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Diaphragm electromyograms recorded from multiple surface electrodes following magnetic stimulation

J.C. Gierant, N. Mustfa, W.D. Man, Y.M. Luo, G. Rafferty, M.I. Polkey and J. Moxham

ABSTRACT: The diaphragm compound-muscle action potential (CMAPdi), elicited by unilateral magnetic stimulation (UMS) of the phrenic nerve can be recorded using surface electrodes. However, there is no consensus on the best positioning of surface electrodes and there are no data on the reproducibility of the signal.

Using 36 surface electrode pairs, in five healthy subjects, the CMAPdi elicited by UMS and electrical stimulation (ES) were compared and 12 pairs were identified as providing acceptable signals. The latency and amplitude were measured for each CMAPdi, following UMS at 60–100% of maximal stimulator output, in 12 healthy subjects, on two occasions.

Latencies obtained using UMS and ES ranged between 6.1–7.33 and 6.25–7.17 ms, respectively. Optimum CMAPdi were not recorded from the same electrode pair in all subjects, or for both hemidiaphragms in each subject. However, the optimal recording site for a particular individual remained unchanged on subsequent testing. When recorded from the optimal site, latencies and amplitudes of CMAPdi elicited on the two occasions were not significantly different.

The current study suggests that the use of multiple chest wall electrodes can identify an optimal electrode pair, from which it is possible to obtain reproducible compound-muscle action potential signals.

KEYWORDS: Diaphragm, magnetic stimulation, reproducibility, surface electrodes

AFFILIATIONS
Respiratory Muscle Laboratory, King's College London School of Medicine, King's College Hospital, London, UK.

CORRESPONDENCE
J. Moxham
Dept of Respiratory Medicine
King's College Hospital
Bessemer Road
London
SE5 9PJ
UK
Fax: 44 2073463589
E-mail:
john.moxham@kingsch.nhs.uk

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The diaphragm compound muscle action potential (CMAPdi), elicited by phrenic nerve stimulation, reflects phrenic nerve and diaphragm function and provides diagnostic and prognostic information [1]. The measurement is useful in patients with neuromuscular disease and respiratory muscle involvement [2], including those in the intensive care unit (ICU).

The phrenic nerve can be stimulated using electrical or magnetic techniques [3]. Electrical stimulation (ES) is a well-established method of phrenic nerve activation [4–7], but it can be painful and due to a narrow field of activation it can also be technically difficult to locate the phrenic nerves [8–10]. Therefore, false-negative results are relatively common, particularly in the ICU or ward settings and in patients with suspected respiratory muscle weakness and with unfavourable neck anatomy. Although the phrenic nerve is more reliably located using magnetic stimulation (MS), which has a wider field of activation and is more comfortable for patients [11], it may co-activate extradiaphragmatic chest wall muscle and contaminate the electromyogram (EMG) signal, affecting CMAPdi reproducibility [11, 12]. However, it is possible to avoid co-activation of extradiaphragmatic muscles when performing MS of the phrenic nerves, particularly with careful placement of the stimulation coils [13], and silent EMG traces in patients with diaphragm paralysis have been recorded with surface electrodes during MS [14, 15].

The CMAPdi can be recorded from needle electrodes placed in the diaphragm [16] or from an oesophageal electrode [1]. Although with these techniques for EMG acquisition the electrodes are placed close to the diaphragm, they are invasive, uncomfortable, technically difficult and have not been widely adopted for diaphragm assessment. Chest wall electrodes are easily applied and more acceptable to patients. Although a number of different sites have been reported for recording the diaphragm EMG using surface electrodes, the optimal position for achieving a reproducible CMAPdi is not well established. Different investigators have described a variety of positions for chest wall

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electrodes for MS, most commonly close to the anterior axillary line, the midclavicular line, or between the xyphoid process and the costal margin [8, 13, 17, 18]. Various positions have also been presented for ES by investigators with the most common recording sites being the anterior axillary line over the sixth to the eighth intercostal spaces [2, 8, 9, 17], between the xyphoid process and the costal margin [5] and in the eighth intercostal space close to the midclavicular line [19]. Thus, CMAPdi can be recorded from multiple positions using MS, and the optimal position of electrodes may vary between individuals. In clinical practice, it is crucial to achieve a reproducible signal so that the technique can be used to serially monitor neuromuscular function of the diaphragm. The current authors hypothesised that testing all recording sites, with surface electrodes during the same procedure, would identify the optimal positions for each patient.

Using multiple chest-wall surface electrodes, the purpose of this study was: 1) to determine the optimal position of electrodes for recording the CMAPdi elicited by unilateral magnetic stimulation (UMS) in healthy subjects; and 2) to assess the reproducibility of CMAPdi and latency with UMS.

MATERIALS AND METHODS

Healthy volunteers, free of neurological and respiratory disease and members of the laboratory staff, participated in the studies. The ethics committee of King's College Hospital (London, UK) approved the study and subjects gave their informed consent.

