Enhancement of Arm and Leg Locomotor Coupling With Augmented Cutaneous Feedback From the Hand

E. Paul Zehr,1–3 Marc Klimstra,1 Katie Dragert,1 Yasaman Barzi,1 Mark G. Bowden,5 Bahar Javan,1 and Chetan Phadke4

1Rehabilitation Neuroscience Laboratory and 2Centre for Biomedical Research, University of Victoria, Victoria, British Columbia and 3Human Discovery Science, International Collaboration on Repair Discoveries, Vancouver, British Columbia, Canada; 4Departments of Physical Therapy and Neuroscience, University of Florida, Gainesville and 5Brain Rehabilitation Research Center, Rehabilitation Research and Development Service, Malcom Randall Veterans Affairs Medical Center, Gainesville, Florida

Submitted 20 May 2007; accepted in final form 24 June 2007

Zehr EP, Klimstra M, Draget K, Barzi Y, Bowden MG, Javan B, Phadke C. Enhancement of arm and leg locomotor coupling with augmented cutaneous feedback from the hand. J Neurophysiol 98: 1810–1814, 2007. First published July 5, 2007; doi:10.1152/jn.00562.2007. Cutaneous feedback from the hand could assist with coordination between the arms and legs during locomotion. Previously we used a reduced walking model of combined arm and leg (ARM&LEG) cycling to examine the separate effects of rhythmic arm (ARM) and leg (LEG) movement. Here we use this same paradigm to test the modulation of H-reflexes with and without interlimb cutaneous conditioning evoked by stimulating a nerve innervating the hand (superficial radial, SR). It was hypothesized that both ARM and LEG would contribute significantly to suppression of H-reflex amplitude during ARM&LEG. We also predicted a conservation of interlimb cutaneous conditioning during movement and an interaction between arm and leg rhythmic movement control. Subjects were seated in a recumbent ARM&LEG cycle ergometer and maintained a low-level soleus contraction for all tasks. H-reflex amplitude was facilitated by cutaneous conditioning evoked by stimulation of the SR nerve. H-reflex amplitudes were taken from recruitment curves and included modulation of 50% \( H_{\text{max}} \) and \( H_{\text{rms}} \). The suppressive effect of ARM was less than that for LEG and ARM&LEG, while suppression during LEG and ARM&LEG were generally equivalent. For H-reflexes conditioned by cutaneous input, amplitudes during ARM&LEG instead were in between those for ARM and LEG modulation. Multiple regression analysis revealed a significant contribution for ARM only in trials when SR stimulation was used to condition H-reflex amplitudes. We suggest that there is a measurable interaction between neural activity regulating arm and leg movement during locomotion that is specifically enhanced when cutaneous input from the hand is present.

INTRODUCTION

There is uncertainty about linkages between the limbs during human locomotor behaviors involving rhythmic arm and leg activity such as occurs in walking. Dietz and colleagues have shown task-modulated interlimb effects and have also ascribed these to the output of central-pattern-generating (CPG) elements (Dietz et al. 2001). Evidence for interlimb coupling during walking was observed by evoking cutaneous reflexes in both arm and leg muscles by stimulation at the hand (SR) and foot (SP) (Haridas and Zehr 2003). Observations of similar interlimb reflexes were also shown recently during combined arm and leg cycling (Sakamoto et al. 2006). These data provide compelling evidence of the reflex effects of sensory feedback evoked by activation of distant skin fields during movement and also of the influence of CPG activity regulating the arms and legs during walking (Haridas and Zehr 2003). However, examination of interactions between control of the arms and legs is difficult during locomotion because of the “interference” between rhythmic arm and leg activity. Interestingly, facilitation of soleus H-reflex amplitude induced by SR nerve stimulation interferes with the suppression occurring during arm cycling (Zehr et al. 2004). This contrasts with lack of interaction of facilitatory conditioning evoked by stimulation of a local cutaneous nerve innervating the foot (sural) (Frigon et al. 2004). This suggests that the remote cutaneous inputs are not regulated in the same way as local segmental ones.

