Use of mouth pressure twitches induced by cervical magnetic stimulation to assess voluntary activation of the diaphragm

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Use of mouth pressure twitches induced by cervical magnetic stimulation to assess voluntary activation of the diaphragm. P.F.C. De Bruin, R.A. Watson, N. Khalil, N.B. Pride. ©ERS Journals Ltd 1998.

ABSTRACT: There is a need for a simple method to assess the adequacy of diaphragm activation during voluntary inspiratory efforts in patients with suspected respiratory muscle weakness.

We have compared mouth ($P_{mo,t}$), oesophageal ($P_{oes,t}$) and transdiaphragmatic ($P_{di,t}$) twitch pressure elicited by cervical magnetic stimulation (CMS) in five normal men (mean (SD) age 32.2 (1.8) yrs) on two separate study days. Single magnetic stimuli were delivered at functional residual capacity during relaxation and during graded voluntary inspiratory efforts against a closed airway.

As voluntary-effort transdiaphragmatic and oesophageal pressure increased, $P_{di,t}$ and $P_{oes,t}$ decreased linearly (r range, respectively, 0.82–0.98 and 0.87–0.95). During relaxation, $P_{mo,t}$ was unreliable due to the poor transmission of intrathoracic pressure, but during inspiratory efforts, the relation between voluntary mouth pressure and $P_{mo,t}$ was also linear (r range 0.84–0.95). On average, our subjects voluntarily generated 99, 100 and 102% of the maximum transdiaphragmatic, oesophageal and mouth pressures predicted by the respective linear regression equations. $P_{mo,t}$ was correlated to both $P_{oes,t}$ and $P_{di,t}$ during inspiratory efforts, but not during relaxation.

These studies confirm that twitch pressures induced by CMS during inspiratory efforts can be assessed at the mouth in normal subjects, providing a simple and non-invasive technique for assessing diaphragm activation during voluntary inspiratory efforts. Potentially, this technique could be made more sensitive and accurate and applied to detect submaximal efforts in patients.

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Although reliable assessment of diaphragm and inspiratory muscle strength and activation is important in many clinical situations, it is in practice still difficult to obtain. The most direct way of assessing muscle strength *in vivo* is provided by maximum tetanic stimulation of the motor nerve, but transcutaneous tetanic stimulation is painful, and needle stimulation carries a potential danger. As an alternative method, BELLEMARE and BIGLAND-RITCHIE [1] applied single transcutaneous bilateral shocks to the phrenic nerves. They demonstrated that, similarly to limb muscles, the amplitude of a diaphragm twitch was inversely proportional to the voluntary force upon which it was imposed. This permitted the determination of maximum transdiaphragmatic pressure as the voluntary pressure at which no superimposed twitch could be detected (twitch-occlusion). Also, by recording the amplitude of single twitches during relaxation and graded inspiratory efforts, maximum-effort transdiaphragmatic pressure could be estimated from submaximal force levels. Twitch occlusion of voluntary efforts using bilateral transcutaneous electrical phrenic stimulation (BPS) has proved useful in assessing patients with diaphragm weakness and chronic obstructive pulmonary disease [2] as well as in the study of the effects of drugs on the strength and contractility of the diaphragm [3]. Recently, it has been proposed that

mouth twitch pressure ($P_{mo,t}$) could be used as an indicator of transdiaphragmatic twitch pressure ($P_{di,t}$) and more specifically, oesophageal twitch pressure ($P_{oes,t}$) during voluntary inspiratory efforts [4], during relaxed expiration against high resistance [5] or during a gentle expiratory effort against a closed airway [6].

