

Research article

Magnetic versus electrical stimulation in the interpolation twitch technique of elbow flexors

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Abstract

The study compared peripheral magnetic with electrical stimulation of the biceps brachii m. (BB) in the single pulse Interpolation Twitch Technique (ITT). 14 healthy participants (31±7 years) participated in a within-subjects repeated-measures design study. Single, constant-current electrical and magnetic stimuli were delivered over the motor point of BB with supra-maximal intensity (20% above maximum) at rest and at various levels of voluntary contraction. Force measurements from right elbow isometric flexion and muscle electromyograms (EMG) from the BB, the triceps brachii m. (TB) and the abductor pollicis brevis m. (APB) were obtained. The twitch forces at rest and maximal contractions, the twitch force-voluntary force relationship, the M-waves and the voluntary activation (VA) of BB between magnetic and electrical stimulation were compared. The mean amplitude of the twitches evoked at MVC was not significantly different between electrical (0.62 ± 0.49 N) and magnetic (0.81 ± 0.49 N) stimulation ($p > 0.05$), and the maximum VA of BB was comparable between electrical (95%) and magnetic (93%) stimulation ($p > 0.05$). No differences ($p > 0.05$) were revealed in the BB M-waves between electrical (13.47 ± 0.49 mV.ms) and magnetic (12.61 ± 0.58 mV.ms) stimulation. The TB M-waves were also similar ($p > 0.05$) but electrically evoked APB M-waves were significantly larger than those evoked by magnetic stimulation ($p < 0.05$). The twitch-voluntary force relationship over the range of MVCs was best described by non-linear functions for both electrical and magnetic stimulation. The electrically evoked resting twitches were consistently larger in amplitude than the magnetically evoked ones (mean difference 3.1 ± 3.34 N, $p < 0.05$). Reduction of the inter-electrodes distance reduced the twitch amplitude by 6.5 ± 6.2 N ($p < 0.05$). The fundamental similarities in voluntary activation assessment of BB with peripheral electrical and magnetic stimulation point towards a promising new application of peripheral magnetic stimulation as an alternative to the conventional ITT for the assessment of BB voluntary activation.

Key words: Electrical stimulation, magnetic stimulation, interpolation twitch technique, voluntary activation, elbow flexors.

Introduction

Interpolation Twitch Technique (ITT) has become standard for assessment of human voluntary activation in healthy (Allen et al., 1998; Man et al., 2004; Merton, 1954) and impaired muscles (Horemans et al., 2004; Martin et al., 2004; Pap et al., 2004) although there is not an agreed 'gold standard' method for muscle activation assessment. The presence of a twitch-like increment in force evoked by electrical stimulus during maximal voluntary contraction (MVC) suggests that not all the motor units are recruited by the voluntary effort or that they are not

firing fast enough to drive the muscle maximally at the moment of stimulation (Gandevia, 2001; Taylor and Gandevia, 2008). This method has been considered as a valid measure of assessing the central drive to muscles despite some methodological pitfalls, such as non-linearity of the twitch force-voluntary force relationship, the activation of synergists, antagonists, and the intermuscular differences (De Haan et al., 2009). ITT is mainly applied in isometric contractions via single pulse techniques but doublets or train of stimuli have also been used without altering the sensitivity of the technique (Behm et al., 1996; Millet et al., 2011).

However, application of peripheral electrical stimulation of underlying nerves using surface electrodes often activates sensory fibre endings thus causing pain when high current levels or trains of stimuli are used and may hinder its successful application for the assessment of voluntary activation in clinical settings (Bampouras 2006; Man et al., 2004). While needle or implantable electrodes are used clinically for certain neurophysiological assessments, these have the added risk of infection, trauma or bleeding (Man et al., 2004). Peripheral magnetic stimulation of the nerve trunk for the assessment of muscle function has been proposed as an alternative to peripheral electrical stimulation (Barker 2002; Hovey and Jalinous 2006; Luo et al., 2006; O' Brien et al., 2008; Polkey et al., 2000).

Peripheral magnetic stimulation, based on electromagnetic induction, produces an electric field, proportional to the rate of change of the generated magnetic field, without electrical contact with the tissue (Barker 2002; Hovey and Jalinous 2006). The induced current of commercially available magnetic stimulation devices is of sufficient amplitude and duration to depolarize nerve membranes and generates action potentials in a similar way to conventional electrical stimulation (Barker 2002; Hovey and Jalinous 2006). It has therefore been proposed to be more suitable for use in clinical environments as it can ensure nerve trunk stimulation without involving high currents in the skin, and thus, without causing painful sensations (Hovey and Jalinous 2006; Luo et al., 2006; Man et al., 2004; O' Brien et al., 2008; Polkey et al., 2000). Indeed, it has been used for assessment of muscle strength in patients (Harris et al., 2001) and even for neonatal use (Rafferty et al., 2000). Additionally, there is increased interest in using the peripheral magnetic stimulation as an alternative to ITT in assessing the activation level of the upper (Harris et al., 2000) as well as the lower limb muscles (Goodall et al., 2009; Hamnegård et al., 2004; Kremenec et al., 2004; Vivodtzev et al., 2005).

Some limitations of the technique, such as the supra-maximality which is in some cases problematic with peripheral magnetic stimulation (Hamnegård et al., 2004; Matsumoto et al., 2010; Millet et al., 2011), or the limited stimulus strength which is affected not only by the spatial distribution of the magnetic field (Lin et al., 2008; Tomazin et al., 2010), but also by the subcutaneous adipose tissue (Tomazin et al., 2011), may be the reason for not widespread acceptance as a viable alternative to peripheral electrical stimulation or as the 'gold standard' method for muscle activation assessment.

