No effect of arm-crank exercise on diaphragmatic fatigue or ventilatory constraint in Paralympic athletes with cervical spinal cord injury

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Taylor BJ, West CR, Romer LM. No effect of arm-crank exercise on diaphragmatic fatigue or ventilatory constraint in Paralympic athletes with cervical spinal cord injury. J Appl Physiol 109: 358–366, 2010. First published May 20, 2010; doi:10.1152/japplphysiol.00227.2010.—Cervical spinal cord injury (CSCI) results in a decrease in the capacity of the lungs and chest wall for pressure, volume, and airflow generation. We asked whether such impairments might increase the potential for exercise-induced diaphragmatic fatigue and mechanical ventilatory constraint in this population. Seven Paralympic wheelchair rugby players (mean ± SD peak oxygen uptake = 16.9 ± 4.9 ml·kg⁻¹·min⁻¹) with traumatic CSCI (C5–C7) performed arm-crank exercise to the limit of tolerance at 90% of their predetermined peak work rate. Diaphragm function was assessed before and 15 and 30 min after exercise by measuring the twitch transdiaphragmatic pressure (Pdi,tw) response to bilateral anterolateral magnetic stimulation of the phrenic nerves. Ventilatory constraint was assessed by measuring the tidal flow volume responses to exercise in relation to the maximal flow volume envelope. Pdi,tw was not different from baseline at any time after exercise (unopposed responses to exercise in relation to the maximal flow volume envelope. Pdi,tw). However, only two subjects showed expiratory flow limitation, and operating lung volumes and an eightfold increase in the work of breathing were observed. In conclusion, highly trained athletes with CSCI do not develop exercise-induced diaphragmatic fatigue and rarely reach mechanical ventilatory constraint.

neuromuscular disorder; respiratory mechanics; respiratory muscles; quadriplegia; upper body exercise

CERVICAL SPINAL CORD INJURY (CSCI) causes reductions in baseline pulmonary function, including combined restrictive and obstructive ventilatory impairment (9, 45). These reductions in pulmonary function are thought to be related to weakened respiratory muscles (34), reduced lung and chest wall compliance (44), reduced expanding effect of the diaphragm at the zone of apposition due to elevated abdominal compliance (16), and unopposed parasympathetic activity secondary to loss of sympathetic innervation to the lungs (41). The consequent decrease in ventilatory capacity is accompanied by an increase in demand on the respiratory muscles for pressure generation due to chest wall distortion (54), increased airway resistance (41), and elevated tonic activity of the diaphragm (47). During exercise, the increase in ventilatory requirements would exacerbate the potential imbalance between ventilatory capacity and respiratory muscle demand.

High respiratory muscle demand in the face of reduced ventilatory capacity may predispose people with CSCI to exercise-induced inspiratory muscle fatigue. Alternatively, the low active muscle mass in people with CSCI may not impose enough stress on the respiratory system to elicit inspiratory muscle fatigue. In the only study to investigate this postulate, Sinderby et al. (48) found a significant reduction in the center frequency of the diaphragm electromyogram (EMG) power spectrum during maximal arm-crank exercise in recreationally active subjects with chronic CSCI (C5–C7). However, shifts in the EMG power spectrum are related more to disturbances in action potential transmission than to a fatiguing process at the sarcomere level, and are rapidly reversed with rest even though the muscle may remain in a fatigued state (51). A more objective index of diaphragmatic fatigue is the twitch transdiaphragmatic pressure (Pdi,tw) response to phrenic nerve stimulation (51). In healthy able-bodied subjects, this technique has been used to show that sustained high-intensity whole body exercise (85–95% maximum oxygen uptake) elicits diaphragmatic fatigue, as demonstrated by 15–30% reductions in Pdi,tw within 15 min after exercise that did not return to preexercise baseline values until at least 1–2 h into recovery (43).

The aim of the present study, therefore, was to measure Pdi,tw before and after sustained high-intensity upper body exercise in highly-trained athletes with CSCI to determine whether exercise-induced diaphragmatic fatigue occurs in this population. An additional aim was to evaluate the mechanical properties of the respiratory system at rest and during upper body exercise, and to determine the degree to which tidal breaths approach the mechanical limits for generating respiratory volume and flow.