To address the issue of the relative coupling between the arms and legs, we have used reflex modulation studies. Recently we studied the role of arm, leg, or arm and leg movement on modulation of cutaneous reflex amplitudes in leg muscles by separating the rhythmic arm movement from the rhythmic leg movement (Balter and Zehr 2007). The main finding was that the effect of arm cycling on reflexes in leg muscles when the legs were not moving was relatively minor; full expression of the effect of rhythmic arm movement was only revealed when both the arms and legs were moving. In that case, the relative contribution from the arms was linked to the functional state of the legs such that the contribution from the arms was functionally gated throughout the locomotor cycle in a manner that appeared to facilitate the action of the legs. These observations support an interaction between rhythmic arm and leg movement during human locomotion. However, using similar methodology but with uncoupled arm and leg ergometers, Sakamoto et al. (2006) concluded that the modulation of cutaneous reflexes in leg muscles is not influenced strongly by arm movement. These two studies highlight the uncertainty that currently exists in regard to arm and leg coupling during human locomotor movement. Here we tested the hypothesis that further evidence of neural coupling between arm and leg movement would be obtained by examining the amplitude modulation of soleus H reflexes using the general procedures of arm, leg, and arm and leg cycling from Balter and Zehr (2007). Additionally, our earlier observation of functionally relevant and phase-modulated interlimb reflexes in leg

Address for reprint requests and other correspondence: E. P. Zehr, Rehabilitation Neuroscience Laboratory, PO Box 3010 STN CSC, University of Victoria, Victoria, BC V8W 3P1, Canada (E-mail: pzehr@uvic.ca).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
muscles after stimulation of SR nerve (Haridas and Zehr 2003) suggested that cutaneous feedback from the upper limb could have priority access to interneuronal reflex networks directed to leg muscle motoneuronal pools. This, coupled with our observation that SR nerve facilitatory conditioning of soleus H-reflex amplitudes in stationary legs could interfere with the strong suppression of H-reflex amplitude induced by rhythmic arm cycling (Zehr et al. 2004), allowed us to theorize that arm to leg locomotor coupling might be revealed more clearly by superimposing cutaneous conditioning onto the H-reflex modulation. We therefore also tested the hypothesis that additional strong evidence of locomotor coupling during arm and leg cycling would be revealed in SR nerve conditioned H reflexes. This approach was also selected to counter any possible floor-related effects of strong soleus H-reflex suppression during leg cycling.

METHODOLOGICAL APPROACH

The experimental protocol and methodology were similar to that described in previous experiments involving reflex modulation during leg and arm and leg cycling (Balter and Zehr 2007; Zehr et al. 2001). Participants provided informed written consent in a protocol approved by the Human Research Ethics Committee at the University of Victoria and performed in accordance with the Declaration of Helsinki. Seventeen participants (age range: 24–40 yr; 13 females and 4 males), free of any known history of neurological or metabolic disorders completed three 4–min movement tasks at a frequency of 1 Hz: arm cycling with legs stationary with knees bent at a 90° angle (ARM); leg cycling with stationary arms held at the side (LEG); and combined arm and leg cycling (ARM&LEG). On-line display of cycling cadence was used by the subjects to aid in maintaining this 1-Hz frequency. This frequency is similar to those used during leg cycling (Brown and Kukulka 1993) and arm cycling (Zehr and Kidwai 2001) and is considered to be equivalent to a typical walking cadence. Reflexes were also evoked while participants performed static postures matching the three cycling tasks to provide control, nonmoving conditions for each task. During all cycling and static tasks a consistent electromyographic (EMG) level (~20% MVC) was maintained in the soleus muscle, ipsilateral to the site of stimulation (the right leg was stimulated in all experiments). To aid in maintaining this contraction, participants wore an ankle-foot orthosis (AFO) on their right side and were provided visual feedback of contraction level on an analogue oscilloscope.