Since 1985, time-varying magnetic fields have been increasingly employed to stimulate central and peripheral nervous structures. This technique involves the generation of a magnetic field pulse when energy stored in a capacitor is discharged through a coil of wire. At the tissue level, this pulse induces an electric field that stimulates neuromuscular tissue in the same way as with electrical stimulation. However, as no current is actually injected into the body, magnetic fields can stimulate deep nervous structures without causing pain [7, 8]. Cervical magnetic stimulation (CMS) in normal subjects has been shown to induce maximum bilateral stimulation of the diaphragm and to produce $P_{di,t}$ during relaxation comparable with that obtained in studies using electrical stimulation [9]. In the present study, we examined $P_{mo,t}$ as an indicator of $P_{oes,t}$ and $P_{di,t}$ elicited by CMS during relaxation and during graded inspiratory efforts in normal subjects. An abstract describing these results has been previously published [10]. The long-term objective was to determine whether

the persistence or absence of $P_{mo,t}$ evoked by CMS could be used to assess the adequacy of diaphragm activation during voluntary maximum inspiratory efforts in patients.

Methods

Five normal male volunteers (mean (SD) age 32.2 (1.8) yrs) took part in the study. Informed consent was obtained from all participants, and the study was approved by the Research Ethics Committee of the Royal Postgraduate Medical School. Cervical nerve root activation was produced by a magnetic stimulator (Magstim 200, Magstim Company, UK) connected to a 90-mm-diameter coil lodged in a circular plastic case with a central hole. The magnetic field developed at the centre of the coil at maximum output of the stimulator was 2.0 T.

Oesophageal (P_{oes}) and gastric pressures (P_{ga}) were measured by two balloon catheters coupled to two differential pressure transducers (Validyne MP 45, Northridge, CA, USA). The transdiaphragmatic pressure (P_{di}) was obtained by electronic subtraction of P_{oes} from P_{ga} . The resting P_{di} at end-expiration was used as the zero reference point. The mouth pressure (P_{mo}) was measured by another similar transducer and was displayed on an oscilloscope in front of the subject. Inspiratory P_{oes} and P_{mo} are both presented as positive values, for simplicity. The flow signal from a Fleisch pneumotachograph (Lausanne, Switzerland) was integrated to provide change in lung volume. Pressure, flow and volume signals were continuously recorded on a multichannel chart recorder (HP Sanborn 7700, Waltham, MA, USA).

Procedure

Subjects were studied on two separate occasions (2–6 month interval), in the sitting position, with the neck flexed at approximately 60° from the vertical, wearing a noseclip and breathing through a conventional mouthpiece. The maximum inspiratory effort (MIE) voluntary pressure was measured at functional residual capacity (FRC) against a closed airway. At least three attempts were performed, and the most negative P_{mo} that could be sustained for 1 s was taken for analysis. No attempts were made to control chest wall configuration or the type of inspiratory effort made.

Cervical magnetic stimulation

The coil was positioned posteriorly on the midline of the neck in the axis of the vertebral column. The initial position was centred on the spinous process of the seventh cervical vertebra. The optimal stimulation site was determined during relaxation by comparing the amplitude of the transdiaphragmatic twitch-pressure ($P_{di,t}$) in relation to the longitudinal position of the coil at a low constant stimulation intensity and this position was marked on the skin. The stimulus maximality was then assessed by progressively increasing stimulus intensity until no further increase in $P_{di,t}$ was obtained. In all subjects, a plateau could be reached from at least 95–100% of the maximum power output of the stimulator. To assess twitch responses with the diaphragm relaxed, tidal breathing was moni-

tored, and subjects were asked to breathe out and to relax at end-expiration. After the airway was closed, one magnetic stimulus at maximum power was delivered. If relaxation of the diaphragm could not be confirmed by baseline transdiaphragmatic pressure, the measurement was discarded. The manoeuvre was repeated at 1-min intervals until five technically satisfactory twitches were recorded. The mean of the three largest results at rest was considered for analysis. Twitch occlusion was assessed by superimposing a magnetic stimulus at maximum power on voluntary contractions of the diaphragm during progressive inspiratory efforts made against a closed airway at FRC. Subjects were asked to generate predetermined levels of mouth pressure as indicated on the oscilloscope. Each effort was sustained for 2–3 s, during which one magnetic stimulus was delivered. Target pressures were increased in steps of 10 cmH₂O, and at least two twitches were obtained for each level of mouth pressure.

