Neural adaptations to strength training: Moving beyond transcranial magnetic stimulation and reflex studies

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Abstract
It has long been believed that training for increased strength not only affects muscle tissue, but also results in adaptive changes in the central nervous system. However, only in the last 10 years has the use of methods to study the neurophysiological details of putative neural adaptations to training become widespread. There are now many published reports that have used single motor unit recordings, electrical stimulation of peripheral nerves, and non-invasive stimulation of the human brain [i.e. transcranial magnetic stimulation (TMS)] to study neural responses to strength training. In this review, we aim to summarize what has been learned from single motor unit, reflex and TMS studies, and identify the most promising avenues to advance our conceptual understanding with these methods. We also consider the few strength training studies that have employed alternative neurophysiological techniques such as functional magnetic resonance imaging and electroencephalography. The nature of the information that these techniques can provide, as well as their major technical and conceptual pitfalls, are briefly described. The overall conclusion of the review is that the current evidence regarding neural adaptations to strength training is inconsistent and incomplete. In order to move forward in our understanding, it will be necessary to design studies that are based on a rigorous consideration of the limitations of the available techniques, and that are specifically targeted to address important conceptual questions.

Keywords H-reflex, muscle strength, single motor unit, transcranial magnetic stimulation, V-wave.
Neural adaptations to strength training • T J Carroll et al.

Acta Physiol 2011

The purpose of this review is to critically evaluate evidence about the neural responses to strength training obtained from single motor unit, reflex, and TMS studies. The physiological and technical principles that underlie these techniques, and their limitations and complications, are emphasized in order to make the point that care is required when interpreting data from these electrophysiological methods in humans. We also consider the potential of some alternative applications of these techniques to provide new information regarding the neural adaptations to strength training. Subsequently, methods to assess nervous system functions that have only very recently been applied to strength training will be considered. These include techniques for studying brain function through functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). The overall goals are to summarize the current evidence regarding neural adaptations to strength training, and to identify the most promising avenues to address the key conceptual questions that remain.

Single motor unit studies

Since its introduction in the late 1920s (Adrian & Bronk 1929), intramuscular recording of single motor unit activity has provided valuable insight into the neural control of movement in humans. The key advantage of recording single motor unit activity is that the discharge properties of the motoneuron, whose cell body originates in the spinal cord, can be obtained from the discharge of the single motor unit. This is achieved because every action potential generated in the motoneuron will result in an action potential in all muscle fibres innervated by the parent motoneuron, because of the high safety factor for action potential transmission at the neuromuscular junction (Bigland-Ritchie et al. 1979). Accordingly, single motor unit recording is one of only a few neurophysiological techniques that can provide unambiguous information about the behaviour of motoneurons during voluntary contractions in humans.

Technical considerations

The conventional approach to record single motor unit activity is to insert an electrode into the muscle of interest to record the extracellular action potentials from a group of muscle fibres associated with one motor unit. An intramuscular electrode commonly consists of a set of flexible fine wires or a needle. A fine wire electrode is usually custom made and can consist of several (2–4) insulated wires that are inserted into the muscle with a hypodermic needle (Milner-Brown et al. 1973). With this technique the needle is withdrawn leaving the fine wires within the muscle, with the cut ends of the wires representing the exposed recording surface. More recently, concentric needle electrodes have been used to record single motor unit activity, which usually consist of a stiff needle (~250 μm in diameter) that remains within the muscle during the voluntary contraction (Stalberg et al. 1996). One advantage of this technique is that the needle can be advanced (as opposed to only withdrawn) to optimize the motor unit recording, or manipulated to record from other locations within the muscle, which can allow recordings at high forces under some circumstances. The obvious drawback is that the needle can generate some discomfort within the muscle during a voluntary contraction, and it is not suitable for recording action potentials when there is a change in muscle length. Furthermore, recordings at high forces with this technique are often limited by the inability to identify the recruitment threshold or to obtain a sufficient number of action potentials for each motor unit, because the location of the electrode is often manipulated throughout the contraction. Nonetheless, it seems that measuring motor unit activity with a concentric needle electrode has become more commonplace over recent years, with a growing number of studies utilizing this technique during isometric contractions.

In addition to intramuscular electrodes, motor unit potentials can be recorded with subcutaneous electrodes or with surface electrode arrays. Subcutaneous electrodes comprise a branched bipolar configuration that is positioned under the skin but over the muscle (Gydikov et al. 1986, Enoka et al. 1988). Although more technically difficult to fabricate and use compared with conventional fine-wire electrodes, these electrodes are capable of providing selective recordings of single motor unit potentials up to maximal contractions (Oya et al. 2009), and provide the necessary stability to isolate and identify the same motor unit during different fatiguing tasks (Miller et al. 1996, Mottram et al. 2005). Electrode arrays consist of a grid of electrodes placed on the skin above the muscle, and were originally used to provide a non-invasive assessment of the conduction velocity of motor unit potentials along the muscle fibres (Schneider et al. 1989, see Merletti et al. 2003 for review). However, the development of more advanced processing methods has expanded the utility of this technique through decomposition of the surface electromyogram (EMG) to identify the discharge times of individual motor units (De Luca et al. 2006, see Merletti et al. 2008 for review), which can be accurate up to maximal contractions (Nawab et al. 2010). While these techniques are limited to superficial motor units (Farina et al. 2010), they offer a promising alternative to more invasive
procedures where interpretations are constrained because of a low motor unit yield.

Despite the emergence of some new hardware and software, longitudinal strength training studies pose an additional challenge for reliable assessment of motor unit activity in humans. The main problem is that it is not yet possible to identify the same motor unit before and after the training program, in order to clearly demonstrate an effect of the intervention. Longitudinal tracking of the same motor unit is possible under some circumstances (Doherty & Brown 1994), but the usefulness of the technique is likely to be limited to patient populations with substantial motoneuron loss (Gooch & Harati 1997), and does not provide information on motor unit discharge behaviour during voluntary contractions. Therefore, with current motor unit recording techniques, studies that involve strength training require a large sample of motor units in each subject, with a sufficient number of subjects, to adequately characterize the change with training. Because of these technical constraints, coupled with the time consuming nature of the experiments, there are only a few studies that have adequately addressed the effect of strength training on motor unit activity in humans.

**Single motor unit activity**

One possible neural mechanism to increase muscle strength with training is an increase in motor unit discharge rate during maximal contractions. Because these measures are technically challenging, only a limited number of studies have examined maximal motor unit discharge rates after a strength training intervention. Specific details of these studies are provided in Table 1. Using both isometric and dynamic training protocols that produced significant increases in strength, these studies have demonstrated an increase in maximal motor unit discharge rates in upper and lower limb muscles after training, although this is not always a consistent finding (e.g. Pucci et al. 2006). The greatest changes in maximal discharge rates with training (up to 49% increase) have been observed in older adults (Kamen & Knight 2004). This may be because maximal discharge rates are lower in the untrained state (Kamen et al. 1995), reflecting a greater potential for change in the elderly. However, there is a poor association between increases in muscle strength and maximal motor unit discharge rates after training ($r^2 = 0.15$ for studies in Table 1), presumably because it is only possible to sample from a small proportion of the active motor units, and several muscles are likely to contribute to the mechanical action at the relevant joint. Nonetheless, these findings suggest that other factors must also be contributing to the early gains in strength with training.

Experimental evidence suggests that more subtle changes in single motor unit activity, such as an increased incidence of brief interspike intervals (known as double discharges or doublets), may have the potential to influence the neural control of force with strength training. When present at the beginning of a voluntary contraction, double discharges have been shown to substantially increase low-frequency (unfused) motor unit force (Macefield et al. 1996), which may be important in the maintenance of force during a submaximal fatiguing contraction (see Garland & Griffin 1999). After rapid force development training of the ankle dorsiflexors, Van Cutsem et al. (1998) has shown that an increase in the rate of force development (RFD) was associated with an increased incidence of double discharges from 5% before training to 33% after training. This finding suggests that it may be an appropriate neural strategy to utilize when performing rapid muscle contractions. However, other evidence suggests that the implementation of double discharges may not be a strategy used to improve the functional outcome, but represent a byproduct of a change in the intrinsic properties of the motoneurons. For example, the incidence of double discharges is not associated with the speed of the voluntary contraction (Bawa & Calancie 1983, Christie & Kamen 2010), is reduced in older adults (Klass et al. 2008, Christie & Kamen 2010), and is greater in patients with neuromuscular disorders (see Thomas et al. 2002). The lack of any consistent finding on the functional significance of double discharges may be caused by sampling from only a small number of motor units in each contraction, and may depend on the muscle investigated, the contraction intensity, or the type of motor unit (low vs. high threshold) examined (see Garland & Griffin 1999, Christie & Kamen 2006).

