Diaphragm EMG measured by cervical magnetic and electrical phrenic nerve stimulation

Y. M. Luo, M. I. Polkey, L. C. Johnson, R. A. Lyall, M. L. Harris, M. Green, and J. Moxham. Diaphragm EMG measured by cervical magnetic and electrical phrenic nerve stimulation. J. Appl. Physiol. 85(6): 2089–2099, 1998.—The purpose of the study was to compare electrical stimulation (ES) and cervical magnetic stimulation (CMS) of the phrenic nerves for the measurement of the diaphragm compound muscle action potential (CMAP) and phrenic nerve conduction time. A specially designed esophageal catheter with three pairs of electrodes was used, with control of electrode positioning in 10 normal subjects. Pair A and pair B were close to the diaphragm (pair A lower than pair B); pair C was positioned 10 cm above the diaphragm to detect the electromyogram from extradiaphragmatic muscles. Electromyograms were also recorded from upper and lower chest wall surface electrodes. The shape of the CMAP measured with CMS (CMS-CMAP) usually differed from that of the CMAP measured with ES (ES-CMAP). Moreover, the latency of the CMS-CMAP from pair B (5.3 ± 0.4 ms) was significantly shorter than that from pair A (7.1 ± 0.7 ms). The amplitude of the CMS-CMAP (1.00 ± 0.15 mV) was much higher than that of ES-CMAP (0.26 ± 0.15 mV) when recorded from pair C. Good-quality CMS-CMAPs could be recorded in some subjects from an electrode positioned very low in the esophagus. The differences between ES-CMAP and CMS-CMAP recorded either from esophageal or chest wall electrodes make CMS unreliable for the measurement of phrenic nerve conduction time.

esophageal electrode; cervical magnetic stimulation; phrenic nerve conduction time

THE DIAPHRAGM ELECTROMYOGRAM (EMG) elicited by phrenic nerve stimulation can provide useful information on diaphragm function and for the diagnosis of neuromuscular disease. By using electrical stimulation of the phrenic nerve (ES) with an esophageal electrode, phrenic nerve conduction time (PNCT) can be accurately measured (13). Whether it is possible to specifically record the diaphragm compound muscle action potential (CMAP) and accurately measure PNCT with magnetic nerve stimulation is uncertain.

Cervical magnetic stimulation of the phrenic nerves (CMS) is a recently described technique of phrenic nerve stimulation that is both easy and painless (9, 19) but that stimulates many of the muscles of the upper thoracic cage as well as the diaphragm. To assess the extent of stimulation of these muscles, investigators have used chest wall electrodes to record the CMAP (9, 11, 14, 19, 21). These studies, including our own (21), initially suggested that increasing stimulator output results in the CMAP amplitude reaching a plateau. However, further studies have revealed difficulty in obtaining good-quality surface signals (11) as well as contradictory results in terms of the leveling off of the amplitude of the CMAP elicited by CMS (CMS-CMAP) of increasing intensity (11, 14, 21). Moreover, the amplitude of the CMS-CMAP was often not the same as that of the CMAP elicited by ES (ES-CMAP) (9), and PNCT measured with CMS (CMS-PNCT) was frequently shorter than PNCT with ES (ES-PNCT) (20). These phenomena indicate that the diaphragm EMG recorded from surface electrodes after CMS is potentially unreliable, perhaps because chest wall electrodes also record electrical activity from other muscles (15).

To address this possibility, Similowski and co-workers (19, 20) have used a single-pair esophageal electrode to record EMG responses to CMS in two studies. However, their results were not reproducible, with a PNCT of 7.92 ms in the first study (19) and 5.88 ms in the second (20).

In the present study we used a specially designed esophageal electrode as well as chest wall surface electrodes to assess whether PNCT can be reliably measured with CMS. We also studied whether the latency of CMS-CMAP was influenced by the recording position of the esophageal electrode.

METHODS

Subjects

Ten healthy volunteers (6 men and 4 women) aged 28–38 yr (mean age 33 yr) participated in the study. The subjects were members of the laboratory staff; all were free of neurological and respiratory disease. The study was approved by the King’s College Hospital Ethics Committee, and all subjects gave their informed consent to participate.

Phrenic Nerve Stimulation

CMS. CMS of the phrenic nerves was performed by using a 90-mm coil (P/N 9784-00) powered by a Magstim 200 stimulator (Magstim, Whitland, Dyfed, UK). We placed the coil over C6-C7 with the coil current flowing clockwise or counterclockwise depending on which produced the highest amplitude CMS-CMAP at 80% output. During CMS, subjects were seated in a chair with the neck flexed. Stimulation was performed at relaxed end expiration with the abdomen unbound.

ES. The phrenic nerves were stimulated bilaterally at the posterior border of the sternomastoid muscle at the level of the cricoid cartilage with bipolar surface-stimulating electrodes (Medelec; Old Woking, UK). The cathode was below the anode. Square-wave impulses of 0.1-ms duration were delivered. Stimulation was begun at low voltage. The subjects adopted a similar position for ES as they had for CMS; in particular, forward flexion of the neck was maintained. Once the action potential was observed, stimulus voltage was progressively increased until no further increase in amplitude of CMAP occurred. To ensure that supramaximal stimulation of the phrenic nerves was maintained, the stimul
voltage was increased by 30% for the remainder of the study. Stimulation was also performed at relaxed end expiration.

