* In: *Annual International Conference of the IEEE Engineering in Medicine and Biology Society*: 5560-5563, 2008.

4. Babb TG, Rodarte JR. Estimation of ventilatory capacity during submaximal exercise. *J Appl Physiol* 74(4): 2016-2022, 1993.

5. Babcock MA, Pegelow DF, Harms CA, Dempsey JA. Effects of inspiratory muscle unloading on exercise-induced diaphragm fatigue. *J Appl Physiol* 93(1): 201-6, 2002.

6. Babcock MA, Pegelow DF, Taha BH, Dempsey JA. High frequency diaphragmatic fatigue detected with paired stimuli in humans. *Med Sci Sports Exerc* 30(4): 506-511, 1998.

7. Banzett RB, Mead J, Reid MB, Topulos GP. Locomotion in men has no appreciable mechanical effect on breathing. *J Appl Physiol* 72(5): 1922–1926, 1992.

8. Cardozo C. Respiratory Complications of Spinal Cord Injury. *J Spinal Cord Med* 30(4): 307-308, 2007.

9. Carroll T, Taylor J, Gandevia S. Recovery of central and peripheral neuromuscular fatigue after exercise. *J Appl Physiol* 122(5): 1068-1076, 2017.

10. Celli B, Criner G, Rassulo J. Ventilatory muscle recruitment during unsupported arm exercise in normal participants. *J Appl Physiol* 64(5): 1936-1941, 1988.

11. Coutts KD, Rhodes EC, McKenzie DC. Maximal exercise responses of tetraplegics and paraplegics. *J Appl Physiol Respir Environ Exerc Physiol* 55(2): 479-482, 1983.

12. Dempsey JA, Amann M, Romer LM, Miller JD. Respiratory system determinants of peripheral fatigue and endurance performance. *Med Sci Sports Exerc* 40(3): 457-461, 2008.

13. Green M, Road J, Sieck G, Similowski T. Tests of respiratory muscle strength. *Am J Respir Crit Care Med* 166: 528-547, 2002.

14. Grimby G, Sóderholm B. Spirometric studies in normal subjects. *Acta Med Scand* 173(2): 199–206, 1963.

15. Guenette J, Romer L, Querido J, Chua R, Eves N, Road J. et al. Sex differences in exercise-induced diaphragmatic fatigue in endurance-trained athletes. *J Appl Physiol* 109(1): 35-46, 2010.

16. Hodges P, Cresswell A, Daggfeldt K, Thorstensson A. In vivo measurement of the effect of intra-abdominal pressure on the human spine. *J Biomech* 34(3): 347-353, 2001.

17. Hodges P, Eriksson A, Shirley D, Gandevia S. Intra-abdominal pressure increases stiffness of the lumbar spine. *J Biomech* 38(9): 1873-1880, 2005.

18. Johnson B, Babcock M, Suman O, Dempsey J. Exercise-induced diaphragmatic fatigue in healthy humans. *J Physiol* 460(1): 385-405, 1993.

19. Laghi F, Jubran A, Topeli A, Fahey P, Garrity E, Arcidi J. Effect of lung volume reduction surgery on neuromechanical coupling of the diaphragm. *Am J Resp Crit Care Med* 157(2): 475-483, 1998.

20. Li X, Rymer W, Li G, Zhou P. The effects of notch filtering on electrically evoked myoelectric signals and associated motor unit index estimates. *J Neuroeng Rehabil* 8: 64, 2011.

21. Luo YM, Moxham J, Polkey MI. Diaphragm electromyography using an oesophageal catheter: current concepts. *Clin Sci (Lond)* 115(8): 233-244, 2008.

22. Macintyre N, Crapo R, Viegi G, Johnson D, Van Der Grinten C, Brusasco V et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J* 26(4): 720-735, 2005.

23. Mador MJ, Khan S, Kufel TJ. Bilateral anterolateral magnetic stimulation of the phrenic nerves can detect diaphragmatic fatigue. *Chest* 121(2): 452-458, 2002.

24. Mahler DA, Shuhart CR, Brew E, Stukel TA. Ventilatory responses and entrainment of breathing during rowing. *Med Sci Sports Exerc* 23(2): 186–193, 1991.

