



Corticomotor excitability of arm muscles modulates according to static position and orientation of the upper limb



Jeremy P.M. Mogk^{a,b,c}, Lynn M. Rogers^{b,d}, Wendy M. Murray^{b,c,d,e,*}, Eric J. Perreault^{b,c,d}, James W. Stinear^{b,c,f}

^a Environment and Ergonomics Research Group, Autodesk Research, Toronto, ON, Canada

^b Sensory Motor Performance Program, Rehabilitation Institute of Chicago, Chicago, IL, USA

^c Department of Physical Medicine & Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

^d Department of Biomedical Engineering, Northwestern University, Evanston, IL, USA

^e Edward Hines, Jr. VA Hospital, Hines, IL, USA

^f Department of Sport & Exercise Science, University of Auckland, Auckland, New Zealand

ARTICLE INFO

Article history:

Accepted 13 February 2014

Available online 22 February 2014

Keywords:

Transcranial magnetic stimulation

Peripheral nerve stimulation

Corticomotor excitability

Upper extremity

Upper limb posture

Tendon transfer

HIGHLIGHTS

- Multi-joint changes in static, functionally relevant upper limb posture altered the overall corticomotor excitability of the resting target muscles.
- Forearm orientation impacted the overall excitability of both target muscles, but in a more robust manner for the muscle whose length was mechanically altered by forearm posture.
- Posture-mediated changes in overall corticomotor excitability are not likely predominated by variables related to target muscle length alone, particularly for muscles crossing multiple joints.

ABSTRACT

Objective: We investigated how multi-joint changes in static upper limb posture impact the corticomotor excitability of the posterior deltoid (PD) and biceps brachii (BIC), and evaluated whether postural variations in excitability related directly to changes in target muscle length.

Methods: The amplitude of individual motor evoked potentials (MEPs) was evaluated in each of thirteen different static postures. Four functional postures were investigated that varied in shoulder and elbow angle, while the forearm was positioned in each of three orientations. Posture-related changes in muscle lengths were assessed using a biomechanical arm model. Additionally, M-waves were evoked in the BIC in each of three forearm orientations to assess the impact of posture on recorded signal characteristics.

Results: BIC-MEP amplitudes were altered by shoulder and elbow posture, and demonstrated robust changes according to forearm orientation. Observed changes in BIC-MEP amplitudes exceeded those of the M-waves. PD-MEP amplitudes changed predominantly with shoulder posture, but were not completely independent of influence from forearm orientation.

Conclusions: Results provide evidence that overall corticomotor excitability can be modulated according to multi-joint upper limb posture.

Significance: The ability to alter motor pathway excitability using static limb posture suggests the importance of posture selection during rehabilitation aimed at retraining individual muscle recruitment and/or overall coordination patterns.

Published by Elsevier Ltd. on behalf of International Federation of Clinical Neurophysiology.

1. Introduction

Re-educating muscles and learning to control an impaired limb is a common challenge following neurological impairment. Reduced or paralyzed function of the upper limb can dramatically

* Corresponding author at: Rehabilitation Institute of Chicago, 345 E. Superior, Suite 1408, Chicago, IL 60611, USA. Tel.: +1 312 238 6965; fax: +1 312 238 2208.

E-mail address: w-murray@northwestern.edu (W.M. Murray).

encumber one's ability to perform common activities of daily living, and thus functional independence. Under certain circumstances, lost function can be surgically restored by transferring the distal tendon of a non-paralyzed muscle to that of a paralyzed muscle (i.e., tendon transfer). One such procedure involves the restoration of active elbow extension following triceps (TRI) paralysis, which involves transfer of either the posterior deltoid (PD) or biceps brachii (BIC) muscle to the distal tendon of the triceps (Leclercq et al., 2008; Mulcahey et al., 2003). In either case, individuals must learn to recruit the transferred muscle to actuate its new function. Successful training of each muscle as an elbow extensor has been reported, with some evidence that elbow extension against gravity (i.e., overhead) is less successful following PD-TRI transfer (Mulcahey et al., 2003). Mechanical differences exist between the BIC and PD based on musculoskeletal anatomy and muscle architecture (Holzbaur et al., 2005; Langenderfer et al., 2004); however, differences in the ability to voluntarily activate these two muscles during functional tasks (e.g., Johanson et al., 2006, 2011) might also contribute to disparities in performance.

Because the amplitudes of the motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) change with joint posture, it has been suggested that limb posture modulates the overall functional state (or excitability) of a motor pathway (i.e., how accessible a muscle is by the motor cortex). For example, changes in the excitability of hand and forearm muscles have been reported to result from static changes in shoulder position (Domini et al., 2005; Ginanneschi et al., 2005, 2006). Since none of the hand or forearm muscles cross the shoulder joint complex, the authors hypothesized that joint posture modulates excitability according to how relevant the overall limb position is to a particular muscle's function. Other studies have demonstrated that, when a target muscle crosses the joint of interest, MEP amplitudes tend to increase at joint angles that place the muscle at shorter lengths (Lackner and Hummelsheim, 2003; Lewis et al., 2001; Mitsuhashi et al., 2007; Renner et al., 2006). Such results have also been interpreted as posture-dependent changes in corticomotor excitability, and have been used to suggest that a target muscle's length helps to shape its accessibility by the motor cortex.

The hypothesis that muscle length influences corticomotor excitability has not been tested explicitly. Rather it has only been inferred from experiments of a limited scope. Specifically, these experiments have involved a change in position of only a single joint, resulting in a tight coupling between muscle length and joint position. This is problematic since functional behaviors, such as activities of daily living, often involve postural changes at multiple joints. Moreover, because many upper limb muscles (including BIC, for example) cross more than a single joint, muscle length is not always uniquely defined. Thus, how different multi-joint upper limb postures that are adopted during functional use of the hand and arm relate to muscle length is not always intuitive. To complicate matters, apparent length-mediated changes in MEP amplitude parallel length-dependent changes in EMG signal amplitude (Frigon et al., 2007; Hashimoto et al., 1994; Lateva et al., 1996). As such, a strong relationship between posture-dependent changes in muscle length and MEP amplitude could simply reflect electrophysiological changes at the muscle level, rather than central modulation of overall excitability.

