REVIEW ARTICLE

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Assessing Voluntary Muscle Activation with the Twitch Interpolation Technique

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Contents

Abstract

The twitch interpolation technique is commonly employed to assess the completeness of skeletal muscle activation during voluntary contractions. Early applications of twitch interpolation suggested that healthy human subjects could fully activate most of the skeletal muscles to which the technique had been applied. More recently, however, highly sensitive twitch interpolation has revealed that even healthy adults routinely fail to fully activate a number of skeletal muscles despite apparently maximal effort. Unfortunately, some disagreement exists as to how the results of twitch interpolation should be employed to quantify voluntary activation. The negative linear relationship between evoked twitch force and voluntary force that has been observed by some researchers implies that voluntary activation can be quantified by scaling a single interpolated twitch to a control twitch evoked in relaxed muscle.

Observations of non-linear evoked-voluntary force relationships have lead to the suggestion that the single interpolated twitch ratio can not accurately estimate voluntary activation. Instead, it has been proposed that muscle activation is better determined by extrapolating the relationship between evoked and voluntary force to provide an estimate of true maximum force. However, criticism of the single interpolated twitch ratio typically fails to take into account the reasons for the non-linearity of the evoked-voluntary force relationship. When these reasons are examined, it appears that most are even more challenging to the validity of extrapolation than they are to the linear equation. Furthermore, several factors that contribute to the observed non-linearity can be minimised or even eliminated with appropriate experimental technique. The detection of small activation deficits requires high resolution measurement of force and careful consideration of numerous experimental details such as the site of stimulation, stimulation intensity and the number of interpolated stimuli. Sensitive twitch interpolation techniques have revealed small to moderate deficits in voluntary activation during brief maximal efforts and progressively increasing activation deficits (central fatigue) during exhausting exercise. A small number of recent studies suggest that resistance training may result in improved voluntary activation of the quadriceps femoris and ankle plantarflexor muscles but not the biceps brachii. A significantly larger body of evidence indicates that voluntary activation declines as a consequence of bed-rest, joint injury and joint degeneration. Twitch interpolation has also been employed to study the mechanisms by which caffeine and pseudoephedrine enhance exercise performance.

When a supramaximal electrical stimulus is applied to the nerve trunk or intramuscular nerve branches of an active muscle during a voluntary contraction, those motor units that have not already been recruited respond by generating a twitch response.[1] Those motor units firing at sub-maximal rates and whose motoneurones are not in a refractory state respond with a twitch-like increment in force.[1] With increasing neural drive to the muscle fewer units are available for recruitment, the twitch-like response of others diminishes and the superimposed twitch becomes smaller and ultimately undetectable if the muscle can be fully activated (figure 1). The progressive occlusion of the interpolated twitch by voluntary effort was first reported by Denny-Brown[2] and subsequently applied to the assessment of muscle activation by Merton.[3] Merton[3] reported a negative linear relationship between adductor pollicis twitch force and voluntary isometric force measured during attempted thumb adduction. He also saw no evidence of an interpolated twitch during maximal voluntary contractions (MVCs) and concluded that the muscle could be activated completely by voluntary command.[3]

In accord with Merton's observations,[3] subsequent work indicated that a majority of healthy individuals could fully activate most of the muscles to which twitch interpolation was applied.[1,4-12] However, the methods employed in these early studies were not particularly sensitive and higher resolution techniques[13,14] have since revealed that full activation occurs less frequently and in fewer muscles than was previously suggested.[14-23]

Unfortunately, some controversy exists regarding the appropriate means of quantifying muscle activation. This review addresses the issues involved and some of the important technical considerations with the twitch interpolation technique. Also included is a brief summary of what the technique has revealed regarding: (i) the levels of muscle activation in brief and prolonged MVCs; and (ii) the role of the nervous system in strength development consequent to resistance training and strength loss consequent to immobilisation, injury and joint de-

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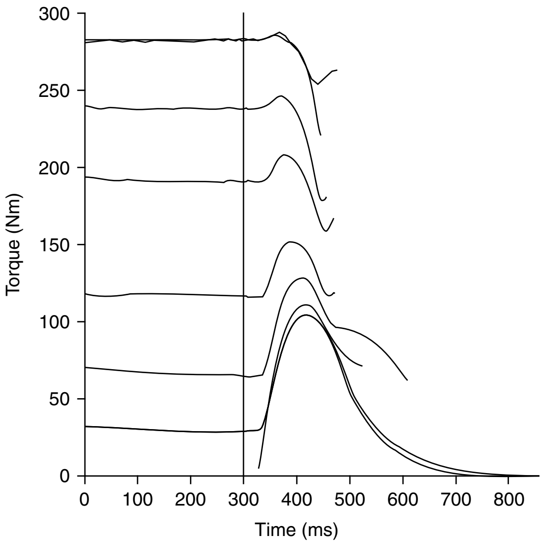

Fig. 1. Superimposed twitch-like responses evoked in the quadriceps with twin stimuli during isometric actions of the knee extensors (traces from bottom to top): two potentiated control responses (those evoked in relaxed muscle), and at approximately 10, 20, 40, 60, 80 and 100% (two contractions) of maximal voluntary contraction. The vertical line represents the timing of the initial stimulus. Supramaximal stimuli (each 50μs duration, 10ms inter-pulse interval) were applied via electrodes placed over the proximal and distal quadriceps femoris.

generation. We also discuss the application of twitch interpolation to the study of ergogenic drugs.