As described previously (Balter and Zehr 2007), an arm and leg cycle ergometer (PRO II, SCIFIT Systems, Tulsa OK) in which the arm and leg cranks were mechanically coupled to maintain a constant rigid out-of-phase relation between arm and leg movement was used. The movement cycle was divided into 12 phases, equivalent to a clock-face with 12 o’clock at the top (see Fig. 1 in Balter and Zehr 2007) using the output obtained from two optical encoders (i.e., 1 each for the arms and legs). Reflexes were evoked at approximately the late 200 – 300 Hz (P511 Grass Instruments, AstroMed). However, for ipsilateral SOL, EMG was filtered from 100 to 1,000 Hz.

Soleus H reflexes were evoked by stimulating the posterior tibial nerve at the popliteal fossa with 1-ms square wave pulses using bipolar surface electrodes with either a Digitimer (Medel) constant current stimulator (model DS7A) or a Grass S88 stimulator (Grass Instruments, AstroMed) connected in series with a SIU5 isolator and a CCU1 constant current unit. Nerve stimulation was delivered pseudo randomly between 3 and 5 s apart during all trials. Full H-reflex recruitment curves (n = 40 sweeps) were obtained in all conditions. Delivered current was measured using a mA-2000 Noncontact Milliammeter (Bell Technologies, Orlando, FL). Control recruitment curves were constructed at the beginning and the end of each experiment and were taken for each condition. Using single, unrectified sweeps of EMG from soleus, H-reflex peak-to-peak amplitudes were analyzed in all trials. For each subject M-waves and H-reflexes were normalized to the corresponding M_max to reduce inter-subject variability. As used recently, (Zehr et al., 2007b) the recruitment curves

FIG. 1. A: H-reflex recruitment curves for all 3 movement tasks and static control for a single subject. The fitted lines represent the best-fit sigmoidal representation of the data. The largest effect of cycling movement is seen during LEG. Data are normalized to the maximum M-wave amplitude in each condition. B: group data for all conditions with unconditioned H reflexes. All movement conditions induced significant suppression of H-reflex amplitude relative to static control (indicated by * within bars). LEG and ARM&LEG were significantly different from ARM but not from each other (indicated #). Data are normalized to the maximum M-wave amplitude in each condition and are given means ± SE for 17 participants. ARM (arm cycling), LEG (leg cycling), ARM&LEG (combined arm and leg cycling), M_max (maximal M-wave amplitude).
(ascending limb only) were fit using a general least squares model of a custom three-parameter sigmoid function according to Eq. 1

\[ H(s) = \frac{H_{\text{max}}}{1 + e^{s - s_50}} \]

where \( H_{\text{max}} \) is the upper limit of the curve, \( m \) is the slope parameter of the function, \( s_{50} \) is the stimulus at 50% of the \( H_{\text{max}} \) value, and \( H(s) \) is the H-reflex amplitude at a given stimulus value (s). Average \( H_{\text{max}} \) was calculated from the five largest peak-to-peak H reflexes. Variables analyzed were: \( H_{\text{max}}, 50\% \ H_{\text{max}}, H\)-reflex threshold, and the slope of the ascending limb of the recruitment curve at 50% of the \( H_{\text{max}} \) value. This slope was determined using Eq. 2

\[ \frac{m(H_{\text{max}})}{4} \]

Also, the variables \( H_{\text{max}}, 50\%H_{\text{max}}, \) and \( H_{\text{threshold}} \) taken from the static control curves were compared with the reflex amplitudes obtained from the same current values on the conditioned curves (Zehr and Klimstra 2006). That is, the same relative current needed to evoke a certain sized H reflex on the static control recruitment curves was used in the curves fit to the movement trials and the “predicted” value obtained. To differentiate the description of reflex parameters taken from the fitted curves, they are described as ”*@” the value from static control. For example, modulation of the value for \( H_{\text{max}} \) during static is \( H_{\text{max}} \) during cycling tasks. This is similar in principle to a previously applied procedure using linear fits (Zehr and Stein 1999).