The principal aim of the current study was to investigate the effects of multi-joint changes in static upper limb posture on the overall corticomotor excitability of the PD (a muscle that crosses only the shoulder) and BIC (a multi-articular muscle) in healthy, non-impaired individuals. We evaluated the hypothesis that muscle length influences corticomotor excitability, postulating that MEP amplitudes of both muscles would vary with posture, such that the response amplitudes would increase as the target muscles were placed at shorter lengths. To accomplish this, we (1)

measured MEP amplitudes in both the BIC and PD in four functionally relevant static upper limb postures, and (2) used a biomechanical model to assess the degree to which changes in target muscle length alone could describe the posture-dependent variations in MEP amplitude. Additionally, we conducted a control experiment, using nerve stimulation to assess the effect of forearm orientation on M-wave amplitude in the BIC, to determine whether muscle electrophysiology alone dictates the recorded changes in MEP amplitude. We chose to focus on the PD and BIC based on our specific interests in tendon transfer surgeries. Consequently, the upper limb postures were selected based on the restoration of voluntary function following cervical spinal cord injury (SCI), and varied in shoulder and elbow angle. In addition, three different forearm orientations were investigated within each functional posture. Since isolated changes in forearm orientation have been reported to modulate MEP amplitude in muscles crossing, and distal to, the elbow (Mitsuhashi et al., 2007), we wanted to evaluate whether forearm orientation has a robust effect in modifying MEP amplitude (and excitability) throughout the workspace.

2. Methods

2.1. Subjects

Twelve healthy subjects, aged 23–35 years (three females and nine males; mean age 26.5 ± 3.3 years), were recruited for this study. Subjects had no neurological impairment or injury to the upper limb. The relationship between corticomotor excitability and arm posture was evaluated in the dominant arm, as self-identified by each subject. All subjects gave their written informed consent to participate in this study and were free to withdraw at any time. The experimental protocol was approved by the Northwestern University Institutional Review Board in accordance with the Declaration of Helsinki.

2.2. Transcranial magnetic stimulation

Responses evoked via the corticospinal pathways projecting to proximal upper limb muscles were assessed using TMS delivered when the muscles were at rest. Single-pulse TMS was delivered to the contralateral motor cortex using a Magstim 200 stimulator (Magstim, Dyfed, Wales, UK) via a 70 mm figure-of-eight coil. The coil was placed tangentially on the scalp with the handle rotated $\sim 45^\circ$ from the midline to induce a posterior-to-anterior cortical current. A single stimulation site, located where the largest peak-to-peak amplitude MEP was evoked in BIC using the lowest stimulation intensity, was marked on the cap and was the coil location used for all subsequent stimulation. The stimulus intensity for experimental trials was set at 120% of the resting threshold (RTh) for the BIC, which was determined with the limb hanging relaxed by the side, and was defined as the stimulus intensity that induced MEPs of $\leq 50 \mu\text{V}$ in no more than 5 of 10 consecutive stimuli. Changes in corticospinal excitability were quantified in both BIC and PD simultaneously by the changes in MEP amplitudes across the thirteen postures investigated. During experimental trials, the stimulator was triggered to deliver 20 stimuli at a rate of 0.2 Hz, and the trigger pulses recorded using Spike2 software (Cambridge Electronic Design, Cambridge, UK). The coil position and orientation were maintained manually throughout each trial.

2.3. Electromyography

Surface electromyography (EMG) was used to monitor muscle activity prior to each stimulus event and to record the TMS-induced responses in the target muscles of interest. Recording sites

were lightly abraded and cleaned with alcohol, and disposable dual Ag–AgCl electrodes (Noraxon U.S.A. Inc., Scottsdale, AZ) were positioned over the posterior deltoid and biceps brachii muscles. For the PD, the electrodes were centered over the proximal third of the muscle belly, as determined while the subject isometrically contracted against resistance with the arm abducted to 90° and the elbow flexed. For the BIC, the electrodes were placed over the proximal half of the muscle belly, as determined during isometric contraction with the elbow flexed to 90° and the forearm supinated, centered about a location approximately 40% of the distance between the acromion process and lateral epicondyle. These electrode placements correspond well with recommendations made according to the common locations of muscle innervation zones (Barbero et al., 2012; DeFreitas et al., 2010). The reference electrode was placed over the acromion process. EMG signals were amplified (1000×) and bandpass-filtered (10–500 Hz) using an AMT-8 amplifier (Bortec Biomedical, Calgary, Alberta, Canada), prior to A/D conversion (CED Micro 1401 MkII, Cambridge Electronic Design, Cambridge, UK). All EMG data were sampled at 2 kHz using Spike2 software (Cambridge Electronic Design, Cambridge, UK) and stored on a personal computer for offline analysis.

2.4. Experimental protocol

Subjects were seated in a comfortable, armless chair with their dominant arm positioned and supported in each of five primary upper limb postures, including a single “reference” posture and four “functional” postures (Fig. 1). The reference posture (“side”) had the subject hang their arm naturally at their side (shoulder neutral, elbow extended and forearm in neutral rotation – thumb directed anteriorly), and served as the baseline condition. The four functional postures (“forward reach”, “horizontal reach”, “overhead reach”, “pressure relief”) incorporated changes in both shoulder and elbow posture, and mimicked upper limb positions that are required for tasks that have been identified as being important for functional independence following cervical SCI. While positioned in each of the four functional postures, the forearm was rotated into three different static orientations (full pronation, neutral, and full supination), resulting in a total of thirteen

postures (4 functional postures × 3 forearm orientations + 1 reference posture) in which MEP amplitudes were measured.

