Functional magnetic stimulation of expiratory muscles: a noninvasive and new method for restoring cough

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Lin, Vernon W. H., Caleb Hsieh, Ian N. Hsiao, and James Canfield. Functional magnetic stimulation of expiratory muscles: a noninvasive and new method for restoring cough. J. Appl. Physiol. 84(4): 1144–1150, 1998.—The purpose of this study was to assess the effectiveness of functional magnetic stimulation (FMS) for producing expiratory function in normal human subjects. Twelve able-bodied normal subjects were recruited for this study. FMS of the expiratory muscles was performed by using a magnetic stimulator and placing the magnetic coil along the lower thoracic spine. Results showed that peak expired pressure, volume, and flow rate generated by FMS at the end of normal inspiration (102.5 ± 13.62 cmH2O, 1.6 ± 0.16 liters, and 4.8 ± 0.35 l/s, respectively) were comparable to their voluntary maximal levels (P > 0.1). The optimal coil placement was between T7 and T11, and the optimal stimulation parameters were a frequency of 25 Hz and 70–80% of maximal intensity. We conclude that 1) FMS of the lower thoracic nerves in normal subjects resulted in a significant expiratory function comparable to their voluntary maximum; 2) FMS was noninvasive and was well tolerated by all subjects; and 3) FMS may be useful to produce cough in patients in critical care or perioperative settings, or in patients with neurological disorders.

thoracic nerve stimulation; expired pressure; respiratory muscles; abdominal muscles

PATIENTS IN CRITICAL CARE or perioperative settings often develop increased airway secretions and impaired cough mechanisms caused by endotracheal tube irritation, anesthesia, muscle relaxants, infection, or impaired respiratory muscle function. Aggressive pulmonary toilet, with frequent suctioning, chest percussion, and postural drainage, has become the mainstay of critical care or postoperative prescriptions. Spinal cord injury (SCI) disrupts the central nervous system and is often associated with weakness of the expiratory muscles. This results in frequent respiratory tract infections, which are a major cause of morbidity and mortality in subjects with SCI (3, 8, 19, 22). Current management of expiratory muscle dysfunction in SCI includes postural drainage, chest percussion, airway suctioning, and “quad coughing” (10). In addition, functional electric stimulation (FES) of the expiratory muscles has been developed in recent years to restore effective cough (6, 9, 15). However, the FES technique is inconvenient to use and can be quite painful to patients who have preserved sensation.

Magnetic stimulation has been used in recent years as a noninvasive method for stimulating the nerves. Magnetic stimulation applies Faraday’s law, which states that, whenever a magnetic field changes, an electric field is induced. This induced electric field, if of adequate amplitude and duration, may generate sufficient current to stimulate nerves (4). In recent years, investigators have used magnetic stimulation to evaluate the respiratory system by stimulating the phrenic nerves (23, 24), thoracic spinal nerves (5), and the cortex (16, 25). Magnetic stimulation is not painful, does not require direct physical contact with the patient, and can be applied outside the clothing. In addition, our laboratory has demonstrated, by using a high-speed magnetic stimulator, significant inspired volume generation by functional magnetic stimulation (FMS) of the inspiratory muscles as well as significant expired pressure production by FMS of the lower thoracic nerves in dogs (12) and significant improvements in expired function in patients with SCI (13).

The objectives of this study were 1) to assess the effectiveness of FMS of the expiratory muscles in normal subjects by measuring the expired pressure, volume, and flow rate generated by FMS; 2) to determine the optimal magnetic coil (MC) placement for FMS of the expiratory muscles; 3) to determine the optimal stimulation frequency and intensity for FMS of the expiratory muscles; and 4) to compare FMS of the expiratory muscles with the existing FES technology to induce cough.

MATERIALS AND METHODS

Twelve neurologically normal, nonsmoking male subjects were recruited for the study. The purpose of this study was explained, and written informed consent was obtained. This study was in accordance with the Stanford University Human Subjects Administrative Panel. Each subject first received a screening history and physical examination followed by pulmonary function tests (PFT). A Medical Graphics model 1070 was used for measuring pulmonary function, and the following measurements were recorded for comparison: total lung capacity (TLC); slow vital capacity; functional residual capacity; residual volume; expiratory reserve volume (ERV); maximal expired pressure (MEP) measured from the end of a normal inspiration (Ins); forced expiratory flow (FEF) rate from TLC (FEF-TLC); and FEF rate from the end of a normal Ins (FEF-Ins). The above flow measurements were obtained as peak flow rates.