1. Quantifying Voluntary Activation

The term 'voluntary activation' is quite common in the literature although there are potential ambiguities in its use.[24] In this review we use the term to define the completeness of skeletal muscle activation during voluntary contractions.

1.1 The Interpolated Twitch Ratio

The negative linear relationship between evoked and voluntary force described by Merton[3] and others[6,25,26] implies that the extent of inactivation can be quantified by expressing the interpolated twitch as a percentage of the twitch evoked in relaxed muscle. It also suggests that the muscle's 'true maximum' force can be determined on the basis of a single interpolated twitch ratio. Accordingly, voluntary activation of the stimulated muscle(s) is frequently quantified with the linear equation (equation 1):

$$\text{voluntary activation (\%)} = [1 - (\text{superimposed twitch/control twitch})] \times 100 \quad \text{(Eq. 1)}$$

where the superimposed twitch is the force increment noted during a maximal contraction at the time of stimulation and the control twitch is that evoked in the relaxed muscle.[15,16] The control twitch is typically evoked 1.5–5 seconds after the MVC[15,16,18,19,27] and it is assumed that it and the superimposed twitch are equally potentiated by the voluntary effort.

Since Merton's original twitch interpolation study[3] the relationship between evoked and voluntary force has been re-examined for a wide range of muscles. Numerous studies have shown that the relationship is concave upward at medium forces and asymptotic at high voluntary forces.[1,14,28,29] Some studies also indicate an upward convexity in the relationship at low voluntary forces,[1,30] although this is not always the case.[16,26,31]

Observations of non-linear evoked-voluntary force relationships have led to the claim that the aforementioned linear equation is invalid and that voluntary activation can not be determined from a single interpolated twitch ratio.[14,28,30] However, those who make this claim fail to consider that non-linearity in the evoked-voluntary force relationship may occur for reasons other than a non-linearity in the relationship between the activation of the stimulated muscles and evoked force. It must be acknowledged, however, that the linear equation can not provide an accurate estimate of the true maximum force when the relationship between evoked and voluntary force is non-linear.[28]

1.2 Extrapolating the Evoked-Voluntary Force Relationship

An alternative method of quantifying voluntary activation involves modelling the relationship between evoked and voluntary force and extrapolating it to the estimated true maximum, where the curve crosses the voluntary force axis.[14,28,30,32] Voluntary activation is then determined by expressing the MVC force as a percentage of the estimated true maximum. The evoked-voluntary torque relation-

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ship has been modelled in various ways. Some have estimated true maximum force by fitting a straight line to data points above 25% of maximum voluntary force[30] while others have employed polynomial[28] or exponential functions.[14] Alternatively, the relationship has been linearised by replacing evoked force with [normalised evoked force]^k where k gave the best linear fit to the data for each individual.[32]

Regardless of the method employed to model the relationship, curve fitting has significant limitations. For example, when polynomial functions are employed, the estimate of true maximum force will be very sensitive to slight variation in the values obtained during maximal contractions. Consequently, slight errors in determining the amplitude of the twitches superimposed over MVCs could significantly alter estimates of voluntary activation. Furthermore, the best fitting relationships may not always provide curves that cross the x-axis[14,32] and when they do, their flat slopes dictate that the 95% confidence intervals for the relationship will envelop a large range of voluntary forces. Because of these limitations, the estimates of true maximum force obtained via extrapolation are sometimes unrealistically large[33] or even less than the measured MVC forces.[32] Furthermore, stimulus-evoked increments in force are sometimes observed during MVCs that are equal to or greater than the predicted true maximums.[18,32] A further practical problem arises because the extrapolation technique requires the performance of numerous submaximal contractions in addition to maximal ones. Consequently, the method is time consuming and unsuited to the study of fatigue-related reductions in voluntary activation when instantaneous determinations of activation are required.[19,22,34,35]

1.3 Mechanisms Underlying the Non-Linearity of the Evoked-Voluntary Force Relationship: Implications for Quantifying Voluntary Activation

Equation 1 and various non-linear extrapolation techniques typically provide different results[14,31,32] (figure 2) and considerable disagreement exists as to which is the most appropriate.[14,16,28,30,33] Criticism of the single interpolated twitch ratio often fails to take into account the reasons for the non-linearity of the evoked-voluntary force relationship. When these