Techniques of stimulation of phrenic nerves

Unilateral magnetic stimulation of the phrenic nerves

During UMS, subjects were seated upright in a chair. The phrenic nerves were stimulated anterolaterally in the neck with a 43-mm mean diameter double-circular (figure of eight) coil (P/N 9784-00; Magstim, Co., Dyfed, UK) powered by a Magstim 200 stimulator (Magstim Co.). The lower border of the coil was placed at the level of the upper border of the cricoid cartilage. Each stimulation was performed at the end of a relaxed expiration, with the mouth closed, wearing a nose-clip and with the abdomen unbound. The CMAPdi was recorded using anterolateral MS either at 80% of maximal intensity or at different percentages of maximal power output. In the latter case, stimulation began at 60% of maximal intensity and then the stimulus intensity was increased in steps of 10% up to the maximal power output. Care was taken to minimise co-stimulation of the brachial plexus, as indicated by visible muscle contractions and arm movements.

Electrical stimulation of the phrenic nerves

The subjects were positioned as for UMS and stimulations were performed at resting end-expiration. ES was performed using a surface bipolar stimulating electrode (Medelec, Old Woking, UK) with the felt tips soaked in saline. The electrode was connected to a constant voltage stimulator (Digitimer type 3072; Digitimer Ltd, Welwyn Garden City, UK) and a gated pulse generator (Digitimer type 2521; Digitimer Ltd) which generated square-wave impulses of 100 μs throughout. The electrode was positioned at the posterior border of the sternomastoid muscle, at the level of the cricoid cartilage, with the cathode at the lower level.

Stimulation began at low intensity. When a CMAPdi was observed, the stimulus voltage was progressively increased in steps of 10 volts (V) until no further increase in the size of CMAPdi was observed, indicating supramaximal stimulation. The voltage was increased by a further 10% for the remainder of the study to ensure that supramaximal stimulation was achieved throughout. The voltage achieving supramaximal stimulation varied between subjects, from 100 to 160 V. Care was taken to avoid co-stimulation of the brachial plexus, as indicated by visible muscle contractions and arm movements.

Diaphragm compound-muscle action potential acquisition

The skin was initially cleaned with alcohol wipes to reduce skin resistance. Silver/silver chloride electrodes (Arbo Medical, Stratford, CT, USA) were then positioned at multiple sites, as per protocol. The CMAPdi was recorded following phrenic nerve stimulation. EMG signals were amplified, band-pass filtered between 10–10,000 Hz (Magstim Co) and sampled at 10 kHz using Power Lab (AD Instruments Pty Ltd, Castle Hill, NSW, Australia). The signals were available in real time to the investigators. Phrenic nerve conduction time (PNCT), CMAPdi amplitude and stability of the baseline trace were measured. PNCT was defined as the time from the stimulation, identified by a computer-generated mark, to the onset of the positive deflection of the CMAPdi. CMAPdi amplitude was measured from positive to negative.

Procedure

Two study protocols were followed.

Protocol one

Five males aged 26–35 yrs (mean 30 yrs) received unilateral MS and ES of the right phrenic nerve. The mean height and weight were 1.75 ± 0.06 m and 78.8 ± 8.3 kg, respectively. Surface electrodes were placed on each subject, whilst seated upright in a chair, to cover the lower right hemithorax. The position of the electrode pairs were defined by their level (L) above the costal margin, with electrodes at the costal margin being labelled as L1 and the next tier superior to these being L2 *etc.* The distance lateral from the sternal border was labelled as C so that eight columns were identified from the anterior axillary line (C1) to the anterior position close to the xyphoid process (C8).

As recommended by CHEN *et al.* [5], a surface electrode was placed 5 cm superior to the tip of the xyphoid process and a second electrode at the costal margin on the right side with an interelectrode distance of 16 cm. The position of the second electrode (L1C4) corresponded to the seventh intercostal space (7CS). Seven other electrodes were then applied on both sides of L1C4, along the costal margin (four on the left side and three on the right side), from close to the xyphoid process (in the sixth intercostal space) to the anterior axillary line (eighth intercostal space). Other electrodes were then closely apposed above this first line of electrodes, as eight electrodes for the second line (L2), seven electrodes for the third line (L3) and four electrodes for the fourth line (L4). The edges of the adhesive discs were in contact so that the distance between two adjacent electrodes was kept to a minimum. Therefore, 27 electrodes were positioned both on the right and left hemi-thorax. An earth plate was placed a few centimetres below the

costal margin on both sides. Positioning of electrodes is shown in figure 1.

The CMAPdi was recorded from 36 electrode pairs (some electrodes were used for several electrode pairings) using anterolateral MS at 80% of maximal intensity and supramaximal ES. For each electrode pair, at least five stimulations were performed with ES and UMS. The right hemidiaphragm was studied twice with an interval of at least 1 week between studies. PNCT, CMAPdi amplitude and stability of the baseline trace were measured. Study of baseline stability from the stimulation marker to the CMAPdi, necessary for accurate measurement of phrenic nerve conduction time and the regularity of the CMAPdi waveform of all the action potentials recorded from the different electrode pairs, identified the optimal electrode pairs for recording CMAPdi (fig. 2).