Recording of CMAP

Esophageal electrode. Esophageal electrodes (Fig. 1) were individually constructed for each subject from a polyethylene tube 80 cm in length, 1.1 mm in internal diameter, and 1.5 mm in external diameter. Five Teflon-insulated copper wires 0.25 mm in diameter were passed through the tube and exteriorized at distances of 22, 18, 11, 7, and 3 cm from the distal end through five holes created by a 21-gauge needle. After being stripped of their insulation, the wires were tightly wound around the tube toward the distal end to form coils of 1 cm in width. Thus the completed electrode had an array of 1-cm electrodes placed 3 cm apart. A 6-cm gap lay between the lower three coils and the upper pair. We designated the most distal electrode coil number 1 and the most proximal coil number 5. Recordings were obtained from three pairs: electrodes 1 and 2 (pair A), electrodes 2 and 3 (pair B), and electrodes 4 and 5 (pair C).

The esophageal electrode was passed through the nose and swallowed into the esophagus. Electrode 2 was connected to the positive-input terminal of a differential amplifier and was the common electrode for bipolar pairs A and B; electrodes 1 and 3 were connected to negative-input terminals. The position of the esophageal electrode was then adjusted so that electrode 2 lay over the center of the electrically active region of the diaphragm (EARdi). With the electrode setup used in the present study, this point is characterized by both the amplitude and polarity being the same when recorded from pairs A and B (3) (Fig. 1). Electrode positioning was achieved by visual inspection of diaphragm CMAPs elicited by bilateral ES to minimize the influence of muscles other than the diaphragm. When the optimal position had been obtained, the electrode catheter was securely fixed at the nose.

Chest wall electrodes. Bipolar skin silver-silver chloride electrodes (Arbo Medical) were placed on the abraded skin in the sixth, seventh, or eighth intercostal space in the anterior axillary line on both the left and right side in 7 of the 10 subjects.

Data Acquisition

The EMG signals, from both esophageal and surface electrodes, were amplified and band-pass filtered between 10 Hz and 10 kHz (Magstim). The signals were then passed to a

![Esophageal Electrode](image)

**Fig. 1.** Experimental setup. Left: esophageal electrode configuration. Each electrode is 1 cm in length. Distance between electrodes within an electrode pair is 3 cm. Electrode 2 is a common one for pair A and pair B and is connected to positive-input terminal of both amplifiers. Electrode 2 is placed at center of diaphragm electrically active region. Right: compound muscle action potential (CMAP) recorded from 2 pairs with same negative polarity and similar amplitude. Data are from subject 1.
12-bit analog-to-digital converter (NB-M10-16, National Instruments, Austin, TX) and stored and displayed on a Macintosh Centris Computer running Labview 2.2 software (National Instruments). The signals were available in real time to the investigators. The sampling rate was 10 kHz.

Esophageal pressure (Pes) and gastric pressure (Pga) were recorded by using conventional balloon catheters (17). The pressures were measured by differential pressure transducers (model MP45, Validyne, Northridge, CA) and were recorded with Labview software. Transdiaphragmatic pressure (Pdi) was measured by subtraction of Pes from Pga. The Pdi elicited by phrenic nerve stimulation was termed twitch Pdi (Pdi\text{trw}).

Study Protocols

Protocol 1: Differences of the EMG recorded from pair A and pair B electrodes with CMS and ES. Simultaneous recordings from pair A and pair B were obtained during CMS and bilateral ES. A minimum of five twitches were performed with ES and at 60, 80, and 100% of maximum Magstim power output.

Protocol 2: Differences of the EMG recorded from pair C with CMS and ES. In this protocol we compared the CMAP from pair C during ES and CMS. CMAP was also recorded from pair A to monitor that the phrenic nerves were properly stimulated. A minimum of five stimulations were performed with supramaximal ES and CMS at maximal power output. Because the apparatus had the capacity to record only two channels simultaneously at the desired sampling rate, we were obliged to separate protocols 1 and 2.

Protocol 3: Differences of the EMG recorded from chest wall surface electrodes with CMS and ES. Similar to protocol 1, CMS at 60, 80, and 100% of stimulator output and supramaximal ES were delivered to elicit the CMAP. Left and right EMGs were recorded simultaneously. At least five twitches were performed for ES and for each output level of magnetic stimulation. Seven subjects participated in this study.

In three subjects (subjects 2, 4, and 7), a simplified protocol was performed on a separate day. Simultaneous recordings from pair A and pair B were obtained during CMS at 100% output and bilateral ES. A minimum of five twitches were performed for each method of stimulation. The purpose of this protocol was to examine the reproducibility of the measurements.

Additional Studies

We were able to study a patient (age 60 yr, height 170 cm) with a 3-yr history of diaphragm paralysis due to neuralgic amyotrophy (16). The CMAP was measured by using an esophageal electrode in response to both CMS at 100% of stimulator output and supramaximal bilateral ES. Pdi\text{trw} was also measured. Because there was no diaphragm response to ES, we placed electrode 2.45 cm from the nose instead of precisely positioning the esophageal electrode at the center of EARDi.

In a further study of four normal subjects, we placed surface electrodes at the second and third intercostal space in the anterior axillary line to record the EMG from muscles near to the site of phrenic nerve stimulation. ES and CMS with 100% output were used. The EMG from the surface electrodes on the upper chest wall and the diaphragmatic EMG recorded from the lower chest wall electrodes were recorded simultaneously. The purpose of this study was to compare the EMG recorded from the two sites.

