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Corticospinal Excitability Is Lower During Rhythmic Arm Movement Than During Tonic Contraction

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Carroll, Timothy J., Evan R. L. Baldwin, David F. Collins, and E. Paul Zehr. Corticospinal excitability is lower during rhythmic arm movement than during tonic contraction. *J Neurophysiol* 95: 914–921, 2006. First published October 26, 2005; doi:10.1152/jn.00684.2005. Humans perform rhythmic, locomotor movements with the arms and legs every day. Studies using reflexes to probe the functional role of the CNS suggest that spinal circuits are an important part of the neural control system for rhythmic arm cycling and walking. Here, by studying motor-evoked potentials (MEPs) in response to transcranial magnetic stimulation (TMS) of the motor cortex, and H-reflexes induced by electrical stimulation of peripheral nerves, we show a reduction in corticospinal excitability during rhythmic arm movement compared with tonic, voluntary contraction. Responses were compared between arm cycling and tonic contraction at four positions, while participants generated similar levels of muscle activity. Both H-reflexes and MEPs were significantly smaller during arm cycling than during tonic contraction at the midpoint of arm flexion ($F = 13.51$, $P = 0.006$; $F = 11.83$, $P = 0.009$). Subthreshold TMS significantly facilitated the FCR H-reflex during tonic contractions, but did not significantly modulate H-reflex amplitude during arm cycling. The data indicate a reduction in the responsiveness of cells constituting the fast, monosynaptic, corticospinal pathway during arm cycling and suggest that the motor cortex may contribute less to motor drive during rhythmic arm movement than during tonic, voluntary contraction. Our results are consistent with the idea that subcortical regions contribute to the control of rhythmic arm movements despite highly developed corticospinal projections to the human upper limb.

INTRODUCTION

Although there is detailed information about the regions within the CNS that regulate motor behavior in many species, there is an incomplete understanding of the extent to which cortical, subcortical, and spinal structures contribute to different movements in humans. Spinal networks known as central pattern generators (CPGs) play a major role in the production of rhythmic, stereotyped movements in many invertebrate and vertebrate species (Grillner 1981; Grillner and Dubuc 1988; Hill et al. 2003; Marder and Calabrese 1996; Yamaguchi 2004). In quadrupeds, CPGs generate the basic pattern of locomotor drive, which is modified to meet functional requirements by descending inputs and afferent information from sensory receptors (Barbeau and Rossignol 1994; Forssberg et al. 1977; Pearson et al. 1998). It has been proposed that a similar cooperation between CPG, afferent, and descending systems underlies the basic control of rhythmic activities in humans (e.g., Dietz 2002; Duysens and Van de Crommert 1998; Zehr and Duysens 2004a), despite the extensive corticospinal projections that exist in primates (Phillips and Porter 1977; Porter and Lemon 1993). Evidence for this proposal comes from studies on the movement capabilities of spinal cord–injured patients (e.g., Dietz and Harkema 2004; Fouad and Pearson 2004), and the striking similarities that exist between humans and quadrupeds in the regulation of spinal reflexes during locomotion (e.g., Zehr and Stein 1999).

The importance of spinal circuitry for the control of rhythmic, human leg movements is well documented (for review see Brooke et al. 1997; Zehr and Stein 1999), although there is also evidence from transcranial magnetic stimulation (TMS) studies that the corticospinal pathway plays at least some direct role in the production of locomotor drive in humans during walking and leg cycling (Capaday et al. 1999; Petersen et al. 1998, 2001; Pyndt and Nielsen 2003; Schubert et al. 1997, 1999). Here we assessed the excitability of the motor cortex during the execution of rhythmic, locomotor-like movements of the human upper limbs. We previously showed, in a series of reflex studies, that spinal circuits are part of the neural control system for rhythmic arm movement (Carroll et al. 2005; Zehr et al. 2000, 2001, 2003, 2004b). Our results are consistent with the possibility that CPGs may contribute to the execution of rhythmic arm movement (e.g., Dietz 2002; Yamaguchi 2004; Zehr et al. 2004b). On the other hand, the human hand and forearm muscles are strongly innervated by direct corticospinal projections and frequently used for tasks (such as tool use) that rely heavily on cortical control (Phillips and Porter 1977; Porter and Lemon 1993). Thus it might be expected that corticospinal pathways play a proportionally greater role in the control of rhythmic movement of human arms than of human legs, or of the limbs in animals with less well developed corticospinal projections (e.g., Heffner and Masterton 1975). We addressed this issue in the current study by comparing corticospinal excitability during arm cycling with that during tonic contraction. Our hypothesis was that the corticospinal pathway would be less excitable during arm cycling, which would indicate that alternative circuits (e.g., CPGs or spinal reflex pathways) provide a proportionally greater contribution to the control of rhythmic arm movements than of tonic contraction in humans. Such a result would supplement evi-

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dence from reflex studies that the basic mechanisms of rhythmic motor behavior are conserved across species, despite differences in the strength of corticospinal projections.