MATERIALS AND METHODS

Subjects

Seven subjects with traumatic CSCI (C5–C7) volunteered to participate in the study. The subjects were members of the 2008 Great Britain wheelchair rugby squad who competed at the Beijing Paralympic Games. Other sporting activities included swimming and resistance training, with a total weekly activity of 11 ± 3 h. None of the subjects smoked, had a history of cardiopulmonary disease, or was taking medications known to influence the exercise response. Each subject provided written informed consent to the procedures as approved by Brunel University’s research ethics committee. Before the study, the subjects were classified by an independent observer using the International Standards for Neurological Classification of Spinal Cord Injury (2) and the International Wheelchair Rugby Federation classification system (15). Subject characteristics are shown in Table 1.

Experimental Protocol

The procedures were conducted during two laboratory visits separated by at least 48 h but no longer than 1 wk. At the initial visit, preliminary measures of pulmonary function and peak responses to incremental arm-crank exercise (5 W every 2 min starting at
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Lesion Level</th>
<th>AIS Grade</th>
<th>IWRF Classification</th>
<th>Time After Injury, yr</th>
<th>Age, yr</th>
<th>Stature, m</th>
<th>Body Mass, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>C6-7</td>
<td>B</td>
<td>2.0</td>
<td>15</td>
<td>36.3</td>
<td>1.78</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>C5-7</td>
<td>A</td>
<td>1.0</td>
<td>14</td>
<td>36.5</td>
<td>1.68</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>C5-6</td>
<td>A</td>
<td>1.0</td>
<td>12</td>
<td>23.5</td>
<td>1.62</td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>C6-7</td>
<td>A</td>
<td>1.5</td>
<td>12</td>
<td>35.3</td>
<td>1.85</td>
<td>72</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>C6-7</td>
<td>A</td>
<td>2.5</td>
<td>10 ± 5</td>
<td>30.9 ± 5.1</td>
<td>1.79 ± 0.12</td>
<td>70 ± 14</td>
</tr>
</tbody>
</table>

Values are for individual subjects and group mean ± SD. C, cervical spine; AIS, American Spinal Injury Association Impairment Scale (A = least function to E = normal); IWRF, International Wheelchair Rugby Federation classification (0.5 = least function to 3.5 = most function).

Additional detail on the methods of measurement is provided in an online supplement.

Preliminary measures. Pulmonary volumes, capacities, and flows were assessed by spirometry (Oxycon Pro; Jaeger, Höchberg, Germany) and body plethysmography (Zan 530; Oberhutla, Würzburg, Germany) in accordance with ATS/ERS guidelines (37, 55) modified for use in SCI (29). Maximal inspiratory pressure (Pimax) and maximal expiratory pressure (Pmin) were assessed at functional residual capacity (FRC) with a handheld mouth pressure meter (MicroRPM, Micro Medical, Chatham, UK) in accordance with ATS/ERS recommendations (18).

Phrenic nerve stimulation. Gastric pressure (Pga) and esophageal pressure (Pes) were measured with two latex balloon catheters (no. 47-9005; Ackrad Labs, Cooper Surgical, Berlin, Germany) that were passed nasally into the stomach and lower one-third of the esophagus, respectively, after local anesthesia was administered to the nasal mucosa. Each balloon was filled with 1 ml of air, and the esophageal catheter was placed with the use of the “occlusion” technique (7). The catheters were coupled to two differential pressure transducers (DP45; Validyne, Northridge, CA; range ±229 cmH2O) that were calibrated across the physiological range with an electromanometer (model C9553; JMW, Harlow, UK). The pressure signals were amplified (model 1902; Cambridge Electronic Design, Cambridge, UK), digitized at sampling rates of 150 Hz with an analog-to-digital converter (micro 1401 mkII; Cambridge Electronic Design), and acquired with computer software (Spike 2 version 7; Cambridge Electronic Design). Transdiaphragmatic pressure (Pdi) was obtained online by subtracting Peso from Pga.