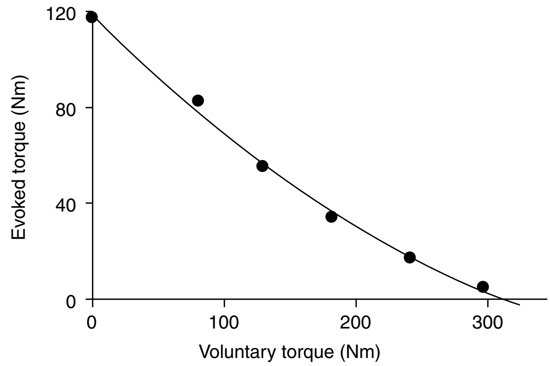

Fig. 2. The relationship between evoked and voluntary knee extensor torque fitted with a polynomial function and extrapolated to an estimate of true maximum force. Maximal voluntary activation levels determined via the equation: voluntary activation = [1 – (super imposed twitch/control twitch)] × 100 and via extrapolation are 96.4% and 90.3%, respectively. Supramaximal twin stimuli (each 50μs duration, 10ms inter-pulse interval) were applied via electrodes placed over the proximal and distal quadriceps femoris.

reasons are examined,[16,33] it appears that some are even more challenging to the validity of extrapolation than they are to the linear equation (see paragraph below). Furthermore, several factors that contribute to the observed non-linearity can be minimised or even eliminated with appropriate experimental technique.

To provide a valid estimate of voluntary activation, equation 1 actually requires a linear relationship between evoked force and activation of the stimulated muscle(s) and a non-linear relationship between evoked and voluntary force does not necessarily invalidate the equation. The evoked-voluntary force curve may be non-linear because unstimulated synergists contribute disproportionately to increases in voluntary force in near maximal contractions. This is quite likely in the case of the elbow flexors because the often studied biceps brachii can be almost fully activated while the brachioradialis exhibits a significant activation deficit.[16] Furthermore, small increases in muscle length that occur during supposedly isometric contractions of near-maximal and maximal intensity[16,36] may also increase force independently of voluntary activation. Together, these effects could account for the asymptotic nature of the evoked-voluntary force relationship at high voluntary forces (figure 3, see also Gandevia[24]). Neither effect invalidates the use of a single interpolated twitch ratio as a means of esti-

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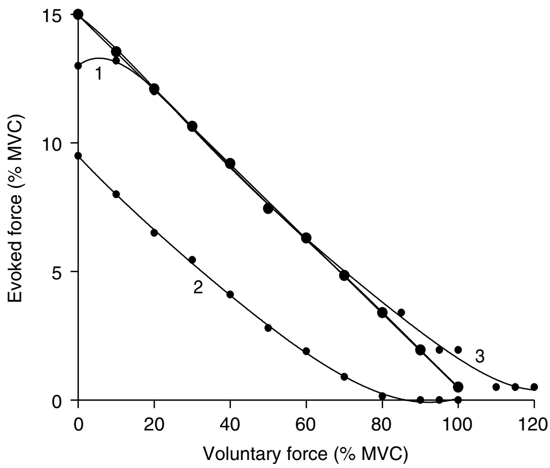

Fig. 3. Three mechanical factors that may distort the expected linear relationship between evoked and voluntary force. The bold line is the hypothetical relationship between evoked and voluntary force (note the twitch is not fully occluded at MVC). **MVC** = maximal voluntary contraction; **1** = effect of series elastic slackness when tests are conducted at short muscle lengths; **2** = effect of a compliant myograph and the resulting shortening of the muscle during evoked twitches; **3** = effect of the increasing role of unstimulated synergists and small increases of muscle length (note that the same interpolated responses are observed across a range of voluntary forces).

mating activation because activation of the stimulated muscle is determined by scaling-evoked forces (the superimposed and control responses) measured on the y-axis, while the distortion in the relationship between activation of the stimulated muscle and voluntary force occurs on the x- or voluntary force axis. This distortion does, however, create doubts about the validity of extrapolation because the extent to which it occurs will influence the predicted true maximum forces (and the estimate of muscle activation) independently of the stimulated muscle's level of activation.

At least three other factors may contribute to the asymptotic nature of the evoked-voluntary force relationship. The first is the failure to detect small increments in force superimposed over near-maximal contractions (see section 2.3). The second is the inadvertent stimulation of antagonistic muscles (see section 2.1). As discussed in section 2, the influence of both factors can be reduced and the linearity of the evoked-voluntary force relationship improved by careful attention to experimental detail. Finally, the use of a compliant myograph causes the otherwise near-linear evoked-voluntary force relationship to become asymptotic at considerably submaximal forces.[37] Consequently, care must be taken to prevent muscles from shortening during superimposed responses and failure to do so will impact upon estimates of voluntary activation regardless of how it is quantified.