In four subjects (subjects 1, 4, 5, and 6) anterior unilateral magnetic stimulation (UMS) (15) at 100% output was performed on the right phrenic nerve. The diaphragm CMAP was recorded from pair A. Unilateral supramaximal ES was also performed. Five twitches were obtained for each method of stimulation. The purpose of this simple experiment was to examine the suggestion of Mador et al. (11) that the CMAP could be affected by stimulus artifact.

In four subjects, Pes, Pga, and the CMAP (pair A and pair B) were recorded simultaneously during CMS. The sampling rate was 2 kHz. The purpose of this study was to investigate whether any extradiaphragmatic muscle contraction generated pressure before the CMAP after CMS.

Data Analysis and Statistics

The diaphragm CMAP was analyzed off-line. To eliminate the influence of electrocardiogram, we only analyzed CMAPs with constant shape and a stable baseline before and after stimulation. More than 80% of CMAPs were acceptable for analysis. The PNCT was defined as the time from stimulation artifact to the onset of the CMAP. The time from the onset of the CMAP to first peak was defined as first peak time (T1). Amplitude was measured from peak to peak rather than from baseline to peak because the baseline of the CMAP-CMAP was not always stable, especially from pair B. The phase of the CMAP was taken to be the net excursion of the amplitude of the signal in either the positive or negative direction. The values reported in RESULTS correspond to the average of three to five CMAPs.

Paired t-tests were used to assess the differences in amplitude and conduction time between ES and CMS. The difference between esophageal EMG and chest wall EMG was tested by an unpaired t-test. The differences with different intensities of magnetic stimulation were analyzed by repeated paired t-tests. Results are expressed as means ± SE, and a P value of < 0.05 was considered significant.

RESULTS

The electrode catheter was well tolerated by all subjects. A satisfactory position for the esophageal electrode could be found in all subjects by making careful minor adjustments to the position of the catheter on the basis of the polarity and amplitude of the CMAP during supramaximal ES. The CMAP recorded simultaneously from pairs A and B then had the same negative polarity and similar amplitude (Fig. 2), and the common electrode of pair A and B was at the center of EARDi.

Differences of the EMG Recorded From Pair A and Pair B Electrodes With CMS and ES

With supramaximal ES, clear signals could be obtained from the esophageal electrode pairs A and B in all subjects (Figs. 1–3). There was always a level baseline and no electrical activity preceding the down-turn of the CMAP. The onset of the CMAP was always clearly identified. The latency of the CMAP recorded from pair A was exactly the same as that from pair B (7.0 ± 0.6 ms). The amplitude of the ES-CMAP was 1.85 ± 0.59 and 1.90 ± 0.58 mV for pair A and pair B, respectively [P = not significant (NS)]. However,
the CMS-CMAP from pair A and pair B was different from the ES-CMAP (Table 1). The baseline was not always at the same level and sometimes had superadded short-latency electrical activity; this activity was more prominent from pair B (Figs. 2 and 3). The amplitude of the CMAP elicited by maximal CMS was more variable among individuals compared with ES. The coefficients of variation from pair A and pair B

**Fig. 2.** CMAP recorded simultaneously from pair A and pair B. Left: CMAP elicited by electrical stimulation (ES) (ES-CMAP). Latency is equal from pair A and pair B. Right: CMAP elicited by 100% cervical magnetic stimulation (CMS) (CMS-CMAP). There is a small short-latency wave before prominent negative wave of CMS-CMAP recorded from pair B; therefore, latency recorded from pair B is shorter than that recorded from pair A. Five stimulations were superimposed. A: small waves (indicated by arrow) in pair B are completely merged with prominent negative wave of diaphragm CMS-CMAP. Data are from subject 2. B: small waves do not merge with prominent negative wave of diaphragm CMS-CMAP, therefore forming 2 separate waves. Data are from subject 3.

**Fig. 3.** CMAP recorded simultaneously from pair A and pair B. Left: ES-CMAP. Latency recorded from pair A is equal to that from pair B. CMAP begins with a prominent negative wave. Right: CMS-CMAP. There is a baseline change before prominent negative wave, particularly when recording from pair B. Before the prominent negative wave, there are small waves that differ in polarity between pair A and pair B. Onset of diaphragm CMAP is therefore difficult to determine. Data are from subject 5. Three stimulations were superimposed.
Latency could not be measured because of nearly unidentifiable CMAP. Latency could not be measured because of movement of baseline.

The main difference between the shape of the CMAP elicited by ES and CMS was at the beginning of the CMAP waveform (Figs. 2 and 3). For pair B, in some subjects the small wave completely merged with the main negative wave (Fig. 2A), whereas in other subjects the small wave was followed by a brief silence of electrical activity that was then followed by the prominent negative wave, there being therefore two separate waves (Fig. 2B).