Magnetic stimuli were delivered simultaneously to the phrenic nerve roots via two 45-mm figure-of-eight coils, each of which was powered by a magnetic stimulator (Magstim 200; Magstim, Whitland, UK). A digital output from the analog-to-digital converter was used to simultaneously discharge both stimulators. The coils were positioned on either side of the neck at the posterior border of the sternocleido-mastoid muscle at the level of the cricoid cartilage (32, 38). The area of stimulation that evoked the greatest Pdi,tw was located, marked, and used for all subsequent stimulations. Three single twitches were obtained at 50%, 60%, 70%, 80%, 85%, 90%, 95%, and 100% of each stimulator’s maximum power output to determine whether depolarization of the phrenic nerves was maximal. All subsequent twitches were performed at 100% of maximum power output.

Diaphragm function was assessed before and at 15 and 30 min after constant-load exercise. Four stimulations were delivered to the phrenic nerves at the end of a tidal expiration against an occluded airway such that four unpotenti ated Pdi,tw values were obtained. The potentiated twitch is a more sensitive measure of diaphragmatic fatigue than the unpotentiated twitch, particularly when the degree of fatigue is small (31). Therefore, Pdi,tw was measured between 5 and 10 s after a 5-s maximal Mueller maneuver; this procedure was repeated six times such that six potentiated Pdi,tw values were obtained. The first two measurements were discarded because the degree of potentiation was slightly smaller after the first and, to a lesser extent, after the second inspiratory effort. Baseline-to-peak amplitude of the pressure responses (Pdi,tw, Pga,tw, Pes,tw) was analyzed for each stimulation. Maximal rate of pressure development (MRP), maximal relaxation rate (MRR), contraction time (CT), and one-half relaxation time (RT0.5) were analyzed for each of the Pdi traces. Voluntary activation of the diaphragm during the maximal inspiratory efforts was assessed with twitch interpolation (35). Within-day between-trial reliability of inspiratory muscle function was assessed in five of the subjects before and after 30 min of quiet breathing.

Exercise responses. The exercise tests were conducted on an arm ergometer (Angio; Lode, Groningen, The Netherlands). The ergometer was set so that the scapula-humeral joint and the distal end of the crank pedal were aligned. When necessary the hands were fixed to the handle with a gripping aid (Active Hands, Woodley, UK). The tests were terminated when the subject was unable to maintain cadence >50 rpm despite verbal encouragement. During the incremental test, ventilatory and pulmonary gas exchange measurements were collected with an online system (Oxycon Pro). During the constant-load test, ventilatory parameters were measured with an ultrasonic flowmeter (Birmingham Flowmetrics, Birmingham, UK). Other measurements included arterial oxygen saturation (Sao2) by earlobe pulse oximetry (Biox 3700e; Ohmeda, BOC Healthcare, Louisville, CO); cardiac frequency (f) by telemetry (Polar Vantage NV; Polar Electro Oy, Kempele, Finland); earlobe capillary blood lactate concentration ([Lact, b]) by an enzymatic method (Biosen C line; EKF Diagnostik, Barleben, Germany); and perceived respiratory (dyspnea) and arm discomfort with Borg’s modified CR10 scale (8).
inspiratory flow as described previously (36). The diaphragm and esophageal pressure-time products (PTP_d and PTP_e) were obtained by multiplying the area subtended by each pressure trace by f_R (30). The PTP_d-to-PTP_e ratio was calculated to evaluate the pressure contribution of inspiratory muscles of the chest wall and neck relative to that of the diaphragm (30).

The degree of ventilatory constraint was estimated by measuring changes in operating lung volumes, expiratory flow limitation, inspiratory flow reserve, and end-inspiratory lung volume (EILV) and end-expiratory lung volume (EELV) were estimated by measuring inspiratory capacity (IC) relative to forced vital capacity (FVC) at baseline, at the first minute of exercise, every 2 min thereafter, and at the end of exercise. EELV and EILV were expressed as ratios of expiratory reserve and inspiratory reserve volume relative to FVC (ERV/FVC, IRV/FVC). To verify that a maximal inspiratory effort was made during each IC maneuver, we confirmed that peak inspiratory P_e values matched those obtained at baseline (baseline = −39.5 ± 14.2 cmH2O, first minute = −37.3 ± 10.8 cmH2O; final minute = −38.8 ± 9.6 cmH2O; P > 0.05). The degree of expiratory flow limitation was defined as the percentage of the spontaneous flow-volume loop that met or exceeded the boundary of the expiratory portion of the maximal volitional flow-volume loop obtained either immediately before exercise or <2 min after exercise cessation. Inspiratory flow reserve was determined by how close the inspiratory portion of the tidal breath came to the inspiratory flows generated during the maximal volitional flow-volume maneuver. V_ECAP was estimated based on the maximal available inspiratory and expiratory airflow over the range of the actual tidal breath placed at the estimated EELV.