For some muscles, the evoked-voluntary force relationship may be upwardly convex at low voluntary forces and control twitches may be equal to or even smaller than those evoked over weak (10–15%) voluntary contractions[1,30] (figure 3). This upward convexity, which has been attributed to the effect of series elastic slackness,[1] creates a problem when using a linear equation which clearly implies that control twitches should be larger than those evoked during voluntary efforts. By testing muscles at longer lengths, the impact of series elastic slackness is reduced and the relationship becomes more linear at low voluntary forces.[30] Furthermore, interpolation techniques employing two or more stimuli are influenced less by series elastic slackness than the traditional single stimulus[34,38] and may be more appropriate for tests of muscle activation across a range of joint angles. It should also be acknowledged that estimates of voluntary activation are relatively insensitive to small variations in the size of the control twitch. However, underestimates of voluntary activation caused by the upward convexity at low voluntary forces become increasingly significant when low levels of activation are achieved. Consequently, the suitability of scaling superimposed twitches to control twitches should be seriously considered when muscles are to be tested at short lengths, particularly when low levels of activation (<80%) are expected as the result of injury,[39] disuse[38] or disease.[9,40,41] When an unavoidable upward convexity in the evoked-voluntary force relationship exists at low voluntary forces it may be more appropriate to extrapolate to true maximum force by fitting a straight line to data points above 25% of maximum.[30]

Mechanical factors are not the only ones that influence the relationship between evoked and voluntary force. Twitch amplitude is also influenced by collisions between orthodromic and antidromic action potentials and by the spinal effects of stimulation that create the subsequent electrical silent

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period.[33] During voluntary contractions, both effects reduce the force generated by low threshold motor units that are already firing at rates sufficient for the fusion of successive twitches. Consequently, soon after the unrecruited motor units and those firing at suboptimal rates start to develop extra force, those that are already fully activated start to relax and the amplitude of the superimposed response is diminished. Simulation experiments conducted by Herbert and Gandevia[33] employing a model of the adductor pollicis indicate that this effect has its greatest influence at voluntary forces between 40 and 80% of maximum because a significant proportion of motor units start to relax prior to the peak of the superimposed response.[33] During a weak voluntary contraction (<40%), the superimposed response is influenced to only a very small extent, because the proportion of units that respond with an increase in force is very much greater than that of the units that respond with a decrease in force. At forces higher than 80% of maximum the superimposed response is diminished to only a small extent, by the collision effect alone, because the rising phase of the superimposed response is complete or almost complete before the spinal influence of stimulation has had time to reduce voluntary force.[33] Consequently, scaling superimposed twitches to control twitches will tend to overestimate voluntary activation but only to a small extent for healthy individuals who are typically capable of activating 85% or more of their muscles.[15,16,18,20,21,23,25,28,29,32]

It has been suggested that twitch interpolation involving a single superimposed stimulus may be incapable of detecting sub-optimal motor unit firing rates[42,43] and that the evoked-voluntary force relationship becomes less steep or even asymptotic at forces at which recruitment is complete and rated coding becomes the sole means of enhancing force.[31] This view is contradicted by two observations. First, it is well known that force increments (the catch-like property) do occur when an extra stimulus is applied to muscles or motor units that are being stimulated at sub-optimal rates.[1,33,44,45] Secondly, if superimposed stimuli were almost completely occluded once full recruitment occurred, the evoked-voluntary force relationship for the adductor pollicis would become asymptotic at approximately 50% of MVC force[46] and this does not occur when a non-compliant myograph is employed.[3,37]

2. Technical and Practical Considerations with Twitch Interpolation

2.1 The Site of Stimulation

Electrical stimulation is typically applied via electrodes placed over the nerve trunk that innervates the studied muscle(s) or over the muscle belly, in which case the stimulus activates the muscle via intramuscular nerve fibres.[47] With either technique, it is possible that both the studied muscles and their antagonists will be activated. For example, when the tibialis anterior is stimulated via the common peroneal nerve, the plantarflexing peroneal muscles are also activated.[25,48] Similarly, when the femoral nerve is stimulated, the quadriceps femoris and the sartorius muscles contract. In these circumstances, the appropriate muscles are more selectively stimulated via electrodes judiciously placed over the muscle belly, preferably near the motor points.[1,25] However, placing electrodes too far apart, too close to antagonists, using excessively large electrodes or intensities of stimulation[49,50] may lead to the activation of antagonists. The small twitch torques generated by antagonists may only slightly reduce the amplitude of control twitches; however, during near maximal and maximal voluntary efforts they may completely mask the small force increments produced by the agonists.[49] The impression will be that muscles are fully activated during clearly submaximal contractions.

2.2 Stimulation Intensity

Twitch interpolation is often performed with submaximal stimulation, perhaps on the basis of an early but inexhaustive investigation which indicated that submaximal and maximal stimulation provide similar estimates of voluntary activation in unfatigued muscle.[9] The use of submaximal stimulation reduces the discomfort associated with twitch interpolation. It may also provide a more selective recruitment of agonists and thereby lessen the risk of activating antagonistic muscles.[49] However, a potential disadvantage of employing submaximal stimulation is that successive stimuli may activate differ-

