Coordinated Interlimb Compensatory Responses to Electrical Stimulation of Cutaneous Nerves in the Hand and Foot During Walking

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Haridas, Carlos and E. Paul Zehr. Coordinated interlimb compensatory responses to electrical stimulation of cutaneous nerves in the hand and foot during walking. \textit{J Neurophysiol} 90: 2850–2861, 2003. First published July 9, 2003; 10.1152/jn.00531.2003. It has been shown that stimulation of cutaneous nerves innervating the hand (superficial radial, SR) and foot (superficial peroneal, SP) elicit widespread reflex responses in many muscles across the body. These interlimb reflex responses were suggested to be functionally relevant to assist in motor coordination between the arms and legs during motor tasks such as walking. The experiments described in this paper were conducted to test the hypothesis that interlimb reflexes were phase-dependently modulated and produced functional kinematic changes during locomotion. Subjects walked on a treadmill while electromyographic (EMG) activity was collected continuously from all four limbs, and kinematic recordings were made of angular changes across the ankle, knee, elbow, and shoulder joints. Cutaneous reflexes were evoked by delivering trains of electrical stimulation pseudorandomly to the SP nerve or SR nerves in separate trials. Reflexes were phase-averaged according to the time of occurrence in the step cycle, and phasic amplitudes and latencies were calculated. For both nerves, significant phase-dependent modulation (including reflex reversals) of interlimb cutaneous reflex responses was seen in most muscles studied. Both SR and SP nerve stimulation resulted in significant alteration in ankle joint kinematics. The results suggest coordinated and functionally relevant reflex pathways from the SP and SR nerves onto motoneurons innervating muscles in nonstimulated limbs during walking, thus extending observations from the cat to that of the bipedal human.

\textbf{INTRODUCTION}

There is a linkage between rhythmic hind- and forelimb movements resulting in coordinated locomotor movement in the cat (Miller and Van Der Meche 1975; Miller et al. 1975). Both ascending (Gernandt and Megirian 1961), and descending (Skinner et al. 1980) pathways may assist in this coordination between the cervical and lumbar spinal cord. Phase-dependent reflex transmission from the fore- to hindlimbs has been shown during fictive locomotion in the cat (Schomburg et al. 1977), and a reflex reversal of inputs from the forelimb onto the hindlimb was shown during stepping in decerebrate cats (Miller et al. 1977). We recently showed that stimulation of both the superficial peroneal (SP; innervating the dorsum of the hand) nerves could evoke prominent reflex responses in arm and leg muscles of subjects maintaining tonic contractions (Zehr et al. 2001a). We speculated that these responses could function to assist in coordination of the limbs during movement. In quadrupeds, reflex connections from fore- to hindlimbs for the rapid transmission of information about the terrain make functional sense. However, it is uncertain to what extent such pathways might persist in the bipedal human. Just as in the cat, extensive phase-dependent modulation of cutaneous reflex responses within the arms has been shown in humans during arm cycling (Zehr and Kido 2001) and during walking (Zehr and Haridas 2003). It might be theorized that cutaneous reflex responses evoked by stimulation of the hand may affect leg muscles via interlimb pathways.

Electrical stimulation of the SP nerve elicits a stumble-corrective response during human walking (Van Wezel et al. 1997; Zehr et al. 1997). Because a perturbation to the leg during swing can easily result in a fall, thus necessitating the use of the upper limbs to break the fall, reflex activation of upper limb muscles should be observed after SP nerve stimulation during locomotion. Interestingly, McIlroy and Maki (1995) described compensatory arm-muscle activation during perturbation of upright stance and suggested that the arms were being used to stabilize posture. That is, interlimb reflex responses evoked by stimulation of the foot surface may act to coordinate protective responses in the upper body.

Other groups have recently addressed this question as well (see for review Dietz 2002a). It was shown that electrical stimulation of the distal tibial nerve (innervates the heel, primarily cutaneous) could evoke interlimb reflex responses in arm muscles during walking (Dietz et al. 2001). Furthermore, it was demonstrated that this reflex linkage was only expressed during locomotion, thus suggesting task dependency. However, although that paper showed important support for the presence of interlimb reflex responses during human walking, the concept of phase-dependent modulation (an important hallmark of reflex function) (Zehr and Stein 1999) was not addressed. Thus the nature of any reciprocal linkages from cutaneous fields in the hand and foot onto leg and arm muscles during walking have not yet been addressed. Thus this current study was conducted to test the hypothesis that interlimb cu-
taneous reflex responses undergo functionally relevant modulation during human locomotion.