Statistical Analyses

Changes in respiratory function and exercise responses were analyzed by repeated-measures ANOVA with pairwise comparisons and Bonferroni correction. Reliability was assessed with the coefficient of variation (CV). Relationships between selected variables were calculated with the Pearson correlation coefficient. Statistical significance was set at P < 0.05. Data are expressed as mean ± SD. Statistical analyses were performed with SPSS 15.0 for Windows (Chicago, IL).

### RESULTS

**Preliminary Measurements**

Group mean values for pulmonary function and peak responses to incremental exercise are shown in Tables 2 and 3, respectively. The data suggest a mild restrictive ventilatory impairment, with reduced TLC, IC, and vital capacity (VC) relative to predicted normal values. Forced expiratory volume in 1 s (FEV_1), peak expiratory flow (PEF), and maximal voluntary ventilation (MVV) were reduced, consistent with a decrease in flow reserve. Inspiratory muscle strength (P_max) was not different from normal values, but expiratory muscle strength (P_max) was lower than predicted. During incremental exercise there was a progressive metabolic acidosis as exercise intensity increased (peak [L_c]_b = 4.1 mmol/l) and an acute

Table 3. Peak responses to incremental arm-crank exercise

<table>
<thead>
<tr>
<th></th>
<th>Absolute</th>
<th>% Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work rate, W</td>
<td>59 ± 19</td>
<td></td>
</tr>
<tr>
<td>VO_2, l/min</td>
<td>1.20 ± 0.45</td>
<td></td>
</tr>
<tr>
<td>VCO_2, l/min</td>
<td>1.32 ± 0.47</td>
<td></td>
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<tr>
<td>RER</td>
<td>1.10 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>V̇E/ḞE</td>
<td>52.4 ± 25.7</td>
<td></td>
</tr>
<tr>
<td>V̇E/VO_2</td>
<td>40.3 ± 4.9</td>
<td></td>
</tr>
<tr>
<td>V̇E/VCO_2</td>
<td>38.4 ± 7.3</td>
<td></td>
</tr>
<tr>
<td>PETCO_2, mmHg</td>
<td>27.4 ± 4.9</td>
<td></td>
</tr>
<tr>
<td>SpO_2, %</td>
<td>95 ± 4</td>
<td></td>
</tr>
<tr>
<td>f_R, beats/min</td>
<td>115 ± 14</td>
<td></td>
</tr>
<tr>
<td>V̇E/f_R, ml/beat</td>
<td>10.2 ± 3.0</td>
<td></td>
</tr>
<tr>
<td>[L_c]_b, mmol/l</td>
<td>4.1 ± 1.0</td>
<td></td>
</tr>
<tr>
<td>RPE (dyspnea)</td>
<td>6.2 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>RPE (arm discomfort)</td>
<td>8.1 ± 1.1</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD for 7 subjects. VO_2, oxygen uptake; VCO_2, carbon dioxide output; RER, respiratory exchange ratio; V̇E, minute ventilation; PETCO_2, end-tidal PCO_2; SpO_2, arterial oxygen saturation by pulse oximetry; f_R, cardiac frequency; [L_c]_b, blood lactate concentration; RPE, ratings of perceived exertion. 

Fig. 1. Individual subject (dashed lines) and group mean (solid line) twitch transdiaphragmatic pressure (P_d,tw) in response to magnetic stimulation of increasing stimulation intensity. The incremental protocol was applied after 10 min of rest and 20 min before the baseline assessment of diaphragm function.

*P < 0.05, group means significantly different from those at 100% of stimulator power output. Note that individual subject and group mean P_d,tw leveled off at ~85% of stimulation power output.
hyperventilation as indicated by respiratory exchange ratio (RER) > 1, elevated ventilatory equivalents, and a decline in end-tidal \( \text{P}_{\text{CO}_2} \) (Pet\text{CO}_2).

