Corticospinal excitability of the biceps brachii is higher during arm cycling than an intensity-matched tonic contraction

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Forman D, Raj A, Button DC, Power KE. Corticospinal excitability of the biceps brachii is higher during arm cycling than an intensity-matched tonic contraction. J Neurophysiol 112: 1142–1151, 2014. First published June 4, 2014; doi:10.1152/jn.00210.2014.—Human studies have not assessed corticospinal excitability of an upper-limb prime mover during arm cycling. The purpose of the present study was to determine whether supraspinal and/or spinal motoneuron excitability of the biceps brachii was different between arm cycling and an intensity-matched tonic contraction. We hypothesized that spinal motoneuron excitability would be higher during arm cycling than an intensity-matched tonic contraction. Supraspinal and spinal motoneuron excitability were assessed using transcranial magnetic stimulation (TMS) of the motor cortex and transmastoid electrical stimulation (TMES) of the corticospinal tract, respectively. TMS-induced motor-evoked potentials (MEPs) and TMES-induced cervicomedullary-evoked potentials (CMEPs) were assessed at three separate positions (3, 6, and 12 o’clock relative to a clock face) during arm cycling and an intensity-matched tonic contraction. MEP amplitudes were 7.2 and 8.8% maximum amplitude of the compound muscle action potential (Mmax) larger during arm cycling compared with a tonic contraction at the 3 (P < 0.001) and 6 o’clock (P < 0.001) positions, respectively. There was no difference between tasks during elbow extension (12 o’clock). CMEP amplitudes were 5.2% Mmax larger during arm cycling compared with a tonic contraction at the 3 o’clock position (P < 0.001) with no differences seen at midflexion (6 o’clock) or extension (12 o’clock). The data indicate an increase in the excitability of corticospinal neurons, which ultimately project to biceps brachii during the elbow flexion portion of arm cycling, and increased spinal motoneuron excitability at the onset of elbow flexion during arm cycling. We conclude that supraspinal and spinal motoneuron excitability are phase- and task-dependent.

motoneuron; transmastoid; transcranial

RHYTHMIC AND ALTERNATING MOTOR outputs, such as locomotion, are initiated via descending commands (Jordan et al. 2008) that enhance the excitability of spinal interneurons, thereby causing the central pattern generator (CPG; Grillner 1981; Jordan 1998) to oscillate and recruit spinal motoneurons. Occurring simultaneously with CPG operation is a drastic reorganization of intraspinal excitability, including modulation of spinal reflex pathways and changes in the presynaptic regulation of sensory transmission and interneuronal excitability. Essentially, a new functional locomotor “state” is created within the spinal cord compared with rest. Ultimately, however, it is the spinal motoneuron that must transform all inputs from descending, sensory, and spinal circuitry into action potentials to produce movement. In the adult decerebrate cat, the “excitability” of spinal motoneurons is enhanced before and throughout locomotor tasks via a reconfiguration of their intrinsic electrical properties (Brownstone et al. 1992, 1994; Krawitz et al. 2001; Power et al. 2010). For example, during fictive locomotion and scratch, motoneurons are characterized by a decreased rheobase current (Krawitz et al. 2001; Power et al. 2010), reduced afterhyperpolarization (AHP) amplitude (Brownstone et al. 1992; Power et al. 2010), the emergence of intrinsic voltage-dependent depolarizations (Brownstone et al. 1994; Power et al. 2010), and hyperpolarization of the voltage threshold (VT_H) for action potential initiation (Krawitz et al. 2001; Power et al. 2010). Importantly, these state-dependent changes in motoneuron excitability are also “task-dependent.” We (Power et al. 2010) previously examined the excitability of the same motoneuron during two different motor outputs in the adult decerebrate cat: rhythmic scratching and stance, a tonic motor output. We demonstrated that when a motoneuron was engaged in rhythmic scratching, the VT_H hyperpolarized and the AHP was reduced. When the same motoneuron was active during stance, the VT_H depolarized and the AHP amplitude was unchanged. This suggests that there are different neural control mechanisms regulating spinal motoneuron excitability between scratch and stance in the cat.

In humans, it is well-known that central nervous system excitability is modulated during rhythmic and alternating motor outputs. Furthermore, indirect evidence from studies examining corticospinal excitability (Capaday et al. 1999; Carroll et al. 2006; Pyndt and Nielsen 2003), interlimb coordination (Zehr et al. 2009), and spinal reflexes (Zehr and Stein 1999) in humans indicates that a spinal CPG likely contributes to the production of rhythmic and alternating motor outputs, such as locomotion and cycling, as it does in quadrupeds. The majority of studies involving assessment of nervous system excitability during locomotor tasks in humans tend to focus on the modulation of supraspinal and/or spinal reflex excitability. For example, in the lower limb, Capaday et al. (1999) demonstrated that transcranial magnetic stimulation (TMS)-induced motor-evoked potentials (MEPs) in the soleus were smaller during the stance phase of locomotion compared with an intensity-matched tonic contraction, whereas the tibialis anterior showed larger MEPs in the same period. They suggested that cortical input was less to the soleus during walking compared with a tonic contraction, whereas the opposite occurred for the tibialis anterior. In the upper limb, Carroll and colleagues (2006) showed a decrease in corticospinal excitabil-
ity (i.e., decreased MEP amplitude) during the flexion phase of rhythmic arm movement and a subthreshold TMS-evoked facilitation of spinal reflexes during tonic contraction but not arm cycling. They concluded that a spinal CPG was likely involved in the production of arm cycling. It is presently unclear, however, whether the observed changes in TMS-evoked MEPs and/H-reflex excitability in these studies could be partially explained by changes in the excitability of the final common path, the spinal motoneuron.