A Dantec MagPro magnetic stimulator with a round coil (13.7 cm OD) was used in this study. This stimulator was capable of generating biphasic pulses (280–us pulse width) with a magnetic gradient up to 50 kT/A, which could be used to generate a magnetic field up to 50 kT/A. Flow and volume measurements were taken by using a pneumotachometer (model 3800, Hans Rudolph) connected to a desktop diagnostic flow module (Medical Graphics). MEP was determined by using a separate circuit composed of a mouth piece, a nonheated pneumotachometer (model 3800, Hans Rudolph), and a transducer (DD250, no. 32, Valdyne) capable of reading pressure up to ±250 cmH2O. For measurement of MEP,
subjects were asked to breathe quietly and then to expire maximally against an occluded shutter, and the mouth pressure (Pm) was measured. Airway occlusion was accomplished by occluding the breathing circuit at the patient's mouth with a manually triggered shutter. The measurements were relayed to a laptop computer and, through display of tidal volume, FMS was performed at the end of normal Ins. To ensure accurate measurements, the pressure transducers and pneumotachographs were calibrated before each study.

Nerve-conduction study. A preliminary nerve-conduction study was conducted by using 10-mm surface disc electrodes (no. 6030-3, TECA). Compound muscle action potential (CMAP) recordings were made according to standard motor nerve-conduction techniques by using a commercially available electromyogram (EMG) machine (Nicolet Viking). The low-pass and high-pass filters were set at 5 kHz and 2 Hz, respectively. The external preamplifier had a voltage gain of 10 V. The sweep speed used for CMAP recordings was either 5 or 10 ms per division, and the sensitivity used was either 1 or 2 mV per division. CMAP was recorded from three muscles: seventh intercostal, rectus abdominis, and external oblique. Electrode placements were in accordance with the method of Chokroverty et al. (5). The active recording electrode for intercostal muscle was placed in the 7th intercostal space along the anterior axillary line. The rectus abdominis and external oblique active electrode placements were at the junction of the upper one-fourth and lower three-fourths of the line joining the xiphoid process and the anterior superior iliac spine, and at the junction of the upper one-half and lower one-half of the same line, respectively. The corresponding reference electrodes were placed 3 cm lateral to the active electrodes. For each individual muscle, a placement profile was conducted by moving the center of the MC along the spinous processes ranging from T4 to L1. The placement that produced the highest CMAP amplitude in each individual muscle was used for generating intensity profiles of magnetic stimulation. Stimulation intensities were increased from 40 to 90%. The motor conduction latencies and amplitudes were taken into consideration.

FMS protocol. Subjects were asked to be in a seated position and to breathe quietly through a breathing circuit. Inspiratory and expiratory manifolds were instrumentally monitored via the desktop diagnostic flow module and displayed on a computer screen. When the subject's tidal breathing was established, FMS was applied at the end of normal inspiration. All subjects were instructed not to exert their own voluntary efforts during FMS, and subjects were not prewarned of the delivery of the stimulation. Each measurement was taken multiple times at random intervals to ensure consistent and repeatable values, and the most consistent value was used for data analysis. Optimal coil placement was determined by measuring the changes in mouth pressure (ΔPm) while the center of the coil moved between T6 and T11 spinous processes. The stimulation parameters were 70% intensity, 20-Hz frequency, and a 2-s stimulation duration. The coil placement that produced MEP was used for subsequent magnetic stimulations.

After the optimal coil placement was established, intensity and frequency profiles were generated. In the intensity profile, stimulation intensities were varied from 40 to 90% while the frequency and duration were kept constant at 20 Hz and 2 s, respectively. For the frequency profile, the stimulation was performed at varying frequencies (5, 10, 15, 20, 25, and 30 Hz), with the intensity and stimulation duration maintained at 70% and 2 s, respectively. The maximal ΔPm generated by FMS (MEP-FMS) was selected from the above data regardless of the stimulation intensity and frequency.