Comparisons between electrical and magnetic stimulation twitch interpolation during maximal voluntary contractions revealed close agreement between supra-maximal twitch and close onset latencies when studied over long segments of nerve such as the median nerve (Olney et al., 1990). Close agreement between supra-maximal potentiated twitch of adductor pollicis for electrical and magnetic stimulation was also found by Harris et al., (2000), demonstrating that, with optimal magnetic coil orientation the strongest electric field maximally excite the ulnar nerve without activation of the median nerve, and is comparable to electrical stimulation. In addition, resting peak force and M waves of quadriceps muscle produced by both single and paired stimulation were similar for both electrical and magnetic nerve stimulation (Verges et al., 2009). Furthermore use of the magnetic stimulation technique was well tolerated in patients who reported no signs of discomfort (Harris et al., 2000; Rafferty et al., 2000). Peripheral magnetic stimulation has been also compared with electrical stimulation in assessing leg muscle function as for clinical interest in locomotor activity (Hamnegård et al., 2004; Verges et al., 2009; Vivodtzev et al., 2005). Magnetic stimulation of the upper limb muscles has been limited to investigate the intrinsic hand muscles, e.g., m. adductor pollicis (Cros et al., 1990; Harris et al., 2000) because of the more convenient stimulation sites along the brachial nerve, i.e, ulnar nerve compared to muscles innervated by the musculocutaneous nerve. Voluntary activation of human elbow flexors has been tested with using transcranial magnetic stimulation (TMS) of motor cortex but not peripheral nerve magnetic stimulation where electrical stimulation is typically more prevalent in use (Todd et al., 2003; 2004). However, the evoked twitches produced by a cortical stimulus superimposed during maximal isometric contractions test degree of volitional drive to muscle for supraspinal contributions, while the evoked twitch force to peripheral stimulation assesses spinal neural drive (Lee et al., 2008).

No detailed comparison between these two methods of peripheral nerve stimulation has been undertaken for elbow flexors with respect to the use of twitch interpolation for the assessment of voluntary activation-force relationship. A detailed comparison is therefore necessary which could facilitate more widespread adoption of peripheral magnetic stimulation in clinical settings and for other useful neuromuscular performance assessments.

The aim of this study therefore, was to make detailed comparisons of the use of magnetic versus electrical stimulation for assessment of voluntary activation using the Interpolation Twitch Technique (ITT). We examined

the twitch force evoked by single pulse electrical and magnetic stimulation not only at rest and at maximal contractions -as mainly examined by other studies- but also at various levels of voluntary contraction of elbow flexors. The Time to Peak (TTP) for the resting twitches, the M-waves of the biceps brachii m. (BB), triceps brachii m. (TB), and the abductor pollicis brevis m. (APB) obtained by electrical and magnetic stimulation were also examined.

Methods

Participants

A group of 8 healthy participants (by chance these were all females) with an average age of 30 ± 7 years (range 23–41 years), with all but one right-handed, took part in this study of a within-subjects design for comparisons between magnetic and electrical stimulation. Participants were students/staff volunteers from the university community who gave written informed consent to participate in this study. Participants underwent this assessment of both peripheral electrical and magnetic stimulation within the same session. An additional group of 6 (3 males, 3 females) healthy participants of mean age 33 ± 9 years (range 24–47 years) took part in a subsequent experiment which tested the effect of the inter-electrode distance of electrical stimulation in the spread of the electrical current. These 2nd group of participants only received peripheral electrical stimulation condition. This study had the ethical approval of the Brunel University Research Ethics Committee.

Apparatus

Measurement of Isometric Force and Surface Electromyography (sEMG)

Force measurements were obtained from right elbow isometric flexion by using a purpose-built static rig containing a force transducer (Model 615, S-Type Load Cell, TedeA-Huntleigh Electronics, UK). The participants were seated in the rig with their shoulder immobilized in a flexed position, supinated forearm, 90° flexion of the elbow and the wrist secured with straps. The analogue force signals were amplified 300 or 1000 times, filtered [(high pass DC-offset, low pass 2 KHz), (Quad 1902, 4 channels, Cambridge Electronic Design (CED), Cambridge, UK)], and simultaneously sampled and digitized (4 KHz, micro 1401, 12 channels, CED, Cambridge, UK). The force transducer signal was recorded simultaneously with all surface EMG (sEMG) signals.

Muscle electromyograms (EMG) were recorded from the biceps brachii m. (BB) (as a surrogate of the agonist elbow flexors). The triceps brachii m. (TB) was also chosen as a surrogate of the antagonist elbow extensors, to monitor the degree of spread of stimulation from the chosen stimulation site over BB which is likely to occur at supramaximal intensities. The abductor pollicis brevis m. (APB) was also recorded because as a surrogate of those muscles innervated by underlying nerves in the upper arm (e.g., median nerve) whose trajectory is parallel and superficial to BB muscle, it was essential to moni-

tor the possible effect of stimulation on these nerves). Pairs of silver/silver chloride (Ag/AgCl) disposable self-adhesive electrodes (KENDAL, SOFT-E, H59P, Henleys Medical, Welwyn Garden City, UK) were affixed onto cleaned skin and were placed parallel to the muscle fibres over the muscle belly of each muscle respectively using standard recording sites for arm and hand muscles (Cram *et al.*, 1998). A ground electrode was placed over the medial epicondyle of the humerus bone. The bipolar, differentially recorded EMG signals were amplified 1000 or 3000 times, filtered [10 Hz high pass (to pass frequencies related to muscle activity 10Hz-1KHz, 2KHz low pass (to reject frequencies associated to electromagnetic noise (De Luca, 1997), (Quad 1902, 4 channels, CED, Cambridge, UK), digitized (4 KHz, micro 1401, 12 channels, CED, Cambridge, UK)]. All digitized data (force and sEMG) were stored for subsequent analysis (Spike2 v6 and Signal v4 for Windows, CED software).