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ent portions of the muscle,[28] particularly if slight changes in voluntary drive occur immediately prior to stimulation.[51] The proportion of the quadriceps activated via submaximal stimulation of the femoral nerve has been observed to be less during maximal voluntary efforts than during rest, presumably because the stimulating electrode was displaced by contraction of the surrounding muscles.[28] This effect would diminish the superimposed responses and result in overestimation of voluntary activation when the superimposed response is scaled to the control twitch. When stimulation is clearly supramaximal, small movements of the electrodes relative to the underlying muscle or nerve trunk should have no effect on the proportion of the muscle that is activated. Submaximal stimulation is also particularly unsuited to studies of fatigue because the threshold of motor axons increases during fatiguing contractions and stimulation at any particular intensity will activate progressively fewer motor units.[52]

2.3 The Signal to Noise Ratio of Twitch Interpolation

The signal to noise ratio of twitch interpolation decreases considerably with increasing voluntary activation because the superimposed responses diminish while fluctuations in voluntary force increase.[53] Thus, the force increments superimposed over near-maximal and maximal voluntary efforts may remain undetected unless efforts are made to enhance the technique's sensitivity.[14,25,54]

2.3.1 The Number of Interpolated Stimuli

The original twitch interpolation technique described by Merton[3] and subsequently employed by many others[1,5-9,12,15,29] involved a single stimulus interpolated over voluntary contractions. Recently, it has become common for two or more stimuli (50–100Hz) to be employed[14,18,34,38,51] because the evoked force increments are larger and more readily detected.[16,32,43,45,54-58] There is also evidence that supramaximal twin, triple and quadruple stimuli (at 125Hz) evoke less variable force increments than single stimuli when superimposed over voluntary isometric contractions at 50% of maximum.[45] Furthermore, single stimuli are unsuited to studies of muscle fatigue because alterations in excitation-contraction coupling (low frequency fatigue) dictate that the resulting evoked responses will decline more than those evoked with multiple stimuli delivered at a high rate.[5,22] Thus, twin stimuli separated by 10ms are typically employed to study central fatigue during exhausting exercise.[19,22,34]

A practical problem introduced by the use of two or more supramaximal stimuli is the increased discomfort involved. Consequently, submaximal stimuli are often employed[43,56,58,59] and this introduces the potential problems outlined previously.[60] The use of multiple stimuli has also been criticised on the grounds that spinal reflexes have more time to influence the superimposed response.[33,60] This possibility must be carefully considered, particularly in light of evidence that single stimuli can reveal very small deficits in voluntary activation when high resolution measurements of force[13] and triggered averaging methods are employed[14,25] (see section 2.3.2). Modelling suggests that the use of twin stimuli has minimal effect on estimates of voluntary activation[33] and estimates of true maximum force obtained from extrapolation do not differ significantly when 1, 2 or 5 stimuli are employed.[28] We have also observed that almost identical estimates of voluntary activation are provided by single interpolated twitch ratios when 1, 2 and 4 stimuli are applied to the quadriceps during MVCs (unpublished observations). Thus, the impact of employing 2–5 stimuli on estimates of voluntary activation appears to be negligible. In contrast, longer trains of submaximal stimuli do appear to influence estimates of voluntary activation. It has been reported that while the force increments evoked by both submaximal trains of 20 stimuli (100Hz) and single supramaximal stimuli decline linearly with increasing voluntary force, the 95% confidence intervals for the relationship are considerably wider when trains were employed.[61] Thus, submaximal trains appear to provide less precise estimates of voluntary activation than single supramaximal stimuli.

Regardless of the potential problems involved, trains of 10–100 stimuli (at 50–100Hz) are quite commonly employed to assess the maximality of voluntary activation.[32,43,55-58,62] As with interpolated twitches, activation is then sometimes quantified by scaling superimposed force increments to control responses evoked in relaxed muscles.[32,56] Alterna-

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tively, MVC force is expressed as a percentage of the total force produced during the superimposed response[55,57] and this index of activation has become known as the central activation ratio (CAR).[55] The clear and often false assumption of the CAR is that the combination of the superimposed train and the MVC will evoke the muscle's true maximum force.

Superimposed train stimulation of the tibialis anterior via the peroneal nerve revealed CAR values of less than one, while under the same circumstances the single and double pulse stimulation did not.[55] However, in this study, the inadvertent stimulation of the peroneal muscles (also innervated by the peroneal nerve) would have evoked plantarflexion torques that could well have concealed small superimposed dorsiflexion torques evoked by single and twin stimuli (the use of train stimulation protocols is frequently justified by the findings of studies such as this one that have used flawed twitch interpolation methodology). Nevertheless, comparing the CAR values obtained when single, twin and trains of stimuli are employed is inappropriate because the evoked force increment and therefore the CAR value, depends critically on the duration of stimulation.[43,55,57,58,60] An even more fundamental flaw with the CAR is that MVC force is typically determined by a number of synergists while only the stimulated muscles produce the force increment. Consequently, the CAR value will vary with the number of synergists that are stimulated and can therefore not provide a valid measure of muscle activation.