We conducted two experiments to determine whether there are differences in the extent of corticospinal control between tonic contractions and rhythmic, stereotyped movements of the human upper limbs. First we compared the amplitude of motor-evoked potentials (MEPs) evoked by transcranial magnetic stimulation (TMS) of the motor cortex, and H-reflexes evoked by electrical stimulation of a peripheral nerve during tonic contractions and arm cycling. We predicted that transmission by both the corticospinal and Ia afferent pathways would be depressed during arm cycling. Because changes in MEP amplitude could be mediated by cortical or subcortical alterations in corticospinal transmission, we conducted a second experiment to provide specific information about the excitability of the motor cortex during arm cycling. *Experiment 2* involved the use of subthreshold TMS to condition H-reflexes. We expected to see a reduction in motor cortical excitability during rhythmic arm cycling compared with tonic contraction, consistent with the idea that subcortical regions contribute to the control of rhythmic upper limb movements in humans as in quadrupeds.

METHODS

Participants

Nine individuals (two women, seven men; aged 22–27 yr) without any known neurological deficits participated in *expt 1* after providing informed, written consent. Six of these people also participated in *expt 2*. The procedures conformed to the Declaration of Helsinki and were approved by the Human Research Ethics Board at the University of Alberta.

Protocol

All tasks were carried out on the same custom-built, arm cycle ergometer described previously (e.g., Zehr and Kido 2001; Fig. 1). The two arm cranks were fixed at 180° out of phase. Participants were seated so that the center of rotation of the arm crank was approximately aligned with their shoulder, and they gripped the ergometer handles with forearms pronated. A brace was worn to restrict movement about the right wrist joint. Responses were evoked in separate trials at four equidistant positions in the movement cycle defined relative to the clock face (12, 3, 6, and 9 o'clock), with the "top dead center" arm position specified as 12 o'clock. Stimuli were triggered automatically from the crank position by custom software. Arm extension was defined as movement from the 9 to the 3 o'clock position, while the hand was moving away from the body. Arm flexion was classified as the part of the cycle in which the hand was moving toward the body (from 3 to 9 o'clock). In each cycling trial, subjects cycled at a comfortable rate (about 60 rpm), and stimulation was applied every two to four crank revolutions. For each trial, stimuli were delivered at one of the four positions and the order of the four positions was randomized across subjects. During the tonic contraction trials, participants were asked to match their contraction to the level of muscle activity recorded immediately before stimulation in the corresponding cycling trial (i.e., at the same arm position). Stimulation was applied every 2 to 4 s.

Electromyography

Ensemble electromyographic (EMG) signals were recorded from the right flexor carpi radialis (FCR) using custom-built, fine-wire, intramuscular electrodes, to ensure selective recordings. Each electrode consisted of a single strand of Teflon-coated stainless steel (0.12 mm diameter, A-M Systems, Carlsbourg, WA) inserted through the barrel of a 27-gauge hypodermic needle. The Teflon was stripped from about 2 mm at either end of the wire, and the wire was bent to create a hook at the recording end. Two electrodes were placed in the belly of the muscle, approximately 1 cm apart. The needles were retracted, leaving the wire in the muscle. This electrode configuration provided ensemble EMG signals. EMG activity was preamplified (200–500 times) and band-pass filtered (30–3,000 Hz) by Grass P511 amplifiers. EMG activity was also rectified, low-pass filtered at 3 Hz, and recorded on a separate channel. Data sweeps of 350-ms duration (prestimulus, 100 ms; poststimulus, 250 ms) were recorded at 5 kHz by a 12-bit A/D converter (National Instruments) connected to a computer running custom-written Labview (National Instruments) software. Before the main experiments, the EMG activity during a brief maximal voluntary contraction (MVC) was measured. All prestimulus EMG amplitudes were expressed as a percentage of the average, rectified EMG amplitude recorded during the MVC.

