Phrenic motoneuron firing rates before, during, and after prolonged inspiratory resistive loading

J. D. ROAD AND A. M. CAIRNS
Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada V5Z 3J5

Road, J. D., and A. M. Cairns. Phrenic motoneuron firing rates before, during, and after prolonged inspiratory resistive loading. J. Appl. Physiol. 83(3): 776–783, 1997.—Phrenic motoneuron firing rates during brief inspiratory resistive loading (IRL) are high, and nearly all the motoneurons are recruited. Diaphragmatic fatigue has been difficult to demonstrate during IRL. Furthermore, evidence from studies in limb muscles has shown variable motoneuron responses to prolonged high-intensity loads. We studied phrenic motoneuron firing rates before, during, and after prolonged IRL in anesthetized rabbits. Of 117 phrenic axons, only 2 axons were not recruited; 41 axons were silent during unloaded breathing but were recruited at higher loads. Silent axons showed a more rapid increase in firing rate as the load increased. Phrenic motoneuron firing rates increased throughout the period of loading, whereas airway pressure swings did not. After prolonged IRL, higher motoneuron firing rates were needed during brief loads to produce the same airway pressure. No evidence of a decline in motoneuron firing rates was seen at any point. We conclude that the respiratory muscles can be shown to demonstrate physiological responses consistent with fatigue during prolonged IRL, and activation rates are high and remain so throughout this prolonged loading.

Methods:

A detailed description of methods has been given previously (29). New Zealand White rabbits of either sex, weighing 3–4 kg, were anesthetized with ketamine (35 mg/kg im) and xylazine (7 mg/kg im) and maintained with one-third to one-half of the initial dose every 30 min. The trachea was cannulated and connected to a pneumotachograph (Fleisch no. 00) and differential pressure transducer (Validyne MP45) for measuring inspiratory flow. A miniature two-way nonrebreathing valve (model 2814, Hans Rudolph) divided inspiratory and expiratory flows. A side port in the endotracheal tube was connected to a second Validyne pressure transducer for measurement of airway opening pressure (Pao). Dividing Pao by inspiratory flow gave inspiratory resistance that could be adjusted from near zero up to 4 cmH2O·mL−1·s by means of a needle valve at the inspiratory port of the nonrebreathing valve. Expiration was unimpeded.

A laparotomy was performed, and two stainless steel hooks were placed in the anterior margin of the left costal diaphragm for recording electromyograms (EMGs), which were amplified ×1,000, filtered 10–10,000 Hz, rectified, integrated (τ = 100 ms), and recorded on a chart recorder (Gould, Cleveland, OH). The laparotomy incision was closed in two layers. Arterial blood-gas samples were taken from a carotid catheter.

In 17 experiments, balloon catheters were placed in the esophagus and under the diaphragm to obtain transdiaphragmatic pressure (Pdi). However, during severe prolonged loads, measurement of Pdi was often distorted by esophageal contractions. Pao measured in the tracheal tube did not suffer from this problem. Plots of Pao vs. Pdi showed a linear relation that was unchanged after inspiratory loading. When Pdi was not distorted by swallowing, it gave the same qualitative...
results as Pao, although Pao was ~5 cmH2O less than Pdi for unloaded breathing and exceeded Pdi by 5–10 cmH2O during severe loads (see Fig. 5B). In 15 experiments, Pao alone was measured. Results in this paper refer to Pao, but Pdi showed very similar behavior when it was recorded.

Activity in axons of phrenic motoneurons was recorded from small filaments pulled from the C3 branch of the phrenic nerve and placed on a platinum wire under mineral oil. Unitary recordings were obtained as judged from the uniform size of action potentials, the absence of interspike intervals <5 ms, and the all-or-none response to electrical stimulation of the distal nerve. Electrical stimulation also detected “silent” axons, those with no spike activity during unloaded breathing. When a filament contained two intact axons, one active and the other silent, the unloaded firing rate of the active axon and the inspiratory pressure at recruitment of the silent axon were recorded. Otherwise, observations were made only on filaments containing a single intact axon.

Unit action potentials were discriminated with the trigger circuit of an oscilloscope (model 1421, Gould), and a synchronized pulse of fixed size was integrated (t = 50 ms) to give a signal proportional to motoneuron firing rate. This rate signal was calibrated with trains of pulses at known rates, while the interpulse interval on the oscilloscope was observed, and was linear between 10 and 100 Hz.