Table 1. CMAPs recorded from esophageal electrode during ES and maximal CMS

<table>
<thead>
<tr>
<th>Subj. No.</th>
<th>n</th>
<th>Amplitude of CMAP, mV</th>
<th>Latency of CMAP, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ES</td>
<td>CMS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pair A</td>
<td>Pair B</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>2.55±0.13</td>
<td>1.13±0.07</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>1.86±0.05</td>
<td>1.77±0.03</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>2.41±0.22</td>
<td>2.76±0.09</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1.01±0.04</td>
<td>0.50±0.02</td>
</tr>
<tr>
<td>5</td>
<td>3-5</td>
<td>1.67±0.03</td>
<td>1.32±0.14</td>
</tr>
<tr>
<td>6</td>
<td>4-5</td>
<td>0.99±0.04</td>
<td>0.56±0.15</td>
</tr>
<tr>
<td>7</td>
<td>3-5</td>
<td>2.39±0.10</td>
<td>1.89±0.11</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>2.65±0.11</td>
<td>3.02±0.05</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>1.45±0.12</td>
<td>1.49±0.11</td>
</tr>
<tr>
<td>10</td>
<td>4-5</td>
<td>1.94±0.21</td>
<td>0.87±0.14</td>
</tr>
</tbody>
</table>

Mean±SE 1.85±0.59  | 1.43±0.71  | 1.90±0.58  | 1.52±0.72  | 0.26±0.15  | 1.00±0.15  | 7.0±0.6  | 7.1±0.7  | 7.0±0.6  | 5.3±0.04  | 2.6±0.7  | 1.7±0.5  
Values are means ± SD; n, no. of observations. CMAP, compound muscle action potential; ES, electrical stimulation; CMS, cervical magnetic stimulation. 
*Latency could not be measured because of nearly unidentifiable CMAP. †Latency could not be measured because of movement of baseline.

were 34 and 32 for ES and were 53 and 49 for CMS, respectively. The amplitude of the CMAP elicited by 100% CMS was lower than the amplitude of the CMAP elicited by ES for pair A and pair B, but the difference achieved statistical significance (P < 0.05) only for pair A.

In four subjects, with CMS we were unable to measure PNCT from either pair A or pair B because of movement of the baseline and reversal of the CMAP polarity because of superimposed short-latency waves (Fig. 3). The small waves in pair A and pair B were opposite in polarity, indicating an origin distant above the diaphragm. These small waves were followed by prominent negative waves that were similar to those of the ES-CMAP in their polarity. Latency could be measured in six subjects in whom the baseline was relatively stable, and the CMS-CMAP polarity was the same as the ES-CMAP polarity (Fig. 2). The PNCT measured from pair A was 7.1 ± 0.7 ms with CMS and 6.9 ± 0.7 ms with ES in the six subjects studied (P = NS); PNCT measured from pair B was shorter (5.3 ± 0.4 ms with CMS and 6.9 ± 0.7 ms with ES; P < 0.001). The main difference between the shape of the CMAP elicited by ES and CMS was at the beginning of the CMAP waveform (Figs. 2 and 3). For pair B, in some subjects the small wave completely merged with the main negative wave (Fig. 2A), whereas in other subjects the small wave was followed by a brief silence of electrical activity that was then followed by the prominent negative wave, there being therefore two separate waves (Fig. 2B).

Differences of the EMG Recorded From Pair C With CMS and ES

In nine subjects a CMAP could be detected from pair C with both ES and CMS. However, the amplitude of the ES-CMAP was very small and was much less than that of the CMS-CMAP (P < 0.001; Table 1, Fig. 4). The latency for pair C with ES and CMS was different (P < 0.05). In one subject, the CMAP was barely detectable from pair C during ES (0.03 mV), whereas the amplitude of the CMAP was 0.88 mV with CMS.

Effect of Magnetic Stimulator Output on the Amplitude of CMAP Recorded From the Esophageal Electrode

The amplitudes of the CMAPs elicited by 60, 80, and 100% output of the magnetic stimulator were 0.57 ± 0.35, 0.99 ± 0.53 and 1.43 ± 0.71 mV for pair A and were 0.60 ± 0.33, 1.08 ± 0.53, and 1.52 ± 0.72 mV for pair B, respectively. There were significant differences in amplitude between all the different outputs of the stimulator (P < 0.05).

Fig. 4. CMAP recorded simultaneously from pair A and pair C. Left: ES-CMAP. Pair A only detects a small short-latency potential. Right: CMS-CMAP. Pair C detects a high-amplitude potential. Data are from subject 3.
Table 2. CMAPs recorded from surface electrodes during ES and maximal CMS

<table>
<thead>
<tr>
<th>Subj. No.</th>
<th>n</th>
<th>Latency, ms</th>
<th>T1, ms</th>
<th>No. of Phases</th>
<th>Amplitude, mV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ES</td>
<td>CMS</td>
<td>ES</td>
<td>CMS</td>
</tr>
<tr>
<td>Left side</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4–5</td>
<td>6.7±0.2</td>
<td>5.9±0.1</td>
<td>9.2±0.3</td>
<td>4.3±0.5</td>
</tr>
<tr>
<td>3</td>
<td>4–5</td>
<td>6.4±0.1</td>
<td>4.7±0.1</td>
<td>3.8±0.5</td>
<td>0.8±0.2</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>8.2±0.2</td>
<td>6.7±0.1</td>
<td>7.7±0.4</td>
<td>1.5±0.2</td>
</tr>
<tr>
<td>5</td>
<td>4–5</td>
<td>7.9±0.3</td>
<td>5.7±0.1</td>
<td>8.0±0.6</td>
<td>1.4±0.1</td>
</tr>
<tr>
<td>7</td>
<td>3–5</td>
<td>7.2±0.3</td>
<td>4.2±0.3</td>
<td>9.0±0.3</td>
<td>2.3±0.2</td>
</tr>
<tr>
<td>8</td>
<td>3–5</td>
<td>6.6±0.1</td>
<td>5.8±0.1</td>
<td>6.2±0.2</td>
<td>8.2±0.1</td>
</tr>
<tr>
<td>10</td>
<td>3–5</td>
<td>7.8±0.2</td>
<td>5.6±0.6</td>
<td>9.2±0.4</td>
<td>1.4±0.0</td>
</tr>
<tr>
<td>Mean±SE</td>
<td></td>
<td>7.3±0.7</td>
<td>5.5±0.8</td>
<td>7.6±1.8</td>
<td>2.8±2.4</td>
</tr>
</tbody>
</table>