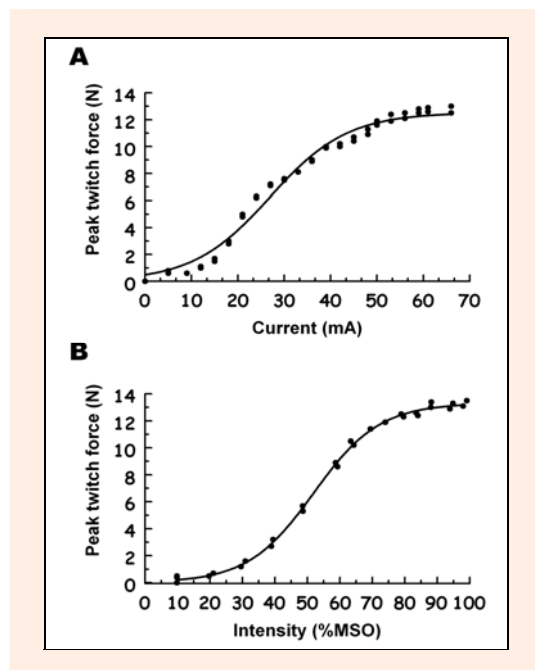


Figure 1. Examples of evoked twitch response curves to range of (A) electrical stimulation and (B) magnetic stimulation from same single subject. Two responses at each stimulus level are shown and points were fit with sigmoid curve. For estim: $y=12.52/[1+\exp(-(x-26.94)/8.39)]$, $R^2=0.99$. For mag stim: $y=13.30/[1+\exp(-(x-51.92)/10.12)]$, $R^2=0.99$.

Electrical muscle stimulation

Single, constant-current electrical stimuli (1 ms duration) were delivered to the musculocutaneous nerve over the motor point of BB previously identified according to standard position sites (Digitimer, DS7A, UK, range from 1 to 100mA, fixed durations between 0.05 to 2 ms). A pair of self-adhesive, circular (2.5 cm), gel electrodes (PALS Platinum, neurostimulation electrodes, model J10R00, Axelgaard manufacturing, Denmark) were positioned with surface cathode over the motor point of BB and the surface anode placed over the bicipital tendon (inter-electrodes distance 6 cm). A supramaximal stimulus intensity (mean supramaximal intensity = 53 ± 11 mA (range = 35 to 66 mA) (n=8) was used which was 20%

higher than the intensity used to produce a twitch of maximum amplitude in a relaxed muscle. A stimulus response curve of single twitch force versus stimulus intensity was first used to determine the required maximal intensity (Figure 1). The amplitude was measured from baseline to peak of each twitch response.

In a second experiment the inter-electrodes distance of the electrical stimulation was reduced from 6cm to 1cm (both electrodes to the muscle belly) with the cathode specifically positioned over the motor point. The experiment was conducted after the main experiment and mainly to examine whether the significantly larger resting twitches evoked by electrical stimulation compared to magnetic stimulation during the main experiment (see Results Section) was due to spread of electrical current. It has been reported that widely spaced electrodes (more than 5 cm in the case of biceps) increase the degree of current spread to antagonists and may activate both superficial as well as underlying agonists (e.g. brachialis) (Allen *et al.*, 1998). Thus, changing the inter-electrode distance was tested to determine if this resulted in a more selective stimulation of the BB through minimizing current spread and reducing coactivation of synergistic and antagonist muscles. Five resting twitches were evoked by electrical stimulation at supramaximal intensity (20% above maximum) in each of the two electrode pair configurations.

Magnetic muscle stimulation

Single pulse magnetic stimulation with supramaximal intensity (20% above the current intensity used to produce a resting twitch of maximum amplitude in a relaxed muscle determined by stimulation-response curve) was performed using a 70mm figure of eight coil powered by a Magstim Rapid (pulse duration 250 μ s) biphasic stimulator (Magstim Company Ltd, Spring Gardens, Whitland, Wales, UK). The coil was positioned perpendicularly to the trajectory of the musculocutaneous nerve and firmly against the skin with the crossover positioned on the motor point of BB which was detected before the experiment and was marked with a pen to ensure consistent placement of the coil during the experiment. The perpendicular orientation of the figure of eight coil was determined experimentally as the optimum orientation for inducing maximal current flow in underlying nerve. The optimal stimulation site was also determined by moving the coil over the BB near the cathodal electrical stimulation site, and it was defined as the stimulation site that yielded the largest force twitch elicited from the muscle. Tests with and without stimulating electrodes showed that no interference of the affixed cathodal electrode occurred. The mean supramaximal intensity, determined from an online stimulus response curve (see Figure 1) from subthreshold to maximal stimulator output (MSO = 100%) was 89 ± 13 (SD) %MSO (range = 66 to 100) (n = 8).

M-waves

Muscle action potentials (M-waves) evoked by peripheral electrical and magnetic stimulation were also recorded while elbow flexors were at rest and during isometric elbow contractions of various levels of voluntary force

(10, 25, 50, 75, 90 and 100% of every individual's MVC). Due to stimulus artifacts which could not be removed, the M-waves of BB were analyzed only in 6 out of the 8 participants. Additionally, the M-waves of APB and TB were analyzed in all participants. These evoked responses-M waves were collected with all EMG and force recordings and they were amplified (4 channels, Cambridge Electronic Design (CED), Cambridge, UK), filtered, digitized (4 KHz, micro 1401, 12 channels, CED, Cambridge, UK) as already described in the EMG section. A standard interface with 1902 as bioamplifier was used. All digitized data were stored for subsequent analysis (Signal v4 for Windows, CED software).