**Table 1. Pulmonary function test results**

<table>
<thead>
<tr>
<th>Pulmonary Function Test</th>
<th>Actual</th>
<th>Predicted</th>
<th>%Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC, liters</td>
<td>7.0 ± 0.39</td>
<td>7.2 ± 0.23</td>
<td>97</td>
</tr>
<tr>
<td>SVC, liters</td>
<td>5.0 ± 0.27</td>
<td>4.9 ± 0.11</td>
<td>102</td>
</tr>
<tr>
<td>FRC, liters</td>
<td>3.3 ± 0.26</td>
<td>3.9 ± 0.15</td>
<td>85</td>
</tr>
<tr>
<td>RV, liters</td>
<td>2.0 ± 0.19</td>
<td>2.0 ± 0.13</td>
<td>100</td>
</tr>
<tr>
<td>ERV, liters</td>
<td>1.4 ± 0.18</td>
<td>1.6 ± 0.10</td>
<td>80</td>
</tr>
<tr>
<td>MEP, cmH2O</td>
<td>114.7 ± 6.74</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>FEF-TLC, l/s</td>
<td>11.0 ± 0.47</td>
<td>9.6 ± 0.14</td>
<td>107</td>
</tr>
<tr>
<td>FEF-Ins, l/s</td>
<td>5.3 ± 0.51</td>
<td>6.02 ± 0.12</td>
<td>89</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 12 subjects. TLC, total lung capacity; SVC, slow vital capacity; FRC, functional residual capacity; RV, residual volume; ERV, expiratory reserved volume; MEP, maximal expired pressure; Ins, inspiration. *Predicted value not available for end of normal inspiration.

The MEP-FMS was later used for comparing the pressure generated by FMS with patients’ voluntary maximum. Similarly, maximal ERV-FMS (calculated from functional residual capacity by the computer software) and FEF-FMS were compared with their voluntary maximal efforts (ERV and FEF-Ins).

**Statistical methods.** Data obtained from the pulmonary function tests are expressed as means ± SE. ΔPm, ERV-FMS, and FEF-FMS are also expressed as means ± SE and compared with results obtained from the PFT. Statistical analyses were performed by using a one-way ANOVA and post hoc t-tests. A P value of ≤ 0.05 was considered significant, except when multiple comparisons were made. In those cases, the Bonferroni statistical correction of the P value was used.

**RESULTS**

The 12 normal subjects ranged in age between 21 and 52 yr, in height from 66 to 74 in., and in weight from 125 to 260 lb. Their PFT data are listed in Table 1; all measurements were within normal range.

Nerve-conduction study. The results of the nerve-conduction studies are listed in Table 2. CMAPs from the 7th intercostal muscle were optimally obtained by placing the center of the MC at the T7 spinous process. As the MC was moved to the T5 and T10 spinous processes, the CMAP amplitude from the 7th intercostal muscle was only 25% of the value obtained at the T7 spinal level. CMAPs of rectus abdominis or external oblique muscles were best obtained when the MC was placed at T10. Figure 1 illustrates a pattern of external oblique muscle activation caused by placing the MC along the spinous processes between T4 and L1. Maximal amplitude was observed when the MC was placed along the T10 spinous process; the amplitude was reduced to 15% and 12% of the maximal value when placed at T7 and L1, respectively (Fig. 1A). The CMAP
amplitudes increased as the magnetic stimulation intensity increased from 50 to 80% (Fig. 1B). No significant increase in amplitude was observed when the intensity increased from 80 to 90%.

FMS protocol. FMS of the expiratory muscles produced a significant $\Delta P_m$ at all coil placements (T6–T11) that were studied; the magnitude of $\Delta P_m$ proved to be a function of the position of the coil ($P < 0.0001$) (Fig. 2). When a set of fixed stimulation parameters (70% intensity, 20-Hz frequency, and a 2-s stimulation duration) was used, the maximum $\Delta P_m$ generated was at the T8 spinous process (86.5 ± 13.5 cmH$_2$O); paired t-test comparisons between the other levels of stimulation with the T8 level showed that only FMS at the T6 level produced significantly less $\Delta P_m$ ($P = 0.0002$). However, there was significant individual variation.

