Mechanical contribution of expiratory muscles to pressure generation during spinal cord stimulation

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DiMarco, A. F., J. R. Romaniuk, K. E. Kowalski, and G. Supinski. Mechanical contribution of the expiratory muscles to pressure generation during spinal cord stimulation. J. Appl. Physiol. 87(4): 1433–1439, 1999.—Lower thoracic spinal cord stimulation (SCS) results in the generation of large positive airway pressures (Paw) and may be a useful method of restoring cough in patients with spinal cord injury. The purpose of the present study was to assess the mechanical contribution of individual respiratory muscles to pressure generation during SCS. In anesthetized dogs, SCS was applied at different spinal cord levels by using a 15-lead multicontact electrode before and after sequential ablation of the external and internal obliques, transversus abdominis (TA), rectus abdominis, and intercostal muscles. Paw was monitored after tracheal occlusion. SCS at the T9 spinal cord level resulted in maximal changes in Paw (60 ± 3 cmH2O). Section of the oblique muscles resulted in a fall in Paw to 29 ± 2 cmH2O. After subsequent section of the rectus abdominis and TA, Paw fell to 25 ± 2 and 12 ± 1 cmH2O, respectively. There was a small remaining Paw (4 ± 1 cmH2O) after section of the internal intercostal nerves. Stimulation with a two-electrode lead system (T9 + T13) resulted in significantly greater pressure generation compared with a single-electrode lead due to increased contributions from the obliques and transversus muscles. In a separate group of animals, Paw generation was monitored after section of the abdominal muscles and again after section of the external intercostal and levator costae muscles. These studies demonstrated that inspiratory intercostal muscle stimulation resulted in only a small opposing inspiratory action (≤3 cmH2O). We conclude that, during SCS, 1) contraction of the obliques and TA muscles makes the largest contribution to changes in Paw, and 2) stimulation with a two-electrode lead system results in more complete abdominal muscle activation and enhanced mechanical actions of the obliques and transversus muscles.

electrical stimulation; mechanical action; airway pressure; dogs

ELECTRICAL CURRENT applied to the epidural surface of the lower thoracic spinal cord results in the generation of large positive airway pressures (Paw) and holds promise as a method of restoring an effective cough mechanism in spinal cord-injured patients (5, 6). With a single electrode, substantial positive changes in Paw can be generated with stimulation applied over the entire lower thoracic and upper lumbar spinal cord. Maximal pressure generation, however, occurs when stimulation is applied in the vicinity of the T9–T10 spinal cord level (4–7). Although it is likely that stimulation applied in the region of the lower thoracic spinal cord results in the activation of several different expiratory muscles, the mechanical contribution of individual muscles to pressure generation during spinal cord stimulation (SCS) is unknown. Moreover, recent electromyographic data indicate that stimulation over the lower thoracic spinal cord also results in activation of the inspiratory intercostal muscles (5). The magnitude of the opposing action of these latter muscles on Paw generation is unknown. A better understanding of the specific expiratory muscles responsible for positive-pressure generation and the degree of opposing inspiratory action during SCS is important for the further development and refinement of this technique, including optimal electrode design and placement.

METHODS
All studies were approved by the Animal Care and Use Committee of Case Western Reserve University. Experiments were performed in nine mongrel dogs (weight, 17.2 ± 1.0 kg; range, 13.0–24.5 kg) anesthetized with pentobarbital sodium. Animals were initially anesthetized with 25 mg/kg, supplemented with 1–2 mg/kg as required to maintain an absent corneal reflex and response to noxious stimuli. Body temperature was maintained with a heating blanket at 38 ± 0.5°C. Auffed endotracheal tube (10 mm ID) was placed via cervical tracheostomy in each animal. An arterial cannula (P23, Statham) was inserted into the femoral artery to monitor blood pressure and for intermittent arterial blood-gas analysis (arterial blood-gas analyzer ABL-30, Radiometer, Copenhagen, Denmark). Another catheter was placed in the femoral vein to administer intravenous fluids and to provide additional doses of pentobarbital sodium. End-tidal PCO2 was monitored at the tracheal opening with a rapidly responding CO2 analyzer (O. R. SARA; PPG Biomedical System, Lenexa, KS). Tracheal pressure was recorded with a differential pressure transducer (Validyne MP-45, Validyne, Northridge, CA). A laminectomy was performed between the L3 and L4 vertebral bodies, through which a multicontact disk electrode was inserted onto the epidural surface of the spinal cord and was advanced cephalad to the region of the T7 spinal cord level. The electrode consisted of 15 electrode leads (4 mm diameter) that were embedded in polyurethane plastic and