Experimental procedure

All participants underwent a familiarization procedure at the start of session to ensure comfort and accuracy in brief sustained isometric force levels with appropriate arm positioning. The main experimental session started with the electrical stimulation series, and after 10 minutes break was followed by the magnetic stimulation series, without randomizing the pattern of delivery.

Measurements taken

MVC Recordings: Due to participation of amateur volunteers in the experiment, and to variation in MVC responses the MVC was determined for each participant from the average of the three maximum contractions which were produced under strong verbal encouragement to ensure a maximum effort was undertaken (Shield and Zhou, 2004). MVCs were performed at the start of both the electrical and magnetic stimulation series.

Target force levels: The force signal and required force levels were displayed to the participant on a PC monitor to ensure good production of visually guided stable isometric contractions. Both electrical and magnetic stimulation were delivered while elbow flexors were at rest and during isometric elbow contractions of various levels of voluntary force (10, 25, 50, 75, 90 and 100% of each individual's MVC as it was recorded at the beginning of the electrical or magnetic stimulation series respectively). The target force levels were performed in random order while the contractions but the trials of each target force was performed consecutively in sets of three, with a 30 sec rest in between each trial to minimize fatigue.

Supramaximal stimulus: During each contraction and when the force reached a plateau, a supramaximal stimulus was delivered to the musculocutaneous nerve over the motor point. Two single pulses of magnetic or electrical stimulation were delivered to the biceps muscle while relaxed (resting twitches) 20 sec after the initial three MVCs (Kufel et al., 2002), and between every set of contractions so as they are equally potentiated with the superimposed twitches by the voluntary contractions (Shield and Zhou, 2004; Verges et al., 2009).

Display of recordings: The twitches evoked by the stimulation (interpolated twitch) were displayed on the PC screen while an automated twitch peak analysis was used by first setting cursors for the peak search within user specified regions of the force record. A segment of

the voluntary contraction force data immediately prior to the twitch force was averaged to set a baseline for measurement of the twitch force.

Analysis of data

SEMG amplitude (mV) was quantified by root mean square (rms) method of analysis of 1.5 second period during sustained peak force during voluntary contractions under visual inspection. For each muscle the M-wave area was calculated between pair of cursors set at the onset and offset of the evoked potential. The sEMG signals and the voluntary force were normalized to the corresponding maximal values of each participant. The mean values of three contractions of each level of contraction were used in the statistical analysis. Force, and not torque level is reported here because the moment arm of the muscle and the centre of rotation of the joint remained constant throughout the experiments, and therefore, the net torque could be reasonably and directly related to the net force acting in the joint (De Luca, 1997). Voluntary activation was calculated from force data by the formula: $voluntary\ activation = 100 \times (1 - superimposed\ twitch / control\ twitch)$, where the superimposed twitch is the force increment evoked during a voluntary contraction at the time of the stimulation and the control twitch is that evoked by identical nerve stimulation in potentiated relaxed muscle (Shield and Zhou, 2004).

Repeated measures analysis of variance (ANOVA) was used to find the effect of the level of voluntary force contraction and of the type of stimulation (electrical or magnetic) on the twitch force, the M-waves, the EMG, and the voluntary activation. Post-hoc comparisons using Bonferroni corrections and Greenhouse-Geisser correction when sphericity was violated, were used (Field, 2005). A paired-samples *t*-test was used to compare mean values of the resting twitch force, M-waves, background sEMG and resting twitch force evoked by electrical stimulation between different inter-electrode distances. The significance level was set at a *p* value ≤ 0.05 . The results in the text are presented as mean values \pm Standard Deviation and as means and Standard Error of Means (SEMs) are shown for figures unless otherwise indicated.

To estimate the relationship of the evoked twitches with the level of voluntary force Generalized Estimating Equations (GEE) analysis were employed, using an exchangeable correlation structure for non-independent data (Hanley et al., 2003). GEE analysis is based on a generalized linear model to estimate more efficiently unbiased regression parameters than ordinary least squares regression, where an unknown correlation is present (Ballinger, 2004). This method was chosen for its applicability to within subjects repeated measures research designs in which data are clustered (Ballinger, 2004; Hanley et al., 2003). There is one statistically significant fit determined by this method of equation estimation that identifies the best relationship. The evoked force-produced force relationship defined by the GEE analysis is presented by the formula: $Tw\%MVC = a_0 + a_1EFrc + a_2EFrc^2 + a_3EFrc^3$ for electrical stimulation, and $Tw\%MVC = a_0 + a_1MFC + a_2MFC^2 + a_3MFC^3$ for magnetic stimulation, where $Tw\%MVC$ is the amplitude force of the superim-

posed twitches normalized to MVC, EFrc and MFrc are the levels of voluntary force (% MVC) undertaken when electrical or magnetic stimulation was used respectively, and a^1 , a^2 , a^3 represent the coefficient of 1st (linear), 2nd (quadratic) or 3rd (cubic) order polynomial. The voluntary activation-force relationship was presented by a similar formula. STATA statistical software (release 12.0, College Station, Texas: STATA Corporation 2011) was employed for the GEE analysis. All the other statistical tests were performed using SPSS version 15; SPSS for Windows, 2007. Chicago: SPSS Inc).