IRL. IRL were either brief or prolonged. Brief loads at resistances of 0.5 to 4.0 cmH2O·m·1·s−1 were applied for <1 min (20–40 breaths) to determine the peak firing rates of phrenic motoneurons at inspiratory peak pressures up to 50 cmH2O. Six loads of different intensity were placed in random order, with 5 min recovery between each, to span the range of phrenic motoneuron firing rates and interspike intervals. Prolonged loads were resistances of 1–2 cmH2O·m·1·s−1. These loads produced peak Pao (Pao peak) of 40–50 cmH2O and were applied for 20–30 min. During unloaded breathing, the inspired gas was pure O2, to keep arterial PO2 >70 cmH2O, a level of effort that was usually avoided to reduce the risk of hypoxic or mechanical injury. The two experiments were pooled below with new results from 15 rabbits in which Pao alone was measured, with two exceptions: 1) Table 1 is from the 15 present experiments only and 2) results on instantaneous firing rates and interspike intervals are reported only for the present experiments in which a computer was used to acquire the data.

RESULTS

Brief loads. A total of 117 phrenic axons were classified into three major categories: those that showed spike activity during unloaded breathing, those that became active only during IRL, and those that showed no activity even at the highest inspiratory pressures. Only two axons fell into the third category. Of the remainder, 74 (63%) were active during unloaded breathing, and 41 (35%) were initially silent but began to fire as peak inspiratory pressure increased under the stimulus of an inspiratory load.

As inspiratory effort increased under loading, the inspiratory pressure at which an initially silent motoneuron first showed activity was termed the threshold for recruitment of that motoneuron. This recruitment pressure varied from axon to axon but was a fixed and reproducible value for any given axon. Motoneurons recruited at low or moderate pressures were more common than those recruited at high pressures (Fig. 1). Of 41 silent phrenic motoneurons, 27 (66%) were recruited at a Pao peak of <30 cmH2O, which is about half the maximal Pao in these rabbits. One phrenic motoneuron was not recruited until Pao peak rose to >70 cmH2O, a level of effort that was usually avoided to reduce the risk of hypoxic or mechanical injury. The two axons categorized above as unresponsive were tested only to a Pao peak of 50 cmH2O and therefore may have been high-threshold phrenic motoneurons.

The time of the first spike activity was measured with reference to the raw diaphragm EMGdi. Early onset of activity was by far the most common finding. Onset times were measured for 64 motoneurons active during unloaded breathing. Of these, 56 (88%) began to fire within the first 20% of the inspiratory time (Ti). Two motoneurons that were silent for some unloaded breaths but active for others showed late onset times, from 30 to 55% of Ti. For motoneurons only recruited during brief IRL

Table 1. Phrenic motoneuron firing rates vs. Pao during brief IRL

<table>
<thead>
<tr>
<th>Pao, cmH2O</th>
<th>Activity During Unloaded Breathing</th>
<th>Yes</th>
<th>n</th>
<th>No</th>
<th>n</th>
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</thead>
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<tr>
<td>Noload</td>
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<td>34</td>
<td>26</td>
<td>30±6.7</td>
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<tr>
<td>10</td>
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<td>26</td>
<td>45±6.0</td>
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</tr>
<tr>
<td>20</td>
<td>39±7.7</td>
<td>27</td>
<td>45±6.0</td>
<td>6</td>
<td></td>
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<tr>
<td>30</td>
<td>44±9.2</td>
<td>25</td>
<td>56±4.4</td>
<td>7</td>
<td></td>
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<tr>
<td>40</td>
<td>47±11</td>
<td>23</td>
<td>60±8.4</td>
<td>8</td>
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</tr>
</tbody>
</table>

Values are means ± SD given in spikes/s; n, no. of motoneurons. Pao, peak pressure at airway opening; IRL, inspiratory resistive loading. Data are from 15 experiments (see Previously reported results).
during loads, onset time at recruitment was often not captured because the computer data acquisition was intermittent, but onset was clearly delayed relative to that of units active during unloaded breathing, sometimes to 70% of TI. Onset for initially silent units became earlier as inspiratory effort increased during a load.