Along with the gain in maximal strength, several lines of evidence suggest that training alters the activity of single motor units and improves performance of submaximal tasks. In particular, after several weeks of strength training, the variability of motor unit output (referred to as steadiness) is reduced during isometric (Keen et al. 1994) and slow lengthening contractions (Laidlaw et al. 1999). Although multiple factors are likely to be responsible (Taylor et al. 2003), one candidate mechanism for improved steady motor performance after training is a reduction in the variability of motor unit discharge rate (Moritz et al. 2005, Tracy et al. 2005). This hypothesis was examined following a training intervention (Kornatz et al. 2005) that involved 2 weeks of practicing a steadiness task with a light load (10% of maximum) followed by 4 weeks of strength training with a heavy load (70% of
<table>
<thead>
<tr>
<th>Study</th>
<th>Muscle</th>
<th>Subject details</th>
<th>Recording technique</th>
<th>Training duration</th>
<th>Training frequency</th>
<th>Training intensity</th>
<th>Strength gain</th>
<th>Discharge rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christie &amp; Kamen (2010)</td>
<td>Tibialis anterior</td>
<td>30 young 30 old (15 controls/group)</td>
<td>4-wire needle (quadrifilar)</td>
<td>2 weeks</td>
<td>3× week⁻¹</td>
<td>3 sets of 10 isometric MVCs</td>
<td>↑17% young</td>
<td>↑7% young</td>
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<td>↑20% old</td>
<td>↑24% old</td>
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<tr>
<td>Kamen &amp; Knight (2004)</td>
<td>Vastus lateralis</td>
<td>8 young 7 old</td>
<td>4-wire needle (quadrifilar)</td>
<td>6 weeks</td>
<td>3× week⁻¹</td>
<td>3 sets of 10 dynamic contractions (85% 1RM)</td>
<td>↑29% young</td>
<td>↑15% young</td>
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<td>↑36% old</td>
<td>↑49% old</td>
</tr>
<tr>
<td>Patten et al. (2001)</td>
<td>Abductor digiti minimi</td>
<td>6 young 6 old</td>
<td>4-wire needle (quadrifilar)</td>
<td>6 weeks</td>
<td>5× week⁻¹</td>
<td>2 sets of 10 isometric MVCs</td>
<td>↑25% young</td>
<td>↑11% young</td>
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<td>↑33% old</td>
<td>↑23% old</td>
</tr>
<tr>
<td>Pucci et al. (2006)</td>
<td>Vastus lateralis</td>
<td>10 training 10 controls (All young males)</td>
<td>Tungsten microelectrode</td>
<td>3 weeks</td>
<td>3× week⁻¹</td>
<td>3 sets of 10 isometric MVCs</td>
<td>↑35% training</td>
<td>↑3% training group (n.s.)</td>
</tr>
<tr>
<td>Van Cutsem et al. (1998)</td>
<td>Tibialis anterior</td>
<td>5 training 5 controls (all young subjects)</td>
<td>Fine-wire needle electrode</td>
<td>12 weeks</td>
<td>5× week⁻¹</td>
<td>10 sets of 10 rapid shortening contractions (30–40% 1RM)</td>
<td>↑30% training</td>
<td>↑29% training*</td>
</tr>
</tbody>
</table>

MVC, maximal voluntary contraction; 1RM, one-repetition maximum; n.s., non-significant difference after training.

*This value was calculated without the presence of double discharges (<5 ms).
maximum). After the first 2 weeks of practice, there were parallel declines in motor unit discharge rate variability in the first dorsal interosseous muscle and the steadiness of slow shortening and lengthening contractions performed by the index finger. No further changes in motor unit discharge rate variability or steadiness were evident after 4 weeks of strength training, suggesting that practice of the task was largely responsible for the changes in motor unit discharge rate variability and improvements in motor performance. Similarly, 6-weeks of strength training the knee extensor muscles resulted in an increase in mean motor unit discharge rates and a decrease in motor unit discharge rate variability during submaximal contractions (Vila-Cha et al. 2010). Furthermore, Knight & Kamen (2004) examined the modulation of motor unit discharge rate during isometric force tracking tasks requiring skill acquisition. The target force comprised an average of 20% maximal voluntary contraction (MVC) that was modulated by 2% MVC with sine waves of 0.15 and 0.5 Hz. Throughout the performance of 15 trials, they found that an improved precision of force matching was accompanied by decreased motor unit discharge rate modulation at the higher of the two modulating frequencies. Taken together, these studies suggest that training to increase maximal strength may have implications for motor unit activity during submaximal tasks that may improve skilled motor performance.

**Correlated motor unit activity**

The correlated activity of motor units is now regarded as an important physiological principle for the neural control of movement. Computer simulation studies have shown that correlated motor unit activity can have a substantial influence on EMG and force fluctuations (Yao et al. 2000, Zhou & Rymer 2004), and experimental studies suggest that it can vary depending on the details of the task that is performed (see Semmler et al. 2002). The correlated discharge of action potentials by motoneurons is caused by common branched pre-synaptic inputs or independent inputs that are themselves synchronized. The effect on motor unit activity can be quantified in the time domain as motor unit synchronization or in the frequency domain as motor unit coherence (Farmer et al. 1997). There is a strong association between motor unit synchronization and high-frequency coherence (~10–30 Hz), indicating that similar mechanisms contribute to these two features of correlated motor unit activity (Farmer et al. 1993, Semmler et al. 2004). Furthermore, low-frequency (~1–2 Hz) motor unit coherence is equivalent to the common fluctuations in mean motor unit discharge rates, which is referred to as common drive (De Luca et al. 1982). As a coherence analysis is able to detect these multiple features of correlated motor unit activity over a range of frequencies, it is now considered the most sensitive approach when examining the discharge patterns from a population of active motor units.

One of the most appealing mechanisms for an increase in strength with training is an increase in correlated motor unit activity. This has largely been driven by an original investigation from Milner-Brown et al. (1975), which found a 128% increase in motor unit synchronization after 6 weeks of isometric strength training that involved the index finger. However, this study used a surface EMG based population index of motor unit synchronization, which has been shown to be an unreliable estimate of correlated motor unit activity (Yue et al. 1995). Nonetheless, this seminal study by Milner-Brown et al. (1975) has been widely cited as one of only a few examples of a chronic neural adaptation induced by strength training. Using the more robust cross-correlation procedure between pairs of concurrently active motor units (see Farmer et al. 1997), several studies have shown that habitual physical activity patterns may influence motor unit synchronization. For example, motor unit synchronization is greatest in strength-trained subjects (weightlifters), intermediate in untrained control subjects, and least in skill-trained musicians (Semmler & Nordstrom 1998).

More recently, motor unit synchronization has been shown to be greater in strength-trained males, but only for the biceps brachii muscle at high forces (80% MVC) and not for the first dorsal interosseous muscle at low (30% MVC) or high (80% MVC) force levels (Fling et al. 2009). However, these cross-sectional studies are difficult to interpret because no training intervention was performed, and therefore they do not account for other genetic or lifestyle factors that may contribute to alterations in motor unit synchronization. In contrast, a 4-week training intervention that resulted in a 54% increase in index finger strength showed no change in motor unit synchronization in the first dorsal interosseous muscle (Kidgell et al. 2006). This definitive interventional study using cross-correlation from pairs of concurrently active motor units indicates that correlated motor unit activity is unlikely to be important for the expression of muscle strength with training.

An alternative explanation for differences in the strength of correlated motor unit activity in skill and strength-trained individuals (Semmler & Nordstrom 1998, Semmler et al. 2004) might be that practice of a task results in reduced motor unit synchronization, which may be beneficial in performing fine motor tasks at low force levels. This hypothesis was addressed in a recent study which examined motor unit synchronization in hand muscles during a pinching task following...
Neural adaptations to strength training • T J Carroll et al.

Acta Physiol 2011

training with light loads to improve force steadiness in older adults (Griffin et al. 2009). After 4 weeks of light-load isometric training (2 and 4% MVC), they found no change in motor unit synchronization both within and between hand muscles despite significant improvements in isometric steadiness at these low force levels. In contrast, there were significant declines in motor unit discharge rate variability in the first dorsal interosseous muscle with training. Thus, it appears that improvements in motor performance with skill training or practice may occur through altered motor unit discharge rate variability, rather than a change in correlated motor unit activity.

Finally, evidence from lengthening (eccentric) muscle contractions has provided new insight into the task-related adjustments of correlated motor unit activity. Lengthening contractions are performed regularly in everyday lives, and are important considerations for training because of their potential to produce large forces with low metabolic cost. Several studies have shown altered motor unit behaviour during lengthening contractions (Del Valle & Thomas 2005, Pasquet et al. 2006), supporting the proposal that lengthening contractions require unique neural activation strategies (Enoka 1996). Interestingly, the modulation of correlated motor unit activity also appears to be an important feature of lengthening contractions. For example, cross-correlation analysis from the same pairs of concurrently active motor units in the first dorsal interosseous muscle has shown an increase in motor unit synchronization during lengthening, compared with postural or shortening muscle contractions (Semmler et al. 2002). This increased motor unit synchronization during lengthening contractions may act as a protective mechanism by distributing the load over a greater number of motor units to reduce the extent of muscle damage that can occur after these types of contractions (see McHugh 2003 for review). This suggestion is supported by recent work showing that motor unit synchronization is increased in biceps brachii motor units for at least 24 h after the muscle has been damaged with repetitive lengthening contractions (Dartnall et al. 2008). These data suggest that lengthening muscle contractions, including the involvement of naturally occurring movements such as the stretch-shortening cycle (see Nicol et al. 2006), may be important in the neural adaptation and the modulation of correlated motor unit activity with training.