For three of the four functional postures (forward reach, overhead reach, and horizontal reach), the upper limb rested on a custom-built padded support, which was secured to a table of adjustable height. In these three functional reach postures, the upper arm was supported at the level of the elbow via a contoured pad mounted on a lockable pivoting frame and stem. The elbow support allowed adjustments to both the pad orientation and height, enabling customization for individual subjects as needed. For the forward and horizontal reach postures, the forearm and hand rested on an additional support. The forearm support was a padded channel that could easily be moved relative to the elbow support to accommodate forearms of different length, and extra foam padding was added between the wrist and the support as needed to maintain the forearm in the desired posture during the testing protocol. In the case of the overhead reach posture, the forearm support was replaced by an assistant who manually held the forearm (at the level of the wrist). In this case, the upper arm remained rested on the elbow support, while the assistant held the subject’s arm to maintain a steady elbow posture and forearm orientation throughout each trial. For the fourth posture (pressure relief), the assistant supported the full weight of the arm and manually maintained forearm orientation throughout each trial. In all cases, shoulder and elbow postures were confirmed using a manual goniometer prior to stimulation.

Data collected in the reference posture were used to normalize the TMS results (MEP amplitudes) across postures and subjects. For each subject, the reference posture was collected first, followed by a randomized sequence of individual trials with the arm positioned in each of the functional arm postures (Fig. 2). The order of forearm orientations was randomized within each functional arm posture. All measures were made with the arm at rest, as confirmed using surface EMG. A rest period of up to two minutes was provided between trials.

2.5. Relating TMS-evoked responses to changes in muscle length

Muscle fiber lengths for the PD and BIC muscles were estimated for each of the thirteen postures examined, using a validated

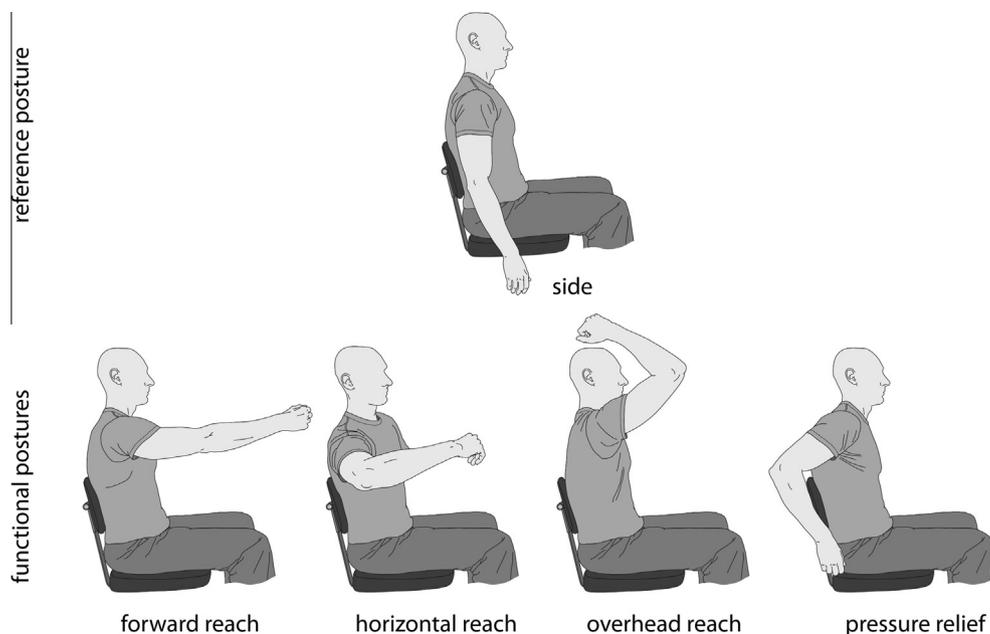


Fig. 1. Illustrations of the reference posture (top), as well as the four functional postures (bottom) used to investigate the effects of upper limb posture on excitability of the posterior deltoid and biceps brachii muscles.

Separate one-way ANOVAs and post hoc comparisons were performed to confirm that the mean RMS amplitude of pre-stimulus EMG did not differ between postures. Separate mixed-effect ANOVAs and post hoc comparisons were performed to examine the main effects and interaction of functional arm posture (forward reach, horizontal reach, overhead reach, and pressure relief) and forearm orientation (full pronation, neutral, and full supination) on normalized MEP amplitude in the PD and BIC muscles. Separate ANCOVAs were performed to evaluate the effect of normalized target muscle length on normalized MEP amplitude. For M-wave data, separate ANOVAs and post hoc comparisons were performed to examine the main effects of forearm orientation on M-wave amplitude, as well as on the MEP/ M_{\max} ratios calculated for the BIC. MEP/ M_{\max} ratios were calculated using each TMS-evoked response and the posture-specific M_{\max} amplitude recorded for that individual. MEP/ M_{\max} ratios were then normalized to the mean ratio calculated for the neutral forearm orientation. All analyses were performed separately for each muscle, treating subjects as a random factor to account for the variability associated with the sample size, as well as recording responses evoked in quiescent muscle. Significance was set at $p = 0.05$ for ANOVAs and ANCOVAs, and a Bonferroni correction applied when necessary for post hoc comparisons.