### Supramaximal Stimulation and Reliability

Individual subject and group mean \( P_{\text{d,tw}} \) values leveled off at \( \sim 85\% \) of stimulator maximum power output (Fig. 1). A similar plateau was observed for \( P_{\text{g,tw}} \) and \( P_{\text{g,tw}} \) (data not shown). There were no systematic differences in respiratory muscle function before versus after 30 min of quiet breathing. The within-subject between-trial CV for \( P_{\text{d,tw}} \) (unpotentiated and potentiated) was 4.5\% and 2.9\%, respectively. The CV for the component parts of \( P_{\text{d,tw}} \) (unpotentiated and potentiated) was 7.2\% and 3.1\% for \( P_{\text{g,tw}} \) and 6.4\% and 3.0\% for \( P_{\text{g,tw}} \), respectively. The CV for the within-twitch measures of diaphragm function and the pressure responses to maximal inspiratory efforts were \( \leq 9\% \) and \( \leq 3\% \), respectively. Additional reliability data are shown in the online supplement (Supplemental Table S1).

### Exercise Effects on Diaphragm Function

Group mean and individual subject ensemble-averaged tracings of \( P_{\text{d,tw}} \) (unpotentiated) at baseline and 15 min after exercise are shown in Fig. 2. \( P_{\text{d,tw}} \) (unpotentiated and potentiated) was not significantly different from baseline at any time after exercise (\( P = 0.16 \) and 0.27, respectively; see also Table 4). The gastric and esophageal components of the twitch were also not different from baseline at any time after exercise. At 15 min after exercise, the change in unpotentiated and potentiated \( P_{\text{d,tw}} \) was 4.2 \( \pm 11.0\% \) (range -8.0 to 23.4\%) and

![Fig. 2.](image-url)
due to a decrease in both inspiratory time (TI) and expiratory VT. As exercise continued, further increases in V˙E were achieved by an increase in fR only. The increase in fR was elevated through to the final minute, reaching 93 ± 5% of peak. No subject experienced dyspnea or arm discomfort at baseline. At end of exercise, five of the seven subjects rated arm discomfort greater than dyspnea, one rated dyspnea greater than arm discomfort, and one rated arm discomfort and dyspnea equally. However, none of the subjects rated arm discomfort or dyspnea as “maximal” at end of exercise.

Respiratory mechanics and ventilatory constraint. The aforementioned increase in V˙E was accompanied by an almost eightfold increase in Wb per minute. Cdyn,L fell progressively from baseline to the final minute of exercise. There was a small but nonsignificant increase in Rt from baseline through to the final minute of exercise, despite a fourfold increase in peak inspiratory flow. Group mean values for PTP at baseline and during exercise are shown in Fig. 3. PTPdi increased sharply to 2.7 times baseline during exercise are shown in Table 5. The subjects exercised for 8.3 ± 6.7 min at a work rate of 53 ± 18 W.

Cardiorespiratory and perceptual. Ventilation increased throughout exercise, reaching 93 ± 16% of peak V˙E (36 ± 15% of MVV) The increase in V˙E from baseline to the first minute of exercise was achieved through increases in fR and V˙T. As exercise continued, further increases in V˙E were achieved by an increase in fR only. The increase in fR was due to a decrease in both inspiratory time (TI) and expiratory time (TE). There was no difference in SPO2 between baseline and the final minute of exercise. There was a sharp rise in fR from baseline to the first minute of exercise and a slight (albeit nonsignificant) increase through to the final minute of exercise, reaching 95 ± 5% of peak. No subject experienced dyspnea or arm discomfort at baseline. At end of exercise, five of the seven subjects rated arm discomfort greater than dyspnea, one rated dyspnea greater than arm discomfort, and one rated arm discomfort and dyspnea equally. However, none of the subjects rated arm discomfort or dyspnea as “maximal” at end of exercise.

During constant-load exercise are shown in Table 5. The subjects exercised for 8.3 ± 6.7 min at a work rate of 53 ± 18 W.

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Responses to constant-load exercise are shown in Table 5. The subjects exercised for 8.3 ± 6.7 min at a work rate of 53 ± 18 W.