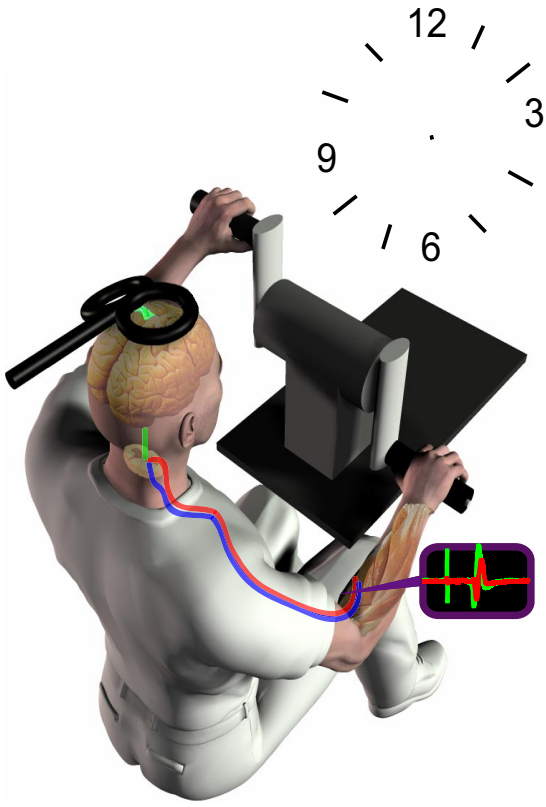

FIG. 1. Schematic illustration of the experimental setup. Positions of the arms were specified relative to a clock face when looking from the participants' right (*top*). In this case, the right arm is at 6 o'clock and the left is at 12 o'clock. Transcranial magnetic stimulation (TMS) was applied to the left motor cortex and nerve stimulation was applied to the right median nerve. Motor-evoked potentials (MEPs) evoked by TMS (*green trace insert*) and H-reflexes (*red trace insert*) were recorded from the right wrist flexors.

Nerve stimulation

The right median nerve was stimulated with 1-ms pulses by a Grass S88 stimulator connected in series with a SIU5 isolator and a CCUI constant-current unit (Grass Instruments, AstroMed). Current was applied with bipolar surface electrodes (1 cm apart) located just proximal to the medial epicondyle of the humerus, near the cubital fossa. The strength of stimulation was varied in different tasks and at different positions to elicit M-waves and/or H-reflexes in the wrist

flexors of specific amplitude as described in detail below. Before the main experiments, the maximal M-wave amplitude (M-max) was measured with the cranks held at each of the four test positions. All subsequently evoked responses were expressed relative to M-max at the corresponding crank position to ensure our comparisons were not confounded by changes in M-wave amplitude with variations in muscle length (Frigon et al. 2003; Simonsen and Dyhre-Poulsen 1999).

Transcranial magnetic stimulation

Stimulation of the left motor cortex was applied using a Magstim 200 stimulator (Magstim, Dyfed, UK) equipped with a figure-of-eight coil. The coil position that yielded MEPs in the wrist flexors at the lowest stimulus intensity was first determined and marked on the scalp with a felt-tip pen. The coil was held firmly in place at this site by an experimenter during all subsequent trials. Particular care was taken to ensure that the coil position was aligned with the scalp markings during every trial. All stimulus intensities were defined relative to the threshold intensity to elicit muscle responses in the wrist flexors during a background contraction of 5% MVC with the arm at the 6 o'clock position. The threshold intensity was identified as the lowest intensity to elicit a clearly discernible MEP in at least three of five trials (typically 50–200 μV). Stimulation intensity varied depending on the task as described below, but intensities at all positions and in all trials were defined relative to the threshold value determined at 6 o'clock.

Experiment 1: H-reflexes and MEPs during arm cycling and tonic contractions

Twenty median nerve stimuli and 20 TMS stimuli were delivered randomly throughout each of the eight trials (i.e., tonic and cycling trials at each of the four positions). Thus each trial of about 2–3 min provided 20 MEPs and 20 H-reflexes for later averaging at each position. The intensity of the electrical stimulation was adjusted at each of the four positions during arm cycling to elicit a small M-wave and a large H-reflex from the ascending limb of the H-reflex recruitment curve. During tonic contraction trials, the stimulus intensity was adjusted at each crank position so that the amplitude of the M-wave matched the M-wave amplitude during the corresponding cycling trials (i.e., at the same arm position). This was done to ensure a similar stimulus intensity for tonic and cycling trials at the same position. The intensity of the TMS was set to 10% above the threshold intensity established before the main experiments. The cycling trials were always conducted before the static trials so that the prestimulus EMG activity could be matched between tasks, although the order of the testing between positions was randomly varied. The average rectified and low-pass–filtered EMG recorded during the 50 ms immediately preceding the stimuli was calculated after each cycling trial. This value was displayed as a target on a computer monitor that provided real-time feedback of muscle activity during tonic contractions.

Experiment 2: motor cortex excitability during arm cycling

We examined the conditioning effects of TMS at 5% below threshold on the size of H-reflexes in the wrist flexors. For each subject, conditioning-test (CT) intervals between −3 and 2 ms (in 1-ms steps) were tested to determine the interval at which the first significant facilitation of the H-reflex was observed. At each CT interval, the mean amplitude of 20 responses to combined H-reflex and TMS stimulation was expressed relative to the average of 20 control H-reflexes (Fig. 5). The first CT interval at which control H-reflexes were facilitated was used subsequently during all cycling and static trials. Twenty control (H-reflex only) and 20 conditioning sweeps (H-reflexes conditioned by subthreshold TMS using the first significant CT interval determined during the setup period) were randomly intermingled in each tonic and cycling trial (eight trials total). The EMG activity was matched between cycling and tonic trials in the same way as for the H-reflex and MEP experiments. The intensity of the electrical stimulation was adjusted to yield a large H-reflex on the ascending limb of the recruitment curve, and we attempted to match the amplitude of H-reflexes across tasks and positions.