3. Results

3.1. Changes in MEP amplitude as a function of arm posture

MEP amplitudes of the posterior deltoid varied with functional arm posture ($F_{3,1428} = 355.95$, $p < 0.0001$); the effect of forearm orientation was also significant ($F_{2,1428} = 3.5$, $p = 0.031$). TMS evoked the largest responses in the PD when the arm was positioned in the pressure relief posture (Fig. 3). Responses evoked in the pressure relief posture were 2.5- to 2.8-fold larger than those recorded in the other three functional postures (all $p < 0.0001$). Relative to the responses evoked with the arm relaxed at the side, MEP amplitudes of the PD increased 2.5-fold when the shoulder was extended to position the arm in the pressure relief posture ($p < 0.0001$). In contrast, with the shoulder flexed in each of the three reaching postures, MEP amplitudes of the PD did not significantly change from the reference posture (Fig. 3). The effect of forearm orientation on PD responses was driven by changes recorded in the pressure relief posture, where MEP amplitudes increased from the pronated to supinated posture ($p < 0.005$; Fig. 3).

MEP amplitudes of the biceps varied differentially with functional arm posture according to the orientation of the forearm ($F_{6,1428} = 35.04$, $p < 0.00001$). Overall, cortical stimulation evoked the largest responses in the BIC when the arm was placed in the horizontal reach posture (Fig. 4). Within each forearm orientation, the horizontal reach posture facilitated responses that were 1.55- to 3.0-fold larger than those recorded in the other functional arm postures (all $p < 0.00001$). Relative to the arm hanging at the side, the excitability of the BIC increased by an average of 4.47 times (range of 2.62–6.58, from pronation to supination) when positioned in the horizontal reach posture ($p < 0.0001$). The responses evoked in the three remaining functional postures averaged 2-fold larger than those induced in the reference posture (all $p < 0.0075$). In contrast to the PD, MEP amplitudes of the BIC increased from the reference posture into all posture combinations ($p < 0.0001$), except for when the forearm was pronated in both forward reach and pressure relief. Within each functional arm posture, orienting the forearm in supination yielded larger BIC responses than either neutral or pronation (all $p < 0.00001$). The neutral forearm posture facilitated larger BIC responses than pronation only in the horizontal reach posture ($p < 0.00001$).

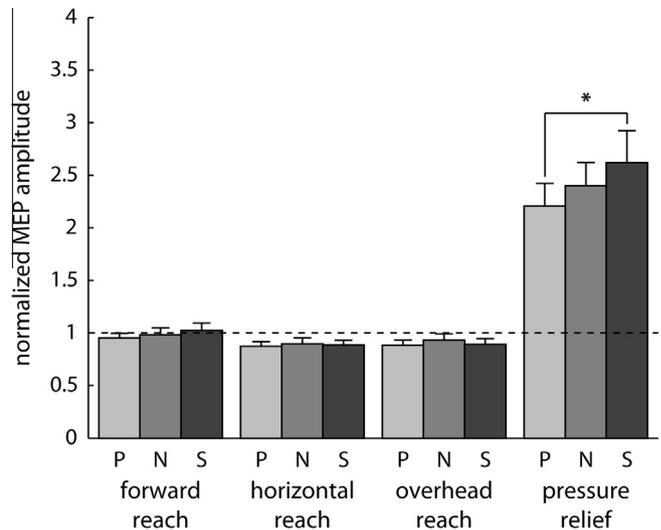


Fig. 3. Normalized MEP amplitude (mean and standard error) of the PD muscle in each of the pronated (P), neutral (N), and supinated (S) forearm postures investigated within each of the four functional postures. MEP amplitudes in each posture are normalized to that evoked when the arm hung relaxed by the side (dotted line). Asterisk indicates significant difference between forearm orientations, within the functional posture.

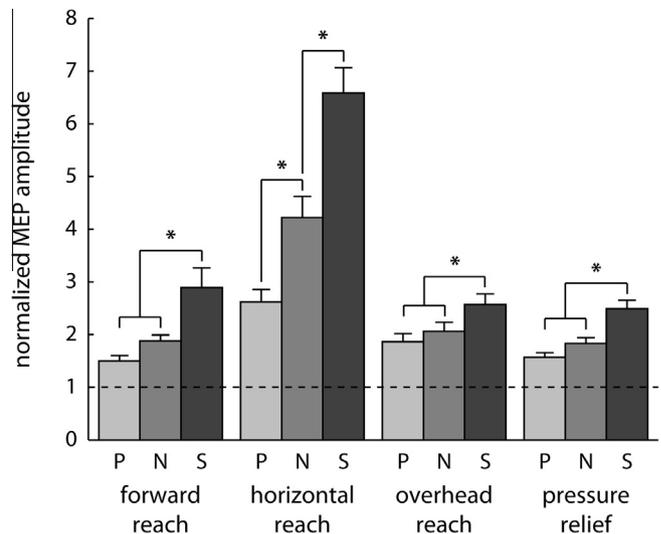


Fig. 4. Normalized MEP amplitude (mean and standard error) of the BIC muscle in each of the pronated (P), neutral (N), and supinated (S) forearm postures investigated within each of the four functional postures. MEP amplitudes in each posture are normalized to that evoked when the arm hung relaxed by the side (dotted line). Asterisks indicate significant differences between forearm orientations, within each functional posture.

3.2. Relating posture-dependent changes in MEP amplitude to target muscle length

The normalized MEP amplitudes evoked in the PD increased as the muscle fiber length decreased ($F_{11,1536} = 122.32$, $p < 0.00001$), but target muscle length alone explained only 60.9% of the variance in normalized MEP amplitudes evoked in the PD. According to the musculoskeletal model, only the pressure relief posture placed the PD muscle at a shorter length than that of the side posture. Relative to the side posture, the normalized PD muscle fiber length shortened by 25.6% for pressure relief, and lengthened by 14%, 24.5% and 25.5% for the horizontal, forward and overhead reach postures, respectively.