METHODS

Much of the methodology is similar to that previously described (Zehr and Haridas 2003; Zehr and Kido 2001; Zehr et al. 1997, 2001a). Thus methods will only be described briefly here.

Terminology

The term interlimb reflex is used to describe reflex responses in muscles that are located in nonstimulated limbs (see Zehr et al. 2001a). For example, while stimulating the right SP nerve, reflex responses in muscles in any of the limbs except for the right leg are interlimb reflexes. Muscles are described as ipsilateral (i) or contralateral (c) with respect to the site of stimulation. In all experiments, nerve stimulation was delivered to the right side of the body.

Subjects and protocol

Subjects between the ages of 18 and 34 yr participated with informed written consent in a protocol approved by the Human Research Ethics Board (Health Research) at the University of Alberta. Sixteen subjects participated in the SP nerve stimulation protocol, and 15 of these subjects also participated in the SR nerve protocol. All subjects were free of documented neurological impairment. Subjects were asked to maintain different static body postures, each lasting ~1 min in duration, while standing on a stationary treadmill (see Komiyama et al. 2000). Subjects were provided with small breaks if it was observed that static postures could not be held stable for the full sample time. Four of these positions mimicked body postures during key points in the step cycle (late stance, early stance, midstance, midswing), while the remaining fifth posture entailed holding the arms out bilaterally. These postures were performed to obtain background electromyographic (EMG) levels in all arm muscles so that we could determine if the stimulus intensity was adequate to elicit a reflex and also for comparison to reflex responses evoked during walking. Subjects then walked on a motorized treadmill at 3 mph for 20 min. Approximately 1,200 steps were collected during the walking task [including both stimulated and nonstimulated (control) steps]. This procedure was performed for each nerve stimulation condition.

Nerve stimulation

Cutaneous reflex responses were evoked with pseudorandomly applied trains (5 × 1.0 ms pulses at 300 Hz) of isolated constant current stimulation (Grass S88 stimulator with SIU5 and CCU1 isolation and constant current units, AstroMed-Grass) applied to the SP or to the SR nerve using flexible 1-cm disposable surface EMG electrodes (H69-P, Jason-Kendall LTP). Stimulus intensity was set as a multiple of the threshold at which a clear radiating paresthesia (radiating threshold, RT) into the innervation area of the nerve was reported. Stimulation intensities were set to evoke a strong cutaneous sensation (during standing) that was not deemed painful by the subjects. This level ranged across subjects from 2 to 4 × RT but was typically set at ~3 × RT (actual means (±SE) 3.34 × RT ± 0.19 for SP, 3.0 × RT ± 0.28 for SR).

EMG

Once the skin was abraded and cleaned with alcohol, disposable 1-cm surface EMG electrodes (Jason-Kendall LTP) were applied in a bipolar configuration over the tibialis anterior (TA), medial gastrocnemius (MG), biceps femoris (BF), anterior tibial (AD), posterior tibial (PD), long head of biceps brachii (BB), and long head of triceps brachii (TB) muscles bilaterally. Ground electrodes were placed over electrically neutral tissue. EMG signals were preamplified and band-pass filtered at 100–300 Hz (IP511 Grass Instruments, AstroMed).

Kinematics and step-cycle detection

Data on the kinematics of the ankle and elbow joints were recorded bilaterally in all subjects using bi-axial electromagnoneters (Biometrics, Cwenfellinfach, Gwent, UK) placed over the joint, secured with two-sided plastic tape and fabric straps using methods described previously (Zehr and Haridas 2003; Zehr et al. 1997). Additionally, in six subjects, kinematic data were also recorded from the knee and shoulder. Step-cycle parameters (e.g., heel contact, toe-off) were obtained with the use of custom-made force sensors, located in the insole of the subject’s right shoe.

DATA ACQUISITION AND EMG ANALYSIS. All 32 channels of data were sampled simultaneously at 1,000 Hz with dual 12 bit A/D converter connected to two Pentium III 500 MHz microcomputers running custom-written (Dr. Romeo Chua, University of British Columbia) LabView software (National Instruments, Austin, TX). For the walking task, custom-written software programs (Matlab, The Mathworks, Natick, MA) were used to separate the step cycle into 16 equal parts (portions), beginning with heel contact. The stimuli occurred randomly throughout the step cycle. During off-line analysis, the EMG signals were full-wave rectified and filtered (see following text). For each portion, the average trace from the nonstimulated steps was subtracted from the corresponding stimulated average trace. This produced a subtracted evoked EMG trace for each subject. From this, the stimulus artifact was removed, and the EMG trace was then filtered using a dual-pass fourth-order Butterworth low-pass filter at 40 Hz. Cutaneous reflex responses (in the subtracted EMG traces) were examined at early (<80 ms to peak amplitude), and middle (80–120 ms to peak) latencies. Reflex responses were only analyzed if they exceeded a 3-SD band (centered about the mean prestimulus EMG level) and had a duration of ≥5 ms. The amplitude of the reflex responses was taken as the average EMG value in a 10-ms time window centered about the peak of the response. For inter-subject comparison, cutaneous reflex amplitude values (baseline to peak) for each subject were normalized to the averaged peak control (nonstimulated) EMG amplitude value occurring during the step cycle for each muscle and were then expressed as a ratio.