Results

All participants reported that magnetic stimulation caused much less discomfort than electrical stimulation and that it was well tolerated even at supramaximal intensities.

Resting twitch force and resting M-waves of three muscles of upper limb

The mean resting twitch force amplitude evoked by the electrical stimulation (14.73 ± 4.83 N) was significantly larger than that evoked by the magnetic stimulation (11.58 ± 3.11 N), (mean difference 3.16 ± 3.35 N, $p < 0.05$) (Figure 2). Additionally, the resting twitches evoked by magnetic stimulation (Time to peak = 75 ± 10 ms) reached their peak force 13 ± 10 ms ($p < 0.05$) later than the twitches evoked by electrical stimulation (Time to peak = 62 ± 11 ms).

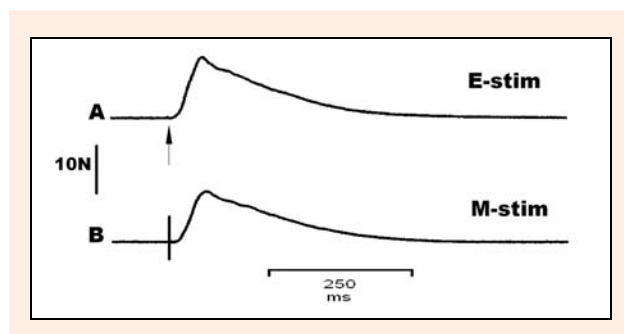


Figure 2. Average evoked resting twitch produced by i) electrical stimulation ii) magnetic stimulation of musculocutaneous nerve from same single subject based on $n=5$ in each. Arrow indicates onset of stimulus in e-stim, while mag-stim produces a small mechanical artefact which is visible prior to twitch response. Time calibration (250ms) and force calibration (10 N) for both average twitch responses.

The mean resting M-wave of BB evoked by electrical stimulation (13.11 ± 4.40 $\text{mV}\cdot\text{ms}^{-1}$) was not significantly different from that evoked by magnetic stimulation (13.57 ± 3.88 $\text{mV}\cdot\text{ms}^{-1}$), (mean difference = 0.05 ± 2.78 $\text{mV}\cdot\text{ms}^{-1}$, $p > 0.05$), (Figure 3). Likewise, the mean evoked M-waves of APB at rest did not differ significantly between electrical (18.49 ± 10.03 $\text{mV}\cdot\text{ms}^{-1}$) and magnetic stimulation (12.95 ± 6.64 $\text{mV}\cdot\text{ms}^{-1}$), (mean difference = 5.55 ± 9.48 $\text{mV}\cdot\text{ms}^{-1}$, $p > 0.05$). Similarly, the mean M-wave of triceps, evoked by electrical stimulation (2.31 ± 0.44 $\text{mV}\cdot\text{ms}$) was not significantly different than that evoked by magnetic stimulation (1.94 ± 1.58 $\text{mV}\cdot\text{ms}^{-1}$) (mean difference = 0.38 ± 1.92 $\text{mV}\cdot\text{ms}^{-1}$, $p > 0.05$)

Position of stimulating electrodes on electrically evoked resting twitch force

The mean resting twitch force evoked by electrical stimulation with the standard-wide placement of electrodes (25.75 ± 9.40 N) was significantly greater than the twitch force evoked by electrical stimulation with closed spaced electrodes (19.24 ± 9.32 N), (mean difference = 6.51 ± 6.17 N, $p \leq 0.05$).

Voluntary force and evoked twitch force at maximal contractions

The MVC did not change significantly due to repeated voluntary contractions: (mean difference before and after electrical stimulation session = 1.55 ± 5.98 N, $p > 0.05$) (mean difference before and after magnetic stimulation session = 1.68 ± 2.71 N, $p > 0.05$). Thus, no pronounced effect of fatigue was observed. The MVC determined prior to the electrical stimulation series (115.57 ± 14.86 N) was not significantly different from the MVC determined prior to the magnetic stimulation series (113.82 ± 17.97 N) (mean difference = 1.74 ± 7.34 N, $p > 0.05$).

The mean amplitude of the twitches evoked at MVC was not significantly different between electrical (0.62 ± 0.49 N) and magnetic (0.81 ± 0.49 N) stimulation ($p > 0.05$). The mean evoked twitch force at rest was about 10% of MVC and significantly reduced to 0.6% of MVC at maximal contractions.

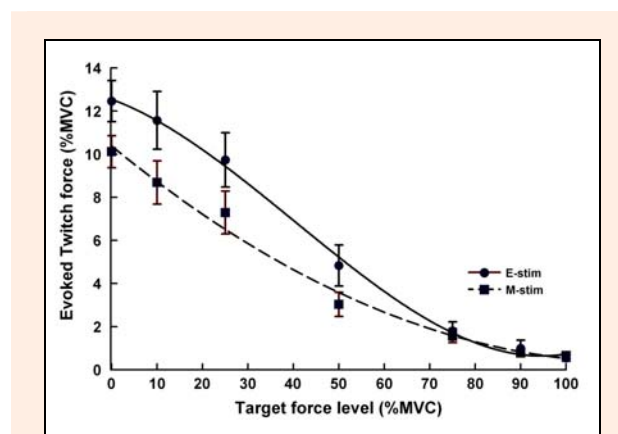


Figure 3. Relationship between the evoked twitch force (%MVC: y-axis) to voluntary force (%MVC: x-axis). This relationship fitted a cubic equation for the electrical stimulation (Fitting Model: $y=a_0+a_1x+a_2x^2+a_3x^3$, $a_0=12.57$, $a_1=-0.089$, $a_2=-0.0021$, $a_3=0.00002$, $R^2=0.99$) and a quadratic equation for the magnetic stimulation (Fitting Model: $y= a_0+ a_1x+ a_2x^2$, $a_0=10.67$, $a_1=-0.19$, $a_2=0.0009$, $R^2=0.99$). Data are presented as mean \pm SEM from 8 participants.