Moving forward with human motor units

Over the last 3 decades, evidence has accumulated to suggest that certain types of strength or resistance training can alter the discharge properties of human motor units. However, the progress in this field at the single motor unit level has not accelerated markedly over the last 10 years. This can largely be attributed to technical difficulties associated with recording single motor units, particularly at high forces. This limitation has been detrimental to studies specifically designed to increase strength, as it is the behaviour of high threshold motor units that are most likely to contribute to the strength gains, but are least amenable to study with invasive motor unit recording techniques. The continued development of hardware and software for use with surface electrode arrays offers many promising avenues for advancing knowledge in this field, as they provide a means of obtaining a high motor unit yield, even during strong contractions (Farina et al. 2010, Nawab et al. 2010). Furthermore, these techniques may also shed new light on the coordination of multiple muscle synergists and antagonists, by facilitating comparisons of common drive between muscles and how this may contribute to changes in muscle strength with training. Finally, for practical reasons, many training studies have been restricted to isometric strength with training. Furthermore, these techniques may also shed new light on the coordination of multiple muscle synergists and antagonists, by facilitating comparisons of common drive between muscles and how this may contribute to changes in muscle strength with training. Finally, for practical reasons, many training studies have been restricted to isometric strength with training. Finally, for practical reasons, many training studies have been restricted to isometric strength with training.

Spinal reflex studies

Technical considerations

Reflex responses produced by electrical stimulation of peripheral nerves have the potential to contribute information regarding the sites and mechanisms of neural adaptation to strength training. The two reflexes that have been applied most commonly in strength training studies are the H-reflex (Magladery & McDo-ugal 1950) and the V-wave (Upton et al. 1971), both of which rely to a large extent on the monosynaptic circuit from Ia afferent fibres to motoneurons. Both reflexes are produced by electrical stimulation of a mixed nerve (i.e. containing axons of motoneurons and afferents of various origin). The afferent volley generated ultimately causes a relatively synchronous discharge of motoneurons, and the earliest part of the response is probably due purely to the monosynaptic connection between Ia afferents and motoneurons (Magladery et al. 1951). With H-reflexes, the response initially grows with stimulation intensity as the afferent volley increases in size, but then progressively falls to zero as the intensity approaches levels supramaximal for activating motor axons (i.e. to produce a maximal M-wave). It is generally accepted that this is because of collision between orthodromic action potentials produced by the reflex with antidromic action potentials generated directly in the motor axons by the electrical stimulus. In contrast, the V-wave is produced by supramaximal
stimulation during voluntary contraction (typically MVC). The cancellation of action potentials that abolishes the H-reflex at high stimulus intensities is prevented in some motoneurons by action potentials produced via volition. That is, in some motoneurons, a voluntary action potential will collide with the antidromic action potential produced by the stimulus, and ‘clear’ the pathway for subsequent reflex activation. The number of motoneurons that are free to respond to the afferent volley will depend on the number and firing rate of the motoneurons involved in the voluntary contraction, and the conduction time from the stimulation site to the spinal cord. The ultimate size of the reflex will also depend on motoneuron responsiveness and the efficacy of synaptic transmission between afferents and motoneurons. Although these two reflexes can provide information regarding the efficacy of the Ia afferent reflex pathway and the output from the motoneuron pool during voluntary contraction, there are a number of technical issues that complicate their interpretation. Because many of the complications with H-reflex interpretation are often neglected, some of the key points will be summarized in the following sections. The reader is referred to Burke & Gandevia (1999) for detailed coverage.

The first complication in interpreting changes in H-reflex amplitude because of an intervention such as strength training is the difficulty in ensuring an identical size of the afferent volley elicited by the stimulation pulse. One way of attempting to control this is by matching the amplitude of a small M-wave between stimulation conditions, and thereby ensuring a similar number of motoneurons are excited by the stimulus (e.g. Zehr 2002, Misiaszek 2003). However, this procedure does not account for potential changes in axonal excitability (e.g. Bostock & Grafe 1985). This is a critical consideration because axonal excitability is susceptible to change in ways that differ for large diameter afferents versus motoneurons (e.g. Mogyoros et al. 1996, Vagg et al. 1998). If strength training were to alter axonal excitability of afferents or motoneurons, this could produce a change in H-reflex amplitude in the absence of central effects (i.e. effects within the central nervous system (CNS)). However, measures of H-reflex responses provided by H-reflex recruitment curves (i.e. recording the reflex size at a range of stimulus strengths from below threshold to supramaximal levels) should be less susceptible to this potential confound. The issue is also less likely to be of concern for V-waves provided that the stimulus intensity was sufficiently supramaximal to account for activity dependent reductions in axonal excitability (see Burke & Gandevia 1999 for details).

The second complication for interpreting the size of H-reflexes is that there are almost certainly considerable non-mono-synaptic contributions to the reflex (e.g. Burke et al. 1984, Marchand-Pauvert et al. 2002, see Burke & Gandevia 1999 for review). While the earliest part of the response is via monosynaptic Ia inputs, this initial excitation is curtailed by disynaptic inhibition (i.e. produced via Ia or Ib afferent activation of an inhibitory interneuron; Marchand-Pauvert et al. 2002). Thus, as pointed out by Burke & Gandevia (1999), the size of the H-reflex is determined by the balance between monosynaptic Ia excitation and disynaptic inhibition. A change in H-reflex or V-wave size could be brought about by an alteration in transmission efficacy in either of these circuits. Clearly, as pointed out previously by many authors (e.g. Burke & Gandevia 1999, Zehr 2002, Misiaszek 2003), the H-reflex does not provide a measure of ‘motoneuron excitability’.

Finally, if one considers only monosynaptic Ia contributions, changes in the size of the H-reflex could be because of changes in the responsiveness of the motoneurons or alterations in the synaptic transmission efficacy at the Ia afferent terminals (see Zehr 2002, Misiaszek 2003 for reviews). With respect to motoneuron responsiveness, intrinsic membrane properties, firing rate and the effects of neuromodulators such as serotonin could contribute (Capaday 1997, Matthews 1999). Alterations to the synaptic transmission efficacy can occur because of pre-synaptic inhibition of Ia afferent terminals and homosynaptic post-activation depression (see Hultborn & Nielsen 1998, Pierronet-Deseilligny & Burke 2005 for extensive review).