TMS did not significantly facilitate H-reflexes in three of our participants, so the subject pool for this part of the study consisted of the remaining six individuals. The lack of effect in these people probably occurred because descending corticospinal volleys of low-amplitude were elicited by TMS at 5% below the active motor threshold. Direct recordings of TMS corticospinal volleys by electrodes chronically implanted in the cervical epidural space indicate that stimuli at this intensity are around the threshold for eliciting a liminal descending volley (Di Lazzaro et al. 1998). However, we were constrained to use such low-stimulus intensities because pilot testing indicated it was necessary to stimulate at 5% of stimulator output below threshold (i.e., as calculated during 5% MVC at 6 o'clock) or less to ensure that MEPs were not elicited in any condition (i.e., at a range of background intensities needed to match background activity during cycling). The validity of our comparisons between cycling and static conditions is not compromised by this interindividual variation because TMS at this intensity was sufficiently large to cause significant H-reflex facilitation in the remaining six individuals.

Data analysis

Data were analyzed off-line using custom-written Matlab software. The peak-to-peak amplitude and the integral of the rectified EMG were calculated for M-waves, H-reflexes, and the responses to TMS. The silent periods after TMS and the average, rectified, prestimulus EMG amplitude for the 50 ms immediately preceding the stimulus were calculated for each sweep. Silent period duration was determined by visual inspection of each individual trail as the period from the MEP onset until the resumption of continuous, poststimulus EMG.

Statistics

A two-way (task × position) repeated-measures ANOVA, with planned comparisons, was used to detect statistically significant differences in H-reflex, M-wave, MEP, and background EMG amplitudes between cycling and static tasks at each arm position (i.e., 3, 6, 9, and 12 o'clock). Separate two-way ANOVAs (conditioning/control × position) were conducted for cycling and static tasks from the H-reflex conditioning experiments. Planned comparisons were used to detect significant facilitation of H-reflex amplitudes arising from TMS conditioning at each arm position during cycling and static tasks. An additional two-way ANOVA (task × position), with planned comparisons at each position, was conducted to detect significant differences in control H-reflex amplitudes between the cycling and static tasks. All tests were performed on group data. Descriptive statistics are given as means ± SE and statistical significance level was set at $P < 0.05$.

RESULTS

Experiment 1: H-reflexes and MEPs during arm cycling and tonic contractions

H-REFLEXES. H-reflexes were smaller during rhythmic movement than tonic contraction at all four positions for the participant shown in Fig. 2, but the depression was largest at the midpoint of arm flexion (6 o'clock). This pattern of response depression was consistent across the group (Fig. 3); H-reflexes were significantly smaller during arm cycling than tonic contraction at 3 o'clock (6% M-max reduction, $F = 11.03$, $P =$

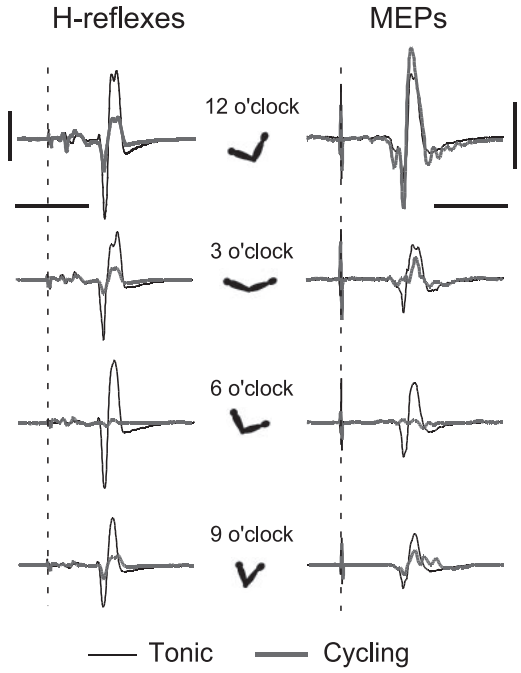

FIG. 2. Average H-reflex and MEP traces after 20 stimuli during arm cycling (thin black lines) and tonic contraction (thick gray lines) at each of the 4 arm positions (12, 3, 6, and 9 o'clock) for an individual participant. Approximate orientation of the arm at each of the 4 positions is shown at center. Horizontal calibration bars represent 20 ms; vertical calibration indicates 5% of the maximal motor response (M-max) for the H-reflexes and 10% of M-max for the MEPs.