Comparison of proximal and distal M-waves during different levels of voluntary elbow flexion

The mean BB M-waves area during all levels of voluntary contractions did not differ significantly between electrical (13.47 ± 0.49 $\text{mV}\cdot\text{ms}^{-1}$) and magnetic (12.61 ± 0.58 $\text{mV}\cdot\text{ms}^{-1}$) stimulation ($F_{(1,4)} = 0.31$, $p > 0.05$, $\eta_p^2 = 0.07$). Specifically, at maximal contractions no differences were revealed between electrical (mean BB M-waves: 14.85 ± 4.04 $\text{mV}\cdot\text{ms}^{-1}$) and magnetic (mean BB M-waves: 12.43 ± 3.08 $\text{mV}\cdot\text{ms}^{-1}$) stimulation ($p > 0.05$).

Similarly, no significant effect of stimulation type was revealed for the TB M-waves ($F_{(1,6)} = 0.16$, $p > 0.05$, $\eta_p^2 = 0.03$) and the TB M-waves evoked at maximal contractions did not differ significantly between electrical ($1.99 \pm 0.84 \text{ mV}\cdot\text{ms}^{-1}$) and magnetic ($1.36 \pm 1.55 \text{ mV}\cdot\text{ms}^{-1}$) stimulation ($p > 0.05$).

The APB M-waves during voluntary contractions, evoked by electrical stimulation were significantly larger than the magnetically evoked ones ($F_{(1,6)} = 10.21$, $p \leq 0.05$, $\eta_p^2 = 0.63$). Additionally, the way the M-waves changed during the various levels of voluntary force was significantly different between electrical and magnetic stimulation ($F_{(1.6, 10.1)} = 8.54$, $p \leq 0.05$, $\eta_p^2 = 0.59$). Specifically, the APB M-waves evoked by magnetic stimulation were reduced after the force level of 25% of MVC (M-waves at 10%MVC = $12.74 \pm 8.32 \text{ mV}\cdot\text{ms}^{-1}$, at 25%MVC = $9.79 \pm 6.74 \text{ mV}\cdot\text{ms}^{-1}$, at 50%MVC = $8.16 \pm 5.92 \text{ mV}\cdot\text{ms}^{-1}$, 75%MVC = $7.81 \pm 5.43 \text{ mV}\cdot\text{ms}^{-1}$, 90%MVC = $7.61 \pm 5.13 \text{ mV}\cdot\text{ms}^{-1}$) while the electrical evoked wave was not significantly different ($p > 0.05$) among these same increasing levels of voluntary contraction (M-waves at 10%MVC = $18.95 \pm 10.03 \text{ mV}\cdot\text{ms}^{-1}$, at 25%MVC = $19.67 \pm 9.87 \text{ mV}\cdot\text{ms}^{-1}$, at 50%MVC = $20.10 \pm 9.28 \text{ mV}\cdot\text{ms}^{-1}$, 75%MVC = $20.45 \pm 8.40 \text{ mV}\cdot\text{ms}^{-1}$, 90%MVC = $20.78 \pm 9.53 \text{ mV}\cdot\text{ms}^{-1}$). At maximal contractions the APB M-waves evoked by electrical stimulation ($18.80 \pm 9.04 \text{ mV}\cdot\text{ms}^{-1}$) were significantly larger than those evoked by magnetic ($7.30 \pm 4.34 \text{ mV}\cdot\text{ms}^{-1}$) stimulation ($p \leq 0.05$).

Background sEMG of agonist & antagonist muscles

The sEMG activity of the antagonist TB, remained low even at maximum contractions (mean rmsEMG: $0.05 \pm 0.03 \text{ mV}$ during electrical stimulation and $0.048 \pm 0.03 \text{ mV}$ during magnetic stimulation) and was not significantly different between the two types of stimulation ($p > 0.05$).

The evoked twitch-voluntary force relationship between the two methods of stimulation

The active twitches decreased with the level of voluntary force and this was significant, ($F_{(6,36)} = 86.37$, $p < 0.001$, $\eta_p^2 = 0.94$). However, the best nonlinear (polynomial) fit of the evoked twitch-voluntary force relationship as it was assessed by GEE analysis was different between electrical and magnetic stimulation (Figure 3). For electrical stimulation, this was best defined by the cubic equation: $[\text{Tw}\% \text{MVC} = 12.57 - 0.089 \text{EFrc} - 0.0021 \text{EFrc}^2 + 0.00002 \text{EFrc}^3$, $p < 0.001$ for the cubic coefficient], and for magnetic stimulation this was best defined by the quadratic equation: $[\text{Tw}\% \text{MVC} = 10.67 - 0.19 \text{MFrc} + 0.0009 \text{MFrc}^2$, $p < 0.001$ for the quadratic coefficient].