In Table 1, firing rates are averaged for 10-cmH$_2$O steps in Pao_{peak}. Units that were active when no load was applied are compared with those that became active only during loading. For each unit, rates at peak pressures from 1 cmH$_2$O below to 1 cmH$_2$O above each step were averaged to obtain the firing rate at that level of pressure. The number of units contributing to each average differs, as indicated in Table 1, because some units were lost before they were fully tested and some initially silent units showed no activity until 40 or 50 cmH$_2$O. When inspiratory loads were applied, firing rates rose. There is a difference between the active and silent motoneurons. Motoneurons that are active during unloaded breathing show a linear increase in rate of 3–6 spikes/s for each 10-cmH$_2$O increase in airway pressure. Motoneurons that are silent during unloaded breathing show a linear increase in rate of 11–15 spikes·s$^{-1}$·10 cmH$_2$O$^{-1}$ of airway pressure, and they reach higher rates on average than motoneurons that are active with no load applied. When Pao_{peak} is 40 cmH$_2$O, the average firing rate among active motoneurons is 47 spikes/s compared with 60 spikes/s for initially silent motoneurons (P < 0.01, unpaired t-test).

Prolonged loads. When a well-isolated axon was found, it was tested with the range of brief loads and then a severe load of 1–2 cmH$_2$O·ml$^{-1}$·s was applied and left in place. Under this loading, Pao_{peak} rose to 40–50 cmH$_2$O within the first few minutes and remained at that level (Fig. 2B). The integrated EMGdi was 4.2 × control at 5 min of load and rose to 5.1 × control at 30 min of load (P = 0.05, Fig. 2C). Arterial Pco$_2$ (P$_{aco_2}$) progressively increased (Fig. 2A) from 60 ± 9 Torr (mean ± SD) just before IRL to 112 ± 43 Torr at 30 min. Arterial pH fell from 7.31 ± 0.05 to 7.09 ± 0.11. PaO$_2$ depended on the effectiveness of the supplementation with pure O$_2$ but remained above 80 Torr (155 ± 62 Torr just before and 164 ± 105 Torr at 30 min of IRL).

Peak firing rate and Pao_{peak} for 15–20 breaths were recorded at 5, 10, 20, and 30 min of loaded breathing. These samples showed that firing rate increased compared with the control rate found previously for the same Pao_{peak} (Fig. 3). This effect was normalized for each motoneuron by dividing its firing rate at 5, 10, 20, and 30 min of load by its control rate for the same Pao_{peak} (obtained from brief loads). There was a progressive increase in this ratio up to the end of the 30-min loaded interval, when rates averaged 15% greater than control (Fig. 4, P < 0.001, one-way repeated-measures ANOVA). Thirteen motoneurons were followed for 30 min of severe IRL. Of these, 10 had been active and three had been silent during unloaded breathing. For the three silent units, the increase in firing rate at 30 min of severe IRL was 7, 14, and 35%, within the same range, 6–39%, found for the 10 active units. Of the 13 phrenic motoneurons followed for 30 min of loaded
breathing, none showed a decrease in firing rate relative to $P_{ao_{peak}}$.

Motoneurons were retested with brief loads after an unloaded recovery interval of 20 min. Although $P_{a_{CO2}}$ returned to control levels (see Fig. 2), an elevation in firing rate with respect to inspiratory pressure often persisted (Fig. 5A). This residual change in rate vs. pressure was largest at the highest pressures. In contrast, the relation between $P_{ao_{peak}}$ and peak transdiaphragmatic pressure was unchanged after the 30-min load (Fig. 5B), which indicates that $P_{ao}$ and $P_{di}$ are not differently affected by IRL and that, therefore, no important information was lost in those experiments that recorded only $P_{ao}$.

In 14 rabbits, it was possible to test a phrenic motoneuron with brief loads both before and after severe IRL lasting 20–35 min. In 10 (7 active, 3 silent) of the 14 cases, firing rates remained significantly elevated after recovery from the load, as shown in Fig. 5A (one-way ANOVA of mean rate, $P < 0.01$). In the other four cases (2 active, 2 silent) the rate vs. pressure relation obtained after the prolonged load was close to the control, even though all four motoneurons had shown higher rates than control, by 6–10%, at the end of the prolonged load. No phrenic motoneuron fired at less than the control rate for a given $P_{ao_{peak}}$ when retested with brief loads after a prolonged severe load. There was no detectable change in the recruitment threshold of silent motoneurons after prolonged IRL.