To explore the extent to which cutaneous feedback from the hand was preserved during rhythmic movement, 12 subjects also performed the ARM, LEG, and ARM&LEG tasks while soleus H reflexes were conditioned with stimulation of the cutaneous superficial radial (SR) nerve in the hand. Trains (5 × 1.0-ms pulses at 300 Hz) of constant current electrical stimulation were applied to the SR nerve at the wrist using flexible surface electrodes. Stimulus intensity was set on the CCU1 unit as ∼2 times radiating threshold using a condition—test (CT) interval of ∼100 ms to facilitate H-reflex amplitude via reduced Ia presynaptic inhibition (Zehr et al. 2004).

STATISTICA software (StatSoft, Tulsa, OK) was used to perform repeated-measures ANOVAs with planned comparisons and Student’s \( t \)-test. To gauge the relative contributions of ARM and LEG to the combined ARM&LEG task, SPSS software (SPSS, Chicago, IL) was used to perform forward stepwise multiple regression for \( H_{\text{max}} \) values. This parameter evoked during the ARM&LEG task (i.e., criterion variable) were compared with those obtained using two predictor variables: the ARM task and the LEG task. This is the same procedure applied in a similar experiment involving ARM&LEG cycling and cutaneous reflexes (Balter and Zehr 2007).

Descriptive statistics included means ± SE. Statistical significance was set at \( P \leq 0.05. \)

Results

H-reflex amplitudes were significantly suppressed for all movement tasks relative to static control. Recruitment curves for a single subject show this suppression in Fig. 1A,g. The recruitment curves show downward and rightward shifts during ARM, ARM&LEG, and leg, in that order. Plotted in Fig. 1B are the group data from all 17 subjects showing H-reflex amplitudes for two measured parameters (\( H_{\text{max}} \), 50% \( H_{\text{max}} \)) across all conditions. Both parameters of H-reflex excitability measured during all three tasks were significantly smaller than static control (indicated by * within each bar). However, LEG and ARM&LEG did not differ from each other and were both significantly smaller than ARM (indicated by #). It is important to note that the suppression of H-reflex amplitude observed during LEG was not increased during ARM&LEG. Percentage change in H-reflex amplitude from static control were calculated for ARM&LEG and compared with the algebraic sum of the changes for ARM added to that of LEG (thus ARM + LEG). For ARM&LEG both \( H_{\text{max}} \) and 50% \( H_{\text{max}} \) parameters were significantly smaller than ARM + LEG (not plotted). There were no significant differences between tasks in the effects of movement conditioning on slope of the ascending limb of the recruitment curve. A minor observation was a rightward shift in the stimulus at 50% of the \( H_{\text{max}} \) value when comparing LEG and ARM&LEG to static.

Analysis of the reflexes conditioned by cutaneous input from the wrist (SR nerve stimulation) are plotted for 12 subjects in Fig. 2A for both parameters examined in the unconditioned reflex conditions. Cutaneous nerve conditioning interfered with the suppressive effect of arm cycling such that there was no significant difference between H reflexes during ARM with SR conditioning and static control.
for $H_{@50\%}$ (as reported previously, Zehr et al. 2004) but not $H_{@max}$. The amplitudes of $H_{@50\%}$ during ARM&LEG and LEG were both significantly smaller than during ARM and were not significantly different from each other. As with the unconditioned reflexes, the suppression of H-reflex amplitude observed during LEG was not increased during ARM&LEG with SR conditioning. Percentage changes in reflex amplitude from static control for ARM&LEG and the algebraic sum of the changes for ARM added to that of LEG (i.e., ARM + LEG) are shown in Fig. 2B. For ARM&LEG, $H_{@max}$ but not $H_{@50\%}$ was significantly smaller than ARM + LEG. This cannot be evidence of a floor effect limiting the suppression of H-reflex amplitude because it persists at both $H_{@max}$ and $H_{@50\%}$. The results of the stepwise regression analysis yielded two interesting observations. During ARM&LEG cycling without conditioning by cutaneous SR stimulation, ARM did not make a significant contribution to the H-reflex modulation during ARM&LEG. That is, LEG was the dominant factor. However, when H reflexes were conditioned with SR stimulation, a significant contribution from the arms was observed ($R^2$ change $= -0.133$; df = 1, 9; F change $= 8.7$, $P < 0.02$) to be superimposed on the dominant effect from the legs ($R^2$ change $= 0.73$; df = 1, 10; F change $= 27.02$; $P < 0.001$).