Protocol two

Following the first protocol, 12 electrode pairs from which a consistently acceptable signal could be obtained were identified. The pairs were: L_1C_7/L_2C_7, active electrode in the sixth intercostal space; L_1C_5/L_2C_5, active electrode in the sixth intercostal space anterior to the midclavicular line; L_3C_3/L_4C_3, active electrode in the sixth intercostal space, between the midclavicular line and the anterior axillary line; xyphoid (Xi)/L_1C_4, active electrode at the costal margin, reference electrode on the xyphoid process; L_2C_5/L_3C_5, active electrode in the fifth intercostal space, just anterior to the midclavicular line; L_3C_2/L_4C_2, active electrode in the seventh intercostal space just anterior to the anterior axillary line; L_3C_1/L_4C_1, active electrode in the seventh or eight intercostal space in the anterior axillary line; L_1C_6/L_3C_6, active electrode in the fifth to the sixth intercostals spaces between the midclavicular line and the anterior line; L_1C_5/L_3C_5, active electrode in the fifth to the sixth intercostal spaces anterior to the midclavicular line; L_1C_3/L_3C_3, active electrode in the sixth to the seventh intercostal spaces between the midclavicular line and the anterior axillary line; L_1C_2/L_3C_2, active electrode in the seventh to the eight intercostal spaces anterior to the anterior axillary line; and L_1C_1/L_3C_1, active electrode in the seventh to the eight-intercostal spaces in the anterior axillary line.

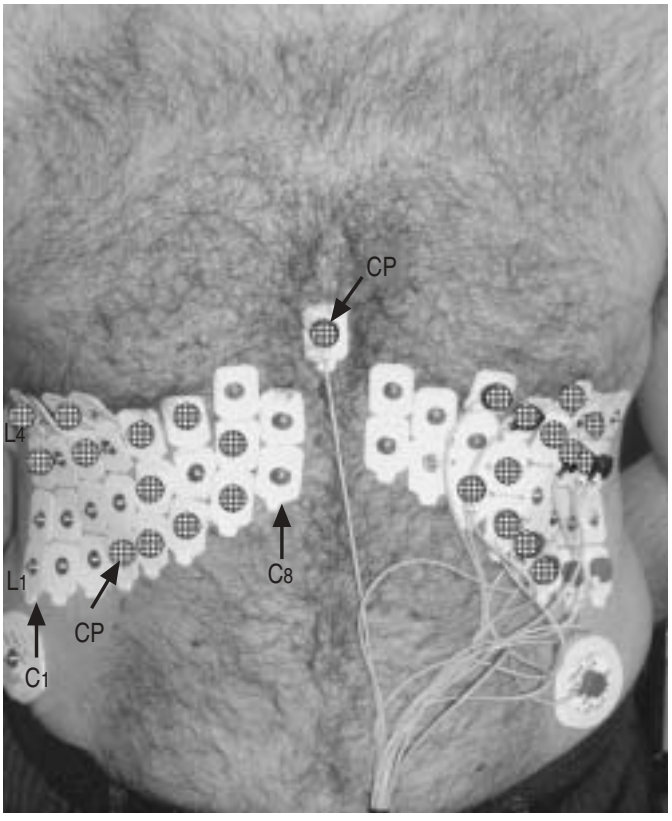

FIGURE 1. Positionning of surface chest wall electrodes for recording diaphragm compound-muscle action potential. CP: indicates the position of the two electrodes described by CHEN *et al.* [5]. C_1: first column; C_8: eighth column; L_1: first line; L_4: fourth line. ■ corresponds to electrodes that protocol two identifies as being the best positions.

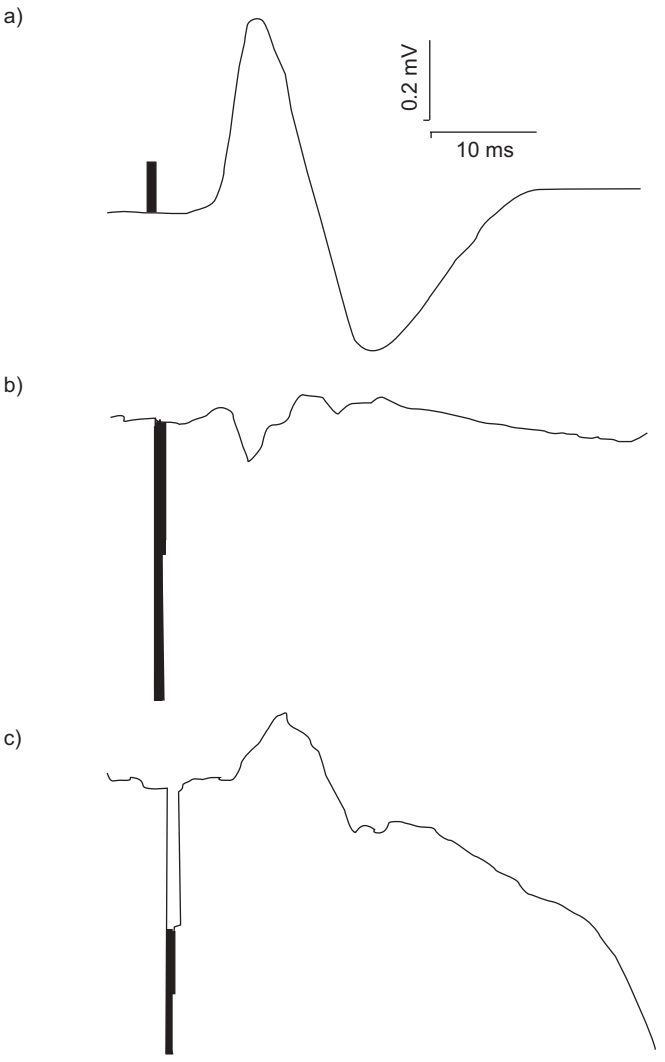

FIGURE 2. Diaphragm compound-muscle action potential elicited by unilateral magnetic stimulation and recorded from three sites on the chest wall. The uncontaminated signal was located close to the anterior axillary line (a); the exact positioning was L_3C_2/L_4C_2. A contamination was noted close to the mid-clavicular line (b, c), the positions of which were L_3C_4/L_4C_4 and L_2C_5/L_3C_5, respectively. L: electrode positioning from costal margin. C: distance lateral from the sternal border.