2.3.2 Triggered Averaging

When muscles are highly activated the superimposed responses will be small and possibly indistinguishable from fluctuations in voluntary force. However, averaging several force traces effectively reduces the impact of these fluctuations and may reveal clear force increments at the appropriate latency after stimulation.[14,25] Triggered averaging may not be necessary when relatively low levels of voluntary activation are achieved and superimposed responses are clearly visible. However, the inference that muscles are fully activated when superimposed force increments are not apparent should be regarded with caution unless triggered averaging has been employed.

2.3.3 The Resolution of Force Measurements

To detect a 1% activation deficit it is necessary to resolve force increments that are 1% of the amplitude of the control twitches. However, because control twitches evoked by single stimuli may be as small as 10% of MVC force,[25,48] the superimposed force increments evoked in a muscle that is 99% activated may be only 0.1% of MVC force. It has been suggested that the resolution of force measurements in many early twitch interpolation studies was insufficient to detect activation deficits of 5% or less.[20,54] Indeed, in one of the earliest twitch interpolation studies, the authors acknowledged that they were unable to detect twitches reduced to less than 3% of the control responses.[1] Significant in the evolution of twitch interpolation was the development and application of a technique that removed the large DC-offset produced by the voluntary contraction and thus allowed further amplification (×10) of the remaining superimposed response without distorting the signal.[13] Unfortunately, the resolution of force measurements is reported in very few studies and the results of those that do not report this information should be considered cautiously.

For a given level of resolution, smaller activation deficits can be detected when the control responses are larger. Consequently, the sensitivity of twitch interpolation is greater when the stimulated muscle is responsible for a high proportion of the total force produced at the joint. Some advantage is also obtained by employing two to five stimuli rather than one. Nevertheless, extremely small deficits in activation can be detected with single stimuli when appropriate methods are employed to amplify the superimposed response.[13]

2.4 Familiarisation of Subjects

Unfamiliarised subjects are typically unable to perform consistent isometric MVCs that display a marked plateau in force. Inadequate familiarisation will therefore result in the reporting of artificially low and highly variable levels of activation. The possible influence of twitch interpolation on voluntary strength should also be considered. Some subjects who are unfamiliar with the technique consist-

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ently perform weaker contractions when stimulation is expected than when it is not (unpublished observations), presumably because they are intimidated by the prospect of receiving noxious stimuli. Consequently, researchers should allow subjects to perform some MVCs without stimulation during the familiarisation process. Only when MVCs with expected stimulation match those without expected stimulation should the subject be formally tested.

2.5 Rejection Criteria for Maximal Voluntary Contractions

Even well familiarised subjects will occasionally perform poorly and it is important that suboptimal trials be identified and rejected. Force traces for each MVC should therefore be examined at the time of the test. Brief isometric MVCs should be rejected and repeated in any of the following cases:
1. the force trace exhibits no clear plateau prior to superimposed stimulation;
2. the superimposed stimulus is delivered when the voluntary force is not at or very close to its maximum for that contraction;
3. the subject perceives that his or her effort was submaximal at the time of stimulation.

Obviously, points 1 and 2 are not applicable to isokinetic contractions in which force varies with joint angle. However, guideline 3 remains applicable to all trials in which maximal effort is expected.

2.6 Verbal Encouragement and Feedback

Loud verbal encouragement has a significant positive impact on exercise performance,[63,64] particularly for untrained subjects.[65] Of particular relevance in the present discussion is the positive impact of verbal encouragement on MVCs of the elbow flexors.[64] It is also important that the subjects are provided with some objective feedback relating to their performance. This typically takes the form of visual feedback provided by computer monitor.

2.7 The Timing of Superimposed Stimulation

When isometric MVCs are performed, steps should be taken to maximise the chance that superimposed stimuli are delivered to the muscle during maximal exertion. It is typically possible to trigger the stimulator automatically soon after voluntary force reaches a peak value, although with this approach it is necessary to delay the stimulus by approximately 300–400ms because without such a delay subjects typically perceive that they have not exerted maximal effort at the time of stimulation.[15] To further reduce the risk of stimulating the muscle during submaximal exertion, a ‘comparator’ can be employed to ensure that the stimulator is only triggered once forces exceed a certain percentage (e.g. 95%) of the subject’s previously recorded MVC. Thus when the subject fails to exceed this torque, no stimulus is applied and the contraction can be repeated.

3. Applications of Twitch Interpolation

3.1 Voluntary Activation During Brief Maximal Contractions

3.1.1 Maximal Isometric Contractions

Sensitive twitch interpolation reveals that healthy individuals are capable of activating the biceps brachii, brachialis and adductor pollicis muscles to within 5% of each muscle’s maximum capacity during maximal voluntary isometric contractions (MVICs).[14-16,19,20,22,51,66,67] Some studies suggest that almost all healthy individuals can fully activate these muscles, although only in 20–50% of maximal efforts.[15,16,20,25] In accordance with earlier observations,[1] more recent work suggests that the tibialis anterior is typically driven to 99% or more of its maximum capacity during MVICs.[25,48] For this muscle, however, full occlusion of superimposed twitches provides convincing evidence of full activation only when efforts are made to avoid stimulating the antagonistic peroneal muscles.[25] Incomplete activation of the ankle plantarflexors is commonly observed and voluntary activation levels of 90–99% have typically been reported.[31,35,68] In comparison with other muscles, relatively low levels of quadriceps femoris activation (85–95%) have frequently been observed.[21,23,40,41,69-75]