Only one study has assessed both supraspinal excitability and spinal motoneuron excitability during a rhythmic and alternating motor output in humans (Sidhu et al. 2012). Since TMS-evoked MEPs can be influenced by changes in cortical and spinal motoneurons, Sidhu and colleagues (2012) used TMS and transmastoid electrical stimulation (TMES) to assess supraspinal excitability and spinal excitability, respectively, of the knee extensors during leg cycling. TMES directly activates the corticospinal axons producing cervicomedullary motor-evoked potentials (i.e., CMEPs) that are independent of changes in supraspinal excitability (Taylor et al. 2002) and are thought to be an effective way to assess spinal motoneuron excitability (McNeil et al. 2013). Sidhu and colleagues (2012) demonstrated that the activation of inhibitory interneurons in the cortex via subthreshold TMS stimulation intensities led to suppression of the electromyogram (EMG) during cycling. They also demonstrated that both MEPs and CMEPs were modulated similarly across all phases of cycling, with MEPs mainly driven by changes at the spinal level. Based on these findings, they concluded that supraspinal centers were directly involved in the generation of cycling and that spinal factors dominated the phase-dependent modulation of corticospinal excitability. They did not compare CMEPs during cycling to CMEPs during an intensity-matched tonic contraction, however, thus it is unclear whether the observed changes in CMEPs were cycling-dependent.

To date, human studies have not assessed supraspinal excitability and/or spinal motoneuron excitability of an upper-limb prime mover during a rhythmic and alternating, cyclical motor output (i.e., arm cycling). Thus the primary objective of the present study was to determine whether corticospinal excitability of the biceps brachii was different during arm cycling compared with an intensity-matched tonic contraction and, if so, to determine whether the observed differences were due to supraspinal and/or spinal mechanisms. We chose to compare these two motor outputs given that the generation of the basic rhythmic and alternating pattern of muscle activity during arm cycling is generated, in part, by spinal interneuronal networks (Zehr et al. 2004). Tonic activation of a key muscle involved in arm cycling (i.e., biceps brachii) was chosen to represent a similar level of motoneuron pool activation but with reduced or absent activation of spinal interneuronal groups contributing to the generation of rhythmic activation during arm cycling. A second objective that arose from the results of our primary study was to determine whether biceps brachii motoneuron excitability was enhanced during the extension phase of arm cycling compared with rest. We hypothesized that 1) supraspinal excitability of the biceps brachii would be lower and spinal motoneuron excitability higher during arm cycling compared with an intensity-matched tonic contraction (experiment 1), and 2) motoneuron excitability would be increased during the extension phase of arm cycling compared with rest (experiment 2).

**METHODS**

**Ethical Approval**

Participants were verbally informed of the procedures and gave informed, written consent to participate in the study. The study conformed to the standards set by the latest revision of the Declaration of Helsinki, and the experimental procedures were approved by the Research Ethics Board at the University of Ontario Institute of Technology (REB# 12-008) and at Memorial University of Newfoundland (ICEHR# 20140358-HK). Experiments were in accordance with the Tri-Council guideline in Canada with full disclosure of potential risks to participants.

**Participants**

Eleven male volunteers (20–23 yr of age) with no known neurological deficits participated in experiment 1. Four separate male volunteers participated in experiment 2 (20–22 yr of age). Before the experiments, all participants completed a magnetic stimulation safety checklist designed to screen for potential contraindications with magnetic stimulation procedures (Rossi et al. 2009).

**Experimental Setup**

The two motor tasks, cycling and tonic contraction (described below), were performed using an arm cycle ergometer (Monark Rehab Trainer, model 881E) mounted on a table (Fig. 1). Participants were instructed to sit upright at a comfortable distance from the ergometer so that when cycling trials began there was no variation in trunk posture (leaning forward or backward) and when the elbow was fully extended at the 3 o’clock position participants were not “reaching.” The participants were not restrained during cycling. The arm cranks were fixed 180° out of phase, and the center of the arm crank shaft was aligned at approximately shoulder height. Participants lightly gripped the ergometer handles with the forearms pronated and wore a brace on the right wrist for all trials to restrict movement of the joint during cycling given the heteronymous reflex connections between wrist flexors and extensors and the biceps brachii (Manning and Bawa 2011).

