Pattern of expiratory muscle activation during lower thoracic spinal cord stimulation

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DiMarco, A. F., J. R. Romaniuk, K. E. Kowalski, and G. Supinski. Pattern of expiratory muscle activation during lower thoracic spinal cord stimulation. J. Appl. Physiol. 86(6): 1881–1889, 1999.—Large positive airway pressures (Paws) can be generated by lower thoracic spinal cord stimulation (SCS), which may be a useful method of restoring cough in spinal cord-injured patients. Optimal electrode placement, however, requires an assessment of the pattern of current spread during SCS. Studies were performed in anesthetized dogs to assess the pattern of expiratory muscle recruitment during SCS applied at different spinal cord levels. A multicontact stimulating electrode was positioned over the surface of the lower thoracic and upper lumbar spinal cord. Recording electromyographic electrodes were placed at several locations in the abdominal and internal intercostal muscles. SCS was applied at each lead, in separate trials, with single shocks of 0.2-ms duration. The intensity of stimulation was adjusted to determine the threshold for development of the compound action potential at each electrode lead. The values of current threshold for activation of each muscle formed parabolas with minimum values at specific spinal root levels. The slopes of the parabolas were relatively steep, indicating that the threshold for muscle activation increases rapidly at more cephalad and caudal sites. These results were compared with the effectiveness of SCS (50 Hz; train duration, 1–2 s) at different spinal cord levels to produce changes in Paw. Stimulation at the T9 and T10 spinal cord level resulted in the largest positive Paws with a single lead. At these sites, threshold values for activation of the internal intercostal (7–11th interspaces) upper portions of external oblique, rectus abdominis, and transversus abdominis were near their minimum. Threshold values for activation of the caudal portions of the abdominal muscles were high (>50 mA). Our results indicate that 1) activation of the more cephalad portions of the abdominal muscles is more important than activation of caudal regions in the generation of positive Paws and 2) it is not possible to achieve complete activation of the expiratory muscles with a single electrode lead by using modest current levels. In support of this latter conclusion, a single lead system resulted in more uniform expiratory muscle activation and significantly greater changes in Paw.

Electrical stimulation; cough; respiratory muscles

METHODS

Experiments were performed on six mongrel dogs weighing 15–21 kg. Each animal was initially anesthetized with pentobarbital sodium (25 mg) given intravenously. Anesthetic level was monitored by the corneal reflex (maintained intact) and response to noxious stimuli (suppressed completely) and was maintained with supplemental doses of pentobarbital sodium (1–2 mg/kg), as needed. A cuffed endotracheal tube was sutured directly into the trachea in the midcervical region. A catheter was placed in the femoral artery to monitor blood pressure (model P23, Statham) and to analyze blood gases (arterial blood-gas analyzer, ABL-30, Radiometer, Copenhagen, Denmark). A catheter was also placed in the femoral vein.
to administer fluids and supplemental anesthesia. Body temperature was maintained with a heating blanket (Harvard Apparatus, Cambridge, MA) at 38 ± 0.5°C. End-tidal Pco₂ was monitored at the tracheal opening with a rapidly responding CO₂ analyzer (O.R. SARAcap, PPG Industries, Lenexa, KS). Tracheal pressure was measured with a differential pressure transducer (model MP-45, Validyne, Northridge, CA).