0.01) and 6 o'clock (23% M-max reduction, $F = 13.51$, $P = 0.006$). The differences between static and cycling H-reflexes at 12 o'clock (6% M-max reduction, $F = 3.33$, $P = 0.105$) and 9 o'clock (16% M-max reduction, $F = 4.89$, $P = 0.058$) were not statistically significant. We ensured a constant stimulus intensity by matching the size of the M-wave between cycling and tonic tasks at each of the four positions (F range = 0.000–1.155, P range = 0.99–0.31). Because there was an equivalent level of muscle activity in the cycling and tonic tasks immediately before stimulation at 3 and 6 o'clock, the differences in reflex size did not arise from differences in motoneuronal excitability. At 9 o'clock, however, there was greater prestimulus muscle activity during tonic contraction than during arm cycling ($F = 14.92$, $P = 0.005$).

MEPS. The responses to suprathreshold TMS are influenced by a range of excitatory and inhibitory circuits at spinal and cortical levels, and provide information regarding transmission through the corticospinal pathway as a whole. The size of MEPs was similar between rhythmic movements and tonic contraction as the arm was extending (12, 3, and 9 o'clock; F range = 0.001–3.066, P range = 0.97–0.12), but was 27% M-max smaller during rhythmic movement than tonic contraction when the arm was in mid-flexion (6 o'clock; $F = 11.83$, $P = 0.009$; Figs. 2 and 4). Thus neural transmission through the corticospinal pathway was depressed during rhythmic upper limb movement at the same position as the most dramatic H-reflex depression, although the mechanism may not be identical (see DISCUSSION). There was no difference in the duration of reduced muscle activity that follows TMS between cycling and tonic contraction (silent period; F range = 0.007–5.81, P range = 0.94–0.07).

Experiment 2: motor cortex excitability during arm cycling

We assessed the extent to which H-reflexes were facilitated by subthreshold TMS to specifically assess the responsiveness of the motor cortex during arm cycling. The rationale for the technique has been described previously (Mazzocchio et al. 1994; Nielsen et al. 1993; Petersen et al. 1998) and relies on timing the peripheral and brain stimuli so that only the earliest (monosynaptic) part of the brain response facilitates the test reflex. With the appropriate controls, the size of the conditioned reflex indicates the responsiveness of cells in the motor cortex. In contrast, the size of motor responses elicited by suprathreshold TMS (*expt 1*) are influenced by excitatory and inhibitory circuits at both cortical and spinal levels. An example of the data used to identify the shortest facilitatory interval between conditioning TMS and the test reflex stimulus is shown in Fig. 5 (group range: −2 to −1 ms; i.e., reflex test stimulus 2 ms before conditioning TMS). Subthreshold TMS facilitated H-reflexes during tonic contraction (main effect $F = 12.36$, $P = 0.017$). The effect was relatively small (18.4%) and was statistically significant only at 12 o'clock (20.3%, $F = 11.41$, $P = 0.020$) and 3 o'clock (17.0%, $F = 9.56$, $P = 0.027$). The conditioning effects were not statistically significant at the 9 o'clock (23.3%, $F = 4.23$, $P = 0.095$) or the 6 o'clock arm position (14.3%, $F = 2.43$, $P = 0.180$). In contrast, TMS conditioning did not increase the size of reflexes at any position during arm cycling (6.3%, main effect: $F = 2.04$, $P = 0.212$; planned comparisons at individual arm positions: F range = 1.39–0.55, P range = 0.291–0.492).

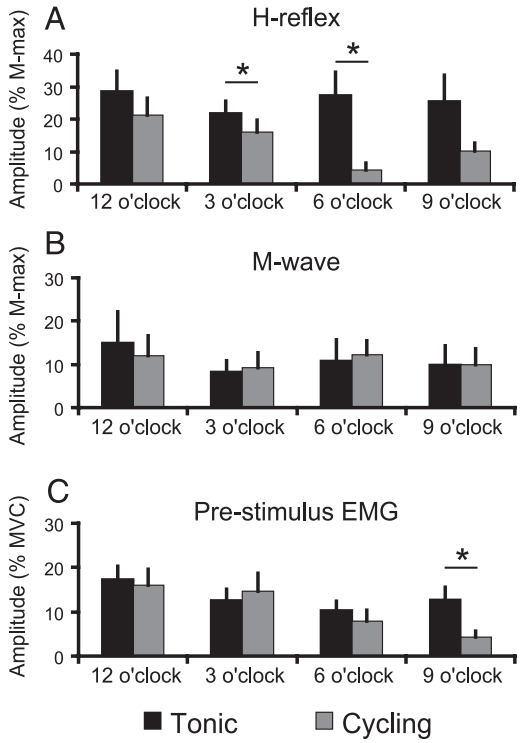

FIG. 3. Group data (mean and SE, $n = 9$) for mean H-reflex (*A*), M-wave (*B*), and prestimulus EMG (*C*) during arm cycling (black bars) and tonic contraction (gray bars) at each of the 4 arm positions (12, 3, 6, and 9 o'clock). H-reflex and M-wave amplitudes are expressed relative to M-max at the same arm position. Mean, rectified, prestimulus EMG is scaled to the amplitude of EMG recorded during maximal voluntary contraction (MVC). Asterisks denote significant differences between cycling and tonic contraction.