25. Miller M, Hankinson J, Brusasco V, Burgos F, Casaburi R. Standardisation of spirometry. *Eur Respir Journal* 26(2): 319-338, 2005.

26. NHLBI workshop summary. Respiratory muscle fatigue. Report of the respiratory muscle fatigue workshop group. *Am Rev Respir Dis* 142(2): 474-480, 1992.

27. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. *Eur Respir J Suppl* 16(5): 5–40, 1993.

28. Scanlon P, Loring S, Pichurko B, McCool F, Slutsky A, Sarkarati M et al. Respiratory Mechanics in Acute Quadriplegia: Lung and Chest Wall Compliance and Dimensional Changes during Respiratory Maneuvers. *Am Rev Respir Dis* 139(3): 615-620, 1989.

29. Schilero GJ, Hobson JC, Singh K, Spungen AM, Bauman WA, Radulovic M. Bronchodilator effects of ipratropium bromide and albuterol sulfate among subjects with tetraplegia. *J Spinal Cord Med* 3: 1-6, 2016.

30. Siegmund GP, Edwards MR, Moore KS, Tiessen DA, Sanderson DJ, McKenzie DC. Ventilation and locomotion coupling in varsity male rowers. *J Appl Physiol* 87(1):233–242, 1999.

31. Silver J, Gibbon N. Prognosis in Tetraplegia. *BMJ* 4(5623): 79-83, 1968.

32. Steinacker JM, Both M, Whipp BJ. Pulmonary mechanics and entrainment of respiration and stroke rate during rowing. *Int J Sports Med* 14(1): S15-19, 1993.

33. Stell I, Tompkins S, Lovell A, Goldstone J, Moxham J. An in vivo comparison of a catheter mounted pressure transducer system with conventional balloon catheters. *Eur Respir J* 13(5): 1158-1163, 1999.

34. Takano N. Ventilatory responses during arm and leg exercise at varying speeds and forces in untrained female humans. *J Physiol* 468(1): 413-424, 1993.

385 35. Taylor B, West C, Romer L. No effect of arm-crank exercise on diaphragmatic fatigue or
386 ventilatory constraint in Paralympic athletes with cervical spinal cord injury. *J Appl Physiol*
387 109(2): 358-366, 2010.
388
389 36. Tiller N, Campbell I, Romer L. Influence of upper-body exercise on the fatigability of human
390 respiratory muscles. *Med Sci Sports Exerc* 49(7): 1461-1472, 2017.
391
392 37. Volianitis S, Secher N. Rowing, the ultimate challenge to the human body - implications for
393 physiological variables. *Clin Physiol Funct Imaging* 29(4): 241-244, 2009.
394
395 38. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F et al. Standardisation of the
396 measurement of lung volumes. *Eur Respir J* 26(3): 511-522, 2005.
397
398 39. Wilson S, Cooke N, Edwards R, Spiro S. Predicted normal values for maximal respiratory
399 pressures in Caucasian adults and children. *Thorax*, 39(7): 535-538, 1984.

400 **TITLES AND LEGENDS TO FIGURES**

401 **Fig. 1.** Ensemble averaged data for respiratory neuromuscular function at rest and during simulated
402 1000 m arms-only rowing time-trial. Inspiration is illustrated by negative flow. Breath-to-stroke ratio
403 was 1:1 for the initial 400 m and 2:1 thereafter. Data are expressed 'per breath' at rest, and 'per stroke'
404 during exercise whereby a given locomotor cycle was anchored such that the end of the power-stroke
405 (start of recovery phase) delineated the start and end-points of each cycle.
406
407 **Fig. 2.** Ratio of inspiratory transdiaphragmatic pressure (ΔP_{di}) to diaphragm EMG (EMG_{di}) (panel A),
408 ΔP_{di} (panel B), EMG_{di} (panel C) and minute ventilation ($\dot{V}_E$) (panel D) during a simulated 1000 m
409 arms-only rowing time-trial.
410
411 **Fig. 3.** Respiratory neuromechanical responses during five breaths at peak-exercise and five breaths
412 immediately after the abrupt cessation of exercise.

Table 1. Pulmonary function.