Crank positions were made relative to a clock face (12, 3, 6, and 9 o’clock, as viewed from the right) with the “top dead center” position of the crank arm defined as 12 o’clock and “bottom dead center” as 6 o’clock. The biceps brachii was the major muscle group of interest, and, as such, we employed terminology to describe the cycling movement based on elbow joint position. Thus elbow flexion was defined as movement from the 3 to the 9 o’clock position, while the hand was moving toward the body. Elbow extension was defined as movement from the 9 to the 3 o’clock position, while the hand was moving away from the body. For the cycling trials, participants were instructed to cycle at a constant power output of 25 W and a cadence of 60 rpm. Responses were evoked at three equidistant positions in the cycle (2, 3, and 6 o’clock). These positions were chosen to ensure that responses in the biceps brachii were evoked during the period of maximal and minimal EMG activity (6 and 12 o’clock, respectively) and just before the maximum EMG burst (3 o’clock). The timing of stimulation was determined by the position of the right arm crank. Responses were triggered automatically as the crank arm passed one of the three predetermined positions (i.e., 12, 3, and 6 o’clock). Each position was tested separately in its own trial, and the order was randomized across participants.
Brachial Plexus Stimulation

Resting $M_{\text{max}}$ of the biceps was first determined by eliciting M-waves by electrical stimulation of the brachial plexus at Erb’s point (200-μs duration, 50–250 mA) with a Digitimer stimulator (DS7AH; Digitimer, Welwyn Garden City, Hertfordshire, United Kingdom). The cathode was placed in the supraclavicular fossa and the anode over the acromion process. The electrical stimulation was gradually increased until the M-wave of the biceps brachii reached a plateau and there was noticeable elbow flexion. At this point, the stimulation intensity was increased by 20% to ensure maximal M-waves were elicited throughout the study. MEP and CMEP amplitudes were normalized to $M_{\text{max}}$ to account for changes in peripheral neuromuscular propagation (Taylor 2006).

TMS

The stimulation intensity for TMS was always performed following TMES because it was easier to match MEPs to CMEPs than vice versa. Stimulation was applied over the vertex using a circular coil (13.5-cm outside diameter) attached to a Magstim 200 (Magstim, Dyfed, United Kingdom). To locate vertex, the distances from nasion to inion and from tragus to tragus were measured, and marks were placed halfway directly on the scalp for both measurements. The intersection of both halfway marks was defined as vertex (Power and Copithorne 2013). The coil was held parallel to the floor with the direction of the current flow preferentially activating the left motor cortex. The coil was held firmly in place by the investigator, and care was taken to ensure the coil position was accurately aligned with the scalp marking during every trial. Stimulation intensity was then increased until the peak-to-peak amplitude of the MEP was matched to that of the CMEP (approximately 5–10% $M_{\text{max}}$). This intensity of magnetic stimulator output was then used for the remainder of the experiment.

TMES

Stimulation was applied via adhesive Ag-AgCl electrodes fixed to the skin slightly inferior to the mastoid processes and current passed between them (100-μs duration, 125–350 mA; model DS7AH; Digitimer). Stimulation intensity was increased until the CMEP peak-to-peak amplitude reached a value of approximately 5–10% of the peak-to-peak amplitude of the participant’s $M_{\text{max}}$. This intensity of stimulator output was then used for the remainder of the experiment.

We were confident that the corticospinal tract and not the ventral roots recorded during an isometric elbow flexion contraction (see below). All participants had prior experience with TMS, TMES, and Erb’s point stimulation procedures (see below).

Before setting the stimulation intensities for TMS and TMES, the maximum EMG of the biceps brachii was determined by having participants cycle for 1 min at a workload of 75 W and a cadence of 60 rpm. The maximum EMG activity was determined by averaging the root-mean-square (rms) amplitudes of the middle six EMG bursts during the 60-s trial. Participants next sat in an upright position with hips, knees, and elbow flexed at 90° and the upper arm supported on a table. The wrist of the right arm was then inserted into a padded strap attached by a high-tension wire to force transducer. Participants were then required to produce an isometric elbow flexion force equal to 20% of the maximum cycling rectified EMG determined in the previous step. This was ensured by having the participants match their biceps brachii EMG to a horizontal line placed on a computer screen. During this intensity of contraction, the stimulation intensities required for TMS and TMES to produce evoked potentials with peak-to-peak amplitudes of approximately 5–10% of $M_{\text{max}}$ were determined. These stimulation intensities were then used for the remainder of the study.

Brachial Plexus Stimulation

Motor responses from the biceps brachii were elicited via 1) brachial plexus electrical stimulation at Erb’s point, 2) TMS, and 3) TMES. TMS and TMES stimulation intensities were set to match the peak-to-peak amplitudes of the resulting MEPs and CMEPs, respectively, to approximately 5–10% of the maximal M-wave ($M_{\text{max}}$).
were stimulated because the latency of the CMEP was typically 4–5 ms shorter than the MEP latency and ~4 ms longer than the maximal M-wave latency.