The normalized MEP amplitudes evoked in the BIC increased as the muscle fiber length decreased ($F_{11,1536} = 12.13$, $p < 0.00001$), but to a lesser extent than the PD. Target muscle length alone explained only 25.6% of the variance in the amplitudes of BIC responses. Although the horizontal reach posture facilitated the largest responses in the BIC muscle, the overhead reach posture placed the BIC at shorter muscle lengths for each forearm orientation (Fig. 5). When the overhead posture was removed from the analysis, relative changes in BIC muscle length explained 61.5% of the variance in normalized MEP amplitude. In contrast to the PD, the model indicated that the side posture was associated with the longest BIC length. Within each functional arm posture, BIC muscle length decreased from pronation to supination. Relative to the side posture, the BIC shortened by an average of 9.7% in pressure relief (range: 1.3–16.8%), 15.7% in forward reach (range: 12.7–19.3%), 32.5% in horizontal reach (range: 23.1–40.3%), and 36.5% in overhead reach (range: 17.1–44.3%). Despite muscle-specific differences in the range of modulation of MEP amplitudes (i.e., more than double the range in BIC), both muscles were placed at a similar range of muscle lengths (55–60% of optimal fiber lengths).

3.3. Changes in M-wave amplitude as a function of forearm orientation

A posture-dependent increase in MEP amplitude occurred when the forearm was supinated that could not be attributed to length-dependent changes in M_{\max} . Specifically, within the horizontal reach posture, MEP amplitudes changed with forearm orientation to a greater extent than did M_{\max} , as evidenced by the MEP/ M_{\max} ratios ($F_{2,113} = 44.85$, $p < 0.00001$; Fig. 6a). Notably, both M_{\max} and MEP amplitudes changed in a common fashion ($F_{2,68} = 102.32$ and $F_{2,113} = 120.17$, respectively, both $p < 0.00001$). For example, relative to responses recorded in the neutral forearm orientation, amplitudes of both the M_{\max} and MEP responses decreased when pronated (both $p < 0.01$) and increased when

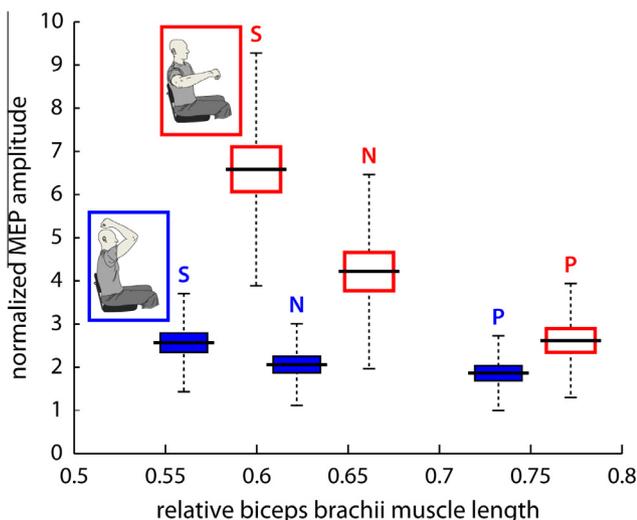


Fig. 5. Changes in normalized MEP amplitudes evoked in the BIC muscle as a function of muscle fiber length in the horizontal (open bars, outlined in red) and overhead reach postures (filled blue bars). For each box plot, the line indicates the mean across subjects, the box indicates the 95% confidence interval, and the error bars indicate 1 standard deviation. Within each functional posture, MEP amplitude versus muscle length differences are shown for the pronated (P), neutral (N), and supinated (S), forearm postures. Despite shorter fiber lengths in the overhead reach posture (i.e., each filled bar is to the left of the respective open bar), the horizontal reach posture facilitated larger responses in the BIC for each of the three forearm postures. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

supinated (both $p < 0.0001$; Fig. 6b and c). When used to calculate MEP/ M_{\max} ratios, the supinated orientation resulted in larger response ratios than either neutral or pronated (both $p < 0.0001$; Fig. 6a).

4. Discussion

The current study was performed to investigate the effects of multi-joint upper limb posture on corticomotor excitability of the PD and BIC muscles. We observed that MEP amplitudes of both target muscles were modulated according to the static, multi-joint position and orientation of the upper limb. Specifically, MEP amplitudes of the multi-articular BIC were modulated by changes in shoulder and elbow posture, and demonstrated a particularly robust response to forearm orientation within each functional posture. In contrast, PD-MEP amplitudes were modulated predominantly by changes in shoulder posture. By comparing TMS-evoked responses within the context of a biomechanical model, we conclude that muscle length alone accounted for a relatively low proportion of the posture-related changes in MEP amplitude observed in this study, particularly for the multi-articular BIC. Finally, for both the BIC and PD, we provide evidence that the observed changes in MEP amplitude with joint posture are consistent with central modulation of excitability, rather than peripheral changes in muscle electrophysiology.

4.1. Influence of limb position and orientation on MEP amplitudes

Our results indicate that the responses evoked in a muscle by TMS represent the collective impact of overall limb posture, and that a fixed relationship between MEP amplitude and the posture of a single joint does not necessarily exist. For example, by examining the same three forearm orientations in each of four functional postures, we demonstrated that BIC-MEP amplitude was dependent on shoulder and elbow posture, in addition to forearm orientation (Fig. 4). Likewise, PD-MEP amplitudes showed some sensitivity to forearm orientation, in addition to the expected changes with shoulder position (Fig. 3). This finding, in particular, provides new evidence of the potential to shape proximal responses (e.g., PD-MEP amplitude) by changes to distal joint postures (e.g., forearm orientation), supplementing previous studies that demonstrated the impact of proximal joint posture on distal muscles (Dominici et al., 2005; Ginanneschi et al., 2005, 2006). Overall, our data support those of previous studies that showed modulation of MEP amplitude, both in muscles that cross the joint of interest (Lackner and Hummelsheim, 2003; Lewis et al., 2001; Mitsuhashi et al., 2007; Renner et al., 2006), as well as posture-related effects on muscles remote to the joint of interest (Dominici et al., 2005; Ginanneschi et al., 2005, 2006).