In protocol two, the CMAPdi recorded from these positions were further investigated. A total of 12 subjects (two females), aged 24–37 yrs (mean 29 yrs) participated in the study. The mean height and weight were 1.77±0.06 m and 75.6±12.7 kg, respectively. A total of 27 electrodes were positioned both on the right and the left hemithorax, as described above in protocol one, and CMAPdi was elicited from the 12 pairs of electrodes following unilateral anterolateral MS of the right and then left phrenic nerves. The right and the left sides were studied separately. The magnetic stimulator was charged to a range of predetermined percentages of maximal power output (60, 70, 80, 90 and 100% of maximal intensity). Five stimulations were performed at increasing levels of intensity on each side of the neck. The latency, amplitude and baseline stability were studied for each CMAPdi. The optimal signal was chosen according to baseline stability and constancy of CMAPdi waveform.

Statistical analysis

The values of CMAPdi latency and amplitude for individual subjects are the average of three to five stimulations. Between-occasion differences are given as the absolute value of the difference between the first and second study. The percentage difference is derived from the absolute value of the difference between the first and second study, divided by the mean of the two studies. Results are expressed as mean and SD.

Latencies and amplitude of the CMAPdi elicited by UMS and ES and the differences between occasions (protocol one), were compared using a paired t-test. To study the reproducibility of anterolateral MS (protocol two), a cross-correlation analysis was performed on latency and amplitude values between occasions. For all studies, a p-value of <0.05 was considered significant [20].

RESULTS

Protocol one

The operators considered that the phrenic nerve was more readily located with MS and, therefore, MS was easier to perform than ES. Nevertheless, it was possible to locate the right phrenic nerve in all subjects, using ES, on all occasions. There was considerable between-subject variability of the position of the optimal electrode pair for recording CMAPdi, whether ES or UMS was used. The optimal position remained unchanged for each individual subject on retesting. The optimal locations with ES and UMS for each individual subject were the same. The best positions were in the anterior axillary line (L_1C_1/L_3C_1, subject 5), between the midclavicular and anterior axillary line (L_1C_2/L_3C_2 subjects 1 and 4; L_3C_3/L_4C_3, subject 3) and in the xyphoid position (Xi/L_1C_4, 2). ES consistently achieved a supramaximal CMAPdi.

PNCT and CMAPdi amplitude obtained using supramaximal ES and UMS were similar (table 1).

Protocol two

Supramaximal nerve stimulation was achieved in 11 subjects for the right side and 10 subjects for the left side. CMAPdi was usually supramaximal at a stimulation intensity of 80–90% of maximum stimulator output. When supramaximality was not clearly demonstrated this may have been due to the contamination of the EMG signal, observed at 100% output. Indeed, at maximal power output, in some subjects, there was a sudden increase in amplitude and a decrease in latency.

The optimum CMAPdi signals were not recorded from the same site in all subjects. In each subject, the optimal signal was not obtained from the same electrode pair position for the right and left hemidiaphragms. The optimal recording site did remain the same for each subject and for both right and left hemidiaphragms on retesting.

The electrode positions yielding optimal CMAPdi signals (fig. 1) were as follows. 1) For the right hemidiaphragm: anterior position, L_1C_7/L_2C_7 (subjects 1 and 11), L_1C_6/L_3C_6 (subject 8); xyphoid position, Xi/L_1C_4 (subjects 2 and 6); close to the midclavicular line, L_3C_3/L_4C_3 (subjects 3, 10 and 12), L_2C_5/L_3C_5 (subject 5), L_1C_5/L_3C_5 (subject 9); close to the anterior axillary line, L_3C_1/L_4C_1 (subjects 4 and 7). 2) For the left hemidiaphragm: xyphoid position, Xi/L_1C_4 (subjects 5 and 12); close to the middle clavicular line, L_2C_5/L_3C_5 (subjects 6 and 10), L_1C_5/L_3C_5 (subjects 2 and 3), L_3C_4/L_4C_4 (subject 4), L_1C_3/L_3C_3 (subjects 1 and 7); anterior position, L_1C_6/L_3C_6

TABLE 1 Diaphragm compound-muscle action potential latency and amplitude recordings from the optimal electrode pairs, following unilateral magnetic stimulation at 80% of maximal intensity and supramaximal electrical stimulation of the right phrenic nerve (protocol one)