Right side

<table>
<thead>
<tr>
<th>Subj. No.</th>
<th>n</th>
<th>Latency, ms</th>
<th>T1, ms</th>
<th>No. of Phases</th>
<th>Amplitude, mV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ES</td>
<td>CMS</td>
<td>ES</td>
<td>CMS</td>
</tr>
<tr>
<td>2</td>
<td>4–5</td>
<td>6.5±0.2</td>
<td>4.7±0.1</td>
<td>8.2±0.3</td>
<td>2.8±0.1</td>
</tr>
<tr>
<td>3</td>
<td>4–5</td>
<td>6.6±0.1</td>
<td>5.0±0.1</td>
<td>6.5±0.5</td>
<td>1.1±0.1</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>8.3±0.2</td>
<td>4.8±0.1</td>
<td>7.8±0.3</td>
<td>1.5±0.1</td>
</tr>
<tr>
<td>5</td>
<td>4–5</td>
<td>8.1±0.2</td>
<td>5.3±0.2</td>
<td>9.4±0.7</td>
<td>2.6±0.1</td>
</tr>
<tr>
<td>7</td>
<td>3–5</td>
<td>8.0±0.2</td>
<td>4.5±0.4</td>
<td>9.1±0.4</td>
<td>2.2±0.9</td>
</tr>
<tr>
<td>8</td>
<td>3–5</td>
<td>7.7±0.2</td>
<td>6.6±0.1</td>
<td>8.1±0.4</td>
<td>1.1±0.6</td>
</tr>
<tr>
<td>10</td>
<td>3–5</td>
<td>8.3±0.3</td>
<td>5.3±0.4</td>
<td>4.9±0.1</td>
<td>1.2±0.0</td>
</tr>
<tr>
<td>Mean±SE</td>
<td></td>
<td>7.6±0.7</td>
<td>5.2±0.6</td>
<td>7.7±1.4</td>
<td>3.2±3.3</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of observations.

Effect of Magnetic Stimulator Output on the Latency of CMAP Recorded From the Esophageal Electrode

In the six subjects whose CMAP signals had a definable starting point, the latency was measured for different outputs of the magnetic stimulator. The latencies for 60, 80, and 100% output were 7.5 ± 0.8, 7.3 ± 0.6, and 7.1 ± 0.7 ms for pair A and were 5.6 ± 0.5, 5.3 ± 0.3 and 5.3 ± 0.4 ms for pair B. The small reduction in latency was significant between 60 and 100% output for pair A (P < 0.05) but not for pair B.

CMAP Recorded From Chest Wall Electrode With ES and CMS

CMAPs were satisfactorily recorded from both sides in all seven subjects with ES. The signals were of good quality with a level baseline and clear onset of the CMAP and latency could be easily measured. The latencies for the left and right sides were 7.3 ± 0.7 and 7.6 ± 0.7 ms, respectively (P = NS). The number of phases of the CMAP was always two. The T1 was 7.6 ± 1.8 ms for left side and 7.7 ± 1.4 ms for the right side with ES. The amplitude was 0.79 ± 0.24 and 0.71 ± 0.25 mV for left and right side, respectively, during ES (Table 2). The shape of the CMS-CMAP was different from that of the ES-CMAP. There were more phases of the CMS-CMAP, and the T1 was shorter for both the left side (P < 0.01) and the right side (P < 0.05). The latency measured with CMS at 100% output was 5.5 ± 0.8 ms for the left side and 5.2 ± 0.6 ms for the right side, which was shorter than that measured with ES for both the left and the right sides (P < 0.01). Although the latency with lower outputs from the magnetic stimulator was slightly longer, this did not reach statistical significance. The amplitude of the CMS-CMAP increased with increasing output of the stimulator (Table 3, Fig. 5). The amplitude of the CMS-CMAP was more variable between individuals when compared with that of the ES-CMAP. The amplitudes of the CMS-CMAP at 100% output were 1.03 ± 0.88 mV for the left side and 1.00 ± 0.97 mV for the right side (Table 2). The coefficients of variation were 33 on the left side and 39 on the right.