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positioned 15 mm apart. Precise position of each electrode lead in relation to specific spinal roots was determined postmortem.

The animal was subsequently placed in the supine posture, and the skin over the lower thorax and abdominal wall was reflected. The following respiratory muscles were exposed: external and internal intercostal muscles of the lower rib cage, external and internal oblique muscles, transversus abdominis, and rectus abdominis.

Electrical stimulation was applied with a two-channel electrical stimulator (Grass model S88, Grass Instruments, Quincy, MA) connected to a stimulus isolation unit. SCS was provided via each lead, in separate trials, with trains of impulses at 50 Hz, 1- to 2-s train duration at 15 mA, and pulse width of 0.2 ms. These stimulus parameters, when applied with a single electrode, have been shown previously to produce near maximal changes in Paw for a single electrode and to result in minimal nonrespiratory muscle activation (5, 6).

Protocol. Animals were hyperventilated to apnea, after which electrical stimulation was applied at each electrode lead under conditions of airway occlusion at functional residual capacity. In group A animals (n = 6), Paw generation was monitored before and after bilateral sequential ablation of each of the following muscles: external and internal obliques in combination, rectus abdominis, transversus abdominis, and internal intercostal muscles (T6–T12). The aponeuroses of the external and internal oblique muscles were sectioned longitudinally along their entire length bilaterally to eliminate their action. The origin and insertions of the rectus abdominis muscles were then sectioned. After reflection of the oblique muscles, the motor nerves to the transversus abdominis muscle were easily visualized and were subsequently sectioned to eliminate the action of this muscle. Finally, the internal intercostal nerves from the T6 to T12 intercostal spaces were sectioned to eliminate the action of the intercostal muscles.

Placement of a single-electrode lead is technically less difficult and is therefore preferable in any potential human application. However, we recently demonstrated (5) that a single-electrode system does not result in complete activation of all the expiratory muscles and that modest but significantly greater changes in Paw can be produced with a properly positioned two-electrode-lead system. Therefore, we also evaluated the mechanical participation of the expiratory muscles during combined stimulation of one-electrode lead in the T9 region and separate electrode leads in the T13 region (each with 15 mA).

Sectioning of the internal intercostal nerves resulted in some damage to the external intercostal muscles in group A studies. We were also concerned that prior section of the external and levator costae muscles could damage the internal intercostal nerves and interfere with our analysis of internal intercostal muscle action. Consequently, the action of the inspiratory intercostal muscles was assessed in a separate group of animals. In group B animals (n = 3), Paw generation was monitored before and after sectioning of the abdominal muscles and was monitored again after section of the insertions of the external intercostal and levator costae muscles between the T6 and T12 interspaces.

Analysis. The values of Paw generated during SCS before and after sequential sectioning of respiratory muscles were plotted against the point of electrical stimulation at specific spinal cord levels. Values (means ± SE) were calculated at specific spinal cord levels by interpolation of curves from individual animals. Statistical analysis was performed with application of one-way analysis of variance and post hoc Newman-Keuls test. P values < 0.05 were taken as indicating statistical significance.