MEP-FMS was 102.5 ± 13.62 cmH$_2$O, which was comparable to the subjects' voluntary MEP ($P > 0.1$). On a few occasions, FMS of the expiratory muscles produced pressures exceeding that generated by voluntary effort. In one subject, the MEP-FMS was 174 cmH$_2$O, which was 160% of his MEP (107 cmH$_2$O). In this subject, FMS was performed at 90% intensity, 20-Hz frequency, with a stimulation duration of 2 s. In another subject, the MEP-FMS was 151 cmH$_2$O, which was 111% of his voluntary MEP (136 cmH$_2$O). In these two subjects, the baseline MEP values fell within the same MEP range as those of the other subjects. Both MEP and MEP-FMS values were reproducible. Stimulation parameters were an intensity of 70%, a frequency of 30 Hz, and a duration of 2 s.

The mean maximal ERV-FMS was 1.58 ± 0.16 liters, which was 14% more than average baseline ERV ($P > 0.1$). In addition, the mean FEF-FMS was 4.8 ± 0.35 l/s, and was similar to FEF-Ins ($P > 0.1$).

The effect of varying stimulation intensity and frequency on pressure, volume, and flow was examined in all 12 subjects. The MEP-FMS generated was a function of stimulation intensity ($P < 0.0001$) (Fig. 3A). The highest value was produced at an intensity of 80% (81.4 ± 14.17 cmH$_2$O). Paired t-test comparisons re-
revealed that intensities ranging from 40 to 60% produced significantly less MEP-FMS than at 80% \( (P < 0.001) \) whereas intensities of 70 and 90% were not significantly different from 80% \( (P > 0.15) \) whereas intensities ranging from 40 to 60% were significantly different from 80% \( (* P < 0.001) \). Maximal MEP-FMS was observed at 25 Hz \( (88.2 \pm 13.02 \text{ cmH}_2\text{O}) \); stimulation frequencies of 5–20 Hz produced significantly less MEP-FMS than frequencies at 25 Hz \( (P < 0.003) \); at 30 Hz, there was no statistically significant difference from 25 Hz \( (P = 0.8552) \).

When ERV-FMS was examined with respect to changes in stimulation intensity, significant effects were found \( (P < 0.0001; \text{Fig. 4A}) \). At 70% intensity, the maximal ERV-FMS was produced \( (1.44 \pm 0.15 \text{ liters}) \). Paired t-test comparisons revealed that intensities ranging from 40 to 60% produced significantly less ERV-FMS than was generated at 70% \( (P < 0.005) \). ERV-FMS produced by intensities >70% (80 and 90%) were not significantly different from 70% \( (P > 0.4) \). Finally, ERV-FMS was sensitive to changes in stimulation frequency \( (P < 0.0001; \text{Fig. 4B}) \). The maximal ERV-FMS was produced at a frequency of 25 Hz \( (1.48 \pm 0.15 \text{ liters}) \).
The major finding of this study was that, in normal subjects, FMS of the expiratory muscles resulted in significant changes in airway pressure, volume, and expiratory flow rate compared with their voluntary maximum. This study also demonstrated that MC placements between T7 and T11 spinal levels produced similar expired pressures. As demonstrated in our nerve-conduction study, the T7 MC placement stimulated spinal nerves between T5 and T10. Therefore, we can infer that the T7-T11 MC placements stimulated spinal nerves between T5 and L2. These stimulations would result in the activation of important expiratory agonists, such as the abdominal muscles, lower intercostal muscles, and serratus posterior inferior muscle (7).

Although the outcomes (expired pressures) produced by varying MC placements between T7 and T11 were similar, the processes (expiratory muscle activation) producing the outcomes could be very different. For example, a T7 MC placement most likely resulted in the recruitment of lower intercostal and abdominal muscle groups that were innervated by lower thoracic spinal nerves (T5-T10). On the other hand, a T11 MC placement would recruit muscle groups predominantly innervated by T9-L2, which would include more abdominal and lumbar muscles and fewer lower intercostal muscles when compared with a T7 MC placement. Furthermore, a significant decrease in expired pressure was observed when the MC was moved from T7 to T6. This may be explained by less recruitment of the expiratory agonists and/or activation of the inspiratory agonists, external and parasternal intercostal muscles, at the T6 MC placement (7).