Table 3. Amplitude of CMAP elicited by ES and CMS recorded with chest wall electrodes

<table>
<thead>
<tr>
<th>Subj. No.</th>
<th>n</th>
<th>CMS 60%</th>
<th>CMS 80%</th>
<th>CMS 100%</th>
<th>ES</th>
<th>CMS 60%</th>
<th>CMS 80%</th>
<th>CMS 100%</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4–5</td>
<td>0.22±0.01</td>
<td>0.38±0.02</td>
<td>0.45±0.02</td>
<td>0.59±0.01</td>
<td>0.09±0.00</td>
<td>0.16±0.04</td>
<td>0.56±0.02</td>
<td>0.73±0.01</td>
</tr>
<tr>
<td>3</td>
<td>4–5</td>
<td>0.22±0.02</td>
<td>0.35±0.03</td>
<td>0.59±0.01</td>
<td>0.46±0.01</td>
<td>0.07±0.01</td>
<td>0.23±0.08</td>
<td>0.43±0.04</td>
<td>0.35±0.01</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>0.29±0.02</td>
<td>0.52±0.02</td>
<td>0.42±0.02</td>
<td>1.12±0.05</td>
<td>0.07±0.01</td>
<td>0.45±0.02</td>
<td>0.60±0.02</td>
<td>0.89±0.01</td>
</tr>
<tr>
<td>5</td>
<td>4–5</td>
<td>0.32±0.02</td>
<td>1.26±0.10</td>
<td>3.12±0.08</td>
<td>0.84±0.05</td>
<td>1.20±0.12</td>
<td>2.96±0.12</td>
<td>3.31±0.09</td>
<td>0.91±0.03</td>
</tr>
<tr>
<td>7</td>
<td>3–5</td>
<td>0.10±0.01</td>
<td>0.45±0.05</td>
<td>0.73±0.02</td>
<td>0.72±0.02</td>
<td>0.18±0.02</td>
<td>0.76±0.04</td>
<td>0.91±0.05</td>
<td>0.89±0.02</td>
</tr>
<tr>
<td>8</td>
<td>3–5</td>
<td>0.13±0.02</td>
<td>0.23±0.01</td>
<td>0.99±0.03</td>
<td>1.14±0.06</td>
<td>0.37±0.02</td>
<td>0.75±0.02</td>
<td>0.89±0.12</td>
<td>0.92±0.02</td>
</tr>
<tr>
<td>10</td>
<td>3–5</td>
<td>0.22±0.04</td>
<td>0.69±0.03</td>
<td>0.92±0.10</td>
<td>0.63±0.05</td>
<td>0.89±0.05</td>
<td>0.21±0.05</td>
<td>0.30±0.02</td>
<td>0.31±0.01</td>
</tr>
<tr>
<td>Mean±SE</td>
<td></td>
<td>0.21±0.07</td>
<td>0.55±0.32</td>
<td>1.03±0.88</td>
<td>0.79±0.24</td>
<td>0.41±0.42</td>
<td>0.79±0.92</td>
<td>1.00±0.97</td>
<td>0.71±0.25</td>
</tr>
</tbody>
</table>

Values are means ± SD in mV; n, no. of observations.
side and 38 on the right for ES and were 92 on the left and 104 on the right for CMS.

Reproducibility

Repeat studies were performed in three subjects. The latency of the ES-CMAP measured from pair A was exactly the same as that measured from pair B and was 7.0 ms for the first study and 7.3 ms for the second. In one subject (subject 4), the latency of CMS-CMAP could not be measured either from pair A or pair B because of the movement of the baseline; this was so on both occasions. The latency could be measured from pair A and pair B in another two subjects. Similar to the first study, the latency of CMS-CMAP measured from pair A was 7.5 ms and was much longer than that measured from pair B (5.5 ms) because of the interference of short-latency signals.

Additional Experiments

In the patient with neuralgic amyotrophy the Pdi was 2 cmH₂O with maximal CMS and 0 cmH₂O with ES, confirming the diagnosis of diaphragm paralysis. We could not detect an EMG from the esophageal electrode pairs A or B despite using high-stimulus intensity (200 V) and attempting for 15 min to locate the phrenic nerve. However, we could detect an EMG signal from pair A and B, which were opposite in polarity during CMS. The amplitudes of the CMAP from pair A and pair B were 0.49 and 0.40 mV (Fig. 6).

An EMG response was consistently detected from the upper chest wall electrodes in all four subjects with CMS but only from three subjects with ES (Fig. 7). The amplitude of the ES-CMAP was very small (0.1 ± 0.11 mV), ~8% of that elicited by CMS (1.25 ± 0.04 mV). The latency for ES-CMAP and CMS-CMAP were similar (4.4 ± 0.7 and 4.0 ± 1.0 ms, respectively).

The shape of the diaphragm CMAP elicited by UMS was the same as that elicited by ES. The latencies of the diaphragm CMAP were 7.3 ± 0.6 ms for ES and 7.2 ± 0.5 ms for UMS (P = NS).

In the four subjects studied, the time from stimulation to the onset of Pes or Pdi was 29.4 ± 2.4 ms with CMS, and the CMAP always preceded pressure generation.

DISCUSSION

In this study we found that the shape and latency of the CMAP were different with ES and CMS, particularly when the diaphragm CMAP was recorded from chest wall electrodes. The CMS-CMAP was often affected by short-latency, small superimposed waves. The latency of the CMS-CMAP from pair B was significantly shorter than that from pair A.

Critique of Methodology

Esophageal electrode design. The EMG response to phrenic nerve stimulation was detected with three pairs of esophageal electrodes. The conventional bipolar configuration is with a 1-cm distance between the electrodes, although 6 cm have also been used (13). We...
Chose a distance of 3 cm between electrodes because the diaphragm consists of two hemidiaphragms that are not at the same level. A 1- to 2-cm change of electrode position in the esophagus is usually necessary for optimal recordings of the EMG from each hemidiaphragm (13). A distance of 3 cm between the bipolar electrodes facilitates optimal recording from both sides. The longer distance between the electrodes might result in high-frequency loss in spectral analysis (1), but this was not addressed in the present study.