Statistical analysis

The relationships between transdiaphragmatic, oesophageal and mouth voluntary and twitch pressures were assessed by linear regression using the least-squares method. The BLAND and ALTMAN [11] method was used to compare measurements between study days. Coefficient of repeatability (CR) was calculated as 2 SDs of the differences between days 1 and 2. Agreement between voluntary pressures measured during MIE and maximum pressures estimated from the regression equations was also assessed according to the recommendations of BLAND and ALTMAN [11]. An unpaired *t* test was used when appropriate. Values are expressed as mean (SD).

Results

Transdiaphragmatic pressure

P_{di} during maximum inspiratory efforts ($P_{di,MIE}$) averaged 140 (15) and 148 (16) cmH₂O on days 1 and 2, respectively (table 1), with a CR between the two study days of 36 cmH₂O. The average relaxed $P_{di,t}$ (mean of 2 days) was 28.0 (2.7) cmH₂O (range 25.7–31.2 cmH₂O). The mean ratio between relaxed $P_{di,t}$ and $P_{di,MIE}$ was 19.8% (16–22%) (table 2). In all subjects, the amplitude of $P_{di,t}$ decreased with the intensity of voluntary contraction on which stimulation was superimposed. Complete occlusion of $P_{di,t}$ by voluntary contractions was consistently obtained in all subjects, except number 2 (fig. 1). In all individuals relationships were well fitted with linear functions of the form:

$$P_{di,t} = a + b \times P_{di} \quad (1)$$

with correlation coefficients ranging 0.82–0.98 on the two study days (all $p < 0.0001$). The potential maximum voluntary P_{di} estimated for each individual by setting $P_{di,t}$ to 0 in Equation 1, *i.e.* extrapolating the relation to the abscissa, ranged from 117–191 cmH₂O, with a CR between study days 1 and 2 of 45 cmH₂O. Subject number 2, who was unable to achieve full muscle activation, generated

Table 1. – Comparison of pressures measured during maximum voluntary efforts with maximum pressures predicted from twitch occlusion

Subject	Day 1						Day 2					
	P_{di} cmH ₂ O		P_{oes} cmH ₂ O		P_{mo} cmH ₂ O		P_{di} cmH ₂ O		P_{oes} cmH ₂ O		P_{mo} cmH ₂ O	
	MIE	Pred	MIE	Pred	MIE	Pred	MIE	Pred	MIE	Pred	MIE	Pred
1	122	117	116	112	108	108	153	151	127	124	118	114
2	127	132	115	127	107	118	134	140	124	122	116	116
3	158	151	136	134	135	134	149	191	127	151	126	164
4	148	142	153	130	155	131	170	166	160	157	160	142
5	144	141	103	103	100	102	132	125	106	101	103	93
Mean	140	136	125	121	121	119	148	155	128	131	125	126
SD	15	13	20	13	23	14	16	25	20	23	22	28

P_{di} : transdiaphragmatic pressure; P_{oes} : oesophageal pressure; P_{mo} : mouth pressure; SD: standard deviation. Amplitudes were measured relative to the resting baseline during maximum voluntary inspiratory efforts (MIE) and values predicted from twitch occlusion (pred). The sign of P_{oes} and P_{mo} is ignored.

96.2 and 95.7% of the predicted maximum P_{di} on days 1 and 2, respectively. On average, our subjects generated 102.5 and 96% of the estimated maximum P_{di} on days 1 and 2, respectively. A plot of the individual differences between $P_{di,MIE}$ and estimated maximum P_{di} against their means on both study days is presented in figure 2. No relation between the size of the difference and the magnitude of P_{di} was observed. Data from subject number 3 on study day 2 (arrows) were clearly outlying the remaining data and, according to the recommendations of BLAND and ALTMAN [11], were excluded from this analysis. The mean difference for nine experiments was 2.6 (9.8) cmH₂O, and the limits of agreement ranged between -7.2–12.4 cmH₂O.