For each of the static postures, 50 rectified EMG sweeps (100 ms pre- and 200 ms poststimulus) were collected using custom-written Labview software. The average sweep was then visually inspected for cutaneous reflex responses using custom-written software (Matlab, The Mathworks) using the criteria identified in the preceding text. KINEMATIC ANALYSIS. Subtracted values for changes in joint angle were obtained as described above for the EMG data. The maximum change was calculated over a time interval of 120–200 ms poststimulus (similar to Zehr et al. 1997). These values were normalized to the maximum range of motion recorded for each subject during the step cycle, and then expressed as percentages.

Statistics

In all cases, analysis was performed using the averaged normalized values for each subject from each part of the step cycle. Repeated-measures (RM) ANOVA was used to determine significant differences in the background EMG level, cutaneous reflex amplitudes, and stimulus-induced kinematic changes between the postures and during walking. Tukey’s highest significant difference (HSD) test was used to post hoc any significant main effects observed. Linear least-squares regression analysis was used to evaluate correlations between the reflex values and changes in joint angle at each part of the step cycle for the muscles involved at a particular joint. Descriptive statistics included means ± SE, and statistical significance was set at $P < 0.05$. 

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RESULTS

SP nerve stimulation

EMG responses. Reflex modulation across the step cycle. Extensive phase-dependent modulation of cutaneous reflex responses was observed bilaterally in most of the muscles sampled. Figure 1 shows subtracted EMG traces across the step cycle for muscles of the leg and arm taken from one subject during SP nerve stimulation. The figure displays subtracted EMG traces for each of the portions of the step cycle moving top to bottom from stance to swing for ipsilateral (i) muscles and from swing to stance for contralateral (c) muscles. To the right of each set of subtracted traces control EMG across the step cycle for each muscle are plotted vertically. As can be seen in Fig. 1A, inhibition occurred during stance (portions 5–7) for iMG, whereas facilitation was observed in stance (portions 11–14) for cMG. The light gray vertical bar on the figure highlights these responses. Figure 1B shows subtracted data for PD in the same subject. Inhibition occurred during the stance portion (portions 6–8) of the step cycle for iPD, and excitation occurred for the same portion of the step cycle (portions 12–15) in cPD as highlighted by the vertical boxes in the figure.

When comparing responses across all subjects, there were no significant early-latency (i.e., <80 ms) reflex responses in any muscles studied (not shown). The sole exception was for a significant inhibition occurring during early stance in iAD. In contrast, however, there were many significant middle-latency (i.e., 80–120 ms) reflex responses when averaged across all subjects. Figure 2 shows the amplitude of the middle-latency responses for the leg muscles, whereas the arm muscles are shown in Fig. 3.

FIG. 1. Subtracted electromyographic (EMG) traces from 1 subject evoked by superficial peroneal (SP) nerve stimulation during the step cycle. A: ipsilateral (i) medial gastrocnemius (MG; left) and contralateral (c) MG (right). B: ipsilateral and contralateral posterior deltoid (iPD, left, and cPD, right, respectively). The gray rectangle highlights the response observed during particular portions of the step cycle. Note the reversal in sign of the reflex response between ipsilateral (suppression) and contralateral (facilitation) muscles during the stance phase. Stimulus artifact has been removed from each trace and replaced by a black vertical bar extending from time 0 out to ~30 ms post-stimulus. Background EMG during the step cycle is shown by the gray line to the right of each muscle’s trace. Calibration bar represents 50 μV.
significant \( (P < 0.05) \) inhibitory response was seen during the latter portion of swing and the swing to stance transition (see asterisks over portions 14–16). In cTA (Fig. 2, top right), inhibition was also seen at end swing and the swing to stance transition of the contralateral leg (thus at the same relative portion of the walking cycle). Therefore for TA, inhibition was observed bilaterally at the same functional portion of the step cycle. This contrasts with the pattern seen in the plantarflexor MG. For MG muscle, while each leg was in the stance phase of the movement cycle, iMG (Fig. 2, middle left) was signifi-
cantly inhibited (portions 5–6), while crossed facilitation was seen in cMG (middle right, portions 11–15). The knee flexor BF showed a pattern of modulation that shared elements of timing with TA (occurring during swing and transitions) and of crossed sign (excitation on ipsilateral and inhibition on contralateral sides) with MG. Facilitation was observed during swing (portions 13–16) for iBF (Fig. 2, bottom left), whereas cBF (bottom right) was significantly inhibited (portions 5–6) during the same part of the step cycle.