In all animals, a laminectomy was performed at the L₃ or L₄ level through which a multicontact disk electrode (15 leads) was inserted onto the epidural surface of the spinal cord and advanced cephalad to the region of the T₇ spinal cord segment. The electrode leads were 4 mm in diameter embedded in polyurethane plastic and positioned 15 mm apart. Precise position of each electrode lead in relation to specific spinal roots was determined in each animal postmortem. Subsequently, the skin over the lower thorax and abdominal wall was reflected to expose the intercostal muscles of the lower rib cage and abdominal muscles to implant the recording electrodes. Because of the large size of the expiratory muscles and the fact that they are innervated by multiple nerve roots, multiple electrodes were placed in each of these muscles to assess the regional activation of the various portions of these muscles. Electromyographic electrodes (bipolar stainless steel wires) were implanted into the external oblique muscles in the midaxillary line at four levels (Fig. 1): 1) superior (within 1–2 cm of muscle origin), 2) upper (3 cm above the costal margin), 3) middle (just below the costal margin), and 4) lower (just above the iliac crest); in the transversus abdominis muscles in the anterior axillary line and in the rectus abdominis muscles just lateral to the midline at three levels corresponding to the upper, middle, and lower portion of the external oblique; in the upper and lower portions of the internal oblique; in the internal intercostal muscles (7th, 9th, and 11th interspaces); in the external intercostal muscles (6th, 8th, and 10th interspaces); and in the parasternal intercostal muscles (5th and 6th interspaces). Electrical stimulation was applied with a Grass stimulator (model S88, Grass Instruments, Quincy, MA) and UltraStim stimulator (model 650–01, Neuromedics) at each electrode lead, in separate trials with single shocks (0.2-ms duration). Recordings of muscle CAP were amplified (model BMI-830, Charles Ward Enterprises) and recorded on an oscilloscope (model 5223, Tektronics) as shown in Fig. 2. The delay between the electrical stimulus and electromyographic response and the threshold for development of the muscle CAP were measured over a wide range of stimulus amplitude (0–50 mA).

Protocol. Initially, the effectiveness of SCS to produce changes in airway pressure was assessed over different regions of the lower thoracic and upper lumbar spinal cord. This was accomplished by monitoring airway pressure after the application of electrical stimulation (50 Hz, 1- to 2-s train duration) at each electrode lead in separate trials, under conditions of hyperventilation-induced apnea and airway occlusion. Subsequently, the effects of single-shock SCS on direct motor root activation were assessed. Single shocks

Fig. 1. Electromyographic electrodes were implanted into superior, upper, middle, and lower portions of abdominal muscles as shown. See text for further explanation.
(0.2-ms duration) were applied with progressively increasing current to determine the threshold for development of the muscle CAP at each stimulating electrode lead and for each recording site. The CAPs were identified as waves of short latency (2–3 ms) and relatively high amplitude (>0.1 mV; Fig. 2).

Data analysis. The electrical current values representing the threshold for activation of each of the respiratory muscles were plotted against stimulus site, identified by spinal cord root level. Threshold values (means ± SE) for stimulation at specific spinal root levels were obtained by interpolation of plots from individual animals. Pressure generation between stimulus sites was compared utilizing analysis of variance and post hoc Newman-Keuls tests. A P value < 0.05 was taken as indicating statistical significance.

RESULTS

Effects of electrical stimulation (50 Hz) on pressure generation. As in previous studies, we found that the optimum site for pressure generation was in the region of the T9-T10 spinal root level (5). The effects of varying stimulus amplitude on airway pressure generation during electrical stimulation (50 Hz) applied in this region are shown in Fig. 3. Increases in stimulus intensity resulted in a steep rise in pressure generation between 0 and 15 mA followed by a much more gradual rise. The application of electrical current >15 mA, however, resulted in visible contraction of the pelvic and leg muscles. In this model, therefore, 15 mA was taken as the optimum stimulus current because it resulted in near-maximal changes in airway pressure (88% of maximum) without causing significant activation of the nonexpiratory musculature. The effects of electrical stimulation at various spinal cord levels on airway pressure generation utilizing 15 mA (50 Hz) is shown for one animal in Fig. 4. Maximum changes in airway pressure occurred with stimulation at the T9 and T10 level and decreased at stimulus sites caudal and cephalad to this region. Mean changes in airway pressure over a broad area of the lower thoracic and upper lumbar spinal cord are shown in Fig 5. Pressure generation was maximal when stimulation was applied in the vicinity of the T9 and T10 spinal root levels (57 ± 3 and 54 ± 1 cmH2O, respectively) and declined progressively at more caudal spinal cord regions. For example, stimulation at the T11, T13, and L-2 spinal cord levels resulted in airway pressures of 43 ± 2, 22 ± 3, and 12 ± 3 cmH2O, respectively (P < 0.01 for each compared with T9).