Voluntary activation

Despite the differences in the resting evoked twitches, the voluntary activation of elbow flexors was not statistically different between the two types of stimulation used in its determination, ($F_{(1,6)} = 0.14$, $p > 0.05$, $\eta_p^2 = 0.02$) (Figure 4). Voluntary activation (VA) significantly increased with the level of voluntary contraction ($F_{(6,36)} = 240.62$, $p < 0.001$, $\eta_p^2 = 0.97$), but the increase in VA with voluntary force was not significantly different between electrical

and magnetic stimulation (no interaction effect between force and type of stimulation: $F_{(6,36)} = 0.91$, $p > 0.05$, $\eta_p^2 = 0.13$). In addition, the maximum voluntary activation of BB was not significantly different between electrical and magnetic stimulation (mean difference $2 \pm 6\%$, $p > 0.05$). During maximum contractions the mean VA of BB determined using electrical stimulation was 95% (range 90%-99%) while that determined using magnetic stimulation was 93% (range 84%-97%).

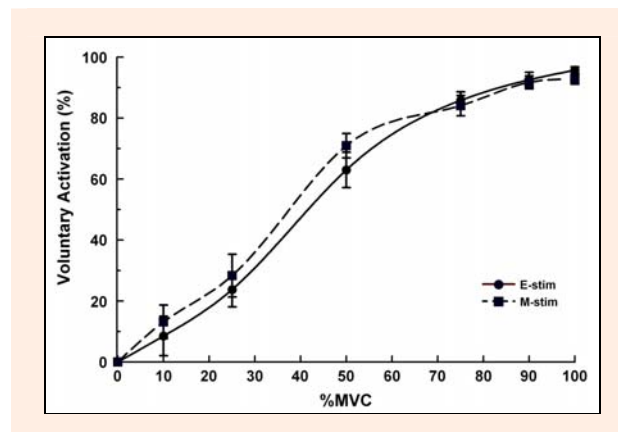


Figure 4. Voluntary activation of BB (% of maximal activation, y-axis) over range of voluntary contraction (0, 10, 25, 50, 75, 90, 100% of MVC, x-axis). Comparison between electrical (solid line) and magnetic (dashed line) type of stimulation. No significant differences revealed between the two modes of stimulation. Data are presented as mean \pm SEM of $n=8$.

Discussion

This study compared the standard assessment of voluntary activation using the ITT between peripheral electrical with magnetic stimulation in healthy individuals in the absence of fatigue. It also assessed the magnetically evoked twitch-voluntary force relationship. The results of this study showed the index of voluntary activation at maximal contractions were similar for the two methods of stimulation and the twitch-voluntary force relationship to fit a curvilinear function for both magnetic and electrical stimulation. In addition the BB evoked twitches at maximum contractions and the M-waves of all tested muscles, but APB, were similar between electrical and magnetic stimulation. The resting twitches however, evoked by electrical stimulation were larger than those evoked by magnetic stimulation.

These results are in accordance with the study of O' Brien et al. (2008) reporting comparable maximal activation level between magnetic and electrical stimulation when ITT was used for quadriceps muscle assessment. The comparable voluntary activation and the similar BB M waves and twitch force evoked at maximal contractions obtained by these two methods of stimulation suggest that both methods are equally sensitive for assessing maximal BB function.

In addition, the non-linearity in the relationship between evoked and voluntary force for both electrical and magnetic stimulation is in agreement with previous studies which report a deviation from the simple linear recip-

rocal electrically evoked twitch-voluntary force relationship (Allen et al., 1998; Behm et al., 1996; Folland and Williams, 2007). This is the first time that the relationship for the magnetic stimulation has been assessed and therefore, no studies exist in order to make comparisons. Our study revealed a cubic relationship for the electrical stimulation and a quadratic fit for the magnetic stimulation. This difference between magnetic and electrical stimulation nonlinear curves for the twitch-voluntary force relationship is novel and it cannot be fully explained. Indeed, in the literature various curvilinear functions have been reported for the electrical stimulation depending on the number of stimuli applied and, or the muscles involved. A quadratic relationship was reported for doublet electrically evoked twitch-voluntary force relationship of knee extensors (Folland et al., 2007) and plantar flexors (Behm et al., 1996). A sigmoidal relationship was also reported by Herbert and Gandevia (1999) for the relationship between excitation of mononeuron pool and interpolated twitch amplitude after electrical stimulation with trains of stimuli over the ulnar nerve. This variability in fitting the appropriate curvilinear function for the electrical stimulation twitch evoked-voluntary force relationship allow for no safe conclusions regarding the similarity in the curve fitting relationship between magnetic and electrical stimulation.

The reasons for this non-linear relationship have been extensively discussed in previous studies (Allen et al., 1998; Behm et al., 1996; Folland and Williams 2007; Herbert and Gandevia 1999; Shield and Zhou 2004). However, the differences in the curve fitting between electrical and magnetic stimulation revealed in our study could be due to the larger resting twitches evoked by electrical stimulation implying larger current spread of electrical stimulation especially with the widely space stimulating electrodes. The greater resting twitches evoked by electrical than magnetic stimulation and the shorter time to peak for the magnetically evoked twitches is not in line with other studies which report agreement between electrical and magnetic resting potentiated twitches but in different target nerves: for stimulation of the ulnar nerve (Harris et al., 2000), and femoral nerve (Hamnegård et al., 2004; Verges et al., 2009). The motor point-tendon configuration for placement of the stimulating electrodes is the most commonly used, as it provides the most selective way of stimulation of the muscle of interest (Shield and Zhou 2004). However, widely spaced electrodes (more than 5 cm in the case of biceps) increase the degree of current spread to antagonists and may activate both superficial as well as underlying agonists (e.g. brachialis m.) (Allen et al., 1998), whereas with magnetic stimulation a much smaller volume of muscle fibres of these muscles may be activated. This larger current spread with widely space stimulating electrodes likely contributes to producing larger twitches evoked by electrical stimulation. However, when the inter-electrode distance was reduced (stimulating electrodes placed closer over the muscle belly), the resting twitches reduced in amplitude to 73% of those evoked with the wide spaced configuration, implying restriction of the electrical current spread and suggest that the difference in focality may be the

underlying reason for this difference between the two methods of stimulation in the assessment of voluntary activation using the ITT.