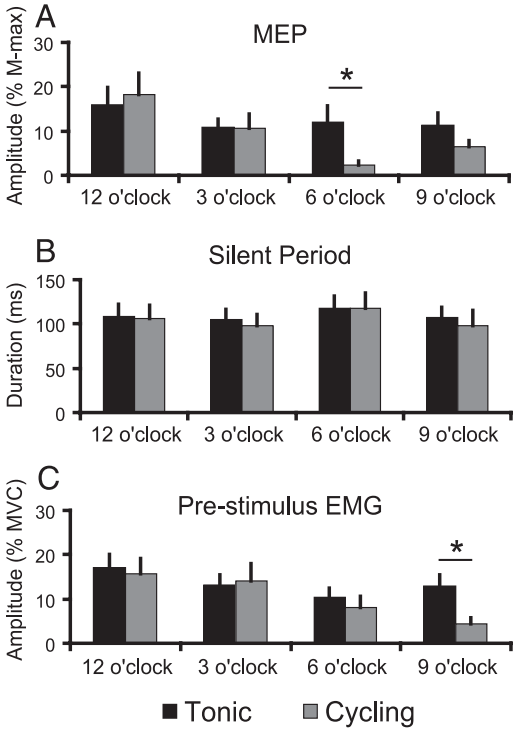

FIG. 4. Group data (mean and SE, $n = 9$) for MEPs (*A*), silent period duration (*B*), and prestimulus EMG (*C*) during arm cycling (black bars) and tonic contraction (gray bars) at each of the 4 arm positions (12, 3, 6, and 9 o'clock). MEPs are expressed relative to the M-max amplitude at the same arm position. Mean, rectified, prestimulus EMG is scaled to the amplitude of EMG recorded during MVC. Asterisks denote significant differences between cycling tasks and tonic contractions.

Because the conditioning effect of TMS is sensitive to the size of the test reflex (Crone et al. 1990), we matched the control H-reflex amplitude between cycling and tonic trials where possible (12, 3, and 9 o'clock; F range = 3.17–0.16, P range = 0.135–0.702). Control H-reflexes could not be matched at 6 o'clock because of strong depression of H-reflexes during arm cycling ($F = 17.77$, $P = 0.008$). There were no significant differences in the level of muscle activity over the 50 ms before stimulation between control and TMS conditioning trials (F range = 0.03–2.41, P range = 0.860–0.181).

DISCUSSION

We have shown that transmission through the H-reflex pathway and the corticospinal pathway is depressed during the flexion phase of rhythmic arm movement and that subthreshold TMS facilitates spinal reflexes during tonic contractions but not during arm cycling. We argue that these data suggest a reduction in the excitability of corticospinal cells during rhythmic arm movement and might reflect a decrease in the contribution of the motor cortex to the generation of motor output during rhythmic movement compared with tonic contraction. This is consistent with the suggestion that reflex and CPG circuits contribute to the control of rhythmic arm movement (Zehr et al. 2004b).

In *expt 1*, we compared H-reflexes and MEPs obtained in the same trials. Our data corroborate findings from leg (Brooke et al. 1997; McIlroy et al. 1992; Pyndt and Nielsen 2003) and arm (Zehr et al. 2003) cycling studies and strengthen the case that the gain of H-reflex (i.e., Group Ia) circuits are reduced during rhythmic locomotor-like movements of both the upper and lower limbs, especially during limb flexion. The most dramatic depression of H-reflexes coincided with the reduction in TMS responses, which indicates that the CNS suppresses excitatory drive from peripheral and descending sources to the wrist flexors during the flexion phase of arm cycling. Despite this coincident timing, the depression of both responses may not share a common mechanism because MEPs can be modulated at spinal and/or cortical levels, and MEPs and H-reflexes may be influenced by entirely different spinal circuits. Thus the depression of each response may be mediated by independent factors. For example, presynaptic inhibition of Ia afferent terminals probably contributes to H-reflex depression during