Experiment 1: Corticospinal Changes During Arm Cycling and Tonic Contractions

Once the TMS and TMES intensities were determined, participants were instructed to relax their arms (hands off of the pedals), and their resting MEP and CMEP amplitude values were assessed. The participants were then repositioned in front of the arm cycle ergometer. While cycling at 25 W and maintaining 60 rpm, each participant was tested at each of the three positions using the three different forms of stimulation. A total of 10 MEPs, 10 CMEPs, and 5 M-waves were delivered at each position. To prevent anticipation of the stimulation, an additional 10 frames without stimulation were added for the MEP and CMEP trials and an additional 5 frames for M-wave. Participants cycled continuously and received stimulation in 50% of the trials, which were pseudorandomized and evoked every 5–10 s. Because \( M_{\text{max}} \) is muscle length dependent (Simonsen and Dyhre-Poulsen 1999) and may change over the course of an experiment (Crone et al. 1999), all \( M_{\text{max}} \) measurements to which MEPs and CMEPs were normalized were made at the same muscle length and at the same time during the experiments as the MEPs and CMEPs.

To compare corticospinal excitability between the two different tasks, it was vital that the intensity of the contractions be matched as closely as possible given the large influence of contraction intensity on evoked potentials. To accomplish this, the average background \( \text{rmsEMG} \) of the biceps brachii from 50 to 0 ms before stimulation at each of the three positions during cycling was assessed as an indication of contraction intensity. EMG was measured before the stimulation to avoid the stimulation artifact. The average prestimulus \( \text{rmsEMG} \) at the selected position was then rectified and displayed on a computer screen via a horizontal line. With the arm crank set at the position corresponding to the cycling trial, the participant was then required to produce a tonic contraction whereby the \( \text{EMG} \) produced in the biceps brachii was equal to the horizontal line displayed on the screen, as was done in Carroll et al. (2006) and Pyndt and Nielsen (2003). During the tonic contractions, the pedals were locked in place, and the participants were instructed to flex at the elbow for the 3 and 6 o’clock positions and to extend at the 12 o’clock position to simulate further the cycling condition. The number of stimulations was the same as that during cycling.

Experiment 2: Spinal Motoneuron Excitability of the Biceps Brachii Using Different Stimulation Intensities At Rest and During the Extension Phase of Arm Cycling

We next compared the effects of varying stimulation intensities on CMEP amplitudes during rest and arm cycling \((n = 4)\). A total of three stimulation intensities were used: CMEP threshold (T), maximum CMEP (Max), and half-maximum CMEP (½ Max). T was defined as the lowest stimulator output that resulted in a CMEP of \( 50 \mu \text{V} \) in \( \geq 50\% \) of trials. For Max, the stimulation intensity was continually increased until the peak-to-peak amplitude plateaued or there was a decrease in the onset latency, indicative of cervical ventral root stimulation rather than the desired corticospinal tract (Taylor and Gandevia 2004). If the latter occurred, the stimulation intensity was decreased until the appropriate onset latency was restored. Finally, \( \frac{1}{2} \) Max was defined as the stimulator intensity required to make CMEP amplitude equal to \( \sim 50\% \) of maximum CMEP. Once the stimulation intensities were determined, the trials began in which all subsequent measurements were recorded with the arm at the 12 o’clock position: 1) rest, 2) 60 rpm, and 3) 90 rpm. The selected cycling velocities were chosen because 60 rpm was used in a similar study (Carroll et al. 2006) and 90 rpm has been used in an incremental test to maximum to assess physiological measures such as peak oxygen consumption (Price et al. 2007). All three stimulation intensities were given during each trial. The trial order and stimulation intensities were randomized.

For the resting condition, a total of 10 CMEPs were elicited for each of the T and \( \frac{1}{2} \) Max stimulation intensities every 8–10 s. For Max stimulations, 5 CMEPs instead of 10 were performed as has been done by others (Taylor et al. 2002) because the stimulation intensities used for Max CMEPs were less variable in amplitude and transiently painful. For the two cycling tasks, CMEPs were elicited automatically when the right hand pedal passed the 12 o’clock position.

Measurements

Data were analyzed offline using Signal 4 software. Measurements of magnetic and electrical responses included the peak-to-peak amplitude and onset latency for MEPs, CMEPs, and M-waves. Peak-to-peak amplitudes for all potentials in all subjects elicited in the biceps brachii were assessed from the initial deflection of the voltage trace from baseline to its third crossing point on the horizontal axis. Changes in MEP and/or CMEP amplitude or latency could be due to changes at the peripheral level, i.e., muscle. Thus MEPs and CMEPs were normalized to \( M_{\text{max}} \). The latency of evoked response onset was defined as the time between the stimulation artifact and the point at which the voltage trace became tangent to a straight line drawn along the horizontal voltage trace at baseline. Measurements for latency were taken from the averaged unrectified traces for each type of response. In experiment 1, the rectified, prestimulus EMG (50 ms) was averaged for each of the trials. All data for cycling and tonic contraction conditions and for each experiment were analyzed in the same manner.