In eight experiments, reliable $P_{di}$ swings were recorded before and after 30 min of severe IRL. Of these, four motoneurons were the active type, and after the prolonged load they all showed elevated firing rates for brief loads very similar to the data for $P_{ao_{peak}}$ shown in Fig. 5A. The other four silent units had $P_{di}$ recruitment thresholds from 15 to 30 cmH$_2$O. Firing rates in two of these were elevated after prolonged IRL, whereas in the other two there was no change in peak firing rate vs. peak $P_{di}$ when retested with brief loads.

Firing patterns. Typical firing patterns are shown in Fig. 6A for active and silent motoneurons. For motoneurons active during unloaded breathing, there was usu-
Fig. 6. A: firing rate profiles of 2 phrenic motoneurons during inspiration. First motoneuron was active during unloaded breathing (x) and showed increased activity during brief IRL (Pao 45 cmH₂O, ▲). Each plot superimposes 6 breaths. Arrow, short initial spike interval when drive is high. Second motoneuron (□) was initially silent, was recruited at a Pao of 17 cmH₂O, and activity shown here is from 3 breaths during brief IRL (Pao 45 cmH₂O). Instantaneous rate is reciprocal of interspike interval. B: same motoneurons as in 6A. Peak firing rate vs. Pao peak as inspiratory effort increases during brief loads. Motoneuron that was active during unloaded breathing (▲) shows more gradual increase in rate than does motoneuron recruited at 17 cmH₂O (□).

Previous results (29) have been confirmed and extended. Nearly all phrenic motoneurons are recruited by IRL. There are phrenic motoneurons that are not active during unloaded quiet breathing but do fire at high rates during loaded breathing. These initially silent motoneurons fire relatively late in the inspiratory phase, at up to 70% of Ti when they are first recruited, but they then fire at progressively earlier times as inspiratory effort increases. Firing rates in initially silent motoneurons increase more rapidly than in motoneurons that are active during unloaded breathing. Motoneurons that are active during unloaded breathing fire early, usually within the first 20% of Ti. Among these active motoneurons, we did not find a bimodal distribution of onset times as has been described in the cat (9, 16). Approximately two-thirds of phrenic motor units were active during quiet unloaded breathing. Both onset times and the proportion of motor units active during unloaded breathing could have been affected by two potentially depressant influences on respiratory drive that were present in our experiments: anesthesia and laparotomy (28). However, although these effects could be significant during unloaded breathing, they did not prevent a high level of recruitment or high firing rates during IRL.

Phrenic motoneuron firing rates, along with our previous results, now strongly suggest that during IRL peripheral fatigue occurs, but drive to the diaphragm remains high. A similar finding has been reported for decerebrate cats, in which integrated phrenic activity and phrenic motoneuron firing rates remained high even when Pdi declined during severe IRL (17). In these cats, there was greater phrenic motor activity during IRL than during CO₂ rebreathing, when compared at equal values of end-tidal CO₂, suggesting to Iscoe (17) that there was a source of respiratory drive in addition to high PaCO₂, for example from afferents in the lungs or respiratory muscles. A twitch-interpolation study also suggests that diaphragm contractions are submaximal during CO₂ rebreathing (8).

In the present study, phrenic motoneuron firing rates increased relative to Pao peak and to Pdi during prolonged severe IRL (Fig. 3). An increase in firing rate during prolonged IRL, without the increase in pressure found during a prior brief IRL, implies that force-generating capacity has been lost. Further evidence of fatigue was seen when phrenic motoneurons were retested with brief loads after 20 min of recovery from a
prolonged load (Fig. 4). Increases in firing rate relative to \( P_{\text{ao}} \text{peak} \) often remained at 20 min postload, at a time when blood-gas values had returned to baseline. Increases were greatest at the highest inspiratory pressures, as would be expected, since fatigue should be greatest at high force levels where large fatiguable motor units make their greatest contribution to overall force generation (12).

Increased motoneuron firing rates were not the only indication of diaphragmatic fatigue during prolonged severe IRL. Although statistical significance was borderline (\( P = 0.05 \)), the peak of the integrated EMGdi tended to increase (by 20% between 5 and 30 min of IRL), whereas the average \( P_{\text{ao}} \text{peak} \) showed no change (see Fig 2). Osborne and Road (26) and Watchko et al. (30) also reported an increase in the EMGdi during IRL, although again the null hypothesis could not be rejected. Motoneuron firing rates may be less subject to variable recording conditions than EMGs, and this may explain their more definitive demonstration of fatigue. Evidence for a similar degree of peripheral diaphragmatic fatigue has also been found in force-frequency curves from rabbits and piglets undergoing IRL (23, 31), but electrical stimulation may differ in some ways from natural drive, as discussed below.