Effects of single-shock stimulation on muscle activation. The effect of electrical stimulation applied at various spinal cord levels on the thresholds for direct activation of upper, middle, and lower portions of the transversus abdominis muscle is shown for a representative animal in Fig. 6. The lowest threshold value for activation of each portion of this muscle occurred during stimulation in the vicinity of the T9-T11, T11-T12, and L1-L3 spinal cord levels, respectively. The threshold for activation of each muscle increased from these optimal sites to form parabolas. Single-shock electrical stimulation applied at the T10 level, for example, results in activation of the upper and middle portions of the transversus abdominis muscle with current levels of <10 mA. However, much higher current levels (>50 mA) are required to activate the lower portion of this muscle. Comparable curves for the internal intercostal muscles of the seventh, ninth and eleventh intercostal space are shown in Fig. 7. These curves are less steep compared with those of the transversus muscle.

These curves were best fit to the following parabolic function: y = ax² + bx + c, where y is the stimulus current (mA), a is a coefficient related to the steepness of the curve, b is a parameter related to electrode position, c is the minimum threshold current, and x is the distance from the stimulating electrode (cm). Mean values of the coefficient a for the various expiratory muscles and intercostal muscles of the lower rib cage are shown in Table 1. Values for the intercostal and rectus abdominis muscles were significantly lower.

Fig. 3. Relationship between stimulus amplitude (0–50 mA) and airway pressure (Paw) generation (expressed as percentage of maximum). There was a steep rise in pressure generation between 0 and 15 mA followed by a more gradual rise between 15 and 50 mA.
than those of the oblique and transversus muscles (P < 0.01), suggesting that the intercostal and rectus muscles are activated with relatively low current levels over a broader area of spinal cord.

The mean threshold values for development of the CAPs of the various respiratory muscles during SCS over a wide range of stimulus sites are shown in Fig. 8. An overview of these data reveals that, with the use of modest current levels (15 mA), it is not possible to activate all portions of the abdominal muscles and the lower intercostal muscles with a single electrode lead. With this current level, stimulation applied between T7 and T12 with a single electrode lead fails to reach threshold values for activation of the lower portions of the abdominal muscles. Conversely, application of current between T12 and L2 fails to reach threshold values for the lower intercostal and upper portions of the abdominal muscles.

Stimulation applied to the T10 spinal cord level (1 of the areas that results in the greatest changes in airway pressure) with 15 mA activates the lower intercostal muscles (8th intercostal and more caudal) and the upper and middle portions of the remaining abdominal muscles. Stimulation is near threshold for activation of the superior portion of the external oblique and intercostal of the seventh interspace and well below threshold for activation of the lower portion of the abdominal muscles. Stimulation applied at the T9 level (which results in similar changes in airway pressure) not only activates the upper portion of the abdominal muscles and lower intercostal muscles but also causes more complete activation of the superior portion of the external oblique and muscles of the seventh intercostal space. Stimulation is below threshold for activation of the middle portion of the abdominal muscles.

Stimulation applied more cephalad at the T7 level, which effects significantly less changes in airway pressure (P < 0.01), results in activation of the lower parasternal intercostal muscles and external intercostals in the fifth and sixth interspaces (muscles that have a proven inspiratory action) but does not activate the upper portion of the transversus muscle.