4.2. Support for central modulation of posture-mediated changes in MEP amplitude

Our data quantifying the sensitivities of both PD and BIC muscles to forearm orientation suggest that the main factors driving the MEP changes with forearm posture, in particular, are central. For the PD, forearm position does not change the length of this single-joint, shoulder extensor muscle. Yet, we observed significant differences in response amplitudes with forearm orientation in the pressure relief posture (Fig. 3). Thus, the significant increase in PD MEP amplitudes we observed with forearm supination is consistent with central modulation because changing forearm position does not result in peripheral changes at the muscle level.

In the case of the BIC, muscle length does change with forearm position. When muscle length changes with posture, it is important

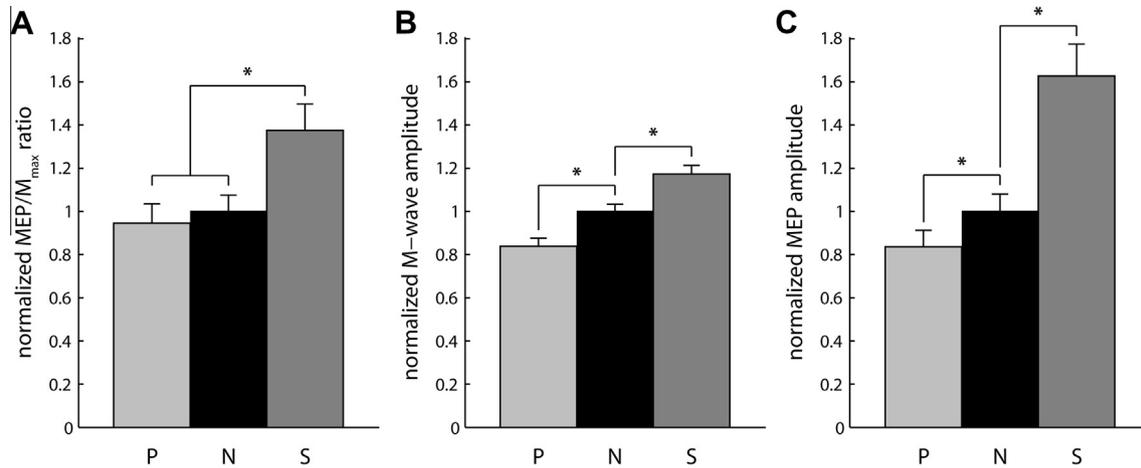


Fig. 6. Changes in (a) normalized MEP/M_{max} ratios, (b) normalized M-wave amplitudes, and (c) normalized MEP amplitudes, as assessed in the BIC muscle in each of the pronated (P), neutral (N), and supinated (S) forearm postures within the horizontal reach posture. Asterisks indicate significant differences between forearm orientations for each of the listed measures.

to note that posture not only impacts factors related to the membrane properties (e.g., fiber length and diameter), but can also alter the spatial orientation of the muscle relative to the electrodes (due to skin movement). This may lead to posture-dependent changes in the measured EMG that are unrelated to changes in muscle activation level (Mesin et al., 2006, 2009; Rainoldi et al., 2000). To address such peripheral factors, we designed the control experiment for BIC. In the control study, both TMS and peripheral nerve stimulation were performed in the same functional arm postures. If a changing electrode-muscle relationship was the prime factor driving the posture-mediated increase in response amplitudes from pronated to supinated, the MEP/M_{max} ratios would be close to one because similar changes to the electrode-muscle relationship should occur for both protocols between forearm orientations. Instead, the ratio between MEP and M-wave amplitudes changed significantly according to forearm orientation (see Fig. 6). Thus, we observed an increase in MEP amplitude above and beyond that expected from the peripheral changes that occurred at the muscle level. This posture-based modulation of BIC excitability mimics its enhanced mechanical advantage relative to the other elbow flexor muscles (Murray et al., 1995), as well as the increase in overall stability of the elbow joint, when supinated (Pomianowski et al., 2001).

We provide data for both PD and BIC that are consistent with a neural link that preferentially facilitates the motor pathway when the forearm is supinated. In addition, across functional postures, we observed that posture-related changes in MEP amplitudes did not scale proportionally with target muscle length, which limited the amount of variance in evoked responses explainable by muscle length alone. Most notably, a decrease in muscle length did not always cause MEP amplitude to increase. For example, the response amplitudes recorded in the BIC were smaller in overhead compared to horizontal reach, despite the shorter BIC lengths in the overhead posture (Fig. 5). This contradiction to the muscle length hypothesis is also consistent with central modulation. That is, if factors related to muscle membrane properties (e.g., fiber length and diameter) were the only mechanism for length-related changes in MEP amplitude, then a more consistent increase in response amplitudes would be expected between *all* postures where muscle length decreased (c.f. Fortune and Lowery, 2012). However, as described above, some of the posture-related changes could be confounded by changes to the electrode-muscle relationship. Such changes are mediated somewhat when using larger recording

electrodes (van Dijk et al., 2009), as we did. Despite this, for those positions where the relative peripheral effects were not directly evaluated by our control study, these potential peripheral mechanisms should also be acknowledged as a possible contributor.