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Responses to constant-load exercise are shown in Table 5. The subjects exercised for 8.3 ± 6.7 min at a work rate of 53 ± 18 W.
Inspiratory flow reserve, % capacity 14 ± 7 43 ± 12† 44 ± 17* 74 ± 8*

Inspiratory flow reserve, % VC 35 ± 8 59 ± 10† 59 ± 8† 47 ± 32*

2.9 cmH\textsubscript{2}O; 1st minute: −5.7 ± 0.9 cmH\textsubscript{2}O; final minute: −6.2 ± 1.4 cmH\textsubscript{2}O. The inspiratory flow generated during the final minute of exercise reached 44% of the maximal available inspiratory flow, and occurred at a lung volume higher than at baseline. The V\textsubscript{E}-to-V\textsubscript{E\textsubscript{CAP}} ratio showed a significantly reduced breathing reserve from baseline (12%) through to the final minute of exercise (47%).

**DISCUSSION**

The main findings of this study were that well-trained subjects with CSCI do not exhibit objective evidence of exercise-induced diaphragmatic fatigue, and rarely reach mechanical ventilatory constraint during sustained high-intensity arm-crank exercise. Using bilateral anterolateral magnetic stimulation of the phrenic nerves, we found that the P\textsubscript{dLw} (unpotentiated and potentiated) and within-twitch contractile properties were not different from baseline at any time after exercise. We also showed, using twitch interpolation, that exercise did not elicit a central decrease in phrenic motor output. Volitional measures of diaphragm function (P\textsubscript{di,max}) and global inspiratory muscle function (P\textsubscript{max}) were also not different from baseline after exercise. During exercise there was a sudden and sustained rise in operating lung volumes. However, there was limited evidence of expiratory flow limitation and substantial capacity to increase both flow and volume. Collectively, these findings indicate that the respiratory system has adequate reserve to cope with the demands placed on it during exercise in well-trained subjects with CSCI.

We believe that our findings in athletes with CSCI may also extend to those who are less fit but otherwise healthy. Our reasoning is that fit, well-motivated subjects might be able to exercise more intensely, and hence it might be easier to elicit respiratory limitation in this population. Even though our subjects provided maximal effort during the exercise tests, diaphragmatic fatigue was not elicited and ventilatory constraint was rare. Thus we believe it unlikely that the respiratory system would be limiting when patients with chronic CSCI perform their normal activities of daily living or undergo exercise training in a clinical setting.

**Technical Considerations**

Our study is the first to use objective measures to evaluate diaphragmatic fatigue in subjects with SCI. In the only other study to investigate whether exercise elicits diaphragmatic fatigue in this population, Sinderby et al. (48) found a reduction in the center frequency of the diaphragm EMG power spectrum during maximal arm cranking in recreationally active subjects with low CSCI (C\textsubscript{5–2}). However, the etiology of power spectral shifts with fatigue is controversial, and hence the utility of diaphragm EMG as an index of fatigue has been questioned (see also introduction). Thus we believe that our study using the bilateral phrenic nerve stimulation technique offers the first objective evidence that high-intensity arm-crank exercise does not elicit diaphragmatic fatigue in subjects with chronic CSCI.

For phrenic nerve stimulation to provide a valid measure of diaphragmatic fatigue it is important to control for several potential sources of error including intensity stimulation (13), lung volume (49), abdominal compliance (23), and twitch potentiation (31). We attempted to control for each of these potential sources of error (see also MATERIALS AND METHODS). First, we demonstrated that nerve stimulation was supramaximal, as shown by the leveling off of P\textsubscript{dLw} at 85% of maximum stimulator power output in all seven subjects (see Fig. 1).
that diaphragm pressure production (PTPdi) increased from baseline to the 1st minute of exercise and leveled off thereafter, while total inspiratory muscle force output (PTPdi/PTPes) decreased as exercise progressed.

Fig. 3. Diaphragm pressure-time product (PTPdi; A), esophageal pressure-time product (PTPes; A), and PTPdi-to-PTPes ratio (B) at baseline and during arm-crank exercise. *P < 0.05, **P < 0.01, significantly different from baseline; †P < 0.05, ††P < 0.01, significantly different from 1st minute. Note that diaphragm pressure production (PTPdi) increased from baseline to the 1st minute of exercise and leveled off thereafter, while total inspiratory muscle pressure production (PTPes) increased through to the final minute of exercise. Thus the relative contribution of the diaphragm to the total inspiratory muscle force output (PTPdi/PTPes) decreased as exercise progressed.