Stimulation at the T12 (P < 0.01) and more caudal levels also effects significantly smaller changes in airway pressure. Stimulation at T12 does not result in activation of the intercostal muscles of the seventh and eighth interspace or the superior portion of the external oblique and is near threshold values for activation of the upper abdominal muscles. Stimulation at the T13 level (which results in even lower pressure generation) results in activation of the middle and lower portion of
the abdominal muscles but not the upper portions of
the abdominal muscles or the lower intercostal muscles.
Stimulation more caudally in the lumbar region (which
results in progressively lower pressure generation)
results in no stimulation of the upper abdominal or
lower intercostal muscles and much less (L1) and
eventually no significant (L2) activation of the middle
portion of the abdominal muscles. Airway pressure
generation resulting from stimulation at the L2 spinal
cord level essentially reflects activation of the lower
abdominal muscles alone without significant contribu-
tion from other respiratory muscles. It should also be
noted that stimulation at L1 and L2 resulted in signifi-
cant contraction of the pelvic and lower extremity
muscles.

Because it was not possible to activate all of the
abdominal musculature with a single electrode lead, we
also evaluated the effects of a two-electrode system
during high-frequency stimulation (50 Hz, 1- to 2-s
train duration). The effects of airway pressure genera-
tion with a two-electrode lead system is shown in Fig. 9.
The simultaneous application of 15 mA with two sepa-
rate electrode leads positioned adjacent to one another
at T9 and T10 levels was employed as a partial control.
This arrangement resulted in only a modest increase in
pressure from 59 ± 3 to 68 ± 3 cmH2O (not significant).
This finding is not surprising because two electrodes
positioned in close proximity would be expected to
result in only a very modest increase in current spread,
resulting in more complete activation of the middle
portion of the abdominal muscles but not activation of
the lower portion of the abdominal muscles. However,
combined stimulation at T9 and T13 results in activation
of the lower intercostal muscles and virtually all por-
tions of the abdominal muscles (Fig. 10) and more marked
increase in pressure generation of 80 ± 3 cmH2O (P <
0.05 compared with a single electrode at T9).

DISCUSSION

Maximal cough efforts in humans are characterized
by the generation of large changes in airway pressure
in the range of +200 cmH2O or greater (13, 17).
Presumably, the generation of pressures of this magni-
itude requires the coordinated contraction of all the
major expiratory muscles, including the internal inter-
-costals, abdominal muscles, and triangularis sterni.
The internal intercostal muscles of the upper rib cage
(T1-T6 interspaces) are very thin (18, 24) and have
negligible capacity to produce changes in airway pres-
sure (1), whereas the internal intercostal muscles of the
lower rib cage (T7-T13) are thick and actively contribute
to rib-cage motion even during resting breathing (8).
We did not assess triangularis sterni activation in this
study because this muscle is less accessible (lying
retrosternally), and its force-generating capacity is
probably small (1). Consequently, the major expiratory
muscles are innervated predominantly by the lower
thoracic and upper lumbar ventral roots (18, 19, 24).
The present investigation demonstrates that the
application of supramaximal high-frequency stimula-
tion in the vicinity of each of the lower thoracic and
upper lumbar segments results in the generation of
positive airway pressures. The results of the single-
shock studies indicate that SCS results in significant
motor root activation via direct stimulatory effects
above and below the sites of current delivery.
The limitation of current spread (21), however, prevented
activation of all motor roots innervating the expiratory
muscles with a single electrode lead with submaximal
current levels (15 mA). The use of an appropriately
placed two-electrode system, however, resulted in more
complete expiratory muscle activation and the conse-
quent development of significantly greater changes in
airway pressure during high-frequency stimulation.

Maximum pressure generation during stimulation in
the present study (80 cmH2O) was far less than that
characterized by maximum cough in humans (170–200
cmH2O) (13, 12, 17). The present studies, however,
were performed at functional residual capacity (FRC),
and recent studies in our laboratory demonstrate that
pressure generation during SCS at high lung volumes
results in approximately twice that generated at FRC
(5). Airway pressures obtained in the present study,
therefore, are in the range of what would be expected
for a cough generated at a lung volume near FRC.