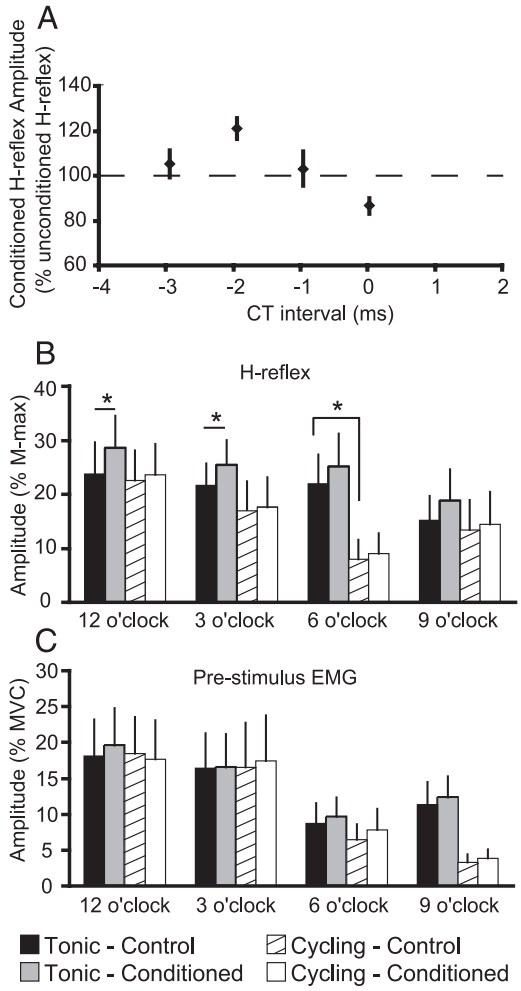

FIG. 5. Muscle responses from the TMS conditioning experiments. *A*: mean H-reflex size (20 sweeps) after conditioning by subthreshold TMS at conditioning-test (CT) intervals between −3 and 1 ms for an individual participant. Reflex size is expressed as a percentage of control H-reflex. A CT of −2 ms was used for this subject because this coincided with the first facilitation of the H-reflex. *B*: group data (mean and SE, $n = 6$) for H-reflex size in the conditioning trials at each of the 4 arm positions (12, 3, 6, and 9 o'clock). Control reflexes are depicted by black or hatched bars and reflexes subject to subthreshold TMS conditioning by gray or white bars. H-reflex size is expressed relative to M-max at the same arm position. *C*: group data (mean and SE, $n = 6$) for mean, rectified, prestimulus EMG, scaled to the amplitude of EMG recorded during MVC, at each of the 4 arm positions (12, 3, 6, and 9 o'clock). Bars are shaded for each condition as in *B*. Asterisks denote significant differences between conditioned and control H-reflexes at each position, or between control H-reflexes in the cycling vs. the static tasks.

rhythmic movement (Pyndt and Nielsen 2003; Zehr et al. 2003), whereas corticospinal–motoneuronal synapses are not subject to classical presynaptic inhibition (Nielsen and Petersen 1994).

There were no significant differences in the silent period after TMS between arm cycling and tonic contraction. The initial part of this silent period (within the first 50 ms) is caused by spinal factors, whereas inhibitory circuits within the motor cortex cause longer-lasting reduction in muscle activity (Chen et al. 1999; Fuhr et al. 1991; Inghilleri et al. 1993). The intracortical inhibitory circuits that lead to the late part of the silent period are subject to independent modulation from the circuits that mediate the excitatory responses to TMS (Inghilleri et al. 1993). Because the silent periods observed here lasted well over 50 ms (Fig. 4), the data indicate that there is little difference in the regulation of the inhibitory circuits within the motor cortex between rhythmic and tonic motor tasks.

We found that H-reflexes were significantly facilitated by subthreshold TMS during tonic contractions, but not during arm cycling, at 12 and 3 o'clock. The situation at the other two positions is less clear because of an inability to match the test H-reflex amplitude or the background EMG amplitude. Furthermore, the trend toward facilitation of H-reflexes by subthreshold TMS during tonic contractions was not statistically significant at either 6 or 9 o'clock. We interpret the lack of H-reflex facilitation during arm cycling to indicate a reduction in the size of descending corticospinal volleys evoked by TMS during rhythmic arm movement compared with those elicited during tonic contraction (i.e., a reduction in the excitability of the motor cortex). However, it is important to recognize that the H-reflex conditioning technique provides an indirect indication of cortical excitability and, moreover, there are alternative explanations. For example, we assume that the degree of H-reflex facilitation is influenced only by transmission through the monosynaptic component of the corticospinal pathway because we used the first CT interval at which the subthreshold TMS facilitated the test reflex. This assumption should be valid because the H-reflex excitatory postsynaptic potential rise time is relatively brief (about 1.5 ms; see Jones et al. 1996), and the first corticospinal volley to reach the motoneurons acts by a direct, monosynaptic connection (see Rothwell et al. 1991). Thus it seems unlikely that modulation of spinal interneurons that receive both corticospinal and group I inputs could underlie changes in the amplitude of test H-reflexes.