Subject	Magnetic stimulation						Electrical stimulation					
	Latency ms			Amplitude μV			Latency ms			Amplitude μV		
	Test 1	Test 2	% diff	Test 1	Test 2	% diff	Test 1	Test 2	% diff	Test 1	Test 2	% diff
1	6.50	6.58	1.20	793	790	0.40	6.42	6.60	2.80	750	844	11.80
2	7.33	7.20	1.80	942	994	5.40	7.15	7.10	0.70	1100	1068	3.00
3	6.17	6.20	0.50	374	446	17.60	7.10	7.17	1	365	426	15.40
4	6.10	6.17	1.10	1099	1055	4.10	6.25	6.33	1.30	1049	1145	8.80
5	7.30	7.13	2.40	592	394	40.20	6.88	7.00	1.70	516	488	5.60
Mean±SD	6.68±0.60	6.66±0.49	1.40±0.70	760±286	736±305	13.50±16.20	6.76±0.41	6.84±0.36	1.50±0.80	756±322	794±328	8.90±4.90

% diff: difference between the first and second study divided by the mean of the first and second study.

(subject 11); close to the anterior axillary line, L_3C_2/L_4C_2 (subjects 8 and 9).

The mean PNCT for the right and left hemidiaphragms are shown in table 2. There is a small progressive reduction in latency and an increase in the coefficient of variation (CV) as stimulation intensity is increased for both hemidiaphragms. The mean CMAPdi amplitudes for both hemidiaphragms elicited at different MS intensities are shown in table 3. There was a broad range of values in the 12 subjects, which is reflected by the wide CV.

No significant differences were noted between latencies and amplitudes of CMAPdi elicited on the two occasions for the right and left hemidiaphragms, at 60–100% MS intensity (fig. 3). Nevertheless, on occasions there was considerable test-to-test variability in amplitude especially with higher levels of stimulation intensity. Tables 2 and 3 show the

TABLE 2 Diaphragm compound-muscle action potential latency measured on both occasions with different intensities of unilateral magnetic stimulation for the right and the left phrenic nerves

Stimulation output % maximal intensity	Test 1			Test 2			Difference between occasions	% difference
	Mean (SD)	Range	CV	Mean (SD)	Range	CV	Mean (SD)	Mean (SD)
Right hemidiaphragm %								
60	6.85 (0.50)	5.75–7.80	7.2	6.86 (0.51)	5.70–7.80	7.4	0.1 (0.08)	1.5 (1.1)
70	6.76 (0.44)	5.75–7.60	6.4	6.66 (0.44)	5.75–7.60	6.7	0.14 (0.11)	2 (1.7)
80	6.61 (0.5)	5.67–7.60	7.6	6.57 (0.48)	5.63–7.60	7.3	0.13 (0.10)	2 (1.6)
90	6.50 (0.48)	5.67–7.70	7.5	6.41 (0.51)	5.50–7.70	7.9	0.09 (0.08)	1.5 (1.2)
100	6.39 (0.6)	5.20–7.50	9.4	6.26 (0.66)	5.13–7.80	10.5	0.18 (0.16)	2.8 (2.4)
Left hemidiaphragm %								
60	6.95 (0.61)	5.58–7.70	8.7	6.95 (0.63)	5.60–7.70	9.0	0.08 (0.08)	1.1 (1.1)
70	6.80 (0.57)	5.60–7.60	8.5	6.78 (0.57)	5.50–7.40	8.4	0.09 (0.05)	1.3 (0.7)
80	6.59 (0.64)	5.40–7.60	9.7	6.65 (0.61)	5.50–7.40	9.2	0.12 (0.05)	1.8 (0.7)
90	6.52 (0.67)	5.30–7.60	10.3	6.45 (0.69)	5.10–7.40	10.7	0.12 (0.07)	1.9 (1.2)
100	6.33 (0.70)	5.10–7.40	11.1	6.35 (0.71)	5.13–7.38	11.2	0.25 (0.11)	4.1 (1.9)

Data presented in milliseconds. CV: coefficient of variation. % difference between occasions: difference between the first and second study divided by the mean of the first and second study.

TABLE 3 Diaphragm compound-muscle action potential amplitude measured on both occasions with different intensities of unilateral magnetic stimulation for the right and the left phrenic nerves

Stimulation output	Test 1			Test 2			Difference between occasions	% difference
% maximal intensity	Mean (SD)	Range	CV	Mean (SD)	Range	CV	Mean (SD)	Mean (SD)
Right hemidiaphragm %								
60	495 (268)	228–1117	54.1	492 (252)	203–952	51.3	45.3 (57.7)	8 (6.4)
70	584 (296)	293–1197	50.6	540 (258)	297–985	47.7	51.2 (58.7)	8.6 (6.4)
80	610 (317)	299–1190	52.0	553 (253)	300–999	45.8	72.2 (66.9)	11.9 (8.2)
90	607 (309)	299–1163	50.8	569 (229)	293–973	40.3	79.3 (73.5)	12.5 (8.3)
100	578 (246)	289–1046	42.6	575 (224)	249–913	39.0	80.5 (55.6)	14.9 (11.5)
Left hemidiaphragm %								
60	556 (268)	221–958	48.2	554 (347)	209–1362	62.6	83.6 (104.7)	15.7 (11.6)
70	647 (297)	197–1067	45.8	637 (387)	236–1372	60.7	122.3 (112.6)	20.6 (20.3)
80	724 (283)	215–1236	39.1	718 (346)	238–1389	48.2	84.6 (99.8)	11.8 (12.4)
90	771 (286)	219–1297	37.0	761 (348)	267–1455	45.7	100.7 (109.1)	14 (1.3)
100	766 (280)	298–1296	36.6	763 (327)	238–1378	42.8	117.3 (100.9)	16.7 (14.2)

Data presented in milliseconds. CV: coefficient of variation. % difference between occasions: difference between the first and second study divided by the mean of the first and second study.