Critique of method. It is important to note that the
focus of this study was limited to an examination of the
direct motor root stimulatory effects that occur via SCS.

Table 1. Coefficient a values for expiratory
and intercostal muscles of lower rib cage

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Coefficient a</th>
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<tbody>
<tr>
<td>External intercostal</td>
<td>0.20 ± 0.02*</td>
</tr>
<tr>
<td>Internal intercostal</td>
<td>0.18 ± 0.02*</td>
</tr>
<tr>
<td>Externol oblique</td>
<td>0.34 ± 0.03</td>
</tr>
<tr>
<td>Internal oblique</td>
<td>0.30 ± 0.07</td>
</tr>
<tr>
<td>Rectus abdominis</td>
<td>0.22 ± 0.04*</td>
</tr>
<tr>
<td>Transversus abdominis</td>
<td>0.47 ± 0.05</td>
</tr>
</tbody>
</table>

Values are means ± SE of 6 dogs. *Values are significantly lower than those of the oblique and transversus abdominis muscles; P <
0.05.
Fig. 8. Mean threshold values for development of muscle compound action potentials during spinal cord stimulation over a wide range of stimulus sites. PA, parasternal; Ext, external; EO, external oblique; Ext Int, external intercostal; Int Int, internal intercostal; IO, internal oblique; TA, transversus abdominis; RA, rectus abdominis. See text for further explanation.
We examined only the short-latency muscle CAP occurring in response to SCS. Although this may be the major mechanism of motor root activation, other pathways may be important, as well (20, 23). There are substantial data in both human and animal studies that various spinal cord pathways are also stimulated during SCS (16). Activation of these pathways exerts both facilitatory and inhibitory influences on various motoneuron pools. For example, previous investigators who have evaluated the effects of SCS in patients who had stimulators implanted for control of pain have demonstrated that SCS activates primary afferents in the dorsal columns, resulting in monosynaptic facilitation of some motoneurons and reduction in transmission in other reflex pathways to motoneurons (10). The potential effects of these reflex pathways on abdominal muscle activation, changes in airway pressure generation, or expiratory airflow, however, were not assessed in these studies.

Another limitation of this study is that the current required for maximum muscle activation was not assessed. Consequently, the degree to which the expiratory muscles were activated is unknown. However, it is likely that maximum muscle activation was achieved when threshold values were small (≤0.5 mA).

Comparison to previous studies. Maximum pressure generation at FRC was greater in this study compared with results obtained in our previous investigation (5). This difference is most likely attributable to the more deeply anesthetized condition of animals in our previous study. We have since determined that the response to electrical stimulation is quite sensitive to the level of pentobarbital sodium anesthesia, a more deeply anesthetized state being associated with smaller changes in airway pressure (22). In this experiment, therefore, a somewhat lighter level of anesthesia was maintained while care was taken to maintain suppression of the corneal reflex and response to noxious stimuli.

Although our studies have consistently demonstrated that maximum changes in airway pressure with a single lead occur with electrical stimulation applied at the T9-T10 spinal cord region, magnetic stimulation results in similar changes in airway and gastric pressure over a more broad area of the lower thoracic spinal cord (2, 11). Lin et al. (14, 15), for example, found that magnetic stimulation applied with coil placements over each of the spinous processes between T7 and T13, in separate trials, resulted in similar changes in mouth pressure. This difference between electrical and magnetic stimulation may be related to the large coil employed with magnetic stimulation (13.7 cm) and potentially greater area of applied stimulation.