Oesophageal pressure

The mean values of $P_{oes,MIE}$ were 125 (20) and 128 (20) cmH₂O on study days 1 and 2, with a CR of 16 cmH₂O. The average (mean of two results) $P_{oes,t}$ during relaxation was 20.7 (2.4) cmH₂O (range 18.2–24.2). The mean ratio between relaxed $P_{oes,t}$ and $P_{oes,MIE}$ was 16.6% (table 2). The mean $P_{oes,t}/P_{di,t}$ ratio during relaxation was 74% compared with a mean P_{oes}/P_{di} ratio during MIE of 88%. The individual relationships between P_{oes} and $P_{oes,t}$ were well described by linear functions of the form:

$$P_{oes,t} = a' + b' \times P_{oes} \quad (2)$$

with correlation coefficients ranging between 0.87 and 0.95 on two study days (all $p < 0.0001$) (fig. 1). The potential maximum voluntary P_{oes} estimated from Equation 2 for each individual ranged 101–157 cmH₂O (table 1) and CR between two study days was 33 cmH₂O. On average, our subjects produced 103 and 98.7% of the estimated maximum P_{oes} on days 1 and 2, respectively (table 1). The mean difference between $P_{oes,MIE}$ and the estimated maximum P_{oes} for nine experiments was -2.2 (11.4) cmH₂O, with limits of agreement ranging -20.6–25 cmH₂O.

Mouth pressure

Mean $P_{mo,MIE}$ was 121 (23) and 125 (22) cmH₂O, respectively, on days 1 and 2 (table 1), with a CR between study days 1 and 2 of 15.2 cmH₂O. There was a large intra- and inter-subject variation in $P_{mo,t}$ when elicited from the relaxed diaphragm. However, when only twitches elicited during inspiratory efforts were taken into account, the relationships between P_{mo} and $P_{mo,t}$ could be appropriately described by linear functions of the form:

$$P_{mo,t} = a'' + b'' \times P_{mo} \quad (3)$$

with correlation coefficients ranging between 0.84 and 0.95 among subjects on the two study days (all $p < 0.0001$) (fig. 1). The potential maximum voluntary inspiratory P_{mo} for each individual estimated from Equation 3 ranged

Table 2. – Transdiaphragmatic, oesophageal and mouth twitch pressures measured with cervical magnetic stimulation during relaxation on two separate days

Subject	Day 1						Day 2					
	$P_{di,t}$		$P_{oes,t}$		$P_{mo,t}$		$P_{di,t}$		$P_{oes,t}$		$P_{mo,t}$	
	cmH ₂ O	%	cmH ₂ O	%	cmH ₂ O	%	cmH ₂ O	%	cmH ₂ O	%	cmH ₂ O	%
1	36.0	29.5	24.3	20.9	5.7	5.3	23.3	15.2	16.0	12.6	3.0	2.5
2	26.0	20.5	19.7	17.1	16.3	15.2	24.7	25.9	28.7	23.2	9.0	7.8
3	27.0	17.1	19.3	14.2	10.0	7.4	32.3	21.7	24.3	19.1	5.7	4.5
4	25.3	17.1	19.7	12.9	6.3	4.1	23.7	13.9	18.3	11.4	18.7	11.7
5	25.7	17.8	19.3	18.7	6.7	6.7	25.3	19.2	17.0	16.0	14.7	14.3
Mean	28.0	20.4	20.5	16.8	9.0	7.8	27.9	19.2	20.9	16.5	10.2	8.2
SD	4.5	5.3	2.2	3.3	4.4	4.4	5.3	4.9	5.4	4.8	6.4	4.9

$P_{di,t}$: transdiaphragmatic twitch pressure during relaxation; $P_{oes,t}$: oesophageal twitch pressure during relaxation; $P_{mo,t}$: mouth twitch pressure during relaxation; %: twitch pressure during relaxation as a percentage of voluntary pressure generated during maximum inspiratory effort.