Positioning at EARdi. Correct positioning of the electrode catheter is essential for our results to be valid. CMAP polarity recorded by a bipolar electrode is related to electrode position and the connection of the electrode to the differential amplifier. If the electrode closest to the electrically active region is connected to the positive-input terminal of a differential amplifier and another electrode away from the electrically active area is connected to the negative-input terminal, the CMAP recorded will be negative in polarity as shown in Fig. 1. To conveniently compare electrode pair A with pair B, we connected electrode 2 to both positive-input terminals of a two-channel amplifier and connected electrodes 1 and 3 to the negative input terminals to produce the same polarity CMAP in both pairs A and B. Because the diaphragm CMAP amplitude and polarity are sensitive to electrode positioning (3), the finding of similar amplitude and polarity waves in pairs A and B after bilateral ES proved that, in every subject, electrode 2 was close to the center of EARdi (Fig. 1).

Source of the Small Superimposed Waves

It is necessary to consider the effect of possible electrode movement on our results during CMS. We securely fixed the electrode catheter at the nose with tape; therefore, the electrode position was constant relative to the esophagus during the study. The unfocussed magnetic stimulation activates extradiaphragmatic muscles during phrenic nerve stimulation, which may generate pressure in the thorax earlier and result in a change of the position of electrode relative to the diaphragm. Additional studies showed that the time from stimulation to the onset of pressure (26–32 ms) was much longer than the latency of the CMAP after CMS. Therefore, it is unlikely that electrode movement affected our results.

The source of the small superimposed waves is of interest because, if they arise from the stimulator, they might be avoidable by changing the nature of the stimulus; conversely, if they arise as a result of coactivation of the upper thoracic muscles, they would probably...
be unavoidable. Several lines of argument suggest they are due to muscle activation. First, because a magnetic pulse duration is $\sim 1$ ms (8), it is unlikely that the artifact from the magnetic stimulator would overlap the CMAP. Moreover, if the artifact from magnetic stimulation was long enough to interfere with the diaphragm EMG, then the CMAP from upper chest wall electrodes would be expected to show more interference than that from lower chest wall electrodes. In fact, the EMG recorded from the upper chest wall electrodes contained less superimposed activity than that obtained from lower chest wall electrodes (Fig. 7). Second, when magnetic stimulation is used to stimulate peripheral nerves, where latency is shorter than that for the phrenic nerves, the stimulator artifact does not preclude analysis of the CMAP (7, 10). Finally, we could always detect a clear CMAP from the esophageal electrode when using unilateral magnetic stimulation with the same stimulation system as that used for CMS but with a different coil.

**Source of the Differences Between Esophageal ES-CMAP and CMS-CMAP**

Unlike ES, CMS simultaneously stimulates other chest muscles, including the latissimus dorsi, trapezius, serratus anterior, and pectoralis muscles (9, 19). If the EMG recorded from an esophageal electrode originates only from the diaphragm, the shape of the CMS-CMAP should be similar to the shape of the ES-CMAP. However, there was a distinct difference in shape between the ES-CMAP and the CMS-CMAP at the beginning of the CMAP. It has been suggested that the amplitude and shape of an observed CMAP are a function of the geometric properties of the motor units, electrode properties (2), and muscle conduction velocity (1). The electrode properties and diaphragm geometry were constant during this study. Therefore, the difference between the ES-CMAP and the CMS-CMAP suggests that the esophageal diaphragm EMG could be affected by contributions from nondiaphragmatic muscles, although this remains to be proven.

There is additional evidence to support the view that the esophageal electrode can pick up contaminating signals. First, by using CMS, we could detect a high-amplitude CMAP from the esophageal pair C electrode, which was far from the diaphragm. This high-amplitude potential was from other muscles as judged by the shape and latency of the CMAP (Fig. 4). Second, in the patient with diaphragm paralysis, it was not possible to detect a CMAP from pair A and pair B electrodes by using ES, whereas a 0.49- and 0.4-mV CMAP, respectively, were detected by using CMS (Fig. 6). Further evidence that the CMS-CMAP recorded from the esophageal electrode may be contaminated by nondiaphragmatic muscle is discussed in Can PNCT Be Measured With CMS?

Nevertheless, it should be noted that any influence on the diaphragm CMS-CMAP by extradiaphragmatic activity may not apply to the EMG of voluntary contractions. For voluntary inspiration, the EMG generated is from only inspiratory muscle, whereas the CMS-CMAP may be contributed to by expiratory muscles, including trapezius and the deep muscles of the back.