**H-reflex and V-wave studies**

Since the earliest cross-sectional (Milner-Brown et al. 1975), and longitudinal studies (Sale et al. 1982, 1983), there have been many reports of H-reflex and V-wave responses to strength training (summarized in Table 2). With the exception of the earliest studies (Sale et al. 1982, 1983), all of these investigations have involved muscles that act at the ankle joint. There have been no reports of an increase in H-reflex amplitude at rest as a consequence of strength training (Aagaard et al. 2002, Scaglioni et al. 2002, Del Balso & Cafarelli 2007, Holtermann et al. 2007, Duclay et al. 2008, Schubert et al. 2008, Finland et al. 2009a, Ekblom 2010) or tetanic electrical stimulation of muscles (Maffioletti et al. 2003, Gondin et al. 2006). In contrast, strength training was reported to increase the amplitude of V-waves in all studies involving plantar flexors (Sale et al. 1983, Aagaard et al. 2002, Gondin et al. 2006, Del Balso & Cafarelli 2007, Holtermann et al. 2007, Duclay et al. 2008, Finland et al. 2009a,b, Ekblom 2010) but not for the thumb abductors (Sale et al. 1982). Thus, for the Soleus muscle, there is clear evidence that resting H-reflexes are unaffected, and
<table>
<thead>
<tr>
<th>Study</th>
<th>Muscle group</th>
<th>Subject details</th>
<th>Methods</th>
<th>Training schedule</th>
<th>Training intensity</th>
<th>Strength gain</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sale et al. (1982)</td>
<td>Thumb abductors</td>
<td>11 trained</td>
<td>V-wave, MVC</td>
<td>18 weeks</td>
<td>Dynamic</td>
<td>† 41% MVC</td>
<td>↔ V-wave</td>
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<td></td>
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<td></td>
<td>74 sessions</td>
<td>5–6 sets up to 1RM Isometric 2 sets 10 MVC</td>
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<tr>
<td>Sale et al. (1983)</td>
<td>Plantar flexors, toe extensors, elbow flexors, finger flexors</td>
<td>14 trained</td>
<td>V-Wave, MVC F-wave</td>
<td>9–21 weeks</td>
<td>Dynamic</td>
<td>Not reported</td>
<td>† 50% V-wave. Pooled across muscles ↔ F-wave</td>
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<td>5–6 sets up to 1RM Isometric 2 sets 10 MVC</td>
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<td>Aagaard et al. (2002)</td>
<td>Plantar flexors</td>
<td>14 trained</td>
<td>H-reflex, rest and 90% MVC V-Wave, 90% MVC</td>
<td>14 weeks</td>
<td>Dynamic</td>
<td>† 20% MVC</td>
<td>↔ H-reflex at rest ↔ 55% V-wave, ↑ 19% H-reflex 90% MVC</td>
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<td></td>
<td>38 sessions</td>
<td>3–10RM multiple exercises 4–5 sets each</td>
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<td>Scaglioni et al. (2002)</td>
<td>Plantar flexors</td>
<td>14 trained</td>
<td>H-reflex, rest</td>
<td>16 weeks</td>
<td>Dynamic</td>
<td>† 18% MVC</td>
<td>↔ H-reflex</td>
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<td>(65–85 years)</td>
<td></td>
<td>48 sessions</td>
<td>50–80% 1RM 1 set of 10</td>
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<td>Maffuletti et al. (2003)</td>
<td>Plantar flexors</td>
<td>8 trained</td>
<td>H-reflex, rest</td>
<td>4 weeks</td>
<td>Dynamic</td>
<td>† 22% MVC</td>
<td>↔ H-reflex at rest ↔ 80% V-wave</td>
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<td>6 control</td>
<td></td>
<td>16 sessions</td>
<td>45 electrical stimulations (max tolerable) ~50–70% MVC</td>
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<tr>
<td>Lagerquist et al. (2006)</td>
<td>Plantar flexors</td>
<td>10 trained</td>
<td>H-reflex, 10% MVC</td>
<td>5 weeks</td>
<td>Isometric</td>
<td>† 15% MVC</td>
<td>↔ H-reflex during 10% MVC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 control</td>
<td></td>
<td>15 sessions</td>
<td>MVC 5 sets of 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gordin et al. (2006)</td>
<td>Plantar flexors</td>
<td>12 trained</td>
<td>H-reflex, rest and MVC V-Wave, MVC</td>
<td>5 weeks</td>
<td>Dynamic</td>
<td>† 22% MVC</td>
<td>↔ H-reflex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 Control</td>
<td></td>
<td>15 sessions</td>
<td>20 electrical stimulations (max. tolerable) ~60% MVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Del Balso &amp; Cafarelli (2007)</td>
<td>Plantar flexors</td>
<td>10 trained</td>
<td>H-reflex, rest, 10% MVC V-Wave, 50, 75, 100% MVC</td>
<td>4 weeks</td>
<td>Isometric</td>
<td>† 20% MVC</td>
<td>↔ H-reflex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 control</td>
<td></td>
<td>12 sessions</td>
<td>MVC 6 sets of 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beck et al. (2007)</td>
<td>Dorsiflexors, Plantar flexors</td>
<td>8 trained</td>
<td>H-reflex during fast contraction</td>
<td>4 weeks</td>
<td>Dynamic ballistic</td>
<td>Not reported</td>
<td>↔ H-reflex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 control</td>
<td></td>
<td>16 sessions</td>
<td>30–40% 1RM 4–6 sets of 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holtermann et al. (2007)</td>
<td>Plantar flexors</td>
<td>12 trained</td>
<td>H-reflex at rest and during 20 and 60% MVC</td>
<td>3 weeks</td>
<td>Isometric</td>
<td>† 18% MVC</td>
<td>↔ H-reflex at rest ↔ H-reflex, 20, 60% MVC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 control</td>
<td></td>
<td>9 sessions</td>
<td>MVC 5 sets of 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Muscle group</td>
<td>Subject details</td>
<td>Methods</td>
<td>Training schedule</td>
<td>Training intensity</td>
<td>Strength gain</td>
<td>Results</td>
</tr>
<tr>
<td>------------------</td>
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<td>-------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Duclay et al. (2008)</td>
<td>Plantar flexors</td>
<td>10 trained 8 control</td>
<td>H-reflex at rest &amp; during passive movement H-reflex and V-wave during max isometric, concentric and eccentric contractions</td>
<td>7 weeks 18 sessions</td>
<td>Dynamic eccentric, 120% 1RM 6 sets of 6</td>
<td>↑ 22% MVC</td>
<td>← H-reflex at rest ↑ V-wave in MVC and max eccentric ↑ H-reflex in MVC, max eccentric and concentric</td>
</tr>
<tr>
<td>Geertsen et al. (2008)</td>
<td>Dorsiflexors</td>
<td>12 trained 6 control</td>
<td>Disynaptic reciprocal inhibition of plantar flexors at onset ballistic dorsiflexion</td>
<td>4 weeks 12 sessions</td>
<td>Isometric MVC ballistic 3 sets of 16</td>
<td>↑ 20% MVC</td>
<td>↑ reciprocal inhibition</td>
</tr>
<tr>
<td>Finland et al. (2009a)</td>
<td>Plantar flexors</td>
<td>10 trained 9 control</td>
<td>H-reflex at rest H-reflex and V-wave during MVC</td>
<td>8 weeks 24 sessions</td>
<td>Dynamic ballistic multi-joint extension 85–90% 1RM 4 sets of 4</td>
<td>↑ 20% MVC</td>
<td>↑ 50% V-wave in MVC ← H-reflexes</td>
</tr>
<tr>
<td>Finland et al. (2009b)</td>
<td>Plantar flexors</td>
<td>15 trained 11 control</td>
<td>H-reflex and V-wave during MVC</td>
<td>4 weeks 16 sessions</td>
<td>Isometric MVC 6 sets of 6</td>
<td>↑ 44% MVC</td>
<td>↑ 72% V-wave in MVC ← H-reflexes</td>
</tr>
<tr>
<td>Ekhblom (2010)</td>
<td>Plantar flexors</td>
<td>9 trained 11 control</td>
<td>H-reflex and V-wave during max concentric and eccentric H-reflex at rest</td>
<td>5 weeks 15 sessions</td>
<td>Dynamic eccentric focused for PF 5–6 sets of 5RM</td>
<td>↑ 19% mean concentric/eccentric</td>
<td>↑ 77% V-wave during maximal eccentric and concentric actions</td>
</tr>
</tbody>
</table>

max, maximal; MVC, maximal voluntary contraction; RM, repetition maximum.
V-wave amplitudes are enhanced, by strength training. The results for H-reflexes elicited during voluntary contractions are less consistent. There have been reports both that strength training increases H-reflex size (Aagaard et al. 2002, Lagerquist et al. 2006, Holtermann et al. 2007, Duclay et al. 2008) and does not change H-reflex size (Gondin et al. 2006, Beck et al. 2007, Del Balso & Cafarelli 2007, Finland et al. 2009a,b, Ekblom 2010), when evoked during contractions ranging in strength from 10 to 100% of MVC. The discrepancies could be due partly to differences in the details of how the reflexes were elicited and measured. For example, some studies determined the maximal H-reflex amplitude, whereas others assessed H-reflex size at matched M-wave amplitudes, or calculated the slope of the stimulus intensity versus response curve. Each of these methods might be differentially affected by methodological factors that can influence H-reflex amplitude such as axonal excitability.

When a change in H-reflex was detected, the result was taken as evidence of neural adaptation to strength training mediated at a spinal level. Whether this is entirely accurate depends on one’s perspective on defining a ‘site’ of adaptation. While it is accepted that the H-reflex is subject to modulation within the spinal cord, it is quite possible that changes in supraspinal inputs to the spinal circuitry could increase H-reflex size (i.e. by modulating pre-synaptic inhibition or the responsiveness of inhibitory interneurons). Increases in V-wave amplitude have frequently been cited as evidence of increased motoneuron activation. There has also been a strong tendency to ascribe the putative increased motoneuron activation to adaptations at supraspinal levels, particularly when V-wave changes were observed in parallel with H-reflexes (e.g. Aagaard et al. 2002, Del Balso & Cafarelli 2007). While an increased supraspinal drive to motoneurons is certainly a plausible explanation for increased V-wave amplitudes, there are numerous alternative possibilities that cannot be discounted. More generally, the notion that comparisons between V-wave and H-reflex allow dissociation between spinal and supraspinal adaptations is ill-founded. For example, the different stimulus intensities associated with the two methods will activate of different populations of afferents and motoneurons (i.e. antidromically), which might also result in different oligosynaptic influences on the reflex amplitude (e.g. greater antidromic activation of motoneurons produced by supramaximal stimulation to generate the V-wave might activate more Renshaw cells), and the reflexes might be differentially influenced by activity dependent changes in axonal excitability. Furthermore, even if an increase in V-wave amplitude could be ascribed entirely to an increase in the number of voluntarily recruited motoneurons (i.e. if one could be sure of an identical reflex excitation of motoneurons), then there is no basis for determining the origin of the extra motoneuronal drive. For example, spinal reflex pathways are known to contribute considerably to the activation of motoneurons during voluntary contraction (e.g. Macefield et al. 1993).