The amplitudes of the middle latency responses for the arm muscles are shown in Fig. 3 with the ipsilateral muscles on the left. The main observation in the arms was a reciprocal crossed effect between the ipsilateral and contralateral PD. Significant inhibition in iPD was seen during the middle to late portions of the stance phase (portions 5–8), whereas significant facilitation was also seen in cPD during stance (portions 10 and 13). Thus the pattern of SP nerve reflex responses in PD muscle was similar to that seen in the leg extensor MG: inhibition was seen ipsilaterally and excitation contralaterally during the stance phase. It is important to note that these crossed effects do not occur simultaneously (e.g., during ipsilateral stance and contralateral swing) but instead are expressed during the same
relative portion of the step cycle on both sides (e.g., during stance on both sides).

Relation between reflex amplitude and background EMG. Early and middle-latency cutaneous reflex amplitudes were each plotted against background EMG across the step cycle and for the five static postures, and linear regression analysis was performed. This was done to determine whether the reflex responses were scaled according to the level of background EMG or were independent of EMG amplitude. The Pearson correlation coefficients are shown in Table 1 for all 14 muscles studied. For the early-latency period, no significant correlations were observed during the static postures (not shown). For the middle-latency period, significant correlations between background EMG and reflex amplitude were found for 11 of the 14 (79%) muscles studied during static contraction. In contrast, during walking significant correlations were found in only 3 of 14 muscles (21%). Interestingly, the correlation values for the static conditions are significantly higher ($P < 0.05$) than those seen during walking. It should be noted that background EMG levels were not identically matched for static contraction and for walking. A difference was mainly seen for the arm muscles where static contraction levels were typically higher than those seen during walking (see Zehr and Haridas 2003). However, as discussed in an early publication (Zehr and Haridas 2003), this does not obscure the general picture of reflex amplitude scaling with background EMG during static but not rhythmic motor tasks. The effects of different postures on the early- and middle-latency reflex amplitudes were also examined. Main effects for posture on the early-latency reflex amplitude were observed for iBF, whereas iTA, iBF, and cBF showed a main effect on the middle-latency reflex amplitude (not shown). These could be explained by scaling with EMG due to posture as these effects occurred only in postures for which there was a change in background EMG activity.

KINEMATIC EFFECTS. In addition to the middle-latency reflex responses described in the preceding text, the kinematic outcomes of SP nerve stimulation are also plotted on Fig. 2.

TABLE 1. Summary of linear regression analysis between middle-latency reflexes and background EMG during standing and walking after SP nerve stimulation

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Task</th>
<th>Ipsilateral $r$</th>
<th>Task</th>
<th>Contralateral $r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg</td>
<td>Static</td>
<td>-0.93***</td>
<td>Static</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Walking</td>
<td>-0.57***</td>
<td>Walking</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Walking</td>
<td>0.52***</td>
<td>Static</td>
<td>0.77***</td>
</tr>
<tr>
<td>MG</td>
<td>Walking</td>
<td>NS</td>
<td>Walking</td>
<td>0.52***</td>
</tr>
<tr>
<td></td>
<td>Static</td>
<td>0.73***</td>
<td>Static</td>
<td>-0.77***</td>
</tr>
<tr>
<td>BF</td>
<td>Walking</td>
<td>NS</td>
<td>Walking</td>
<td>NS</td>
</tr>
<tr>
<td>Arm</td>
<td>AD</td>
<td>Static</td>
<td>NS</td>
<td>-0.96***</td>
</tr>
<tr>
<td></td>
<td>Walking</td>
<td>NS</td>
<td>Walking</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Static</td>
<td>NS</td>
<td>Static</td>
<td>-0.69**</td>
</tr>
<tr>
<td></td>
<td>Walking</td>
<td>-0.50***</td>
<td>Walking</td>
<td>NS</td>
</tr>
<tr>
<td>BB</td>
<td>Static</td>
<td>0.70***</td>
<td>Static</td>
<td>0.61**</td>
</tr>
<tr>
<td></td>
<td>Walking</td>
<td>NS</td>
<td>Walking</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Static</td>
<td>-0.59**</td>
<td>Static</td>
<td>0.88**</td>
</tr>
<tr>
<td></td>
<td>Walking</td>
<td>NS</td>
<td>Walking</td>
<td>NS</td>
</tr>
</tbody>
</table>

Significant Pearson correlation coefficients ($r$) are indicated by asterisks ($*P < 0.05$, $**P < 0.01$, $***P < 0.0001$; NS, no significant correlation).