The nonlinear relationship between the development of the muscle CAP and distance from the stimulating electrode is consistent with previous measurements of electric field distribution performed in our laboratory with upper thoracic SCS (21). Examination of intercostal muscle CAPs reveals that the thresholds for stimulation of motor nerves was lowest in those nerves in closest vicinity to the stimulating electrodes. Increasing amounts of current were required to elicit CAPs in muscles innervated by motor nerves distal to the stimulating electrode according to parabolic functions. Interestingly, the parabolic functions differed among expiratory muscles, the coefficient a (steepness of the parabola) being significantly smaller for the intercostal and rectus abdominis muscles compared with the abdominal muscles. As a result, threshold values for activation of the intercostal and rectus muscles remained low over a broader area of the spinal cord compared with that of the abdominal muscles. The steep parabolic function for the abdominal muscles also suggests that, like each intercostal nerve that inner-

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**Fig. 9.** Effect of spinal cord stimulation at T9 alone and with 2-electrode system (T9+T10 and T9+T13) on Paw generation. *Significantly greater than Paw generation at T9 alone, P < 0.01. See text for further explanation.

**Fig. 10.** Mean threshold values for development of muscle compound action potential of various respiratory muscles during stimulation at T9 spinal cord level (open bars) and T13 (solid bars). Combined stimulation at T9 and T13 results in activation of lower intercostal muscles and virtually all portions of abdominal muscles. See text for further explanation.
vates a specific interspace, each of the lower thoracic and upper lumbar motor roots innervates a specific segment of the abdominal muscles with little overlap.

Although the reasons for these differences in steepness of the parabolic function between muscles is not clear, variation in muscle fiber diameter among the expiratory muscles may be a factor. Smaller fibers would require higher stimulus current to achieve activation. To our knowledge, however, relative differences in fiber size among the different expiratory muscles have not been assessed.

Analysis of threshold stimulation data. Assuming direct motor root activation is the major mechanism of expiratory muscle activation, some inferences concerning the importance of activation of the various expiratory muscles in facilitating pressure generation can be made. Common to areas that resulted in maximum changes in airway pressure with a single electrode lead and modest current levels was activation of the upper portion of the abdominal muscles and lower intercostal muscles. Although T10 stimulation (15 mA) resulted in partial activation of the middle portion of the abdominal muscles, T9 stimulation (which resulted in similar changes in airway pressure as T10) did not. Conversely, stimulation at more caudal sites, which did not result in activation of the upper abdominal and lower intercostals, resulted in significantly smaller changes in airway pressure. Taken together, these results indicate that upper abdominal and/or lower intercostal muscle activation is much more important, in terms of achieving changes in airway pressure, compared with activation of the more caudal portions of the abdominal muscles. This conclusion is further supported by the fact that combined stimulation with electrodes at T9 and T13 results in only a 36% increase in pressure generation.

Clinical significance. The results of this study provide additional insight concerning the potential application of this technique in spinal cord-injured human patients. First, it should be noted that the anatomy of the lower thoracic and upper lumbar spinal cord is similar in humans compared with that of the canine species (18, 24). Moreover, the linear distance between T7 and L2 is virtually the same in the two species (unpublished observations). It is likely, therefore, that lower thoracic SCS may result in comparable levels of expiratory muscle activation in human patients. Although the magnitude of positive airway pressure generation necessary to produce an effective cough is unknown, the results of this study indicate that a multilead electrode system is necessary to achieve uniform expiratory muscle activation and maximal changes in airway pressure. It is conceivable that this electrode can be inserted into the epidural space through a needle under fluoroscopic guidance, as is currently done for control of pain or spasticity (9, 25).

Upper thoracic (T2 level) spinal cord stimulation is presently employed in ventilator-dependent quadriplegic patients to support artificial ventilation (6). Because of their spinal cord injury, spinal cord stimulation is well tolerated in this patient population. It is likely, therefore, that lower thoracic spinal cord stimulation will be well tolerated in spinal cord-injured patients when applied below the level of injury. Restoration of an effective cough by this means may reduce the incidence of respiratory complications and the consequent high morbidity and mortality in patients with spinal cord injury.

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