Second, stimulations were initiated at the same lung volume and diaphragm length, as judged by nonsignificant changes across time in end-expiratory Pes and end-expiratory Pdi, respectively. Third, the relative contribution of Pga to baseline Pdi,tw was reduced in line with the expected increase in abdominal compliance in CSCI (16), but the Pga-to-Pes ratio for Pdi,tw was unchanged after exercise. Finally, we obtained potentiated twitch responses, because the former is a more sensitive measure of diaphragmatic fatigue when the degree of fatigue is small (31).

Our interpretation that exercise does not elicit diaphragmatic fatigue in subjects with CSCI is dependent on our ability to detect relatively small systematic within-day between-trial changes in inspiratory muscle function in this population. When a subgroup of the subjects was tested before and after 30 min of quiet breathing there were no systematic differences in the measurements of inspiratory muscle function, and reliability coefficients were similar to those reported for able-bodied subjects. The CV for unpotentiated Pdi,tw (4.5%), for example, was comparable to the value of 5.1% reported for able-bodied subjects (32). Thus we believe that our methods were sufficiently sensitive and reproducible to detect exercise-induced diaphragmatic fatigue if it had occurred.

Capacity vs. Demand

To determine why exercise-induced diaphragmatic fatigue did not occur it is necessary to consider the balance between respiratory capacity and demand. Group mean values for TLC, IC, and VC were significantly lower than predicted for healthy able-bodied subjects (40). These findings suggest a primarily restrictive impairment, which, along with some mild reductions in expiratory flows (PEF and FEV1), would be expected to reduce the available ventilatory capacity. Maximal inspiratory pressures were relatively well preserved, but maximal expiratory pressures were significantly lower than able-bodied predicted values (10). That FRC was in the normal range implies that the low expiratory pressures were attributable to muscle weakness, secondary to loss of expiratory muscle innervation, rather than to alterations in the operating length of expiratory muscles. The trend toward a decrease in ERV is also consistent with expiratory muscle weakness. Interestingly, the observed values for pulmonary function and maximal respiratory pressures were higher than have been reported for untrained subjects with chronic CSCI (21, 34). While these findings may imply an effect of exercise training on respiratory function, it is unclear whether the hyperpnea of upper body exercise is sufficiently stressful to elicit an adaptive response (46).

Peak VO2 (~17 ml·kg\(^{-1}\)·min\(^{-1}\)) was not significantly different from the value of 19 ml·kg\(^{-1}\)·min\(^{-1}\) predicted for healthy able-bodied subjects (52) but ~25% higher than has been reported for untrained subjects with chronic CSCI (21). The Ve at the end of constant-load exercise (48 l/min) was also higher than typically reported for trained subjects with CSCI (21). Despite these metabolic and ventilatory demands, there was only limited evidence of expiratory flow limitation (see Fig. 4). An intersection of the spontaneous tidal flow-volume loop with the maximal flow-volume envelope was apparent in only two subjects: one during the first and final minutes of exercise and one during the final minute only. Nevertheless, all seven subjects showed a sudden and sustained rise in EELV (i.e., dynamic hyperinflation). This response is in contrast to that in healthy able-bodied subjects for lower body exercise, during which EELV initially decreases and only rises above

Fig. 4. Group mean ensemble-averaged tracings of tidal flow-volume loops plotted within the largest maximal flow-volume loop obtained before and <2 min after exercise at rest and during the 1st and final minutes of exercise. Note that despite limited evidence of expiratory flow limitation, end-expiratory lung volume (EELV) and end-inspiratory lung volume (EILV) increased early during exercise and remained elevated through to the final minute of exercise.
relaxation volume when the ventilatory demand is high and expiratory flow limitation is >50% of \( V_T \) (24, 27). During lower body exercise the expiratory muscles are mainly responsible for the control of EELV (24). During upper body arm-crank exercise, however, the expiratory muscles are also involved in torso stabilization, which suggests that the contribution of these muscles to the regulation of EELV may be reduced (1, 11). This effect would be particularly marked in our subjects with CSCI because of the expiratory muscle weakness that was apparent at baseline (\( P_{E\text{max}} \sim 72\% \) of normal).