In studying phrenic motoneuron firing rates and \( P_{\text{ao}} \text{peak} \), we are looking at both a whole muscle and at individual motor units within it. When firing rates rise without a corresponding rise in \( P_{\text{ao}} \text{peak} \) or \( P_{\text{di}} \), we can assume that fatigue has occurred in some muscle fibers, but not necessarily those innervated by the motoneuron we are recording from, because increases in central drive probably affect all motoneurons in the motor pool. Intracellular recordings from phrenic motoneurons indicate that they all receive a similar profile of excitation from descending inputs during inspiration (1). If so, an increase in central drive would be felt by all phrenic motoneurons and would promote increased firing rates in all, both those innervating fatigue-resistant as well as fatigable motor units.

Previous studies of motor-unit firing rates during sustained contractions have usually not differentiated between motor-unit types. There is some evidence that during sustained maximal voluntary contractions rate declines are more pronounced in high-threshold than in low-threshold motor units (15). This is consistent with our observation of larger rate increases in high-threshold (silent) phrenic motoneurons during brief IRL (Table 1) because rate decreases should therefore be greater when drive is decreased. However, during prolonged IRL, we saw only rate increases. Our sample is too small to determine whether high- and low-threshold phrenic motor units differed in the size of the increase. Variability in respiratory muscle endurance or in anesthetic level from rabbit to rabbit could obscure any such difference between motor unit types.

Although the diaphragm can be fatigued by IRL, the extent of the fatigue seems minor compared with the loss of force seen when motor units are driven with electrical stimulation. When Fournier and Sieck (12) used electrical stimulation to test diaphragmatic motor units in the cat by using the Burke protocol (6), the fast-twitch motor units lost more than one-half of their force-generating capacity in 2 min. These fast-twitch units are the large fibers that should contribute much of the force in the diaphragm during severe IRL. We have shown in rabbits undergoing IRL that most phrenic motoneurons, and in particular the high-threshold motoneurons presumed to be fatiguable, fire at rates that exceed the Burke protocol (40 Hz). How can IRL be tolerated for hours (26) when electrical stimulation leads to substantial loss of force in minutes?

A variety of mechanisms probably promotes better endurance under natural drive than occurs during electrical stimulation. These mechanisms may include adjustments in local blood flow and energy metabolism, recruitment of accessory muscles, and changes in the precontraction length of the diaphragm. The parasternal intercostals assist inspiration, and EMG recordings from these muscles indicate a degree and time-course of activation that closely resembles that of the diaphragm (25). Abdominal muscles recruited during IRL facilitate expiration, which can stretch the diaphragm to a portion of its length-tension curve more favorable for force production. A recent study found that this last factor can be large enough to mask substantial fatigue (23). In piglets, diaphragm force-frequency curves taken after 1 h of IRL were not different from baseline until they were corrected for decreased end-expiratory lung volume. After correction, diaphragmatic force generation was found to have dropped by 20% at all stimulation frequencies. In the present study, we saw evidence of fatigue without taking end-expiratory lung volume into account, but, if such a factor were present during prolonged but not brief IRL, it would cause phrenic motoneuron firing rates to underestimate the true extent of diaphragmatic fatigue. This may account in part for the discrepancy between the well-maintained inspiratory pressures seen during IRL and the rapid fatigue produced by electrical stimulation.

Another difference between IRL and the Burke protocol (6) is the artificial regularity of electrical stimulation. When trains of constant-rate electric shocks are altered to include two short initial intervals, fatiguability is reduced significantly (2). Normal variability in motoneuron interspike intervals may enhance the fatiguability of muscles operating under natural drive. During sustained voluntary contractions, motor-unit spike intervals become less regular, even when the average rate is steady (24), and it is possible that this is an adaptive response that helps to mitigate fatigue. Interval statistics were not a part of our study, but variability was examined in one phrenic motoneuron. The mean ± SD values of the spike interval were derived during the middle one-third of inspiration, when rate had reached a plateau. During severe IRL, the coefficient of variation of the spike interval increased from 0.11 to 0.13, even though the mean interval declined from 15 to 13 ms. For comparison, the coefficient of variation of spike intervals increased from 0.34 to 0.38 at a mean interval of 100 ms in human...
masseter motor units during 15 min of steady activation, a change that was found to be statistically significant (24). The functional significance and cause of changes in discharge regularity are unsettled issues.