This study was consistent with our animal study in which T8–T9 coil placements demonstrated significant expired pressure (12). This human study, however, produced much higher MEP-FMS compared with the animal study (12). This difference could not be explained solely by the differences in species or animal size. In the present study, we used a different power supply and a bigger coil with a different coil configuration. It is conceivable that improvements in the power supply and the MC could activate more spinal nerves, resulting in better recruitment of the expiratory agonists and higher expired pressure. This also explains the higher CMAP amplitudes obtained in this present study when compared with an earlier study by Chokroverty et al. (5). In the present study, supramaximal stimulation was achieved with only 80% of magnetic stimulation intensity, whereas supramaximal stimulation was never achieved in the earlier study (5).

A number of differences and similarities are found when comparing the results obtained from the present study, using FMS, with earlier studies that used FES (6, 9, 15). FES of the abdominal muscles primarily stimulated abdominal muscles and did not activate lower internal intercostal muscles or other expiratory agonists (9, 15). In addition, FES of the lower thoracic ventral roots (6) has been demonstrated to activate lower intercostal and abdominal muscles. In terms of expiratory muscle activation, FMS of the lower thoracic nerves is similar to FES of the lower thoracic ventral roots. The expired pressure generated by FMS resembles that of FES of the lower thoracic ventral roots. Furthermore, the MC placement was also similar to the electrode placement for ventral root stimulation in animals (6). There are several differences between FES and FMS of the lower thoracic nerves/roots, however. FES of the ventral roots stimulates the roots at the electrode placement site near the spinal cord. According to recent studies, the foci of activation by magnetic stimulation is most likely to be at the neuroforamen (5, 17, 18). Technically, FES of the ventral roots is invasive, requires laminectomy for electrode placement, and may be very painful to subjects who have preserved sensation. In contrast, FMS is noninvasive, does not require surgery, is relatively painless, and is well tolerated by all subjects studied to date.

Patients with chronic SCI often have impaired cough because of weakness of the expiratory muscles. For these patients, methods of restoring cough can be of vital importance in improving pulmonary care. This study introduces a new method of stimulating the expiratory muscles to induce cough. By placing the MC in the lower thoracic spine region, major expiratory agonists can be activated via spinal nerve stimulation. The activation of these expiratory muscles results in a

**DISCUSSION**

The activation of these expiratory muscles results in a
forceful expiratory flow that can mimic a physiological cough. However, there is a difference between FMS-induced cough and physiological cough. Physiological cough involves a deep inspiration followed by an explosive outflow of air against a closed glottis. In contrast, FMS-induced cough results in a significant expiratory flow against an open glottis. In a recent preliminary study on patients with chronic SCI (13), we have demonstrated the efficacy of FMS in producing significant expiratory function that was greater than their voluntary maximum. Thus, FMS-induced cough can be an effective means of restoring expiratory function in patients with SCI or patients with other neurological impairments.

The safety of FMS is an area of great concern to both clinicians and patients, particularly in terms of cardiac risks, induced electrical field, and power dissipation. Several studies have been conducted by exposing animals to large, time-varying magnetic fields without inducing ventricular fibrillation (20, 21). We did not observe adverse cardiac effects in our subjects. The peak magnetic field generated by FMS is similar to the static fields used in some magnetic resonance imaging scanners. The maximal change induced by magnetic stimulation is 50 µC/pulse (corresponding to 0.05-0.0005% of the charges used in electroconvulsive therapy). No hazard has yet been reported, despite long-term stimulation (1, 2). It is possible that magnetic stimulators may damage cardiac pacemakers; thus it is important to exclude patients who have a pacemaker from participating in FMS protocols. Other safety concerns that need to be considered are the heat built up by the MC and the power dissipation in tissue. Use of a power supply that has a thermostat connected to the coil will circumvent overheating and prevent thermal injury.

Magnetic stimulation of the spinal nerves is clearly an emerging technology with many important clinical applications. Diagnostically, magnetic stimulation can be used in various cervical, thoracic, lumbar, or sacral motor nerve-conduction studies. Through repetitive stimulation, FMS can produce tetanic muscle contraction and result in useful physiological function. FMS of the sacral nerves has been demonstrated to be an effective means of emptying the bladder in animals and in patients with SCI (11, 14). The present study particularly addresses the usefulness of stimulating the expiratory agonists for generating significant expired pressure, volume, and flow in normal subjects. The future application of this technology is not limited to those patients who have SCI or neurological disorders; it may also be applied to patients with impaired respiratory function, for instance, in the critical care or perioperative settings.

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