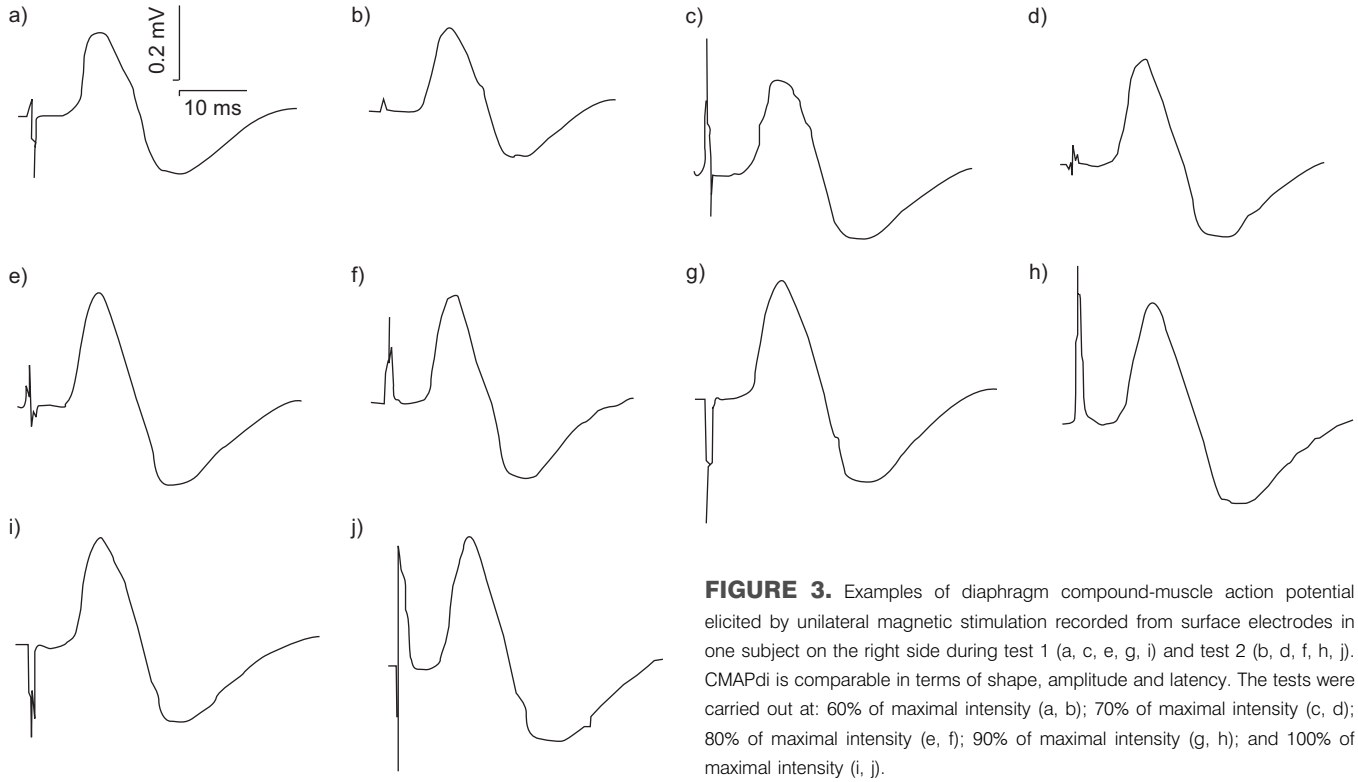

FIGURE 3. Examples of diaphragm compound-muscle action potential elicited by unilateral magnetic stimulation recorded from surface electrodes in one subject on the right side during test 1 (a, c, e, g, i) and test 2 (b, d, f, h, j). CMAPdi is comparable in terms of shape, amplitude and latency. The tests were carried out at: 60% of maximal intensity (a, b); 70% of maximal intensity (c, d); 80% of maximal intensity (e, f); 90% of maximal intensity (g, h); and 100% of maximal intensity (i, j).

between-occasion differences in latency and CMAPdi amplitude, respectively, at increasing intensity of MS. The differences are influenced by the intensity of MS, with 80% providing the most acceptable between-occasion variation, with mean variations of 1.8–2.0% for latency and 11.8–11.9% for CMAPdi amplitude.

When comparing both occasions, the waveforms of CMAPdi were most similar with low intensity stimulation (60–80% of maximum). Increase in magnetic stimulator output could sometimes lead to a change in the waveform of the CMAPdi with a double peak configuration, especially for the highest levels of MS (90–100% of maximum; fig. 4).