The differences in the resting twitches between this study and the previously published ones using magnetic stimulation may also depend on the magnetic stimulation characteristics and the magnitude of the induced electric field in the tissues (Jalinous, 1991). We used a Magstim rapid which generated a biphasic magnetic field waveform but monophasic field waveforms are also in use, and other factors may include coil size and shape. The size and shape of the magnetic coil could have played a significant role in producing resting twitches of smaller amplitude than the electrically evoked ones (Madariaga et al., 2007; Olney, 1990). Indeed, it has been reported that the twitches evoked with the 45-mm coil were higher compared with mean values evoked with the 70-mm coil at all intensities of the stimulator output (Tomazin et al., 2010). Given that the magnetic field falls off by approximately 50% at 10 mm from the coil, the plastic enclosure wrapped around the 70-mm coil may increase the distance from the discharge magnetic field to the stimulating nerve when compared with the 45-mm double coil, which is covered only by a thin, polyurethane coating (Tomazin et al., 2010). It would be of great interest to examine this by using a smaller magnetic coil or also a monophasic stimulator to better suit the typical monophasic electrical stimulation output of most devices in use. Purpose built, higher power magnetic stimulators could also be used to evoke supramaximal compound motor evoked potentials (Matsumoto et al., 2010) and pairs and brief trains of magnetic stimulation may be the preferred method for detection of central activation failure during isometric contractions (Kent-Braun and Le Blanc, 1996; Miller et al., 1999). Trains of stimuli were not used in the present study because its aim was to utilize the most commonly used protocol for electrical stimulation which could be then compared to single pulse magnetic stimulation, however it is suggested that they generate larger force increments at MVCs than single impulse stimulation (Hanley et al., 2003).

The absence of differences in the antagonist TB M waves suggests that magnetic stimulation does not induce more widely distributed electric field than the electrical stimulation within the compartments of the upper arm underlying the stimulation coil. In contrast however, the presence of larger M waves in the distal APB and the significant differences observed for the type of stimulation over the range of voluntary force levels suggest that there is wider electric field effects of the electrical stimulation on the underlying median nerve. The effective induced electric field produced by magnetic stimulation drops off with increasing distance between target tissue and coil surface. Thus the likely decrease in the M wave with increasing force level production in these isometric tasks physically moves the magnetic stimulation coil further away from the underlying median nerve situation beneath BB and other elbow flexors of upper arm. This would not be seen with the electrical stimulation as the current path between the two electrodes would be much less affected by the muscle contraction. This is a likely

explanation given that the magnitude of the induced current is proportional to the distance from the source of the magnetic pulse produced by the coil (Epstein, 2008).

The similarities observed in our study between magnetic and electrical stimulation overall imply that peripheral magnetic stimulation can be a safe alternative for examining neuromuscular function of BB, when an examination of possible changes in neural drive at the level of motoneurons is required. The painless, supra-maximal, reproducible application of magnetic stimulation examined here has been also reported elsewhere in other muscles (Hamnegard et al., 2004; Harris et al., 2000; O'Brien et al., 2008; Polkey et al., 1996; Rafferty et al., 2000). This further suggests an application of peripheral magnetic stimulation for diagnostic purposes of incomplete muscle activation, especially in cases where patients complain of exaggerated effort and chronic fatigue. Post exercise changes in muscle function have been reported to be similar for electrical and magnetic stimulation (Verges et al., 2009) suggesting this method is also suitable for the assessment of muscle activation in studies of both central and peripheral aspect of fatigue in exercise and rehabilitation.

Conclusion

Overall, the results of the study have shown that there are key similarities between magnetic and electrical stimulation in the assessment of voluntary activation with the single pulse Twitch Interpolation Technique. The twitch responses at maximal contractions and the M-waves for agonist BB were comparable. The activation for the antagonist TB was minimal and the curve-fitting for the twitch force-voluntary force relationship was non linear for both electrical and magnetic stimulation. The closeness of BB voluntary activation between electrical and magnetic stimulation at maximal contractions indicate that the use of magnetic stimulation in the single twitch interpolation technique may be an appropriate method of estimating the activation level of BB, despite the factors which contribute to the resting twitch differences and the different curve fitting observed here. The larger resting twitches evoked by electrical stimulation and the different curve fitting may not be significant when investigating the use of peripheral magnetic stimulation with an array of coils and stimulators. Thus, the similar sensitivity of magnetic stimulation to electrical stimulation in assessing voluntary activation and the absence of discomfort from magnetic stimulation offer significant advantages for the assessment of voluntary activation in the clinical environment.

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Key points

- The study compared peripheral electrical and magnetic stimulation in the assessment of voluntary activation using single pulse twitch interpolation of elbow flexors.
- Key similarities between magnetic and electrical stimulation in the assessment of voluntary activation with the single pulse Interpolation Twitch Technique were revealed.
- Voluntary activation at maximal contractions were similar for the two methods of stimulation and the twitch-voluntary force best fit with nonlinear functions for both magnetic and electrical stimulation.
- The fundamental similarities in voluntary activation assessment of elbow flexor, m. Biceps Brachii with these two methods of stimulation support the application of peripheral magnetic stimulation using the conventional Interpolation Twitch Technique.
- The painless assessment of voluntary activation with peripheral magnetic stimulation may strengthen its acceptance for clinical use in neuromuscular assessment.

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