RESULTS

The effects of sequential section of the respiratory muscles on Paw generation during stimulation at the T9 spinal cord level is shown for one animal in Fig. 1. In this example, control Paw was 57 cmH2O. There were progressive reductions in Paw generation with muscle sectioning. After sectioning of the obliques, there was a substantial fall in Paw generation to 30 cmH2O. Sectioning of the rectus abdominis had a negligible effect. Ablation of the transversus abdominis muscle and subsequent section of the internal intercostal nerves (which eliminated the action of the intercostal muscles alone) resulted in further substantial reductions in Paw generation to 13 and 5 cmH2O, respectively.

Mean pressure generation during SCS before and after sequential ablation of the expiratory muscles is shown in Fig. 2. Mean control Paw during T9 stimulation was 60 ± 3 cmH2O. After sectioning of the oblique muscles, pressure generation fell to 29 ± 2 cmH2O (P < 0.01). After sectioning of the rectus muscles, pressure generation fell to 25 ± 2 cmH2O [not significant (NS)]. Subsequent sectioning of the transversus abdominis muscle resulted in a further decrement to 12 ± 1 cmH2O (P < 0.01 when compared with after sectioning of the rectus abdominis). There was a small remaining Paw of 4 ± 1 cmH2O after sectioning of the internal

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Fig. 1. Airway pressure (Paw) generation under control conditions and after sequential ablation of the expiratory muscles in 1 animal. See text for further explanation.
intercostal nerves ($P < 0.01$ compared with after sectioning of the transversus abdominis muscle value).

The mean contribution of the various expiratory muscles to Paw during stimulation at various spinal cord levels is shown in Fig. 3, A and B. In Fig. 3A, bar graphs illustrate the change in Paw production consequent to stimulation applied at each spinal cord level. The change in Paw production resulting from sequential ablation of the various expiratory muscles is also plotted numerically (means ± SE) in Fig. 3B. Paw generation declined progressively with distance both cephalad and caudal to the T9 spinal cord region. During stimulation applied between spinal root levels T7 and T11, the combined effect of contraction of the external and internal oblique muscles made the largest contribution to Paw generation (range: 22–32 cmH2O). Moreover, decrements in Paw generation caudally (between T11 and L1) were, in large measure, consequent to decreases in the contribution of the oblique muscles. Still, contraction of the obliques made a substantial contribution to Paw at all stimulus sites.

Transversus abdominis muscle contraction also resulted in large changes in Paw. These muscles made their largest contribution to pressure generation during stimulation between spinal cord levels T9 and L1 (range: 9–14 cmH2O), and, like the obliques, they made a substantial contribution to Paw at all stimulus sites. The internal intercostal muscles made their largest contribution to changes in Paw during stimulation between T7 and T12 (range: 5–8 cmH2O). Intercostal muscle contribution to Paw that resulted from stimulation in the lumbar region was negligible. The rectus abdominis muscles provided only very small changes in Paw during stimulation at each stimulus site. During stimulation in the T9 region, mean pressure change was $4 ± 1$ cmH2O (range, 0–9 cmH2O).

As shown in Fig. 4, A and B, combined stimulation with two electrodes positioned at the T9 + T13 spinal cord levels resulted in a Paw of $78 ± 6$ cmH2O ($P < 0.01$), compared with T9 stimulation alone. This increased pressure generation occurred as a consequence of a significant increase in the contribution of the transversus abdominis muscles from $16 ± 1$ to $23 ± 6$ cmH2O ($P < 0.01$) and oblique muscles from $30 ± 3$ to $35 ± 3$ cmH2O ($P < 0.05$). The contribution of internal intercostal muscle contraction also increased from $7 ± 1$ to $8 ± 1$ cmH2O (NS when compared with T9 stimulation alone.) The contribution of the rectus muscles remained small, but it also increased from $3 ± 1$ to $5 ± 1$ cmH2O (NS).