Statistics

Experiment 1. A two-way (task × position) repeated-measures ANOVA was used to determine whether statistically significant differences occurred in MEP, CMEP, and M-wave amplitudes and the average of the prestimulus EMG between the three cycling and tonic positions. Separate paired \( t \)-tests were used to determine changes in excitability for each arm position between arm cycling and intensity-matched tonic contraction. All tests were performed on grouped data. For all comparisons, a significance level of \( P < 0.05 \) was used. Group data are reported as means ± SD and shown as ± SE in the figures.

Experiment 2. A two-way (condition × stimulation intensity) repeated-measures ANOVA was used to determine whether statistically significant differences occurred in CMEP amplitudes and the average of the prestimulus EMG between the three conditions (12 o’clock rest and 60 and 90 rpm). Separate paired \( t \)-tests were used to determine changes in excitability for each condition. All tests were performed on grouped data. Additional participants were not recruited given the convincing findings obtained (see RESULTS).

All data for both experiments were analyzed using IBM SPSS Statistics Version 19. For all comparisons, a significance level of \( P < 0.05 \) was used. Group data are reported as means ± SD and shown as means ± SE in the figures.

RESULTS

Experiment 1: Corticospinal Excitability Changes During Arm Cycling and Tonic Contractions

\( \text{EMG} \) patterns of the biceps brachii during arm cycling. Average values of cycling EMG from all subjects during arm cycling are plotted in Fig. 1B. Averages were calculated from files that did not involve stimulation. This was done for all positions, which were made relative to a clock face. The values for each individual were expressed as a percentage of their
maximum biceps brachii EMG recorded during the maximum cycling trial.

Corticospinal Excitability

**MEPs.** The TMS stimulation intensities used to evoke MEPs equal to approximately 5–10% of M<sub>max</sub> are influenced by a range of both excitatory and inhibitory circuits at the cortical and spinal levels and provide information regarding excitability of the corticospinal pathway. Figure 2, left column, shows an example of the differences in MEP amplitude between cycling and tonic tasks at each of the three positions assessed. The left column shows MEPs. In this example, MEPs expressed as a percentage of M<sub>max</sub> were 1.8, 7.0, and 44.2% during cycling and 0.6, 1.0, and 22.7% during tonic contraction. As a group, MEP amplitudes were 7.2 and 8.8% M<sub>max</sub> larger during arm cycling compared with a tonic contraction at the 3 (cycle, 9.8 ± 1.6% M<sub>max</sub>; tonic, 2.6 ± 0.7% M<sub>max</sub>; P < 0.001) and 6 o’clock (cycle, 29.7 ± 4.0% M<sub>max</sub>; tonic, 20.9 ± 2.6% M<sub>max</sub>; P < 0.001) positions (Fig. 3A). These positions correspond to the end of extension/initiation of flexion (3 o’clock) and midflexion (6 o’clock) phases of arm cycling. There was no difference in MEP amplitude between cycling and tonic conditions when the arm was extending at the 12 o’clock position (cycle, 0.75 ± 0.22% M<sub>max</sub>; tonic, 0.41 ± 0.15% M<sub>max</sub>; P = 0.25). TMS intensity was the same for arm cycling and tonic conditions for each subject. MEPs were normalized to M-wave for statistical comparisons.

**Background EMG.** There was no difference in the background EMG of the biceps brachii between the tasks at any of the three positions assessed (P = 0.21). In contrast, the background EMG of the triceps brachii was significantly larger during cycling at the 12 o’clock position (P < 0.001) and during the tonic contraction at the 6 o’clock position (P < 0.001). There was a trend toward significantly higher triceps brachii EMG during the tonic contraction at the 3 o’clock position (P = 0.059). See Fig. 3, B and C, for prestimulus group data.

![Fig. 2. Average motor-evoked potential (MEP) and cervicomedullary MEP (CMEP) traces after 10 stimuli during arm cycling (solid black lines) and tonic contraction (dashed gray lines) at each of the 3 arm positions (12, 3, and 6 o’clock) from 1 participant. M<sub>max</sub>, maximum amplitude of the compound muscle action potential.](image1)

![Fig. 3. Group data (means ± SE, n = 11) for MEP amplitude (A) and prestimulus EMG of the biceps brachii (B) and triceps brachii (C) during arm cycling (black bars) and tonic contraction (white bars) at each of the 3 arm crank positions (12, 3, and 6 o’clock). MEP amplitudes are expressed relative to M<sub>max</sub> amplitudes at the same arm crank position. Prestimulus EMG is expressed relative to the maximum EMG obtained during the maximum cycle test. Asterisks indicate a significant difference (P < 0.001) between the arm cycling and tonic contraction conditions.](image2)
Spinal Motoneuron Excitability