Studies in which individuals have performed MVICs of two or more muscles confirm that the plantarflexors of the ankle are less readily activated than the dorsiflexors[1] and that the quadriceps femoris muscles are less completely activated than

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the elbow flexors, ankle dorsiflexors and plantarflexors.[18] The biceps brachii and brachioradialis muscles are also more fully activated than the brachioradialis muscle during maximal isometric contractions of the elbow flexors.[16]

3.1.2 Maximal Dynamic Contractions

When stimulation is applied during an isometric contraction, the amplitude of the evoked response is typically determined by subtracting the instantaneous force immediately prior to stimulation from the peak force detected during the superimposed response. To accommodate for the changes in voluntary force that occur during dynamic contractions, the force trace prior to stimulation is extrapolated to provide an estimate of what the voluntary force would have been at the time when evoked force reaches its peak.[17,76,77] This extrapolation method has been shown to have a negligible impact on estimates of voluntary activation during isometric contractions.[15]

During elbow flexion, stimulus-evoked increments in force were shown to be extremely small or non-existent and the median level of biceps brachii activation (99.4%) did not differ significantly from that observed during isometric contractions.[77] In contrast, significant deficits in quadriceps femoris activation have been reported during both concentric and eccentric isokinetic actions.[17,76] Furthermore, significant differences in quadriceps femoris activation have been found between dynamic and isometric efforts.[17,76] For example, Babault and colleagues reported voluntary activation levels of $95.2 \pm 1.2\%$ for isometric contractions, $88.3 \pm 1.9\%$ for eccentric contractions at 20°/sec and $89.7 \pm 1.4\%$ for concentric contractions at the same angular velocity (means ± standard errors).[76] These studies suggest, for the quadriceps muscles at least, that the levels of activation reported during isometric actions are not necessarily indicative of those that might occur in dynamic contractions. The possibility should also be considered that the maximal levels of muscle activation in relatively complex multi-joint movements may differ significantly from those observed during the single-joint movements that have been employed for research purposes.

3.2 Voluntary Activation During Fatiguing Contractions

Twitch interpolation, typically involving two or more high-frequency stimuli, is also commonly employed to determine the extent of voluntary activation during fatigue.[3,19,22,34,35,56] Despite early reports to the contrary,[3] more recent studies suggest that the capacity to activate skeletal muscles declines (central fatigue occurs) during exhausting exercise.[19,22,34,35,56] For example, McKenzie and colleagues[22] reported a progressive decline in voluntary elbow flexor activation from 98.4% to 86.8% during a series of 10-second isometric MVCs with a 50% duty cycle. Similarly, voluntary activation of the isometric triceps surae has been reported to decline from 96% to 70% during a series of 100 brief (1–3 seconds) MVCs.[34] Interestingly, transcranial stimulation of the motor cortex has revealed that processes ‘upstream’ of the motor cortex contribute to the progressive reduction in voluntary drive that occurs during fatigue.[19] Further discussion of this topic is beyond the scope of this review and a more detailed account of the nervous system’s role in fatigue can be found elsewhere.[24]

3.3 The Influence of Resistance Training

It has been proposed that maximal voluntary activation increases as a consequence of resistance training. Observations of increases in the surface electromyogram,[78-83] increased motor unit firing rates,[84,85] cross education[81,86-90] and enhanced reflex potentiation[91-93] are consistent with the possibility but none provide conclusive evidence.

Most twitch interpolation studies employing healthy adult subjects suggest that voluntary activation does not increase after resistance training,[7,8,66,71,94-97] although there are exceptions.[31,68,98] Three factors should be borne in mind when interpreting the available evidence. First, in a number of the earlier studies, voluntary activation of the elbow flexors[7,94] and quadriceps femoris muscles[8,95,96] appeared to be complete prior to training although subsequent experiments employing more sensitive techniques have shown that the same muscles are typically not fully activated.[15,16,18,21,66,73] Secondly, when activation deficits have been observed, dynamic resistance training was employed

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whilst the tests of voluntary activation were isometric.[71,97] In these cases, the lack of improvement may be indicative of the highly specific nature of the adaptation[10,99-103] and the known limitations of isometric tests.[104] Thirdly, even with the application of highly sensitive twitch interpolation, some of the tested muscles exhibited only small deficits in voluntary activation and therefore little scope for improvement.[31,66]