Fig. 1. — Individual comparisons of twitch amplitude as a function of the voluntary inspiratory effort on which cervical magnetic stimulation was superimposed, assessed by transdiaphragmatic ($\circ$; ---), oesophageal ($\square$;), and mouth pressure regressions ($\triangle$; —), on the first study day in a) subject No. 1, b) subject No. 2, c) subject No. 3, d) subject No. 4, and e) subject No. 5. In all cases, the linear relationships were highly significant. There was no correlation between mouth and both oesophageal and transdiaphragmatic twitches during relaxation (not shown here). The negative sign of oesophageal and mouth pressure is ignored. Note oesophageal pressure overlaps mouth pressure regressions in (c) and (e).

93–164 cmH₂O (table 1), with a CR between study days 1 and 2 of 29.8 cmH₂O. Our subjects achieved, on average, 103 and 101% of the estimated maximum P_{mo} on days 1 and 2, respectively. The mean difference between $P_{mo,MIE}$ and estimated maximum P_{mo} was 4.9 (10.8) cmH₂O. The limits of agreement ranged between -16.7 and 26.5 cmH₂O (fig. 2). The data from subject number 3, day 2, were again not included in this analysis.

There was a poor correlation between measured $P_{mo,t}$ and $P_{oes,t}$ and between $P_{mo,t}$ and $P_{di,t}$ when the magnetic stimulus was applied to a relaxed diaphragm (correlation coefficient ranging -0.207–0.369 on the two study days); this lack of correlation with $P_{mo,t}$ was found despite the simultaneous presence of a strong correlation between relaxed $P_{oes,t}$ and $P_{di,t}$ (correlation coefficients, respectively, 0.979 and 0.973, on days 1 and 2). However, as shown above, when only small inspiratory efforts were made, good correlations between $P_{mo,t}$ and both $P_{oes,t}$ and $P_{di,t}$ were always observed. The relationships for all the experimental data over the entire range of voluntary inspiratory efforts are shown in figure 3. In all subjects, the relationships between $P_{mo,t}$ and both $P_{oes,t}$ and $P_{di,t}$ during voluntary efforts on both study days were linear, with correlation coefficients ranging 0.920–0.985 and 0.925–0.974, respectively.

Fig. 2. — Differences between pressures measured during maximum voluntary inspiratory effort and maximum pressures predicted from twitch-occlusion plotted against the average between the two results for both mouth ($\circ$) and transdiaphragmatic ($\blacksquare$) pressures, for each of five subjects on both study days. Limits of agreement for mouth (.....) and transdiaphragmatic (----) pressure are also shown. Data from subject No. 3 on the second study day (arrows) were excluded from analysis (for explanations, see text).

Fig. 3. – Group data showing mouth pressure twitches ($P_{mo,t}$) measured from five subjects on two study days plotted against a) oesophageal twitch pressures ($P_{oes,t}$) and b) transdiaphragmatic twitch pressures ($P_{di,t}$). Lines of identity are drawn through each set of data. The negative sign of the oesophageal and mouth pressure is ignored.

Ability to predict best mouth pressure using twitch occlusion during submaximal efforts

In the present studies, twitches were applied over the full range of voluntary efforts in highly motivated normal subjects. However, our interest in the technique was in its eventual use to detect submaximal activation in less motivated subjects and patients. Ideally, twitches could be applied during a series of submaximal efforts to predict pressure during a true MIE with complete twitch occlusion. Therefore, we truncated the data obtained on day 1 in our five normal subjects successively at 90, 80, 70 and 60% of the maximum achieved value and used linear regression on the nontruncated values to predict pressure during a MIE. The mean predicted $P_{mo,MIE}$ was >90% of the maximum achieved value at all levels of truncation, but the standard error increased, and the predicted value slightly decreased as truncation was increased from 90 to 60% of maximum achieved value (fig. 4a). A similar analysis for predicted $P_{di,MIE}$ showed a slightly greater underestimation but smaller standard errors than for $P_{mo,MIE}$ (fig. 4b).