CMEPs. Because changes in MEP amplitude could represent changes at the supraspinal and/or spinal level, we examined spinal changes in excitability using the TMES technique (see METHODS). Figure 2, right column, shows an example of the differences in CMEP amplitude between cycling and tonic tasks at each of the three positions assessed. In this example, CMEPs expressed as a percentage of $M_{\text{max}}$ were 2.4, 13.2, and 50.4% during cycling and 5.5, 1.7, and 38.1% during tonic contraction. As a group, CMEP amplitudes were 5.2% $M_{\text{max}}$ larger during arm cycling compared with a tonic contraction at the 3 o’clock position (cycle, 9.3 ± 1.9% $M_{\text{max}}$; tonic, 4.1 ± 0.9% $M_{\text{max}}$; $P < 0.001$; Fig. 4A). This position corresponds to the end of extension/initiation of the flexion phase of arm cycling. There was no difference in CMEP amplitude between cycling and tonic conditions when the arm was in midflexion at the 6 o’clock position (cycle, 19.4 ± 4.5% $M_{\text{max}}$; tonic, 18.4 ± 3.8% $M_{\text{max}}$; $P = 0.73$) or during the extension phase at the 12 o’clock position (cycle, 1.3 ± 0.4% $M_{\text{max}}$; tonic, 2.2 ± 0.6% $M_{\text{max}}$; $P = 0.10$). TMES intensity was the same for arm cycling and tonic conditions for each subject. Data for each condition were an average of 10 frames. As was done with MEPs (see above), CMEPs were normalized to M-wave for statistical comparisons.

Background EMG. There was no difference in the background EMG of the biceps brachii between the tasks at any of the three positions assessed ($P = 0.35$). In contrast, the background EMG of the triceps brachii was significantly larger during the tonic contractions at the 3 ($P = 0.004$) and 6 o’clock ($P < 0.001$) positions. See Fig. 4, B and C, for prestimulus group data.

Background EMG of Biceps Brachii and Triceps Brachii Between Stimulation Paradigms

Cycling. There was no difference in the background EMG for either biceps brachii or triceps brachii when comparing the background EMG within the cycling task between stimulation paradigms (i.e., TMS and TMES; biceps brachii: $P = 0.41$; triceps brachii: $P = 0.17$).

Tonic contraction. There was no difference in the background EMG for either biceps brachii or triceps brachii when comparing the background EMG within the cycling task between stimulation paradigms (i.e., TMS and TMES; biceps brachii: $P = 0.43$; triceps brachii: $P = 0.32$).

Experiment 2: Spinal Motoneuron Excitability of the Biceps Brachii During the Extension Phase of Arm Cycling

CMEPs. The amplitudes of the CMEPs were assessed using three different stimulation intensities (T, ½ Max, and Max) with the arm at the 12 o’clock position at rest and while cycling at both 60 and 90 rpm. Data for each condition was an average of 10 frames. As was done with MEPs (see above), CMEPs were normalized to M-wave for statistical comparisons. Figure 5 shows an example of the differences in CMEP amplitude between the resting and two cycling tasks at each of the three stimulation intensities. In this example, CMEPs expressed as a percentage of $M_{\text{max}}$ were 3.5, 2.3, and 0.7% at T stimulation, 37.5, 9.1, and 4% at ½ Max stimulation, and 60.4, 29.3, and 21.1% at Max stimulation. In Fig. 6, CMEP amplitudes increased as the stimulation intensity increased for each of the three conditions, as expected. CMEP amplitudes were smaller for all three stimulating intensities during both cycling conditions compared with rest ($P = 0.001$). T CMEPs taken at rest were 37 and 135% larger than T CMEPs taken during cycling at 60 ($P = 0.04$) and 90 ($P = 0.03$) rpm, respectively. ½ Max CMEPs during rest were 319 and 420% larger than ½ Max CMEPs measured while cycling at 60 ($P = 0.01$) and 90 ($P =
The Max stimulation resulted in resting amplitudes that were 117 and 135% greater than the amplitudes seen during cycling at 60 (P = 0.02) and 90 (P = 0.03) rpm, respectively. There were no differences in CMEP amplitudes between cycling at 60 and 90 rpm for any of the three stimulation intensities used (T, P = 0.1; ½ Max, P = 0.25; and Max, P = 0.38).

We initially compared CMEPs with each of the three stimulation intensities during two resting conditions: 1) rest with the hand pronated and resting on the participant’s leg, and 2) rest at the 12 o’clock position as described above. Neither CMEP amplitudes nor the prestimulation EMG (as described in experiment 1) of the biceps brachii were different between the resting conditions (P = 0.88 and P = 0.37, respectively; data not shown). Because of the similarities of background EMG and CMEP amplitudes between the resting conditions, we are reasonably confident that at the 12 o’clock position the arm was at rest. For clarity of results, we only present the rest at 12 o’clock data so as to compare only CMEPs at the same joint position between conditions (rest and cycling at 60 and/or 90 rpm).

**DISCUSSION**

This report is the first to show that corticospinal excitability of an upper-limb prime mover, the biceps brachii, is higher during arm cycling than an intensity-matched tonic contraction and that enhanced spinal motoneuron excitability can partially account for this finding. The results from experiment 2 indicate that spinal motoneuron excitability of the biceps brachii is not increased during the extension phase of arm cycling compared with rest at the same position.