DISCUSSION

The major finding of this study is that recording sites on the chest wall can be identified that allow good-quality CMAPdi signals to be obtained with unilateral magnetic phrenic nerve stimulation, which are comparable in latency, amplitude and waveform to those obtained using ES. This is the first study that demonstrates the reproducibility of CMAPdi amplitude and PNCT recorded by surface electrodes following UMS. The application of MS is technically easier and more comfortable than ES. The optimal CMAPdi is not achieved from the same electrode pair in all subjects, or from the same pair on the right and left hemithorax. The best position remains the same for both right and left sides on retesting. The intensity of MS affects the CMAPdi and an intensity of 80% of maximum output elicited the optimal signal. There is a wide variation in CMAPdi amplitude values in healthy subjects, suggesting that using normal value reference ranges may be less useful than monitoring temporal changes in amplitude for each individual.

Critique of methods

The larger stimulation field allows MS to be more easily applied than ES and the sensation is less uncomfortable. In healthy nonobese young subjects, ES is not difficult to perform and may be as easy as UMS. However, UMS is easier in many clinical situations, especially in obese subjects or in critically ill patients in ICU.

The CMAPdi recorded by surface electrodes may be contaminated by co-activation of the brachial plexus and the upper chest-wall muscles it innervates, the abdominal muscles [21] and the contralateral hemidiaphragm [22], when using the less focused stimulation field of UMS. This could explain the change in the CMAPdi waveform with a double peak configuration observed at the highest levels of MS. However, activation of slower fibres at this intensity may also account for the change in waveform. By observing the upper limb for movement and carefully positioning the magnetic coil in a high position, contamination is minimised. Careful selection of CMAPdi without evidence of contamination also improves analytical accuracy. The use of the second protocol to study fewer positions in more detail, in a greater number of subjects, may appear not to have done justice to some of the electrode positions studied in protocol one. However, it would have required an extensive study of considerable duration to combine protocols one and two. Protocol one allowed the identification of the electrode positions providing acceptable signals with MS, which were then subjected to more detailed study. Surface electrodes, from the same manufacturer, were used throughout the study. In clinical practice, electrodes of varying impedance properties may affect the value of CMAPdi obtained.

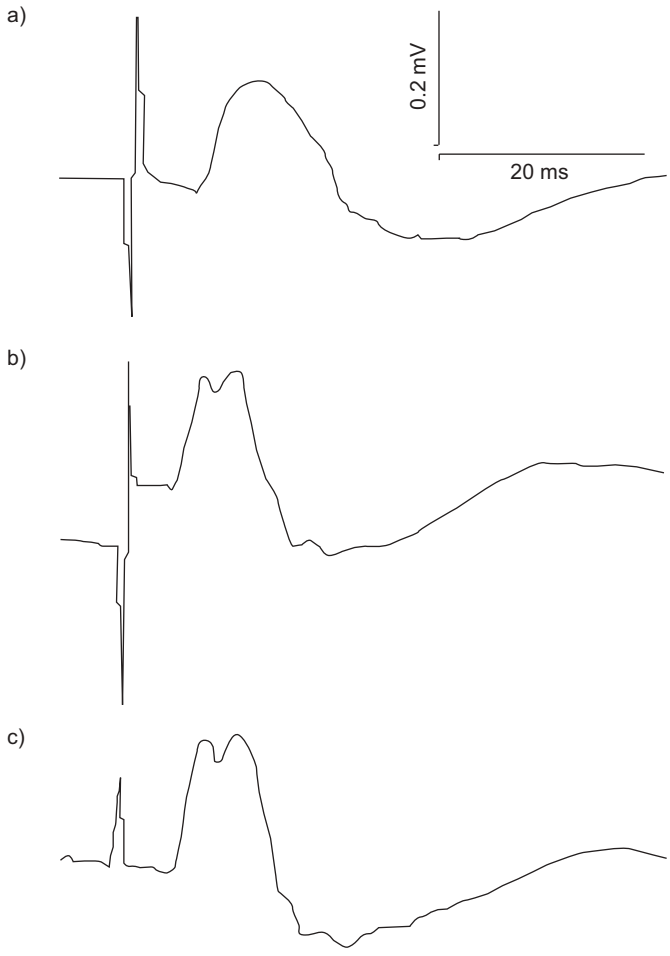

FIGURE 4. Examples of a diaphragm compound-muscle action potential at 80, 90 and 100% of maximal intensity (a–c, respectively). A change in the waveform with a double peak configuration was observed at 90 and 100% of maximal power output.

Although there was good reproducibility of CMAPdi for protocol two, in subject five in protocol one, the test-to-test variability would be unacceptable for clinical decision making. Subject five was overweight (body mass index=37.1) and caution should be exercised in interpreting results in such individuals.

Significance of the findings

The range of latencies obtained were comparable to [8, 18] or slightly shorter than those previously reported [13, 17] and may be a consequence of different recording sites; with latencies elicited from anterior electrodes being shorter than those from electrodes placed in the xyphoid position or close to the anterior axillary line [5, 13]. As previously reported [14, 17], increasing the intensity of UMS led to a decrease in CMAPdi latencies. In the study by LUO *et al.* [17], CMAPdi was recorded using an oesophageal electrode, thereby avoiding contamination of the signal. As MS preferentially recruits fast fibres, as opposed to ES, this decrease in latency could be due to an increase in the recruitment of these fibres rather than contamination from superficial muscles.