In one of very few studies that has employed high resolution measurements of superimposed twitches and identical (isometric) modes of training and testing, voluntary activation of the biceps brachii and brachialis muscles was almost complete (~96%) before training and did not change after 8 weeks.[66] However, it should be acknowledged that the brachioradialis exhibits a significantly greater scope for improved activation than the biceps brachii and brachialis muscles.[16] Therefore, the possibility that brachioradialis activation may improve as a consequence of elbow flexor training should be considered. A study that employed both dynamic and isometric training reported a small (2%) but statistically significant increase in the CAR of the quadriceps in both young and older men after 6 weeks.[98] However, given that only a single stimulus was applied during MVCs, the use of the CAR was inappropriate as larger superimposed force increments and lower CAR values would have been expected if multiple stimuli had been employed.[55,58] Thus, voluntary activation was probably over-estimated and the extent of its improvement under-estimated. The study was also weakened by the absence of a non-training control group.[98] Plantarflexor activation, as determined by the linear equation, has been reported to increase 4% in the trained limb and 3% in the untrained limb after 6 weeks of dynamic unilateral resistance training.[68] Another study of the plantarflexors provided similar results when voluntary activation was quantified with the linear equation; however, the authors also quantified voluntary activation by extrapolating the curvilinear relationship between evoked and voluntary force and the trend towards increasing activation was not statistically significant when expressed in this way.[31] This study further highlights the possible discrepancies between the two methods of quantifying voluntary activation. Unfortunately, the amplitude of superimposed twitches were not reported in this study,[31] but when calculated using the reported mean unpotentiated control twitches and levels of voluntary activation, the mean of the superimposed twitches appears to have been approximately halved after training. The enhanced occlusion of the superimposed twitch suggests that the muscles were more fully activated after training than before.

3.4 The Influence of Disuse, Joint Injury and Degeneration

Twitch interpolation is a valuable tool for assessing the reduction in voluntary activation that may occur as a consequence of traumatic joint injury,[39,72,105-107] arthritis[9,108,109] and muscle pain.[9,40,41] For example, patients with isolated rupture of the anterior cruciate ligament have been reported to exhibit relatively mild reductions in voluntary quadriceps activation (75–84% in patients compared with 90–91% in control individuals),[106,107,110] whilst those with more extensive joint damage exhibit much greater deficits (e.g. mean activation levels of 55%).[39] The technique has also revealed that quadriceps femoris activation is significantly reduced in both the injured and uninjured limbs after anterior cruciate ligament rupture.[106,107,110]

Twitch interpolation is also well suited to the evaluation of rehabilitation programmes,[39] surgical interventions[110,111] and bed-rest.[38] In relation to the last issue, a recent study demonstrated that 20 days of bed-rest resulted in a 6% reduction (86.0 ± 5.3% to 80.2 ± 1.9%) in the extent to which the knee extensors could be activated during MVCs.[38] Furthermore, daily isometric resistance training was shown to completely prevent such a decline in another group of bed-rested individuals.[38]

3.5 The Influence of Pharmaceutical Agents on Voluntary Activation

Twitch interpolation has recently been employed to determine whether drug-induced changes in muscular performance are mediated by muscular or neural mechanisms. Kalmar and Cafarelli[73] showed that caffeine ingestion resulted in a mean improvement in knee extensor strength of approximately 5%

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and that this was accompanied by a mean increase of 3.5% in voluntary activation. Thus, caffeine appears to exert its influence on strength largely via its effects on the central nervous system. Gill and colleagues[112] employed a similar approach to study the effects of pseudoephedrine. Despite an 8.6% improvement in isometric knee extensor torque produced by the drug, no significant change (+1.6%) in quadriceps femoris activation was observed.[112] The results suggest that pseudoephedrine might exert its effects primarily on the quadriceps femoris muscles and not the neural drive delivered to them.

4. Conclusions

Sensitive twitch interpolation is capable of detecting small deficits in voluntary activation during isometric and dynamic contractions. While the technique enjoys widespread use, two distinct methods of quantifying voluntary activation are apparent in the current literature. The negative linear relationship originally reported between evoked twitch amplitude and voluntary force implies that voluntary activation can be determined by scaling a single interpolated twitch to a control twitch evoked in relaxed muscle. The evoked-voluntary force relationship has also been reported to be non-linear and some have argued that the single interpolated twitch ratio is therefore an invalid measure of activation and that extrapolating the relationship to a predicted true maximum force is a more appropriate alternative. However, the relationship between evoked and voluntary force may become curved for a number of reasons, some of which are more challenging to the validity of the extrapolation technique. Furthermore, careful attention to experimental technique produces a more linear relationship and minimises the errors that may be created when using a single interpolated twitch ratio. Careful consideration must also be given to selecting the site and intensity of stimulation, the number of interpolated stimuli and the resolution of force measurements. We argue that when such care is taken, the method of scaling the interpolated response to the control response provides a more valid measure of voluntary activation than that allowed by the prediction of true maximum force via non-linear extrapolation of the evoked-voluntary force relationship. Also, when sensitive methods of twitch interpolation are employed it is unnecessary and potentially problematic to use prolonged trains of stimulation and to quantify voluntary activation via the CAR.

Recently, twitch interpolation has revealed that small deficits are common during MVCs and that the maximum obtainable levels of voluntary activation vary somewhat between muscles. The technique has also allowed researchers to examine the extent to which muscular and neural adaptations influence performance after resistance training, joint damage, bed-rest and drug use.

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