**Conditioning-test reflex approaches**

Given the difficulty in identifying the specific spinal circuits responsible for any changes that might occur in H-reflex (or V-wave) size, it is worth considering the potential of related methods that might provide more specific information about the nature of neural adaptation to strength training. By careful application of conditioning stimulation to various homonymous and heteronymous muscle afferents or skin afferents, it is possible to draw inferences about the efficacy of specific spinal reflex pathways (see Pierrot-Deseilligny & Burke 2005 for extensive review). For example, Geertsen et al. (2008) used conditioning stimulation of the peroneal nerve to suppress the soleus H-reflex in order to study the effect of explosive strength training on disynaptic reciprocal inhibition (i.e. via IA inhibitory interneurons that reduce coactivation of antagonist muscles). They found that 4 weeks of ballistic strength training for the dorsiflexors increased disynaptic reciprocal inhibition from peroneal afferents to the antagonist soleus when assessed at the onset of ballistic dorsiflexion contraction, but not at rest. The lack of change in disynaptic reciprocal inhibition at rest implies that there was no change in the default properties of the pathway per se, and that the increased inhibition prior to ballistic contraction might reflect a training-induced descending modulation of spinal interneuronal responsiveness that is tailored to the functional requirements of the training task (i.e. to ensure that antagonist muscles do not contribute plantar flexion torque at the onset of intended dorsiflexion).

**Moving forward with reflex studies**

Despite the many complications with interpreting H-reflex and V-wave results, it appears that for the plantar flexors, resting H-reflexes are unaffected by strength training and V-waves during MVC are increased. The physiological implications of these results are not definitive, but it is likely that there is little ‘baseline’ alteration to the IA-afferent-motoneuronal circuit, and an increase in motoneuronal output during MVC. An understanding of spinal responses to strength training might be advanced by the application of conditioning-test approaches to study modulation in specific reflex circuits. While these
approaches are powerful in the sense that they have potential to provide specific information about particular afferent and interneuronal pathways, it is important to note that they provide only indirect evidence (i.e. inferences obtained require confirmation from more than one method) and can be technically challenging.

**TMS studies**

**Technical considerations**

Transcranial magnetic stimulation can painlessly activate neurons in the human cerebral cortex through the scalp (Barker et al. 1985), and has been used to study neural transmission from the motor cortex to the muscles in many behavioural contexts. An index of the responsiveness of the entire pathway from brain to muscle (often termed ‘corticospinal excitability’) can be obtained from the size of the compound muscle action potentials (CMAP) recorded at the muscle via electromyography. These responses are known as motor evoked potentials (MEPs). Given that MEPs are generated in response to stimulation of the brain, it can be tempting to interpret alterations in MEP size as being caused by a change in the properties of the motor cortex. This is not inappropriate, however, as the size of TMS responses is subject to potential modulation at each point in the pathway from brain to muscle. Thus, in order to properly interpret the effects of an intervention on MEP size, consideration of all of the biophysical and physiological factors that determine muscle responses to TMS is required. This is particularly important for longitudinal studies involving strength training where there might be substantial changes in spinal cord circuitry (see Spinal reflex studies above).

Transcranial magnetic stimulation can activate corticospinal cells (i.e. output cells from the motor cortex that project to the spinal cord) both directly and indirectly, depending on the magnitude and orientation of the induced electric field to the cortical network (i.e. which are influenced by coil size, shape and orientation, stimulus intensity, and the anatomy of the skull and cortex; e.g. Barker 1991, Ruohonen & Ilmoniemi 1999). Direct activation of corticospinal cells results in a descending corticospinal volley termed a ‘D-wave’, that can be recorded by electrodes implanted in the cervical epidural space (e.g. Di Lazzaro et al. 1998a), and inferred from peri-stimulus time histograms from single motor unit recordings (e.g. Day et al. 1989). Indirect activation of corticospinal cells results in one or more ‘I-waves’ (n.b. numbered in order of appearance latency), the earliest of which (i.e. the I1 wave) appears approximately 1.5–2 ms after the D-wave (Day et al. 1989, Di Lazzaro et al. 2004, Brocke et al. 2005). The size of D-waves produced some distance from the corticospinal cell soma is little influenced by the state of the cortical network (see Di Lazzaro et al. 2004 for review), but the size of I-waves is determined by the net result of multiple synaptic inputs to the corticospinal cells. These inputs could arise from both local cortical interneurons and projections from distant cortical and subcortical sites, are transmitted from the site of (TMS) activation to the corticospinal cells via mono- and oligosynaptic circuits, and contain both excitatory and inhibitory elements (see Reis et al. 2008 for recent review). Thus, the net descending volley produced in the corticospinal tract by a TMS pulse is potentially influenced by the intrinsic responsiveness of the corticospinal cells (i.e. which is influenced by firing rate and membrane properties), the synaptic efficacy of local and distant connections onto corticospinal cells and local interneurons, and the axonal excitability of the cells initially responsive to the TMS pulse. Given the complexity of the system between the sites of stimulation and measurement of the response, the conception that alterations in ‘cortical excitability’, as suggested by TMS studies, might provide a mechanism of strength gains produced by training represents a somewhat superficial consideration of the physiological changes that might be involved.

In addition to the anatomical organization and functional state of cortical circuits (which modulate the descending volley), the size of the MEP induced by TMS is also influenced by factors within the spinal cord. The fact that there are numerous monosynaptic corticospinal connections to distal limb motoneurons in primates (see Porter & Lemon 1993 for review), has perhaps led to excessive focus on the corticospinal cell – motoneuronal connection as a potential site of MEP modulation. It is correct that the responsiveness of motoneurons (i.e. influenced by firing rate and membrane properties) and the efficacy of the corticospinal-motoneuronal synapse can affect the MEP size. However, because many corticospinal cells terminate on interneurons in the spinal cord (see Porter & Lemon 1993 for review), the net motoneuronal output produced by a TMS pulse can be affected by the synaptic efficacy and intrinsic responsiveness of the components of spinal interneuronal circuits. It is quite possible that MEP size might change despite an identical output from the cortex (i.e. due entirely to spinal factors), and this is true even if the level of background EMG does not change. Comparisons of MEP size with H-reflex size, often erroneously interpreted as an index of ‘motoneuronal excitability’ (see Spinal reflex studies section), do not allow dissociation of spinal from cortical effects because the afferent and descending volleys might activate different interneuronal circuits, and because the monosynaptic components of the responses traverse...
Neural adaptations to strength training • T J Carroll et al.

Acta Physiol 2011

different synapses (i.e. the corticospinal-motoneuronal synapse versus the Ia-afferent-motoneuronal synapse; both of which are subject to modulation with voluntary muscle activation; Hultborn & Nielsen 1998, Petersen et al. 2003). Only the response to a descending volley that travels in the same corticospinal axons as those activated by TMS, such as transmastoid electrical or magnetic stimulation, can provide unambiguous evidence about the spinal or cortical location of MEP modulation.

Finally, since the MEP is recorded from the muscles via electromyography, its size is subject to all of the factors that can affect the amplitude of a CMAP. These include electrode impedance and the location of electrodes relative to the muscle architecture and innervation zones (which can be influenced, for example, by muscle length and contractile status; Lee & Carroll 2005, Frigon et al. 2007), the characteristics of tissue between the muscle and the skin, the number and functional state of ion channels in the muscle membrane, the relative timing of action potential firing in different muscle fibres, and synaptic transmission at the neuromuscular junction. Thus, it is conceivable that MEP size might change despite an identical motoneuronal output in response to a TMS pulse (i.e. due entirely to peripheral factors). In order to properly interpret MEP size, it is essential to normalize the responses to a standardized CMAP such as the maximal M-wave (i.e. which is elicited by supramaximal stimulation of the motor nerve).

 MEP studies

The details of studies that have examined the effect of strength training protocols on EMG responses to TMS are summarized in Table 3. These studies show that there is no clear pattern of change in MEP size after short-term strength training (i.e. ~4 weeks). It is possible that the inconsistent results might be because of variations in testing and training protocols, and in the muscle groups studied. For example, the size of MEPs recorded from muscles at rest was unchanged after training of finger (Carroll et al. 2002, Hortobagyi et al. 2009), wrist (Carroll et al. 2009) or leg muscles (Griffin & Cafarelli 2007, Schubert et al. 2008), but was decreased by training of proximal arm muscles (Jensen et al. 2005). Resting MEP size has been used to provide an index of ‘baseline’ corticospinal responsiveness that represents the default characteristics of the pathway from motor cortex to muscle. From this perspective, changes in resting MEP size might reflect training-induced adaptations in the efficacy of synapses and axonal and/or cellular excitability at cortical sites, or in synaptic efficacy or cellular excitability at subcortical sites (n.b. as responses are normalized to the maximal M-wave in most studies, the possibility that the results could be because of muscular factors alone can generally be excluded). However, it is important to consider carefully what conditions represent ‘rest’. MEPs are typically considered to be elicited at rest if the target muscle exhibits EMG silence. However, even in the absence of overt motoneuronal activity, contextual factors such as muscle history (Stuart et al. 2002) and motor imagery (e.g. Hashimoto & Rothwell 1999) can influence MEP size. As it is difficult to control all relevant (i.e. especially cognitive) factors, there is likely to be some ‘noise’ in the assessment of corticospinal responsiveness at rest. If strength training induces corticospinal adaptations that are subtle, resting MEPs may lack the precision to detect them.