**Increased Supraspinal Excitability During Arm Cycling**

In the present study, corticospinal excitability of the biceps brachii was significantly greater at the initiation (i.e., 3 o’clock) and middle (i.e., 6 o’clock) of elbow flexion during arm cycling compared with tonic contraction, as demonstrated via larger MEP amplitudes (Figs. 2 and 3). There was no difference in spinal excitability at the 6 o’clock position (Fig. 4A) between tasks, indicating that the increased MEP amplitude was mediated via changes at the supraspinal level. Corticospinal excitability of the arms during arm cycling has been previously investigated, however. Zehr and colleagues (Carroll et al. 2006) demonstrated a decrease in corticospinal excitability during the flexion phase of arm cycling in the flexor carpi radialis (FCR) accompanied by a decrease in the H-reflex amplitude. This led to the conclusion that during arm cycling there is a suppression of excitatory drive from descending and peripheral pathways to the wrist flexors. Differences between our data and those of Carroll et al. (2006) may be related to muscle function during arm cycling. The main role of the FCR muscle during arm cycling is to stabilize the wrist to allow for a steady grip of the crank handles, which means that the FCR is continuously active during cycling with relatively minor phase-dependent activation changes and no strong propulsive
phase (see Figs. 3C and 4C in Carroll et al. 2006). In contrast, the biceps brachii demonstrates strong phase dependence and propulsive activation during arm cycling (Fig. 1B).

Although different from the results of Carroll et al. (2006), our results are in line with those of Pyndt and Nielsen (2003), who demonstrated an increase in MEP amplitude of the soleus during the propulsion phase of leg cycling. As is the case for the biceps brachii, the soleus is considered a main power producer during cycling (Hug and Dorel 2009). We thus suggest, as did Pyndt and Nielsen (2003), that the increased MEP observed in the present study was due to enhanced excitability of the cortical neurons projecting to the spinal cord, thus making them more susceptible to activation via TMS. This increased descending drive to the spinal motor pools would perhaps be necessary to increase the recruitment and firing rate of spinal motoneurons to ensure adequate muscle activation and power production are obtained during the propulsive phase. Intermuscle differences in corticospinal excitability as measured via TMS-induced MEPs have been previously reported in the ankle muscles during locomotion (Capaday et al. 1999; Sidhu et al. 2012). Capaday and colleagues (1999) showed that soleus MEPs were smaller during stance compared with an intensity-matched tonic contraction, whereas tibialis anterior MEPs were larger.

Increased Spinal Excitability During Arm Cycling

Changes in MEP amplitude can result from changes in neuronal excitability at supraspinal and/or spinal locations. Thus an alternative explanation for the increase in supraspinal excitability at 3 and 6 o’clock during cycling relative to the tonic contraction is an increase in spinal excitability. We thus employed TMES (see METHODS) to assess spinal excitability. Collision experiments have shown that TMES directly activates the corticospinal axons (Gandevia et al. 1999), producing CMEPs that are independent of changes in supraspinal excitability (Taylor et al. 2002), have a large monosynaptic component in biceps brachii motoneuron pool (Petersen et al. 2002), and are free from classic afferent-mediated presynaptic inhibition (Nielsen and Petersen 1994). This technique was particularly important to the current study because one of our main objectives was to determine whether spinal motoneuron excitability was different between arm cycling and tonic contraction. This objective was based on our previous work (Power et al. 2010), which showed that the excitability of the same spinal motoneuron was higher during rhythmic scratch compared with stance in the adult decerebrate cat.

In the present study, we show that spinal motoneuron excitability was higher during arm cycling than an intensity-matched tonic contraction at the initiation of flexion (3 o’clock; Fig. 4A). Task-dependent changes in human motoneuron excitability have been reported using motor unit recordings during either isometric or isotonic contractions. Recruitment thresholds and firing patterns may vary depending on the direction (Thomas et al. 1987), velocity (Desmedt and Godaux 1977), and type (Tax et al. 1990) of contraction. Studies examining human spinal motoneuron excitability during rhythmic and alternating motor outputs thought to be partially generated by spinal CPGs are limited, mainly due to technical constraints. Sidhu and colleagues (2012) examined supraspinal and spinal excitability and concluded that changes in corticospinal excitability were driven mainly by changes at the spinal level. The authors did not discuss the potential spinal mechanisms responsible and were focused on determining the supraspinal and spinal contributions to leg cycling. As such, they did not compare spinal excitability between cycling and a tonic contraction. In the present study, it is possible that motoneuron excitability was higher during cycling even though the background EMG was similar. Background EMG is a crude measure of motoneuron excitability and does not take into account factors such as the activation of voltage-dependent excitation, which may be active in one task and not the other. This could lead to a nonlinear increase in the amplitude of evoked responses even with similar background EMG. However, it is important to recognize that although CMEP amplitudes do represent the excitability of the spinal motoneuron pool, they do not necessarily indicate changes in intrinsic electrical properties such as those observed in cat motoneurons during scratch (see Introduction). The motoneuron pool may have been relatively more excitable during arm cycling due to differences in the balance of excitatory and inhibitory synaptic inputs.

