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Effects of diaphragm activation on airway pressure generation during lower thoracic spinal cord stimulation

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Abstract

Lower thoracic spinal cord stimulation (SCS) results in the generation of large positive airway pressures. The potential effects of diaphragm co-activation during SCS were investigated in 10 anesthetized dogs. Diaphragm compound action potentials (CMAPs) were present during SCS at the T10 and T12 levels. In group 1, airway (Paw) and trans-diaphragmatic (Pdi) pressures were monitored during supramaximal SCS before and after phrenicotomy. In group 2, pressures were monitored before and after C2 section to evaluate the potential influence of supraspinal centers. Following phrenicotomy in group 1, the reduction in Pdi during SCS was associated with increases in Paw. In group 2, diaphragm CMAPs and active Pdi increased following C2 section, while Paw fell. Following phrenicotomy, Paw increased significantly. In intact animals therefore, changes in Paw during SCS are affected by the interaction between inhibitory and excitatory influences on diaphragm activation. We conclude that lower thoracic SCS results in substantial diaphragm co-activation and secondary reductions in airway pressure generation.

Keywords: Respiratory muscles; Expiratory muscles; Diaphragm; Electrical stimulation; Spinal cord stimulation; Cough

1. Introduction

Electrical (DiMarco et al., 1995, 1999a,b, 2002, 2006; Kowalski et al., 2007) and magnetic stimulation (Estenne et al., 2000; Kyroussis et al., 1997; Lin et al., 1998a,b; Polkey et al., 1999) applied in the region of the lower thoracic spinal cord results in expiratory muscle activation and the generation of large positive airway pressures. In previous animal studies (DiMarco et al., 1999b, 2002), we investigated the mechanism of expiratory muscle activation during lower thoracic spinal cord stimulation (SCS) via electrodes placed on the dorsal epidural surface of the spinal cord. We demonstrated that electrical stimulation resulted in direct activation of motor roots in the immediate vicinity of the stimulating electrode and more caudal motor roots via spinal cord pathways (DiMarco et al., 1999b, 2002). The potential effects of cephalad transmission of action potentials however, has never been investigated.

Since lower thoracic SCS results in stimulation of the intercostal nerves in the vicinity of the stimulating electrode (DiMarco et al., 2002) and prior investigations have described intercostal to phrenic reflexes with excitatory influences on phrenic nerve activation (Decima and von Euler, 1969a,b; Decima et al., 1969c; Downman, 1955), we hypothesized that diaphragm co-activation may also occur during SCS. The purpose of the present study therefore, was to systematically evaluate the potential effects of diaphragm co-activation, during lower thoracic SCS, on airway pressure generation, in an acute animal model. In an initial group of studies, airway pressure and trans-diaphragmatic pressures were assessed before and after bilateral phrenictomy. In a second group, the impact of supraspinal influences was examined by monitoring pressures before and after sectioning the spinal cord at the C2 level.

2. Methods

All studies were approved by the Animal Care and Use Committee of Case Western Reserve University. Studies were performed on 10 mongrel dogs (mean weight: 17.3 ± 0.7 kg) in the prone position. Animals were anesthetized initially with intravenous pentobarbital sodium (PB, 25 mg/kg). Additional doses of PB (1–2 mg/kg) were administered to completely sup-

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press any response to noxious stimuli while maintaining corneal reflexes intact. A large bore cuffed endotracheal tube (10 mm ID) was surgically positioned in the cervical region via tracheostomy. A femoral artery catheter was placed to monitor blood pressure (model PT300, Grass Instrument Division, Astro-Med Inc., Warwick, RI). A femoral vein catheter was placed to provide supplemental anesthesia and fluids, as required. A heating blanket (Harvard Apparatus, Cambridge, MA) was used to maintain body temperature at $38 \pm 0.5\,^{\circ}C$. End-tidal pCO_2 was monitored with a rapidly responding CO_2 analyzer (O.R. SARAcap, PPG Industries, Lenexa, KS).

We have previously demonstrated that stimulation applied at the T10 and T12 spinal cord levels in the midline on the dorsal epidural surface, results in the generation of large positive airway pressures (DiMarco et al., 1999a, 2002, 2006). In the present study therefore, stimulating disc electrodes were placed at each of these spinal cord levels via laminectomies, according to previously described techniques (DiMarco et al., 1999a,b, 2002), to assess the effects of electrical stimulation on potential diaphragm co-activation. In studies requiring cervical spinal cord section, laminectomies were also performed in these regions. Electrical stimulation was applied with a Grass 2-channel stimulator (model S88, Grass Instruments, Quincy, MA).

Electromyographic electrodes (bipolar stainless steel wires) were implanted directly into the costal portion of the left hemidiaphragm to monitor the electrical activity of the diaphragm. Spinal cord stimulation was provided during the application of single shocks (5 mA, 0.2 ms pulse duration,) to determine the latencies of diaphragm compound action potentials (CMAPs). These potentials were amplified (model BMI-830 Charles Ward Enterprises) and recorded on a computer utilizing Labview software (Version 6.1 National Instruments Corp., Austin, TX).