**With CMS the CMAP Recorded With Surface Electrodes Is Contaminated by Nondiaphragm Muscles**

We observed that the shape of the CMS-CMAP recorded with surface electrodes differed from that of the ES-CMAP. Similar findings have been reported by Similowski et al. (18). The diaphragm EMG recorded by chest wall electrodes is a far-field potential recorded at a distance from the active muscle (12). Conventionally, the electrodes are placed at the sixth and seventh intercostal space near the superficial pectoralis major muscle, and the distance between the electrodes and the lower margin of the pectoralis major muscle is similar to the distance of the electrodes from the diaphragm. It is therefore likely that during CMS the diaphragm CMAP recorded from chest wall electrodes is contaminated by electrical activity from adjacent muscles, which are also stimulated. Bellemare and Bigland-Ritchie (4) demonstrated that, during unilateral electrical stimulation of the phrenic nerve, contralateral chest wall electrodes can pick up a small amount of diaphragm electrical activity. It has also been noted that the CMAP evoked by a supramaximal stimulus of a peripheral nerve can spread several centimeters from the active muscle by volume conduction (12). Another example of far-field potential is that a CMAP can be recorded with electrodes placed on the hypothenar eminence, far from the actively contracting muscle during stimulation of the median nerve at the wrist (12). These studies lend support to our results for the diaphragm and argue against the assumption that the CMS-CMAP recorded from chest wall electrodes is free of contamination from other chest muscle activity.

In subject 10, the fact that the amplitude of the CMS-CMAP elicited by low-intensity stimulation was higher than that elicited by high-intensity stimulation probably resulted from the difference in polarity and phase between the CMAP of the chest muscles and the diaphragm and from their different responses to stimulation. In another subject (subject 5), the amplitude of the diaphragm ES-CMAP was typical for the surface diaphragm EMG (5, 12), but the amplitude of CMS-CMAP elicited by 100% stimulator output was much higher than would be expected simply from diaphragm contraction (5). These findings can be explained by summation of the CMAP from the diaphragm and other chest wall muscles and provide supplementary evidence that the CMS-CMAP recorded with surface electrodes is contaminated by activation of rib cage muscles.

The amplitude of the CMAP increased with increasing magnetic stimulator output for both the esophageal and the chest wall recordings. This is expected and is in accord with previous studies (11, 14, 20, 21). With maximal CMS the amplitude of the CMAP recorded by the esophageal electrode was less than with ES, but the amplitude of the CMAP recorded with surface electrodes was greater. This finding again supports the
suggestion that the EMG recorded from chest wall electrodes was not a pure diaphragm EMG.

Similowski et al. (20) noted that they could not detect the CMAP from chest wall electrodes with either ES or CMS in patients with diaphragm paralysis as a result of severe amyotrophic lateral sclerosis (ALS). This seems to contradict the findings of the present study. However, a possible explanation for this difference could be that ALS may have affected the chest wall muscles.

Can PNCT Be Measured With CMS?

It is interesting to compare our PNCT results with those of previous studies. Although CMS is considered an easy technique, the CMS-PNCT differs between laboratories. The mean CMS-PNCT measured by Chokroverty et al. (6) with chest wall electrodes was 7.2 ms, whereas the PNCT measured by Similowski et al. (20) was 5.36 ms. In the laboratory of Similowski et al. (19, 20), the results of PNCT were variable between different studies. In the present study, CMS-PNCT measured from chest wall electrodes was similar to that in the recent study of Similowski et al. (20). The CMS-PNCT obtained from the esophageal electrode pair A was affected by stimulus intensity, a finding also noted by Similowski et al. This differs from the results of McKenzie and Gandevia (13), who reported that when moving from submaximal to supramaximal electrical stimulation the PNCT altered by <0.1 ms. The concept that CMS depolarizes the phrenic nerves distally has been proposed as an explanation for the shorter PNCT sometimes obtained with CMS, but this suggestion cannot explain the close similarity between ES-PNCT and CMS-PNCT obtained when recording from esophageal electrode pair A.

Our hypothesis is that the short latency occurs because of superadded signals from extradiaphragmatic muscles. Consistent with this we observed that the PNCT measured by different electrode positions (pairs A and B) was the same with ES in every subject, indicating that slightly different positioning of the esophageal electrode does not affect PNCT, consistent with the observation of McKenzie and Gandevia (13). However, we were surprised to find that the PNCT recorded from different esophageal electrode positions was different when CMS was used (pair A CMS-PNCT 7.1 ± 0.7 ms vs. pair B CMS-PNCT 5.3 ± 0.4 ms). This result shows that short-latency potentials interfere with the esophageal diaphragm CMS-CMAP at pair B. We also observed that there was no difference in latency between different magnetic stimulus intensities when the EMG was recorded from chest wall electrodes or esophageal electrode pair B. However for esophageal electrode pair A PNCT was longer and was also influenced by stimulus intensity. As previously discussed, the diaphragm EMG response to CMS recorded from esophageal electrode pair B, and particularly from the chest wall, is more likely to contain signals from the extradiaphragmatic thoracic muscles than those recorded from esophageal pair A, which is positioned with its lower electrode in the abdomen. This result demonstrates that the latency measured with CMS from the chest wall electrodes and esophageal electrode pair B represent the latency of the extradiaphragmatic muscles rather than PNCT; because these muscles are easily stimulated, an equal response was observed with 60 and 100% of maximal stimulator output. According to this hypothesis the slight shortening of CMS-PNCT measured from pair A at 100% of stimulator output could also be due to the contribution of nondiaphragmatic muscles.

In conclusion, the use of chest wall electrodes with CMS to measure PNCT may lead to misleading results. The relatively small interference in esophageal EMG recordings compared with chest wall recordings usually, but not always, allows PNCT to be measured accurately. The reference electrode of a bipolar esophageal electrode placed in the abdominal part of the esophagus can improve the quality of the diaphragm EMG signal elicited by CMS.

REFERENCES