The functional significance of very short initial intervals, or doublets, is also problematic. Doublets can increase force in motor units (2, 7), but they were not seen in our high-threshold phrenic motoneurons, the force production and fatigability of which are likely to be especially important during IRL, and they were rare in lower threshold phrenic motoneurons and did not become more common when respiratory drive increased. When muscle has been previously activated at high rates, as is likely to be the case in IRL, the force-enhancing effect of doublets is greatly diminished (7).

As illustrated by doublets, even though all motoneurons in the phrenic pool may receive a common descending input, they can respond to it differently. Only some motoneurons are active during unloaded breathing, and there is a substantial range of recruitment thresholds among those that fire only at higher levels of inspiratory effort. In the phrenic motor nucleus, recruitment thresholds have been correlated with input resistance and cell size, showing that small cells are depolarized further by a given synaptic current (19), as the Size Principle predicts. Our results show that, once they are above the recruitment threshold, phrenic motoneurons continue to differ in their response to increasing drive, but in a fashion not explained by the Size Principle.

Phrenic motoneurons that were silent during unloaded breathing showed steeper rate increases, once recruited, both during an individual inspiration and during progressive IRL, than did motoneurons that were active during quiet breathing (see Fig. 6). This finding may be analogous to previous reports that late-onset phrenic motoneurons show greater increases in rate than early-onset motoneurons (16, 18).

Above the depolarization threshold for spike generation, the firing rate of a motoneuron may be strongly dependent on the duration of its afterhyperpolarization (20). Empirically, afterhyperpolarizations are found to vary with motoneuron type in the way needed to explain higher rates in fast vs. slow motoneurons at equal levels of drive (15, 19). Theoretically, there is a need for some mechanism that can allow fast-twitch motor units to be driven at the high rates required for fusion of their brief twitches without at the same time overstimulating smaller slower motor units.

The activation of a motor pool clearly shows adaptation to the requirements of a muscle, although in some cases the mechanisms are not fully understood. During sustained maximal contractions, motor unit firing rates decline as the muscle fatigues and the twitch durations of muscle fibers increase (4). It has been hypothesized that this decline in firing rate, which can still elicit the maximum force available because of the slower relaxation rate and greater fusion of twitches in fatigued muscle, may be a beneficial economy, a concept known as muscle wisdom (22). Alternatively, there would be nothing to be gained from increased firing rates because, during a maximal contraction, there would be no reserve capacity for generating force. The case is different for submaximal contractions, in which there would be reserve force capacity, at least at the outset, so that fatigue could potentially be countered by increasing the activation of the muscle.

In our rabbits, diaphragmatic contractions were probably submaximal during the 30-min IRL protocol. Peak Pao values of 40–50 cmH2O were generated, whereas in the same preparation higher pressures can be maintained longer before respiratory failure occurs (26), and phrenic stimulation at 80 Hz produces a Pdi of 66 ± 7 cmH2O (31), which suggests that our prolonged IRL elicited 60–70% of maximal Pdi.

Previous single-unit work on fatiguing muscle has been done in awake human subjects. In these studies, there are declines in motor unit firing rates during sustained maximal contractions (14, 22), but for submaximal contractions a variety of results have been reported: increases, decreases, and no change in rate (3, 13, 24). Several factors might contribute to differences between our work and these studies. 1) The muscles studied in humans [for example, quadriceps (3), biceps brachii (13), and masseter (24)] have a variety of functions quite different from those of the diaphragm. 2) In anesthetized rabbits, a central pattern generator rather than conscious effort provides the drive to motoneurons. 3) In the case of the diaphragm, any monitoring of the force being produced is internal, whereas human subjects are usually given an external source of feedback to follow. 4) Diaphragm contractions are intermittent and last only seconds, whereas in human studies a constant force is maintained for many minutes. 5) The diaphragm must work continuously and may be better adapted for sustained activity than most skeletal muscles. 6) The diaphragm has comparatively few muscle spindles, and its sensory response to loading probably differs from that of other skeletal muscles.

We saw only increases in diaphragm motor unit firing rates during prolonged severe IRL. During loaded breathing, the need to maintain force and limit increases in PCO2 may override whatever mechanism leads to lower firing rates in some other situations.

Address for reprint requests: J. D. Road, Div. of Respiratory Medicine, Vancouver Hospital and Health Sciences Centre, 2775 Heather St., Vancouver, BC, Canada V5Z 3J5.

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