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

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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

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-µs pulse width) with a magnetic gradient 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 muscles 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 T11. 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 maneuvers were 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>86</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>86</td>
</tr>
<tr>
<td>MEP, mH2O</td>
<td>114.7 ± 6.74</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>FEF-TC, 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).

### Table 2. Nerve-conduction study of thoracic nerves by using magnetic stimulation

<table>
<thead>
<tr>
<th>Magnetic Coil Placement</th>
<th>Recording Electrode Placement</th>
<th>Latency, ms</th>
<th>Amplitude, mV</th>
</tr>
</thead>
<tbody>
<tr>
<td>T7 spinous process</td>
<td>T7 intercostal muscle</td>
<td>5.1 ± 0.20</td>
<td>2.0 ± 0.57</td>
</tr>
<tr>
<td>T10 spinous process</td>
<td>Rectus abdominis</td>
<td>3.6 ± 0.35</td>
<td>2.1 ± 0.58</td>
</tr>
<tr>
<td>T10 spinous process</td>
<td>External oblique</td>
<td>4.4 ± 0.26</td>
<td>3.1 ± 0.81</td>
</tr>
</tbody>
</table>

Values are means ± SE.
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 ΔPm at all coil placements (T6–T11) that were studied; the magnitude of ΔPm 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 ΔPm generated was at the T8 spinous process (86.5 ± 13.5 cmH2O); 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 ΔPm (*P = 0.0002). However, there was significant individual variation.

MEP-FMS was 102.5 ± 13.62 cmH2O, 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 cmH2O, which was 160% of his MEP (107 cmH2O). 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 cmH2O, which was 111% of his voluntary MEP (136 cmH2O). 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 cmH2O). 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). Similarly, MEP-FMS proved to be a function of stimulation frequency (P < 0.0001; Fig. 3B). The maximal MEP-FMS was observed at 25 Hz (88.2 ± 13.02 cmH2O); 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; Fig. 4A). At 70% intensity, the maximal ERV-FMS was produced (1.44 ± 0.15 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; Fig. 4B). The maximal ERV-FMS was produced at a frequency of 25 Hz (1.48 ±

Fig. 3. A: intensity profile. ∆Pm as function of varying stimulation intensity with stimulation frequency and burst length held constant at 20 Hz and 2 s. There was a significant effect of intensity on ∆Pm; P < 0.0001. Maximal ∆Pm was generated at an intensity of 80%; however, intensities of 70 and 90% did not differ significantly from 80% (P > 0.15) whereas intensities ranging from 40 to 60% were significantly different from 80% (*P < 0.001). B: frequency profile. ∆Pm as function of changes in stimulation frequency with stimulation intensity and burst length fixed at 70% and 2 s, respectively. There was a significant effect of frequency on ∆Pm; P < 0.0001. C: maximal ∆Pm was generated at a frequency of 25 Hz. Intensities <25 Hz produced significantly less ∆Pm than at 25 Hz (*P < 0.003) whereas 30 Hz was not significantly different from 25 Hz (P = 0.8552). Error bars represent SE; n = 12 subjects.

Fig. 4. A: intensity profile. Changes in expired volume [expiratory reserved volume-functional magnetic stimulation (ERV-FMS)] as a function of varying stimulation intensity with the stimulation frequency and burst length held constant at 20 Hz and 2 s, respectively. There was a significant effect of intensity on ERV-FMS; P < 0.0001. Maximal ERV-FMS was generated at an intensity of 70%; however, intensities of 80–90% did not differ significantly from 70% (P > 0.40) whereas intensities from 40 to 60% were significantly different from 70% (*P < 0.005). B: frequency profile. ERV-FMS as function of changes in stimulation frequency with stimulation intensity and burst length fixed at 70% and 2 s, respectively. There was a significant effect of frequency on ERV-FMS (P < 0.0001). Maximal ERV-FMS was generated at a frequency of 25 Hz; only a frequency of 5 Hz generated significantly less ERV-FMS compared with 25 Hz (P = 0.0006). Error bars represent SE; n = 12 subjects. *P < 0.0006.
maximal FEF-FMS was generated at intensity of 80%; however, an important 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
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 method 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 charge 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 thermistor 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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