The variability of the results across studies is even more apparent for assessments of MEP size during muscle activation. The majority of studies have assessed MEP size during weak isometric contraction of the trained muscles. Under these conditions MEPs have been shown to increase in the plantar flexor muscles (Griffin & Cafarelli 2007), be unchanged in finger muscles (Carroll et al. 2002, Kidgell & Pearce 2010) or trend lower in arm muscles (Jensen et al. 2005, Carroll et al. 2009). Changes in MEP size during contractions of matched strength could potentially be mediated by all of the factors outlined for resting responses, but are likely to be affected to a relatively greater extent by motoneuron firing rate and intrinsic motoneuron firing properties (Matthews 1999). Only Carroll et al. (2002, 2009) considered MEP amplitudes during strong isometric contractions, and reported reductions in MEP size for contraction strengths over about 50% MVC in both finger and wrist muscles. These reductions in corticospinal responsiveness were likely mediated largely at the spinal level, as similar results were obtained when the descending tracts were activated by transcervical electric stimulation (Carroll et al. 2002) and stimulation of the corticospinal tract via stimulation at the cervicomедullary junction (Carroll et al. 2009). Although both of these techniques are less affected by the state of cortical circuits than TMS (see Di Lazzaro et al. 1998a,b for evidence in relation to transcervical electrical stimulation), stimulation at the cervicomедullary junction is the superior method of dissociating cortical from subcortical effects (Taylor & Gandevia 2004). This is because corticospinal axons are activated well caudal to the cortical circuits (excluding direct influence of cortical excitability to the responses), and peripheral responses to both TMS and cervicomедullary stimulation arise from at least some identical corticospinal axons (Ugawa et al. 1991, Gandevia et al. 1999, Taylor et al. 2002). Unfortunately, the technique is painful (particularly if responses at rest are sought), and it will probably be difficult to recruit large samples
Table 3 Summary of studies examining the effect of strength training on MEP size

<table>
<thead>
<tr>
<th>Study</th>
<th>Muscle group</th>
<th>Subject details</th>
<th>Methods</th>
<th>Training schedule</th>
<th>Training intensity</th>
<th>Strength gain</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carroll et al. 2002</td>
<td>Finger abductors</td>
<td>8 trained</td>
<td>TMS at rest</td>
<td>4 weeks</td>
<td>Dynamic</td>
<td>↑ 30% MVC</td>
<td>Resting MEPs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 control</td>
<td>TMS and TES during 0–60% MVC</td>
<td>12 sessions</td>
<td>70–85% initial 1RM</td>
<td>↓ TES and TMS MEPS at &gt;50% MVC</td>
<td></td>
</tr>
<tr>
<td>Jensen et al. 2005</td>
<td>Elbow flexors</td>
<td>8 trained</td>
<td>TMS at rest</td>
<td>4 weeks</td>
<td>Dynamic</td>
<td>↑ 31% 1RM</td>
<td>Resting MEP max size and slope</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 control</td>
<td>TMS during 10% MVC</td>
<td>12 sessions</td>
<td>10–6RM</td>
<td>↑ 12% MVC</td>
<td>n.s. trend for same at 10% MVC</td>
</tr>
<tr>
<td>Griffin &amp; Cafarelli 2007</td>
<td>Dorsiflexors</td>
<td>10 trained</td>
<td>TMS at rest</td>
<td>4 weeks</td>
<td>Isometric</td>
<td>↑ 18% MVC</td>
<td>MEP size at 10% MVC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 control</td>
<td>TMS during 10% MVC</td>
<td>13 sessions</td>
<td>MVC</td>
<td></td>
<td>remainder at rest</td>
</tr>
<tr>
<td>Beck et al. 2007</td>
<td>Dorsiflexors</td>
<td>8 trained</td>
<td>TMS and H reflex during fast contraction</td>
<td>4 weeks</td>
<td>Ballistic, dynamic</td>
<td>Not reported</td>
<td>H-reflex</td>
</tr>
<tr>
<td></td>
<td>plantar flexors</td>
<td>10 control</td>
<td>SICI and ICF at rest</td>
<td>16 sessions</td>
<td>30–40% 1RM</td>
<td></td>
<td>SICI or ICF</td>
</tr>
<tr>
<td>Schubert et al. 2008</td>
<td>Plantar flexors</td>
<td>12 trained</td>
<td>TMS-conditioning of H reflex during rest and ballistic tasks</td>
<td>4 weeks</td>
<td>Ballistic, dynamic</td>
<td>↑ Rate of force development</td>
<td>TMS during dorsiflexion in TA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 control</td>
<td></td>
<td>16 sessions</td>
<td>30–40% 1RM</td>
<td>MVC not reported</td>
<td>conditioned H-reflex size in ballistic task but not rest</td>
</tr>
<tr>
<td>Carroll et al. 2009</td>
<td>Wrist abductors</td>
<td>8 trained</td>
<td>TMS and CMEPs during 0–75% MVC</td>
<td>4 weeks</td>
<td>Dynamic</td>
<td>↑ 11% MVC</td>
<td>MEP and CMEP at high contraction strength</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9 control</td>
<td></td>
<td>12 sessions</td>
<td>70–85% initial 1RM</td>
<td></td>
<td>MEP at rest</td>
</tr>
<tr>
<td>Hortobagyi et al. 2009</td>
<td>Finger abductors</td>
<td>8 trained</td>
<td>TMS at rest</td>
<td>4 weeks</td>
<td>Isometric</td>
<td>↑ 38% MVC</td>
<td>MEPs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 control</td>
<td></td>
<td>10 sessions</td>
<td>70–80% MVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidgell &amp; Pearce 2010</td>
<td>Finger abductors</td>
<td>8 trained</td>
<td>TMS during 5 and 20% MVC</td>
<td>4 weeks</td>
<td>Isometric</td>
<td>↑ 34% MVC</td>
<td>MEPs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 control</td>
<td>MVC</td>
<td>12 sessions</td>
<td>MVC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TMS, transcranial magnetic stimulation; TES, transcranial electrical stimulation; SICI, short-interval intracortical inhibition; ICF, intracortical facilitation; CMEPs, cervico-medullary evoked potentials; MVC, maximal voluntary contraction; RM, repetition maximum; n.s., non-significant; TA, tibialis anterior.
Neural adaptations to strength training • T J Carroll et al.

for studies involving this technique. Carroll et al. (2002) speculated that the decreases in MEP size after strength training at high forces could be explained by changes in the firing rate of the motoneurons or an increase in the amplitude or duration of motoneuronal after-hyperpolarisation potential.

The group of Beck et al. (2007) and Schubert et al. (2008) assessed TMS responses after a form of strength training involving ballistic contractions. The size of MEPs was greater after training when elicited during the execution of dynamic contractions that resembled the training task, but not at rest (Beck et al. 2007). The data indicate a context-specific increase in corticospinal responsiveness after training. In contrast, the size of H-reflexes conditioned by subthreshold TMS pulses was reduced in a task-dependent manner (Schubert et al. 2008). The H-reflex conditioning technique involves assessing the degree to which a TMS pulse (conditioning pulse), that is subthreshold for producing an MEP on its own, increases the size of an H-reflex (test pulse) that is elicited near simultaneously (see Nielsen et al. 1993). As the precise conditioning-test interval is specified so that the H-reflex is facilitated only by the earliest (monosynaptic) component of the descending volley, the conditioned H-reflex results of Schubert et al. (2008) are consistent with a decrease in the size of the motor cortical output in response to TMS. Although adaptations at the cortico-motoneuronal synapse (see Petersen et al. 2003) could also explain a change in conditioned H-reflex amplitude, the lack of change in this variable at rest argues against this possibility. It is difficult to draw general conclusions from the conflicting results; that is, task-specific increase in corticospinal excitability revealed by MEPs versus task-specific decrease in cortical excitation revealed by TMS conditioning of H-reflexes. However, the studies illustrate the importance of considering task context when attempting to categorize the neural responses to training.