Fig. 4. – Prediction of maximum pressure achieved in five normal subjects during the first study day using linear regression of twitch amplitude versus a) mouth pressure (P_{mo}), or b) transdiaphragmatic pressure (P_{di}) with varying severity of truncation of the available data. When values at higher levels of activation are successively truncated, the predicted maximum pressure falls (see text for further details). MIE: maximum inspiratory effort. Data presented as means $\pm$ SEM.

Discussion

Our results indicate that mouth pressure changes induced by superimposed CMS twitches during voluntary inspiratory muscle contractions can be used to assess diaphragm activation and estimate maximum effort pressures in normal subjects. In clinical practice, inspiratory muscle strength is usually assessed by measuring pressures generated by maximum voluntary efforts, and therefore depends on the degree of muscle activation achieved by the subject; reliance is placed on coaching, encouragement and repetition, and the most negative mouth or oesophageal pressures are taken. Unfortunately, activation of respiratory muscles is frequently submaximal, particularly in patients [12], indicating the need for objective measurements of respiratory muscle strength or activation. Producing maximum excitation of the diaphragm with bilateral transcutaneous tetanic stimulation of the phrenic nerves is painful and sometimes difficult and impractical for clinical use. A more acceptable technique is to use twitch pressures, either during muscle relaxation (at FRC or during a relaxed breath from TLC to FRC) [4–6, 9, 13–17] as an indication of force development or, as in the present study, to assess twitch-occlusion during voluntary efforts [1–4, 18–20]. Most studies have used $P_{di,t}$, but recently, it has been shown that $P_{mo,t}$ can sometimes be substituted and corresponds closely to $P_{oes,t}$ [4–6]. A further simplification has

been to use CMS rather than electrical stimulation to stimulate the phrenic nerves, because CMS requires less skill from the operator and is not painful for the subject [9]. In this study, we combined assessing twitch-occlusion using mouth pressure with stimulating the phrenic nerves by CMS; potentially, this method could be used to detect submaximal diaphragm activation during attempts to generate maximum inspiratory pressures in patients.

Before magnetic stimulation can be applied widely to clinical studies, a number of technical considerations need to be clarified. Although theoretical requirements for placing the coils to obtain maximum stimulation of the phrenic nerve or its roots are not completely understood, in practice, the best position to obtain maximum twitch pressure can be found quickly and maintained without difficulty. In our studies, maximum $P_{di,t}$ during relaxation was achieved in seven experiments at $\approx 90\%$ of the maximum output of 2 T, but in three only at 95%. This output is not painful to the subject; subsequent improvements in coil design have increased the maximum output to 2.5 T [21], which should ensure the stimulus is always supramaximal. The alternative of applying transcutaneous magnetic stimulation directly to the phrenic nerves in the neck [22] is less suitable when studying maximum inspiratory efforts that are accompanied by strong contractions of overlying neck muscles. Ideally, compound diaphragm motor action potentials should be used to assess supramaximality, but this technique is not widely available in pulmonary laboratories, and CMS may interfere with the signal: fortunately, optimizing position by the use of twitch pressure alone has been shown to give comparable results [15]. However, if $P_{mo,t}$ is to be used to find the best location, CMS has to be applied while the subject generates an expiratory or inspiratory pressure of 5 or 10 cmH₂O against a closed airway [6]; this leads to co-activation of upper airway muscles [23] and ensures patency of the upper airway and adequate transmission of alveolar pressure to the mouth, even in the presence of the intrapulmonary airway obstruction of COPD [4]. During relaxation, narrowing of the upper airway impairs pressure transmission as shown in this and previous studies [4, 24]; however, if values of $P_{mo,t}$ cover a sufficient range of voluntary contractions, the derived linear regression can be used to estimate $P_{mo,t}$ during relaxation from the intercept on the ordinate. In the present study, the ordinate intercepts of the linear regressions for $P_{mo,t}$ and $P_{oes,t}$ were almost identical in each subject (fig. 1). The values of $P_{di,t}$ during relaxation are larger with CMS than with BPS due to the generation of a more negative $P_{oes,t}$ with CMS [17]. Originally, CMS was thought to stimulate phrenic nerve roots but one recent study has suggested that it may stimulate phrenic nerves directly [21]. The less focused stimulation of CMS activates other inspiratory muscles, such as the scalenes [15–17], but this only results in a $P_{oes,t}$ ≈ 1 cmH₂O in patients with complete diaphragm paralysis [25], although twitch pressure may be enhanced if there is an associated hypertrophy of neck muscles [26]. Therefore, it has been suggested that the more negative $P_{oes,t}$ mainly results from contraction of the diaphragm with a stiffer upper ribcage [25]. In agreement with this suggestion, the wider activation did not prevent complete twitch occlusion developing in the present study. We applied many CMS twitches during a full range of graded inspiratory efforts in our normal subjects and linear regression