It would have been preferable to match the EMG activity in multiple motor pools between tasks to eliminate possible heteronomous influences. Triceps brachii activity, however, was higher during the tonic contraction at 3 and 6 o’clock during both MEP and CMEP recordings (Figs. 3C and 4C). Thus reciprocal inhibition may have reduced the amplitude of the evoked potentials during tonic contraction even though biceps brachii EMG was matched across tasks and positions. Because reciprocal inhibition affects motoneuron responsiveness, however, it would be expected that both MEPs and CMEPs would demonstrate a similar pattern of between-task modulation. However, MEPs were larger at the 3 and 6 o’clock positions during arm cycling, whereas CMEPs were larger only at the 3 o’clock position. If reciprocal inhibition were reducing motoneuron excitability during the tonic contraction, it would perhaps be expected that CMEPs would be smaller during tonic contraction at the 6 o’clock position as was the case with MEPs. This did not occur (Figs. 3 and 4). Differences between the pattern of MEP and CMEP modulation in the biceps brachii are not likely explained by differences in the degree of triceps brachii activity when comparing MEPs or CMEPs at 3 or 6 o’clock during tonic contraction given that the background EMG was similar. Regardless, we cannot conclude with certainty whether reciprocal inhibition contributed to the observed differences in the present study as it was not directly assessed.

Methodological Considerations

There are a number of other factors to consider in the interpretation of the present results.

A major difference between the motor outputs examined is that cycling involves limb movement, whereas tonic contraction does not. This leads to task-dependent changes in afferent feedback, which could affect both MEPs and CMEPs given that sensory feedback contributes significantly to muscle activity during movement (Nielsen 2004). For example, the muscle is rapidly elongated at the 3 o’clock position during cycling (Fig. 1B), likely activating Ia afferents, which could lead to increased excitatory input to the spinal motoneurons and thus increased MEP and CMEP amplitudes compared with the tonic contraction. Furthermore, as with previous studies...
Spinal Motoneuron Excitability of the Biceps Brachii is Greater At Rest Than During the Extension Phase of Arm Cycling

An additional question we posed and assessed via our second experiment (see METHODS) was, “is biceps brachii motoneuron excitability higher during the extension phase of arm cycling compared with rest?” This question was based on previous findings in the cat (Power et al. 2010). During the approach (flexion) phase of fictive scratch in the adult decerebrate cat, extensor motoneurones are tonically hyperpolarized (Power et al. 2010), whereas both flexor and extensor motoneurones receive reciprocal inhibitory input during the hyperpolarized phase of rhythmical scratch (i.e., when the antagonist is active; Geertsen et al. 2011). Interestingly, the state-dependent enhancement of spinal motoneuron excitability (i.e., hyperpolarized \( V_{\text{th}} \) and AHP suppression) occurred during the inhibitory phase despite these two inhibitory factors (Power et al. 2010). We thus expected, based on the results from the cat, that spinal motoneuron excitability of the biceps brachii would be increased during the extension phase of arm cycling (12 o’clock) relative to rest in experiment 1. This did not appear to be the case, so we furthered this question in experiment 2 (see METHODS) to determine whether motoneuron excitability of the biceps brachii was higher during the extension phase of arm cycling compared with rest, as it was in the cat. As noted in the cat study, even though motoneuron excitability was increased, an increase in intracellular current injection was required to make the cell fire, likely to overcome this background inhibition. In addition, Pyndt and Nielsen (2003) showed that reciprocal inhibition was reduced during lower limb cycling as the pedaling frequency increased. We thus reasoned that if we increased the TMES intensity and/or increased the pedaling frequency of arm cycling, we would see a large increase in CMEP amplitude during the extension phase of arm cycling (12 o’clock) compared with rest if similar changes in motoneuron excitability occurred as those that occurred in the cat. Our results indicate that even with a maximal TMES intensity and a 90 rpm pedaling velocity, spinal motoneurones were less responsive than at rest in the 12 o’clock position. It is concluded that spinal motoneuron excitability of the biceps brachii is not increased during the extension phase of arm cycling with an increase in pedaling frequency and is, in fact, reduced compared with rest.

Conclusion

Increased supraspinal excitability of the biceps brachii occurred during the flexion phase of arm cycling, whereas spinal motoneuron excitability was increased at the initiation of flexion, compared with an intensity-matched tonic contraction. Perhaps spinal motoneuron excitability is enhanced before the propulsive phase (6 o’clock) of the biceps brachii in an attempt to reduce the supraspinal input required to reach firing threshold. It is currently unclear whether the larger CMEP amplitude at the 3 o’clock position during cycling was due to intrinsic changes in spinal motoneuron excitability and/or differences in synaptic input. Our results from experiment 2 indicate that, unlike the cat, spinal motoneuron excitability of the biceps brachii is not increased during the extension phase of a rhythmic and alternating motor output compared with rest.

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