Based on the results from a 2 × 4 repeated-measures ANOVA, background EMG levels in soleus and TA did not differ significantly across conditions. Parameters of M-wave amplitude, including maximal amplitude, also did not differ across conditions. Unsurprisingly, there were differences in EMG levels across conditions for VL (when the legs were moving) and AD (when the arms were moving).

**Discussion**

The main result of this study was the maintenance of interaction between arm and leg movement as measured by the effect of cutaneous input from the hand on the soleus H-reflex amplitude. We conclude that when the influence of rhythmic arm activity interacts with the effects of rhythmic leg activity during ARM&LEG, the result reflects neural processing related to both the ARM and LEG activity. The most striking observation may be that the summation of the individual effects of ARM and LEG did not typically yield the amplitude of ARM&LEG. Instead, the combined effect during ARM&LEG was less than the predicted mathematical summation. The effect from cutaneous SR nerve conditioning persists during arm and leg movement. That is, when the normal locomotor rhythmic activity of all four limbs was ongoing and cutaneous input from the hand was superimposed, an interaction between the arms and legs was revealed.

In a previous paper, we observed interlimb cutaneous reflexes in arm muscles after stimulation of a cutaneous nerve in the leg and in leg muscles after stimulation of the SR nerve at the wrist. We suggested that this interlimb reflex connectivity represented the role that sensory feedback could play in arm and leg coordination during locomotion (Haridas and Zehr 2003; Sakamoto et al. 2006). We also recently showed a subtle but measurable effect of arm movement on cutaneous reflex amplitudes evoked in leg muscles (Balter and Zehr 2007). Using modulation of H reflexes conditioned by cutaneous SR nerve as the neural probe in this study, we arrive at a similar result. We initially suspected that overt modulation of the H reflex might be saturated during LEG such that no effect of ARM could be revealed. However, when the separate effects ARM and LEG were summed and the resulting ARM + LEG compared with measurements taken during ARM&LEG, H-reflex amplitudes were found to be significantly smaller during simultaneous ARM&LEG cycling. The result here during ARM corresponds with our other work with arm cycling and stationary legs (Frigon et al. 2004; Loadman and Zehr 2007; Zehr et al. 2004). Namely, H reflexes are suppressed during rhythmic arm movement. These earlier studies led to the conclusion that the effect of arm cycling was to modulate Ia presynaptic inhibition in the soleus H-reflex pathway. Because modulation of H-reflex amplitude in soleus during leg cycling has also been ascribed to Ia PS (Brooke et al. 1997), strong interaction in the effects of rhythmic arm and leg cycling might be predicted.

We interpret the present observations that the predicted size of suppression of H-reflex amplitude during ARM&LEG (except for $H_{@50\%}$) was less than the experimentally observed values during ARM&LEG (compare $H_{@max}$ for ARM + LEG to ARM&LEG in Fig. 2B) as evidence for a change in the effect of ARM when the legs are moving. That is, now it no longer adds to the suppression generated by LEG and instead the rhythmic actions at cervical and lumbar level converge to a common value. Because this suppression of H-reflex amplitude during LEG may reflect an active “filtering” of excessive afferent feedback (Brooke et al. 1997), this lack of addition of effects may make functional sense. That is, it reflects the physiological filter setting for afferent feedback gain during movement (e.g., see Brooke and Zehr 2006). Notably, the effects for $H_{@50\%}$ show similarity between the mathematically predicted and experimentally derived values (see Fig. 2B, SR $H_{@50\%}$). This suggests that the effects of SR conditioning were strong enough to interfere with the suppression during LEG. Thus the added effects during ARM&LEG are above the physiological filtering gain and are therefore expressed. Related to this point it is interesting to note that the multiple regression analysis revealed a significant contribution from the arms only in trials where H reflexes were conditioned by cutaneous SR stimulation at the wrist. This suggests that interlimb coupling between the arms and the legs is strengthened when cutaneous feedback from the hand is added. Interestingly, the coupling effects detected with the SR nerve conditioned H reflexes may be an extension to interlimb reflexes of the concept of differential regulation of segmental cutaneous and H-reflex pathways suggested earlier during leg cycling (Zehr et al. 2001).