If we accept that the test H-reflex is subject only to monosynaptic corticospinal modulation, some additional, alternative possibilities should be considered before a change in cortical excitability is concluded: *1*) a reduction in the efficacy of transmission at the synapses between corticospinal cells and motoneurons and *2*) a lower recruitment gain of wrist flexor motoneurons (Kernell and Hultborn 1990). A reduced efficacy at the corticospinal–motoneuronal synapse is an unlikely mechanism because impairments in corticospinal–motoneuronal transmission have been shown only after high-intensity contractions, and the effect is reduced as soon as the fatigued muscle becomes active (Petersen et al. 2003). Furthermore, classical presynaptic inhibition does not affect corticospinal–motoneuronal synapses (Nielsen and Petersen 1994). A change in the recruitment gain of the motoneuron pool, such that greater excitatory drive is required to recruit additional motoneurons, cannot account for our findings because such an effect would be expected to depress the responses of the wrist flexor motoneurons to all inputs. In contrast, we found that MEPs were not significantly depressed during arm extension. We conclude that our results indicate that subthreshold TMS activated fewer corticospinal cells projecting to the wrist flexor motor pool during arm cycling. The mechanism for this reduction in cortical excitability is unclear, although one possibility is that the excitability of intracortical circuits could be influenced by the arrival of afferent information from the moving limbs. It is also possible that the decrease in cortical responsiveness occurs because the motor cortex contributes less to the control of rhythmic arm cycling than tonic contraction, which may reflect a shift in the locus of movement control to CPGs.

The importance of cortical inputs to the legs during human locomotion has been assessed using TMS (Capaday et al. 1999; Petersen et al. 2001; Pyndt and Nielsen 2003; Schubert et al. 1997, 1999). Petersen et al. (2001) and Pyndt and Nielsen (2003) showed that the motor cortex plays at least some direct role in the production of locomotor drive to the ankle extensors during the leg extension or stance phase of locomotor-like movements in humans. Thus although subcortical regions may play a major role in the control of rhythmic, human leg movements, the motor cortex probably also contributes to the motor pattern. Indeed, cells in the primary motor cortex have also been shown to contribute directly to the motor output during walking in cats (Armstrong 1986; Armstrong and Marple-Horvat 1996; Drew 1988, 1991), a species known to rely heavily on CPG activity for gait control. The methods used in the current study do not provide evidence regarding the degree to which the direct, corticospinal pathway contributes to human arm cycling per se. Our data indicate, however, that the extent of cortical contribution to arm cycling is less than the contribution of the cortex during tonic forearm contraction. Comparative data from the cat and human legs would suggest that a significant cortical contribution to arm cycling is likely.

Although our data lead to different conclusions from the majority of lower limb studies about the role of the motor cortex in the control of rhythmic human movement, they are directly at odds only with results reported by Pyndt and Nielsen (2003), in which an increase in cortical excitability in the soleus was found during early downstroke in leg cycling. These arm–leg differences might be related to differences in the functional roles of the muscles involved in the upper and lower limb tasks. The activity of the ankle extensors is dramatically modulated during walking and leg cycling, from a strong, propulsive burst during leg extension and stance, to almost complete quiescence during leg flexion and swing (Brooke et al. 1997; Capaday et al. 1999; Pyndt and Nielsen 2003; Schubert et al. 1997, 1999). We chose the wrist flexors for comparison because they have a similar functional role to the plantar flexors (i.e., active during the propulsive phase of movement such as crawling or swimming). However, during arm cycling, the wrist flexors are active continuously and stabilize the wrist to allow a steady grip force on the crank handles (Figs. 3, 4, and 5; Carroll et al. 2005; Zehr and Kido 2001). Although there is some phase-dependent modulation of wrist flexor activity during arm cycling (see Figs. 3, 4, and 5), there is no strong propulsive burst at any point in the cycle. This discrepancy in function might underlie the different re-

sults between arm and leg cycling because the cortical excitability was greater only during the early extension phase of leg cycling (which coincided with the propulsive burst of the ankle extensors) in the Pyndt and Nielsen (2003) study. It is also conceivable that cortical excitability is enhanced during arm cycling (relative to tonic contraction) at arm positions that were not tested in the current study.

In summary, our data suggest a reduction in the excitability of the primary motor cortex during rhythmic arm movement compared with tonic contraction. This contributes to the evidence from reflex studies (e.g., Zehr et al. 2001, 2003) that subcortical regions play a role in the control of rhythmic human arm movements in a similar way to other animals, from cats to lampreys (Grillner 1981; Grillner and Dubuc 1988; Hill et al. 2003; Marder and Calabrese 1996). The possibility that subcortical regions contribute to the control of rhythmic movements in organisms with such a wide range of CNS complexity is consistent with the idea that spinal circuits (e.g., CPGs) may be universally important for the generation of rhythmic, stereotyped motor behavior.

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