4.3. Mechanisms underlying the recorded differences in corticomotor excitability

Explanations of the putative origins of posture-dependent modulation of corticomotor excitability in quiescent muscles have focused on influences arising through peripheral input. The prevailing hypothesis is that corticomotor excitability increases to compensate for the reduced afferent feedback that occurs at progressively shorter muscle lengths (Lewis et al., 2001), presumably related to muscle spindle and/or tendon organ activity. This coincides with findings that corticomotor excitability increases in response to motor inactivity due to withdrawal of afferent input to the motor cortex (Todd et al., 2006). Whether target muscle length changes or stays constant, posture-related excitability is not modulated via intracortical inhibition (Ginanneschi et al., 2005, 2006; Lewis et al., 2001); however, the presence of intracortical facilitation specifies cortical involvement (Ginanneschi et al., 2005, 2006). Since facilitation and inhibition are related to separate mechanisms (Liepert et al., 1997; Ziemann et al., 1996), posture-based increases in corticomotor excitability could involve intracortical disinhibition. Evidence of cortical involvement when muscle length changes comes from results demonstrating posture-dependent modulation in control subjects and following subcortical stroke, but not following cortical stroke (Renner et al., 2006). Contributions from other sensory receptor groups, unrelated to muscle length, are also likely. Most cutaneous and joint receptors respond predominantly near the limits of joint motion (Burke et al., 1988), and thus possess the potential to have impacted responses recorded in the BIC between pronated and supinated forearm postures.

Afferent contributions to posture-related modulation of overall motor pathway excitability are not limited to the cortical level. Posture-dependent changes in H-reflex amplitudes implicate group I muscle afferents at a presumably spinal level, and can vary between excitation and inhibition according to whether the joint position is flexed or extended (Knikou and Rymer, 2002). Without posture-related changes in target muscle length, neural connections between limb muscles might play a role in such modulation

(Katz et al., 1993; Naito, 2004), as well as the activation of cutaneous afferents (Knikou and Rymer, 2002). Since we passively supported the arm in all but the side posture, differences in the pressure and location of skin contact with the support might have influenced the responses evoked in each posture. Additionally, modulation can occur at the level of the motor neuron, where small changes in joint angle have been shown to markedly alter dendritic integration of synaptic input, via the effects of Ia reciprocal inhibition (Hyingstrom et al., 2007). Accordingly, overall measures of corticomotor excitability, as assessed in the current study using single-pulse TMS, reflect a balance between excitatory and inhibitory processes at all levels of the motor pathway.

4.4. Implications for rehabilitation

The current results have implications for the design and implementation of rehabilitation strategies aimed at retraining individual muscles or overall coordination patterns. Since posture has the ability to both facilitate and suppress specific motor pathways, a facilitated pathway would, in principle, make that muscle fundamentally easier to activate and perhaps control. As evidenced in able-bodied individuals, a posture-related increase in corticomotor excitability can decrease the sense of effort during isometric contractions (Gelli et al., 2005). Moreover, when positioned in a posture associated with greater overall excitability, individuals required a lower level of EMG to produce a specific force magnitude, and could generate more force for a specified level of EMG (Del Santo et al., 2007). Since the EMG–force relationship of an intrinsic hand muscle was altered as a function of shoulder posture, the authors interpreted the results as a shift in the gain of the excitatory drive. Should similar principles hold following neurological impairment (e.g., stroke or spinal cord injury), then identifying postures in which a specific muscle is more excitable could aid targeted relearning. For example, the supinated forearm orientation would be expected to reduce the effort to recruit the BIC, facilitating muscle access following paresis or tendon transfer surgery (e.g., BIC-TRI). Alternatively, the desire to more selectively activate the brachialis and/or brachioradialis might be assisted by training in a posture where access to the BIC becomes relatively suppressed (i.e., pronated forearm). Based on interpreted differences in TMS-evoked responses between individuals following cortical and subcortical stroke (Renner et al., 2006), the precise nature of impairment is likely to impact the potential to modulate excitability via posture, as a strategy to facilitate motor retraining.

In summary, we evaluated the influence of multi-joint changes in static upper limb posture on the overall excitability of the motor pathways leading to the PD and BIC muscles. The MEP amplitudes recorded in both target muscles modulated according to the position and orientation of the upper limb, but not necessarily in a manner consistent with posture-related changes in muscle length. Moreover, our results provided evidence of centrally-mediated changes in motor pathway excitability. Consequently, the appropriate selection of upper limb posture may prove beneficial in rehabilitation environments to help selectively modulate the relative accessibility of specific muscles, and thus retrain motor control.

Acknowledgments

Many thanks to Vikram Darbhe for his invaluable assistance with the design and construction of the arm support apparatus, as well as for his help during data collection. This work was supported by the Craig H. Neilsen Foundation (84054).