Given the inconsistent results from studies that have focused on the effect of strength training on MEP size in muscles directly targeted during training, progress toward an understanding of the neural responses to training might be facilitated by reflecting on putative mechanisms that have been proposed on conceptual grounds. If a change in the CNS is to enhance strength, it must act by increasing the activation of motoneurons that contribute to torque in the desired direction (i.e. by recruiting additional motoneurons or increasing the firing rate of motoneurons that innervate agonist and synergist muscles), or by reducing the activation of motoneurons that oppose torque in the desired direction (i.e. antagonist muscles). Since the ability of the CNS to activate many muscles (i.e. when acting as agonists) is near maximal (see Gandevia 2001 for review), one might speculate that the predominant component of the neural adaptation to strength training should be associated with refining circuitry to facilitate activation of synergists and suppress activation of antagonists. This reasoning reinforces the notion that MEPs recorded from agonist muscles may lack the sensitivity to detect corticospinal adaptations in many contexts. How then could TMS be used to identify the neural mechanisms that underlie putative changes in coordination between agonist, synergist and antagonist muscles?

Use of TMS-induced twitch responses

One obvious approach to studying possible changes in coordination between muscles after strength training is to measure MEPs in antagonist and synergist muscles. However, a major impediment to experiments of this kind would be the difficulty in obtaining selective recordings from all of the individual muscles that might be relevant. At most joints, there are many muscles that can contribute non-negligible moments, and it is possible that important functional effects might be brought about by the combined effect of small changes (i.e. that are difficult to measure) in multiple muscles. Some of these muscles will be in close proximity to one-another (i.e. making selective recording difficult), and some will be deep (i.e. making detection with surface electrodes difficult). Another approach is to record the twitch torque evoked by TMS, which will reflect the net response in all agonist, synergist and antagonist muscles. The major difficulty here is to ensure that contractile factors do not contribute to any change in the responses. Carroll et al. (2009) found that TMS-evoked twitches were larger during weak background contraction in the wrist muscles after 4 weeks of strength training involving wrist abduction. Spinal factors were likely dominant, since similar results were obtained for twitches evoked by cervico-medullary stimulation. There were no differences in twitch amplitudes evoked by supramaximal nerve stimulation (at rest or during identical voluntary contractions), suggesting that muscular factors did not underlie the results. Similarly, Lee et al. (2009) reported increased TMS-evoked twitch size during high force contractions in a larger study with an overlapping subject cohort. They also found that the direction of evoked twitches shifted toward the training direction. The differences in the results between the two studies (i.e. no effect on TMS-evoked Twitches at high forces in the Carroll et al. 2009 study), despite identical training parameters, is probably because of subtle differences in TMS intensity and the contractile conditions (i.e. whether subjects matched EMG or torque as a percentage of MVC). Although the results are consistent with the hypothesis that strength training causes corticospinal adaptations
that facilitate coordination between the muscles involved in training, many questions remain about the precise mechanisms involved.

**Cortical voluntary activation**

Although the technique of twitch interpolation (Merton 1954) is not the focus of this review, it is worth noting that a version of the method that involves TMS might have some benefits over ‘traditional’ nerve stimulation methods for identifying changes in the ability of the CNS to activate muscles after strength training (see Todd et al. 2003). Twitch interpolation with nerve stimulation is limited to assessing voluntary activation in a single muscle (with motor point stimulation) or in a group of muscles innervated by a single peripheral nerve. The nerve stimulation technique also provides no information about the site of any failure in the capacity of the CNS to drive the muscles maximally. In contrast, if TMS can elicit extra force during an MVC, it indicates that the output from the *motor cortex* was suboptimal for driving the motoneurons (see Gandevia et al. 1996, Todd et al. 2003). Furthermore, given the relatively poor spatial resolution of TMS, the proximity of cortical representations of functionally related muscles, and the fact that the corticospinal responsiveness of muscles activated voluntarily is considerably higher than resting muscles, the TMS twitch interpolation method can, in many cases, provide information about the ability of the motor cortex to drive all of the relevant agonist and synergist muscles in any given contraction. It is important to note that for TMS methods of twitch interpolation to be valid, it is essential that the stimulus produces a near maximal response in the relevant muscles. Any degree to which the stimulus is submaximal will introduce variability into the measurements, and substantially submaximal stimulations would result in invalid results. Nevertheless, the validity and reliability of the method has been demonstrated in the wrist extensors (Lee et al. 2008), elbow flexors (Todd et al. 2003, 2004) and knee extensors (Sidhu et al. 2009).

Lee and colleagues used twitch interpolation with TMS to study the influence of strength training on the ability of the motor cortex to drive wrist muscles after 4 weeks of strength training (Lee et al. 2009). They found that *cortical* voluntary activation of the wrist abductors was high at baseline (~94%), and did not change as a consequence of strength training. However, the dynamic training was not specific to the isometric conditions under which voluntary activation was assessed, and the improvement in MVC was relatively small (~11%). Lee et al. (2010) subsequently showed that cortical voluntary activation increased for the wrist extensors in the limb contralateral to the trained muscles when there was a 30% increase in MVC in the trained limb (i.e. produced by isometric training). These results suggest that the motor cortex is better able to drive motoneurons during MVC of the untrained, homologous muscles after strength training. This could be due to adaptations at any point upstream of the motor cortical output cells; that is, in the circuitry of the primary motor cortex, or at any of the secondary motor cortical areas or subcortical areas that shape the output of the primary motor cortex. It seems likely that similar mechanisms might contribute to strength gains in the trained limb, which might only be detectible when training causes a considerable increase in MVC.

**Use of repetitive TMS (rTMS)**

In the studies described above, TMS was used to probe the responsiveness of the pathway from motor cortex to muscle. However, in repetitive mode, TMS can also be used to transiently disrupt ongoing cortical processing, or to induce persistent (i.e. that outlast the stimulation by a few minutes to an hour) changes in the responsiveness of cortical (n.b. and/or spinal) circuits (see Fitzgerald et al. 2006, Ziemann et al. 2008 for recent review). In the only strength training study to date to use rTMS in this way, Hortobagyi et al. (2009) applied a low-frequency protocol that is known to induce lasting corticospinal inhibition (1 Hz for 15 min at 110% of resting motor threshold; Chen et al. 1997) to the motor cortex after every session in a 4 week strength training program. The participants who received rTMS showed impaired strength gains relative to control subjects by the end of training, which implies that the cortical or spinal circuits activated by the rTMS were important substrates for the adaptations that increased strength. It is important to note that although rTMS effects are commonly attributed to cortical factors by default, a spinal origin for effects cannot be discounted when the stimulus is above the threshold for a descending volley (n.b. there will be a descending volley from the brain to the spinal cord at stimulus intensities well below resting motor threshold; e.g. Di Lazzaro et al. 1998b).

Although they have yet to be applied to the context of strength training per se, rTMS protocols that induce effects that resemble synaptic plasticity in the motor cortex might allow insights into the nature of corticospinal responses to training. If strength training does cause cortical adaptations, it seems likely that short-term changes might be mediated by synaptic processes similar to those thought to be involved in motor learning, (e.g. Carroll et al. 2001, Carson 2006, c.f. Adkins et al. 2006). Long-term potentiation (LTP) is a likely candidate for the cortical reorganization that underlies some forms of motor learning (Rioult-Pedotti et al. 1998, 2000), and inferences about the induction...
Neural adaptations to strength training • T J Carroll et al.

Acta Physiol 2011

of LTP can be drawn in humans through rTMS protocols that mimic LTP and long-term depression (LTD). The principle that allows rTMS approaches to provide inferences about the induction of LTP- or LTD-like changes in synaptic efficacy is that of ‘metaplasticity’, or ‘plasticity of plasticity’ (see Abraham & Bear 1996). This principle holds that the effects of any given plasticity inducing protocol will be regulated depending on the prior history of synaptic activity. The functional effect of this process is to maintain synaptic efficacy within an appropriate range. Thus, the effect of a protocol that typically enhances corticospinal responsiveness will be reduced if it is applied when the targeted circuits have experienced prior LTP (Ziemann et al. 2004, 2006). Accordingly, the effects of a protocol that typically suppresses corticospinal excitability will be enhanced by prior induction of LTP. A series of studies have used this general approach to argue that a motor learning training protocol that is not dissimilar to strength training (i.e. multiple ballistic contractions that increase peak joint acceleration) causes LTP-like adaptations in the motor cortex (Ziemann et al. 2004, Stefan et al. 2006, Rosenkranz et al. 2007). These studies used a technique known as paired associative stimulation (PAS), which involves the application of peripheral nerve stimulation (to activate muscle afferents) such that the afferent volley arrives near simultaneously at the motor cortex with TMS (Stefan et al. 2000). Approximately 100 stimuli pairs are needed to modulate the synaptic efficacy of cortical synapses for an extended period (see Ziemann et al. 2008 for review). If the afferent volley arrives at the cortex prior to TMS [i.e. inter-stimulus interval (ISI) of 10 ms for hand muscles; PAS10], long lasting depression occurs. If the afferent volley arrives coincident with, or just subsequent to the TMS (i.e. ISI of 25 ms for hand muscles; PAS25), long lasting facilitation results. PAS protocols induce effects that share many characteristics with LTP/LTD; the changes in excitability last for a similar duration (30–60 min), they are dependent on normal N-methyl-D-aspartate receptor function, they are specific to the circuits targeted by stimulation, and are reversible by protocols that have opposite effects on synaptic efficacy (see Ziemann et al. 2008 for review). Although there are many technical challenges in applying PAS and other rTMS techniques that can induce synaptic plasticity to strength training studies, the potential to establish whether strength training induces LTP-like changes in the motor cortex dictate that the experiments should be attempted.