	Absolute	%Predicted
FEV_1, L	5.49	114
VC, L	7.57	130
FEV_1/VC, %	72.5	88
TLC, L	10.1	126
RV, L	2.71	145
FRC, L	4.68	130
IC, L	5.44	124
PEF, $L \cdot s^{-1}$	13.1	124
MVV_{12}, $L \cdot min^{-1}$	262	141
$P_{I,max}$, cmH_2O	217	192
$P_{E,max}$, cmH_2O	252	163
$Raw_{,eff}$, $kPa \cdot s^{-1}$	0.23	77
$sRaw_{,eff}$, $kPa \cdot s \cdot L^{-1}$	1.19	101
$D_{L,CO}$, $mmol \cdot min \cdot kPa^{-1}$	17.2	131

FEV_1, forced expiratory volume in one second; VC, vital capacity; TLC, total lung capacity; RV, residual volume; FRC, functional residual capacity; IC, inspiratory capacity; PEF, peak expiratory flow; MVV_{12}, maximum voluntary ventilation in 12 s; $P_{I,max}$, maximum static inspiratory pressure; $P_{E,max}$, maximum static expiratory pressure; $Raw_{,eff}$, effective airway resistance; $sRaw_{,eff}$, specific effective airway resistance; $D_{L,CO}$, diffusion capacity for carbon monoxide. Predicted values for pulmonary volumes, capacities, and flows are from Quanjer *et al*. (1993. ref 27); MVV from Grimby & Sóderholm (1963, ref 14); maximum static respiratory pressures from Wilson *et al*. (1984, ref 39).

Table 2. Mechanical and cardiorespiratory responses to a 1000 m arms-only rowing time-trial.

	REST	200 m	400 m	600 m	800 m	1000 m
Split time, s	-	44.2	47.3	47.5	47.4	47.2
Power output, W	-	293	239	234	235	240
Mean handle drive force, N	-	458	451	433	414	361
Maximum handle drive force, N	-	933	865	825	771	726
Drive handle travel, m	-	0.84	0.85	0.88	0.89	0.89
Stroke rate, $st \cdot min^{-1}$	-	45	37	37	38	44
$\dot{V}O_2$, $L \cdot min^{-1}$	0.39	2.61	3.13	3.31	3.23	3.30
$\dot{V}O_2$, $ml \cdot kg^{-1} \cdot min^{-1}$	4.3	28.9	34.6	36.6	35.7	36.5
$\dot{V}CO_2$ $L \cdot min^{-1}$	0.33	2.31	3.53	3.91	3.76	3.79
RER	0.84	0.88	1.13	1.18	1.15	1.16
$\dot{V}_E$, $L \cdot min^{-1}$	10.4	71.7	102.9	139.6	144.0	142.3
V_T, L	0.81	1.63	2.84	1.93	1.91	1.99
f_R, $br \cdot min^{-1}$	13	44	37	71	68	64
T_I, s	2.49	0.64	0.77	0.37	0.36	0.40
T_E, s	2.43	0.71	0.86	0.45	0.41	0.45
T_{TOT}, s	4.92	1.35	1.63	0.82	0.77	0.85
T_I/T_{TOT}	0.51	0.47	0.47	0.45	0.47	0.47
V_T/T_I, $L \cdot s^{-1}$	0.33	2.56	3.69	5.18	5.29	5.03
V_T/T_E, $L \cdot s^{-1}$	0.33	2.30	3.30	4.30	4.66	4.42
V_E/VO_2	26.4	27.5	32.9	42.2	44.6	43.1
V_E/VCO_2	31.3	31.0	29.2	35.7	38.3	37.6

$\dot{V}O_2$, O_2 uptake; $\dot{V}CO_2$, CO_2 output; RER, respiratory exchange ratio; $\dot{V}_E$, minute ventilation; V_T, tidal volume; f_R, respiratory frequency; T_I, inspiratory time; T_E, expiratory time; T_{TOT}, total respiratory time; $P_{ET}CO_2$, end-tidal partial pressure of CO_2; SpO_2, peripheral capillary O_2 saturation. Note: Values during exercise are mean data for the final 30 s of each 200 m split.