The results here support the notion of linkage between the control of rhythmic arm and leg movement during human locomotion (Zehr and Duysens 2004). Overall, the current data support the concept that there is arm-to-leg neural interaction during rhythmic locomotor-like movement. However, this coupling is rather loose and is dominated by the legs. This conclusion also corresponds to the recent observation that effects of arm cycling on H-reflex pathways in the legs is related to more general rather than specific features of arm cycling (Loadman and Zehr 2007). Taken together these are compatible with observations of quadrupedal locomotor control in the neonatal rat. Juvin et al. (2005) examined interactions between lumbar and cervical locomotor CPGs in isolated spinal cord preparation. A dominance in locomotor drive from the lumbar over the cervical CPGs was documented and described as an “ascending caudorostral excitability gradient.”
Previously Ballion et al. had suggested that lower cervical spinal cord levels display rhythmogenic capacity and that, in conjunction with the CPG elements in the lumbar cord, contribute to coordinated locomotor activity (Ballion et al. 2001). This general conclusion can also be taken from the recent work of Zaporozhets and colleagues in the neonatal rat that suggested that the cervical motor output is not critical for, but may contribute to, bipedal locomotion (Zaporozhets et al. 2006). Additional recent indirect work, including the current study, support this concept as well in the bipedal human (Balter and Zehr 2007; Sakamoto et al. 2006, 2007). Indeed, the emerging data support the concept that bipedal human locomotion can be considered to be built on elements of quadrupedal coordination as suggested by Dietz (Dietz 2002; Zehr et al. 2007a).

Our results have translational implications for rehabilitation in that they further support incorporating rhythmic arm movement paradigms for locomotor rehabilitation after neurotraumatic injury. Ferris et al. previously argued that to harness interlimb neural coupling gait rehabilitation therapy should incorporate simultaneous arm and leg rhythmic activity after neurotrauma (Ferris et al., 2006). That is, neural commands related to the production of rhythmic arm movement could assist in accessing the neural circuitry underlying coupling between the arms and legs during locomotor retraining. The additional contribution that the current results make is to suggest that cutaneous input from the hand may also help facilitate neural linkage between the arms and legs during locomotion. It is conceivable that the simultaneous arm and leg movement combined with cutaneous input from the hand may lead to facilitation of extensor muscle activity. However, this requires further exploration including a determination of any phase-dependent modulation across the full cycle of movement. Regardless, including specific use of the hands during the arm movement may be of importance in rehabilitation interventions. Elucidating these effects in a neurologically damaged population (e.g., after stroke or spinal cord injury) will be important to further refine effective rehabilitation strategies.

GRANTS

This work was supported by grants to E. P. Zehr from the Natural Sciences and Engineering Council of Canada, the Heart and Stroke Foundation of Canada, and the Michael Smith Foundation for Health Research. M. Klimstra was supported by a Focus on Stroke award from the Heart and Stroke Foundation of Canada. Additional support for M. G. Bowden was provided by the Office of Research and Development Rehabilitation R&D Service, Department of Veterans Affairs and by Dr. Steven A. Kautz. C. Phadke acknowledges support from Dr. Andrea L. Behrman and the University of Florida Locomotor Training and Recovery Laboratory.

REFERENCES