through the data closely predicted actual maximum effort pressures. In patients with suspected weakness, fewer CMS twitches would probably be applied, and more efforts might be submaximal; nevertheless, the persistence of a significant $P_{mo,t}$ would provide objective evidence of a submaximal effort and result in further coaching, or if this fails, the recognition that the measurement should be discarded. To investigate whether twitch amplitude from submaximal efforts could be used to predict pressure during a true MIE, we truncated the present data from normal subjects at various percentages of the best pressures that they achieved. The aim was to simulate the submaximal activation believed to occur commonly in clinical practice [12]. On average, underestimation of the predicted pressure increased as truncation was made more severe; however even using data restricted to $\approx 60\%$ of the maximum achieved value, the underestimate was relatively small, particularly for P_{mo} . The tendency to underestimate pressure during a true MIE probably results from the slight curvilinearity of the plot of twitch size against activation with a reduced slope of twitch amplitude/percentage activation at high levels of activation [1]. BELLEMARE and BIGLAND-RITCHIE [1] found a very similar underestimation of true $P_{di,MIE}$ when calculations were based on extrapolation of data obtained below 70% $P_{di,MIE}$. When sufficient data points are available in the near-maximal effort range, this curvilinearity leads to trivial underestimates.

A problem with using twitch pressures is potentiation after a contraction, which results in a time-dependent increase in the pressure generated [27, 28] and inevitably increases noise in the measurement unless the prior contraction history is strictly controlled. For this reason, it has been suggested that when twitch pressure is used as an indicator of muscle performance, contractions including significant inflations should be avoided for at least 15 min before twitch pressures are measured [27, 28]. When twitch pressures are superimposed on a series of voluntary contractions as in the present study, twitch potentiation is inevitable, but this will enhance the sensitivity of the technique. An alternative approach to this problem has been developed by GANDEVIA and MCKENZIE [29–31] who use a double twitch technique with BPS (using small needle electrodes) in which a first twitch during an attempted maximum voluntary effort is followed by a second twitch during relaxation 5 s later when the muscle is potentiated. They express twitch occlusion as the ratio of the first to second twitch pressures to derive an index of percentage voluntary activation [29–31]. This method is considerably more accurate and sensitive than that which we have used, but necessitates direct measurement of P_{oes} or P_{di} .

In summary, our studies confirm that twitch pressures induced by cervical magnetic stimulation can be assessed at the mouth in normal subjects providing a simple and noninvasive technique for estimating activation and hence true maximum strength of the diaphragm. Potentially, persistence of a superimposed mouth twitch pressure during an attempted voluntary maximal inspiratory effort could be used to identify submaximal activation. Further studies are needed to determine how extensively the relationship between mouth twitch pressure and mouth pressure during graded inspiratory efforts needs to be assessed in order to produce accurate estimates of maximum inspiratory mouth pressure in clinical practice.

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