Moving forward with TMS studies

There is a lack of consistency in the results of studies that assessed the effect of strength training on MEPs at rest or during weak contractions. This suggests that if training changes the properties of cortical and spinal circuits projecting to agonist muscles, then the changes may be too subtle to be detected with MEP approaches in many contexts. Despite this, there is some evidence from TMS studies that the responsiveness of motoneurons during high force contractions is reduced after strength training, that disruption of normal corticospinal processing after training reduces strength gains, and that training increases the capacity of the motor cortex to drive the motoneurons during maximal effort. In order to advance our understanding of the neural adaptations to strength training, studies that target specific sites of modulation via converging techniques (e.g. TMS vs. cervico-medullary stimulation) or conditioning-test approaches are required. Close attention to the functional context under which the methods are applied will also be essential. Finally, rTMS protocols have potential to provide information regarding the nature of any synaptic plasticity that might be induced by strength training.

Imaging and EEG studies

Functional magnetic resonance imaging is a non-invasive technique that detects regional changes in cortical blood flow in response to a task measured as the blood oxygenation level dependent (BOLD) contrast or ratio of oxygenated to deoxygenated haemoglobin (see Logothetis 2003 for review). Changes in BOLD response are interpreted as changes in ‘neural activation’ in fMRI studies but are not direct measures of synaptic activity or neuronal action potentials. While the spatial resolution of fMRI is in the order of a few millimetres, because the signal is sensitive to vascular changes and not neuronal activity, the temporal resolution is in the order of a few seconds.

Using fMRI, Farthing et al. (2007) examined changes in brain activation following 6 weeks of unilateral strength training consisting of a maximum isometric ulnar deviation task. The authors reported widespread changes in the activation profile in both the contralateral (trained) and ipsilateral (untrained) cortices in parallel with increased strength in both the trained (right) and untrained (left) limb. There are, however, several limitations to the interpretation of changes in brain activation from fMRI (see Poldrack 2000, Kelly & Garavan 2005 for review). Firstly, it is not possible to determine the extent to which areas of activation detected by fMRI are functionally related to and share a causal relationship with behaviour, or merely represent correlated activity associated with task-irrelevant processing. For example, changes in behavioural output or cognitive awareness of the imaging process can influence brain activation measured with fMRI. Infor-
trials regarding the mechanisms of cortical changes associated with strength training might be best achieved by testing specific predictions regarding changes in brain activity, based on the known functional roles of cortical areas and likely time course of the hypothesized effects, rather than simply documenting changes in cortical activity in response to training. For example, in assessing transfer of motor skill from one limb to the other, Perez et al. (2007) found that the level of pre-training fMRI activity specific to the ventrolateral posterior thalamic (VLp) nucleus predicted successful future intermanual transfer. These observations are consistent with what is known about the associated connections between VLp, cerebellum and supplementary motor area, which are all implicated in error prediction and correction (Butler et al. 2000, Sakai et al. 2002, Diedrichsen et al. 2005). Secondly, using fMRI, it is not possible to dissociate activity that is excitatory in nature from that which is inhibitory. Therefore, the overall activation profiles observed in fMRI studies are a combination of excitatory and inhibitory neural processes and their associated BOLD signal. As such, it is often unclear how to interpret increases in ‘activity’ based on fMRI.

Another important consideration in interpreting studies that examine the cortical changes associated with strength training is the time course of the changes. For example, observed changes in M1 representation with muscle strength, comparable motor tasks can be performed with a lower level of neural activation (e.g. Carroll et al. 2001, Carson 2006). As the force generating capacity of individual motor units increases with training, fewer motor neurons are required in order to accomplish a given submaximal task. Such a reduction in motor unit recruitment might be reflected in diminished cortical activation.

Finally, frequency-domain coupling between cortical activity and spinal motoneuron firing can be captured in the EEG–EMG coherence signal (see Conway et al. 1995). It has recently been shown that corticomuscular coherence is lower for strength trained than for non-trained individuals (Ushiyama et al. 2010), which suggests that the method may have potential for studying the corticospinal responses to strength training.

General summary and conclusions

In this review, we summarized the available research in which neurophysiological methods were applied to study neural adaptations to strength training. Despite a considerable body of work spanning over 30 years, there remain many inconsistencies in the data and many gaps in our understanding. One possible interpretation of the inconsistent results is that variations in the spatial resolution (i.e. over fMRI, for example). However, the spatial resolution of EEG is much lower than most imaging techniques, such as fMRI. Surface negative potentials detected at the scalp around the time of voluntary movement are referred to as movement-related cortical potentials (MRCP). MRCPs reflect the summed excitatory post-synaptic potentials of apical dendrites and are related to the preparation and execution of self-initiated movement (see Shibasaki & Hallett 2006 for review). The MRCP waveform has an onset 1–2 s prior to movement onset and can be divided into three consecutive phases referred to as (1) the Bereitschaftspotential (preparation), (2) motor execution and (3) movement-monitoring potentials. The amplitude of each component is a function of the number of active neurons, their synchrony and rate of discharge (Siemionow et al. 2000). The later MRCP components have been correlated with force, RFD, and associated EMG amplitude for both elbow flexion (Siemionow et al. 2000), and plantar flexion movements (do Nascimento et al. 2005) suggesting that MRCP is indicative of the level of muscle activation.

A 3-week resistance training program, with increases in MVC, RFD and EMG in the trained leg extensor muscles, resulted in changes in MRCP amplitude at several motor electrode sites (Falvo et al. 2010). For repetitive submaximal leg extensions, Falvo et al. (2010) observed an attenuation of MRCP amplitude. These findings support the hypothesis that by increasing muscle strength, comparable motor tasks can be performed with a lower level of neural activation (e.g. Carroll et al. 2001, Carson 2006). As the force generating capacity of individual motor units increases with training, fewer motor neurons are required in order to accomplish a given submaximal task. Such a reduction in motor unit recruitment might be reflected in diminished cortical activation.

Another technique for monitoring brain activity is EEG, a non-invasive technique that records electrical activity in the brain. Surface EEG electrodes measure voltage changes on the scalp that reflect ion flow caused by excitatory and inhibitory post-synaptic potentials. As EEG is derived from post-synaptic potentials in cortical neurons, it has the advantage of excellent temporal resolution (i.e. over fMRI, for example). However, the spatial resolution of EEG is much lower than most imaging techniques, such as fMRI. Surface negative potentials detected at the scalp around the time of voluntary movement are referred to as movement-related cortical potentials (MRCP). MRCPs reflect the summed excitatory post-synaptic potentials of apical dendrites and are related to the preparation and execution of self-initiated movement (see Shibasaki & Hallett 2006 for review). The MRCP waveform has an onset 1–2 s prior to movement onset and can be divided into three consecutive phases referred to as (1) the Bereitschaftspotential (preparation), (2) motor execution and (3) movement-monitoring potentials. The amplitude of each component is a function of the number of active neurons, their synchrony and rate of discharge (Siemionow et al. 2000). The later MRCP components have been correlated with force, RFD, and associated EMG amplitude for both elbow flexion (Siemionow et al. 2000), and plantar flexion movements (do Nascimento et al. 2005) suggesting that MRCP is indicative of the level of muscle activation.

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Finally, frequency-domain coupling between cortical activity and spinal motoneuron firing can be captured in the EEG–EMG coherence signal (see Conway et al. 1995). It has recently been shown that corticomuscular coherence is lower for strength trained than for non-trained individuals (Ushiyama et al. 2010), which suggests that the method may have potential for studying the corticospinal responses to strength training.
training task and muscle groups targeted fundamentally alter the nature of the neural adaptations produced. However, we do not favour this interpretation. In our opinion, although there is likely to be a continuum of changes that will depend upon the precise details of the training and the characteristics of the involved neuromuscular components, we expect that it should ultimately be possible to identify some general principles of neural adaptation that are applicable to all forms of strength training that involve systematic repetition of actions requiring strong neural drive. Clearly, if these general principles exist, they cannot be identified on the basis of current data. We conclude that in order to advance knowledge in this field, studies should be designed to rigorously account for the limitations of the available techniques, and be specifically targeted to address important conceptual questions. Careful consideration of the likely time course of mechanisms to be studied, and the functional context in which they are investigated will be critical.

**Conflict of interest**

None.

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Neural adaptations to strength training • T J Carroll et al.


Neural adaptations to strength training · T J Carroll et al.


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