Airway pressure (Paw) was monitored with a differential pressure transducer (model MP-45, Validyne, Northridge, CA) at the endotracheal tube and recorded on an 8-channel recorder (model DASH 8, Astro-Med, Warwick, RI). Esophageal and gastric balloons were placed trans-orally to measure changes in esophageal (Pes) and gastric pressures (Pga), respectively. Trans-diaphragmatic pressure (Pdi) was defined as the difference between Pga and Pes. Paw and Pdi were monitored during the application of near supramaximal electrical stimulation (15 mA, 50 Hz, 0.2 ms pulse duration) at each spinal cord level, based upon previously described techniques (DiMarco et al., 1999a,b, 2002). Paw and Pdi were always monitored following hyperventilation-induced apnea and under conditions of airway occlusion, at FRC.

In group 1 studies ($n = 5$), Paw and Pdi were assessed before and after bilateral cervical phrenicotomy to eliminate potential co-activation of the phrenic motoneurons. In group 2 studies ($n = 5$), pressures were assessed before and after spinal cord section at the C2 level, to evaluate the potential influence of supra-spinal centers, and again following bilateral phrenicotomy. C2 section usually resulted in an increase in mean blood pressure of ~30 mm Hg. However, blood pressure returned to baseline values within 15–20 min following which all measurements were taken.

2.1. Data analysis

The latencies of the diaphragm CMAPs were determined from the onset of the stimulus artifact to the onset of the CMAP wave. The average of five CMAPs under each condition was taken for analysis. Pressure measurements were compared utilizing repeated measures ANOVA and post hoc Student's-*t* tests, where applicable.

Control Pdi measurements ($Pdi_{C\text{-}total}$) reflected both the active ($Pdi_{C\text{-}active}$) (consequent to diaphragm contraction) and passive components ($Pdi_{passive}$) of this parameter. The arithmetic difference in Pdi before and after bilateral phrenic nerve section, was taken as $Pdi_{C\text{-}active}$. Pdi active was also determined from the increase in Pdi following C2 section ($Pdi_{C2\text{-}active} = Pdi_{C2\text{-}total} - Pdi_{passive}$). Trans-diaphragmatic pressure following phrenicotomy was taken as Pdi passive ($Pdi_{passive}$). Data are presented as mean ± S.E.

Statistical significance was taken as a p value < 0.05.

3. Results

The effects of single shock SCS on diaphragm CMAPs is shown for one animal in Fig. 1. Diaphragm CMAPs were observed during SCS at the T10 and T12 levels. Similar results were observed in each animal. Mean onset latencies of diaphragm CMAPs at the T10 and T12 spinal cord levels were 16.5 ± 0.2, 17.2 ± 0.2 ($p < 0.05$ compared to T10 stimulation). Diaphragm CMAPs was completely eliminated following bilateral cervical phrenicotomy.

The effects of near supramaximal SCS at the T12 level on Pga, Pes and Paw before and after bilateral cervical phrenicotomy (group 1 studies), is shown for a single animal in Fig. 2. Initial SCS resulted in a Paw of 32 cm H_2O and Pdi of 44 cm H_2O. Following phrenicotomy, airway pressure increased to 45 cm H_2O in association with a decrease in Pdi to 20 cm H_2O. The decrease

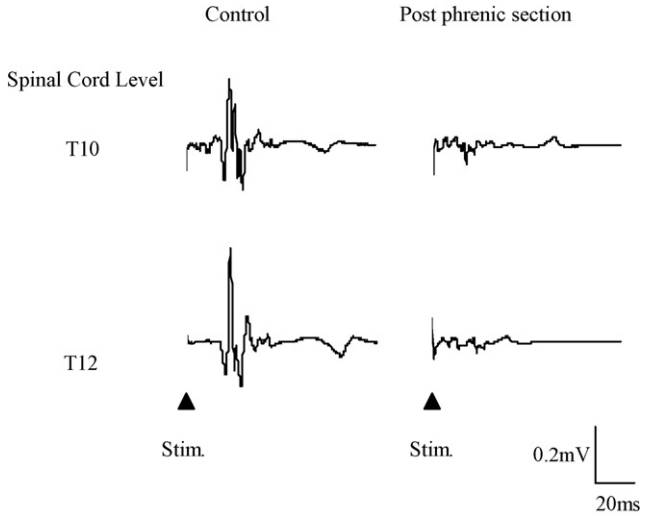

Fig. 1. Diaphragm compound muscle action potentials (CMAPs) recorded during SCS at the T10 and T12 levels under control conditions (left panel) and following bilateral cervical phrenictomy in one animal. See text for further explanation.