An increase in EELV during exercise would be expected to impair the capacity of the diaphragm to generate inspiratory pressure through an inability to operate at or near the optimal length for force generation (14). This decrease in mechanical advantage has been hypothesized to increase the relative pressure contribution of the inspiratory rib cage and neck muscles over that of the diaphragm (57). In the present study, \( P_{TPi}\) leveled off as exercise continued despite further time-dependent increases in \( V_T \) and \( P_{TPe} \) (see Fig. 3). The reason for the leveling off of \( P_{TPi} \) is unclear. Previous studies have suggested that the onset of diaphragmatic fatigue during the early period of high-intensity exercise reflexively inhibits further diaphragmatic recruitment and triggers the recruitment of additional inspiratory muscles (5, 26, 33). That diaphragmatic fatigue was not detected in the present study, however, suggests that the recruitment of additional inspiratory muscles in subjects with CSCI is more likely influenced by reflexes from the chest and/or abdominal wall. Regardless of the mechanism, force development by the diaphragm is an important determinant of exercise-induced diaphragmatic fatigue (4, 6). Thus the apparent sparing of the diaphragm may be one reason why fatigue was not observed in the present study.

An increase in EELV (and EILV) not only decreases the capacity of the diaphragm but also increases the elastic load presented to the inspiratory muscles, as shown by the fall in \( C_{dyn,\text{L}} \) from baseline to end of exercise. Nevertheless, the \( W_b \) at end of exercise (42 J/min; see Table 5) was substantially lower than typically reported for fit able-bodied subjects during lower body exercise (e.g., 510 J/min; Ref. 27). A rise in EELV also increases inspiratory load through the loss of elastic energy in the abdominal wall after expiration that normally aids subsequent inspiration (19). However, an increase in EELV with exercise may spare the negative consequences of expiratory muscle pressure production, which include an increase in the work and oxygen cost of breathing, a decrease in venous return and cardiac output, an increase in dyspnea, and a reduction in exercise tolerance (53).

In addition to the mechanical determinants of diaphragmatic fatigue, exercise may contribute indirectly by compromising blood flow to the diaphragm. In healthy able-bodied subjects performing whole body exercise at high (but not low) relative work rates, the competition between diaphragm and limb locomotor muscles for their share of the available cardiac output may promote inadequate \( O_2 \) transport (22, 56), thereby increasing the likelihood of diaphragmatic fatigue (6). In people with CSCI, however, many of the muscles involved in upper body exercise are paralyzed or weakened such that the exercise intensity may not be high enough to be limited by \( O_2 \) transport (25). In the present study, the \( O_2 \) pulse (\( VO_2/F_C \)) increased throughout exercise and peaked at values similar to those that have been observed in able-bodied subjects during upper body exercise (50). Thus exercise limitation in our subjects with CSCI was more likely due to low active muscle mass than to reduced cardiac output and impaired regional blood flow. Further evidence that exercise was limited peripherally rather than centrally stems from the relatively low blood lactate concentration at peak exercise (~4 mM). Moreover, perceptual responses at end of exercise were submaximal, and most subjects rated arm discomfort over dyspnea as the reason for stopping.

The maximum mechanical capacity of the respiratory muscles to produce flow and volume substantially exceeded the ventilatory requirements during maximal arm-crank exercise. Inspiratory tidal flow was only 44% of the maximal available inspiratory flow, and the ventilatory response to exercise was considerably less than the estimated ventilatory capacity (48 and 103 l/min, respectively) such that the \( V_{E\text{tot}}/V_{E\text{CAP}} \) ratio was only 47%. Importantly, the degree of ventilatory constraint did not appear to influence the adequacy of alveolar ventilation or systemic oxygen delivery. During incremental exercise, hyperventilation occurred with a progressive fall in \( P_{ETCO_2} \). Peak ventilatory equivalents for \( O_2 \) and \( CO_2 \) were elevated and similar to values in able-bodied subjects (50) and fit subjects with CSCI (12). Furthermore, there was no evidence of arterial hypoxemia, as confirmed by \( SpO_2 \); values never decreasing more than 3–4% below baseline (3).

In summary, highly trained athletes with CSCI do not exhibit objective evidence of diaphragmatic fatigue in response to sustained high-intensity arm-crank exercise and rarely reach mechanical ventilatory constraint. These findings suggest that the respiratory system has ample capacity to cope with the demands placed on it during upper body exercise in this population.

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DISCLOSURES

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