The effects of inspiratory intercostal muscle activation on Paw are shown in Fig. 5. Section of these muscles resulted in greater positive pressure generation during stimulation between the T7 and T12 spinal cord levels. However, the magnitude of this effect was small; the maximal increase occurred during stimulation at the T9 spinal cord level ($3.0 ± 1$ cmH2O). As expected, there was negligible or no effect of inspiratory intercostal muscle section during SCS at T13 or more caudal spinal cord levels.

DISCUSSION

Over a broad area of the lower thoracic spinal cord, epidural SCS results in large positive changes in Paw. The results of this study allow some quantification of the mechanical contribution of the various expiratory muscles to Paw generation during stimulation at different spinal cord levels. During stimulation in the vicinity of the T9 spinal cord level, which results in the largest changes in Paw, contraction of the external and internal oblique muscles in combination makes the
largest contribution to Paw. Transversus abdominis and internal intercostal muscle contraction also contributes significantly to pressure generation. In contrast, rectus abdominis muscle contraction makes only a very small contribution to pressure generation (6 ± 2%). SCS also activates the inspiratory intercostal muscles, but this results in only a small opposing inspiratory action during stimulation applied over the lower thoracic spinal cord. Consequently, reduction in pressure generation at sites cephalad and caudal to T9 were secondary to reductions in expiratory agonist activation rather than activation of antagonists.

Critique of method. It was difficult to surgically section the external from the internal obliques without damaging the innervation of these latter muscles. Consequently, the mechanical actions of these two muscle groups could not be separated.

After section of all the expiratory muscles, SCS still resulted in a small positive Paw. This suggests that expiratory muscle ablation was not complete. The magnitude of this pressure however, was < 4 ± 1 cmH2O (6% of total pressure). This suggests that our sectioning technique was successful in eliminating the mechanical action of the major portion of the expiratory muscles. The remaining Paw was most likely secondary to small residual action of muscles incompletely ablated, a portion of the triangularis sterni muscle or other muscles which generally have a minor expiratory action, such as the serratus muscles.

Because of the anatomy of the expiratory muscles, we were limited with regard to the sequence of ablation of the different expiratory muscles. Therefore, it was not possible to exclude a possible order effect that influenced the measured changes in Paw attributable to

Fig. 3. A: mean Paw changes during stimulation at different spinal cord levels. Mechanical contribution of each muscle group to pressure generation is identified by legend key. See text for further explanation. B: changes in Paw attributable to oblique, rectus abdominis, transversus abdominis, and internal intercostal muscles at multiple spinal cord levels between T7 and L2. See text for further explanation.
each of the expiratory muscles. For example, we have previously demonstrated that combined inspiratory intercostal and diaphragm contraction results in a synergistic effect; i.e., changes in Paw that resulted from combined contraction were greater than the arithmetic sum of pressure that resulted from separate contraction of each muscle group (7). We postulated that this phenomenon occurred as a result of the fact that each muscle shortened less during combined contraction; this led to greater force generation (7, 13). It is conceivable that the interaction among the different expiratory muscles is similarly complex. For example, an important function of the external oblique muscles may be to prevent lower rib cage expansion consequent to the increase in intra-abdominal pressure that results from transversus abdominis contraction. If so, after ablation of the obliques, a portion of the pressure generated by transversus contraction would have been dissipated across the lower rib cage. To the extent that this occurred, the changes in Paw that were attributable to the direct action of the transversus muscle as a pressure generator were underestimated, and those attributable to the oblique muscles were overestimated. The magnitude of this effect, however, is unknown. In either case, the pressure attributable to oblique muscle contraction, as determined by our methodology, does accurately reflect the magnitude of the combined fixator and direct agonistic actions of this muscle group.