References

- Barbero M, Merletti R, Rainoldi A. Atlas of muscle innervation zones. Understanding surface electromyography and its applications. Milan: Springer-Verlag Italia; 2012.
- Burke D, Gandevia SC, Macefield G. Responses to passive movement of receptors in joint, skin and muscle of the human hand. *J Physiol* 1988;402:347–61.
- DeFreitas JM, Costa PB, Ryan ED, Herda TJ, Cramer JT, Beck TW. Innervation zone location of the biceps brachii, a comparison between genders and correlation with anthropometric measurements. *J Electromyogr Kinesiol* 2010;20:76–80.
- Del Santo F, Gelli F, Ginanneschi F, Popa T, Rossi A. Relation between isometric muscle force and surface EMG in intrinsic hand muscles as function of the arm geometry. *Brain Res* 2007;1163:79–85.
- Dominici F, Popa T, Ginanneschi F, Mazzocchio R, Rossi A. Cortico-motoneuronal output to intrinsic hand muscles is differentially influenced by static changes in shoulder positions. *Exp Brain Res* 2005;164:500–4.
- Fortune E, Lowery MM. Effect of membrane properties on skeletal muscle fiber excitability: a sensitivity analysis. *Med Biol Eng Comput* 2012;50:617–29.
- Frigon A, Carroll TJ, Jones KE, Zehr EP, Collins DF. Ankle position and voluntary contraction alter maximal M waves in soleus and tibialis anterior. *Muscle Nerve* 2007;35:756–66.
- Gelli F, Del Santo F, Mazzocchio R, Rossi A. Force estimation processing as a function of the input–output relationship of the corticospinal pathway in humans. *Eur J Neurosci* 2005;22:1127–34.
- Ginanneschi F, Del Santo F, Dominici F, Gelli F, Mazzocchio R, Rossi A. Changes in corticomotor excitability of hand muscles in relation to static shoulder positions. *Exp Brain Res* 2005;161:374–82.
- Ginanneschi F, Dominici F, Biasella A, Gelli F, Rossi A. Changes in corticomotor excitability of forearm muscles in relation to static shoulder positions. *Brain Res* 2006;1073–1074:332–8.
- Hashimoto S, Kawamura J, Segawa Y, Harada Y, Hanakawa T, Osaki Y. Waveform changes of compound muscle action potential (CMAP) with muscle length. *J Neurol Sci* 1994;124:21–4.
- Hedeker D, Gibbons RD. Longitudinal data analysis. Hoboken: John Wiley & Sons, Inc.; 2006.
- Holzbaur KR, Murray WM, Delp SL. A model of the upper extremity for simulating musculoskeletal surgery and analyzing neuromuscular control. *Ann Biomed Eng* 2005;33:829–40.
- Hyingstrom AS, Johnson MD, Miller JF, Heckman CJ. Intrinsic electrical properties of spinal motoneurons vary with joint angle. *Nat Neurosci* 2007;10:363–9.
- Johanson ME, Hentz VR, Smaby N, Murray WM. Activation of brachioradialis muscles transferred to restore lateral pinch in tetraplegia. *J Hand Surg [Am]* 2006;31A:747–53.
- Johanson ME, Murray WM, Hentz VR. Comparison of wrist and elbow stabilization following pinch reconstruction in tetraplegia. *J Hand Surg [Am]* 2011;36:480–5.
- Katz R, Mazzocchio R, Penicaud A, Rossi A. Distribution of recurrent inhibition in the human upper limb. *Acta Physiol Scand* 1993;149:183–98.
- Knikou M, Rymer Z. Effects of changes in hip joint angle on H-reflex excitability in humans. *Exp Brain Res* 2002;143:149–59.
- Lackner E, Hummelsheim H. Motor-evoked potentials are facilitated during perceptual identification of hand position in healthy subjects and stroke patients. *Clin Rehabil* 2003;17:648–55.
- Langenderfer J, Jerabek SA, Thangamani VB, Kuhn JE, Hughes RE. Musculoskeletal parameters of muscles crossing the shoulder and elbow and the effect of sarcomere length sample size on estimation of optimal muscle length. *Clin Biomech (Bristol, Avon)* 2004;19:664–70.
- Lateva ZC, McGill KC, Burgar CG. Anatomical and electrophysiological determinants of the human thenar compound muscle action potential. *Muscle Nerve* 1996;19:1457–68.
- Leclercq C, Hentz VR, Kozin SH, Mulcahey MJ. Reconstruction of elbow extension. *Hand Clin* 2008;24:185–201. vi.
- Lewis GN, Byblow WD, Carson RG. Phasic modulation of corticomotor excitability during passive movement of the upper limb: effects of movement frequency and muscle specificity. *Brain Res* 2001;900:282–94.
- Liepert J, Schwenkreis P, Tegenthoff M, Malin JP. The glutamate antagonist riluzole suppresses intracortical facilitation. *J Neural Transm* 1997;104:1207–14.
- Mesin L, Joubert M, Hanekom T, Merletti R, Farina D. A finite element model for describing the effect of muscle shortening on surface EMG. *IEEE Trans Biomed Eng* 2006;53:593–600.
- Mesin L, Merletti R, Rainoldi A. Surface EMG: the issue of electrode location. *J Electromyogr Kinesiol* 2009;19:719–26.
- Mitsuhashi K, Seki K, Akamatsu C, Handa Y. Modulation of excitability in the cerebral cortex projecting to upper extremity muscles by rotational positioning of the forearm. *Tohoku J Exp Med* 2007;212:221–8.
- Mulcahey MJ, Lutz C, Kozin SH, Betz RR. Prospective evaluation of biceps to triceps and deltoid to triceps for elbow extension in tetraplegia. *J Hand Surg [Am]* 2003;28:964–71.
- Murray WM, Delp SL, Buchanan TS. Variation of muscle moment arms with elbow and forearm position. *J Biomech* 1995;28:513–25.
- Naito A. Electrophysiological studies of muscles in the human upper limb: the biceps brachii. *Anat Sci Int* 2004;79:11–20.

- Pomianowski S, O'Driscoll SW, Neale PG, Park MJ, Morrey BF, An KN. The effect of forearm rotation on laxity and stability of the elbow. *Clin Biomech (Bristol, Avon)* 2001;16:401–7.
- Rainoldi A, Nazzaro M, Merletti R, Farina D, Caruso I, Gaudenti S. Geometrical factors in surface EMG of the vastus medialis and lateralis muscles. *J Electromyogr Kinesiol* 2000;10:327–36.
- Renner CI, Woldag H, Hummelsheim H. Central compensation at short muscle range is differentially affected in cortical versus subcortical strokes. *Stroke* 2006;37:2076–80.
- Todd G, Butler JE, Gandevia SC, Taylor JL. Decreased input to the motor cortex increases motor cortical excitability. *Clin Neurophysiol* 2006;117:2496–503.
- van Dijk JP, Lowery MM, Lapatki BG, Stegeman DF. Evidence of potential averaging over the finite surface of a bioelectric surface electrode. *Ann Biomed Eng* 2009;37:1141–51.
- Ziemann U, Lonnecker S, Steinhoff BJ, Paulus W. The effect of lorazepam on the motor cortical excitability in man. *Exp Brain Res* 1996;109:127–35.