The wide range for CMAPdi amplitudes is in agreement with those previously reported [5, 13, 17] and, interestingly, also occurs with ES [2] and between right and left hemidiaphragms of the same subject [2, 6, 23]. This variability between subjects has been attributed to: individual differences in muscle fibre conduction velocity, contraction intensity and recruitment of motors units [16]; anatomical differences, differences in chest-wall thickness [24]; difficulty in maximally stimulating the phrenic nerve [5, 10]; the choice of chest-wall electrode sites [13]; and the interelectrode distance, with greater interelectrode distance increasing contamination [25]. The wide range of CMAPdi amplitudes has led investigators to exercise caution in interpreting CMAPdi amplitude [18].

To the current authors' knowledge, reproducibility of the CMAPdi, elicited by UMS and recorded using chest-wall surface electrodes has not previously been studied. CMAPdi latency reproducibility using surface electrodes has been demonstrated with ES [5, 14, 23] and MS [14]. CMAPdi latency and amplitude are reproducible with UMS when recorded with an oesophageal electrode [12, 17]. However, when recording with surface electrodes placed only in the xyphoid position and using ES, CMAPdi amplitude was not as reproducible, although the variation was $<30\%$ [5]. The xyphoid may not have been the optimal recording position in all subjects. By identifying the optimal surface electrode positions for each subject during MS and ES CMAPdi latency and amplitude reproducibility, similar to other more invasive techniques of EMG recording [5, 12, 17], were obtained.

In the current study, the optimal sites for recording CMAPdi were over the lower region of each hemithorax, between the fifth and seventh intercostal spaces in the anterior position and between the sixth and eighth intercostal spaces in the anterior axillary position. This reflects electrode positions reported by previous studies [1, 2, 13, 18, 23, 25], but it was also found that different electrode pairs are required to record the optimal CMAPdi for different subjects. Moreover, when comparing optimal electrode pairs for the left and right hemidiaphragms, the best signal was not recorded from the same site. This may explain why no consensus has emerged for a single optimal site, as this will be different for each individual. This is not surprising as the CMAPdi recorded from a particular electrode pair can vary between subjects using ES [25] and MS [13], and contamination can differ between subjects when recording from comparable sites [18]. Clinical assessment and monitoring may therefore require the optimal electrode positioning to be ascertained for each individual. A recent, thorough and well-conducted study assessed MS and surface electrodes as a technique for investigating diaphragm EMG [18]. The study compared ES and cervical MS (CMS) for phrenic nerve activation and contrasting surface electrodes and monopolar needles for recording CMAPdi; four electrode positions were studied in detail in five healthy subjects on a single occasion. Two electrode positions, just anterior to the anterior axillary line and an anterior position between the costochondral junction and the midclavicular line, produced signals with CMS and surface electrodes, which were similar to the other methods of stimulation and EMG recording, suggesting an accurate and uncontaminated CMAPdi. However, as acknowledged by the authors, this was a small, preliminary but important study that requires supplementary work. It used

CMS, rather than UMS, and did not present CMAPdi amplitude data or assess reproducibility. CMS does not allow stimulation of each hemidiaphragm individually and is more likely to cause co-activation [11]. CMS and ES can clearly elicit acceptable results when used by an experienced investigator in a laboratory setting, on healthy subjects familiar with receiving CMS and ES and for the recording of PNCT (in the case of CMS) [18]. But in the clinical investigation of patients with respiratory-muscle weakness, with a less favourable noise-to-signal ratio and when measuring CMAPdi amplitude, it would be expected that in future patient studies, UMS will give better results.

The present study's multiple electrode technique could be useful in clinical practice but the acquisition and subsequent analysis of CMAPdi from multiple electrode pairs is time consuming. With practice, putting the electrodes in place for one hemidiaphragm takes 15 mins. However, as optimal positions become established it will not be necessary to employ all the positions described. Initial analysis of recordings is relatively quick because the goal is to identify the optimal CMAPdi. For the future, it would be interresting to pre-mount the multiple electrodes on a wide band and to have an automated analysis selecting the best electrode positions for follow-up. The optimal recording site will be determined by the regularity of the CMAPdi waveform and the baseline stability from the stimulation marker to the CMAPdi. As values of CMAPdi amplitude are variable between subjects and positions of electrodes in the same subject, this can not be used to choose the optimal recording. CMAPdi contamination should be suspected if there is irregularity of the baseline and CMAPdi waveform.

Conclusions

This study demonstrates that there are differences between subjects in the best position for surface electrodes when recording the CMAPdi. These positions tend to be on the costal margin just anterior to the anterior axillary line, at the midclavicular line and between the costochondral junction and the midclavicular line. When the optimal position is identified, CMAPdi latencies and amplitudes are reproducible, for both hemidiaphragms. There is a wide range of values for CMAPdi amplitude in healthy subjects, which limits the use of the measurement for a single evaluation of diaphragm function but as the amplitude is reproducible, temporal surveillance of CMAPdi may be more informative. Therefore, using multiple electrodes optimises the probability of identifying an adequate and reproducible signal for that individual and this signal can be followed up serially to monitor disease progression.

Further evaluation in a large number of normal subjects and the application of the method to appropriate clinical situations would be useful. The authors envisage the technique as having potential for the assessment and ongoing monitoring of critically ill patients in intensive care.

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