Comparison with previous studies. The results of studies that examined the degree of electrical activation and length changes of the different expiratory muscles suggest that the transversus abdominis muscle is the major expiratory muscle (2, 3, 8, 9, 12). During resting breathing, for example, electrical activity is invariably detectable in the transversus but is not consistently present in the external oblique or rectus muscles (3, 9, 12). There is also substantial shortening of the transversus muscle below its relaxation length during resting breathing, but there is only minimal shortening of the external oblique and rectus muscles (1, 12). Previous animal studies have also shown that expiratory threshold loading under unanesthetized con-
tions (3) results in increases in both transversus and external oblique activation, but this result was greater in magnitude for the transversus muscle. Recruitment of rectus activity was infrequent. Preferential recruitment of transversus abdominis muscle has also been demonstrated in human studies (2). Marked activation of the external oblique and rectus muscles, however, occurred in response to postural movements (2).

During hypercapnia and inspiratory loaded breathing, muscle blood flow also increases significantly to the transversus abdominis but not to the other abdominal muscles (15, 16). During expiratory loading, blood flow increases to both the obliques and transversus abdominis muscles, but it increases to a greater extent to the transversus muscle (14). In contrast, rectus abdominis blood flow was unchanged (14).

The results of the present study also support the concept that the transversus abdominis is an important expiratory muscle and plays a major role in the generation of changes in Paw. During combined T9 + T13 stimulation, which results in activation of all portions of the transversus muscle, contraction of this muscle accounted for 42% of the total change in Paw. Also consistent with previous work (9, 12), our results support a negligible expiratory role for the rectus abdominis muscle. During combined T9 + T13 stimulation, rectus contraction contributed <7% to the total change in Paw. Taken together with previous investigations (2, 3, 9, 12), the results of the present study strongly support the concept that the rectus muscles are predominantly postural in function, with only a minimal expiratory function. Somewhat inconsistent with previous studies was the substantial contribution of rectus muscle contraction to changes in Paw (45% of total pressure generation with combined T9 + T13 stimulation). Our results indicate that the oblique muscles are at least as important as the transversus muscle in terms of their capacity to produce changes in Paw. Although the differences between the present and previous studies are not readily apparent, there are a number of possible explanations. First, the present study did not assess potential synergistic actions whereby the pressure-generating capacity of the transversus may have been underestimated. Second, the response of the abdominal muscles to physiological stimuli may not reflect their actual capacity to produce changes in Paw. Finally, the conclusions of the aforementioned prior studies were based predominantly on levels of electromyogram activity and muscle length changes; neither parameter is necessarily reflective of the force-generating capacity of these muscles (17).

Correlation between muscle activation and pressure generation. In a recent study (5), we demonstrated that stimulation with a single electrode at the T9 spinal cord level resulted in activation of the lower intercostals (T7 through T11), the superior and upper portions of the external oblique, and upper portions of the remaining abdominal muscles via direct motor root activation. T9 stimulation resulted in submaximal activation of the middle portion of the abdominal muscles and no activation of the lower portion of the abdominal muscles. However, the addition of a second electrode positioned at the T13 spinal cord level resulted in the additional recruitment of the middle and lower portions of the abdominal muscles and significantly greater changes in Paw. The results of the present investigation indicate that this increase in pressure generation (60–78 cmH2O) is due predominantly to increases in the contribution of the transversus and oblique muscles. Pressure generation attributable to transversus and oblique muscle contraction was clearly less than optimal with T9 stimulation alone and was enhanced by the additional stimulation at the T13 spinal cord level. This occurred most likely as a consequence of the additional recruitment of the middle and lower portions of these muscles via stimulation at the T13 level.

In summary, contraction of the oblique and transversus abdominis muscles make the greatest contribution to changes in Paw during SCS. Although stimulation at the T9 spinal cord level results in the largest changes in Paw with a single-electrode lead, stimulation at this site results in incomplete abdominal muscle activation. Combined stimulation (T9 + T13) results in greater activation of the abdominal muscles and significantly larger Paw values. The increase in Paw is consequent to enhanced mechanical actions of the obliques and transversus muscles. Finally, stimulation of the inspiratory intercostal muscles results in only a small opposing inspiratory action.

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