Graphs on this figure (middle and bottom) show the SP nerve stimulus-induced changes in joint angle across the step cycle for both ankles and both knees (ipsilateral on left-hand side of figure). As shown, there was a significant effect on ankle kinematics during the stance-to-swing transition for each leg. On the ipsilateral side, an increased planar flexion was seen (portions 9–10), whereas on the contralateral side, increased dorsiflexion (portion 1) was observed. Additionally, increased flexion of the ipsilateral knee was also observed during swing (see portion 13). No significant kinematic change occurred in either the ipsilateral or contralateral elbow or shoulder as a result of SP nerve stimulation.

SR nerve stimulation

EMG responses. Reflex modulation across the step cycle. Just as with SP nerve stimulation described in the preceding text, with SR stimulation, cutaneous reflex responses were modulated in the muscles of the lower limbs according to the portion of the step cycle in which the stimulation occurred. Subtracted traces of reflex EMG data evoked by SR nerve stimulation from a single subject are shown in Fig. 4 for MG and PD muscles. Inhibition was apparent in i- and cMG during stance for both the ipsilateral (portions 5–7) and contralateral (portions 12–16) sides, respectively, as depicted by the light gray vertical boxes in the figure. Plotted on Fig. 4B are responses in PD muscle for which excitation is evident bilaterally. Note that the bilateral responses have the same sign for both MG (inhibition) and PD (excitation); this is in contrast to the crossed reciprocal effects (ipsilateral inhibition with contralateral facilitation during stance) seen after SP nerve stimulation (compare with Fig. 1). Only a brief treatment of SR nerve reflex responses in arm muscles is given here as these data were recently described in another paper (Zehr and Haridas 2003).

Just as seen with SP nerve stimulation, there was one muscle (cTA) in which a significant early-latency reflex was observed (inhibition during late stance; not shown). However, significant middle-latency reflex responses were commonly seen. The grouped data across all subjects are shown in Fig. 5 (ipsilateral, left). The common feature was that inhibition predominated. Inhibition was observed during swing for both iTA (portion 15) and cTA (portions 7–8), and during stance for iMG (portion 6) and cMG (portions 13–15). Ipsilateral BF did not display any significant middle-latency reflex responses, whereas in cBF, a significant inhibition was observed in the late portion of the stance phase (portion 1). Notice that the reflex sign was the same across the body for the same part of the step cycle in both TA and MG. It is interesting to note that SR nerve interlimb reflex responses in leg muscles evoked prominent inhibition, whereas a mixture of excitation and inhibition was seen in arm muscles after SP nerve stimulation (see Figs. 2 and 3).

Relation between reflex amplitude and background EMG. Significant correlations between background EMG level and cutaneous reflex amplitude were only observed during the static postures in two of the lower limb muscles with SR nerve stimulation (not shown). For the early-latency period, a significant correlation of 0.96 ($P < 0.05$) was observed in iTA during the static postures. For the middle-latency period, a significant correlation of −0.75 ($P < 0.0001$) between reflex
amplitude and background EMG activity was seen for cBF during the static postures. It is important to note that the EMG levels during static contraction for the lower limb muscles were similar to that seen during walking.

A main effect for posture on the middle-latency reflex amplitudes was observed for iTA and cBF (not shown). However, as was observed with SP nerve stimulation, the cases in which there was a significant difference between postures with respect to reflex amplitude coincided with the cases that showed changes in the background EMG activity.

KINEMATIC EFFECTS. Kinematic responses for the ipsilateral and contralateral ankles evoked by SR nerve stimulation are shown in the middle of Fig. 5. Significant kinematic effects were observed for both the ipsilateral and contralateral ankles during the stance-to-swing transition, with an increased dorsiflexion in both the ipsilateral (portion 8) and contralateral ankle (portion 1).

DISCUSSION

This study concerned the investigation of interlimb cutaneous reflex responses in both the arms and legs evoked by stimulation at the hand (SR) and foot (SP) during walking and there are three major new findings. First, stimulation in both the upper and lower limbs evoked significant changes in lower limb kinematics. Second, interlimb cutaneous reflex responses are phase-modulated during the walking cycle. Third, there is a reciprocally organized pattern and coordination of reflex responses from hand to foot and from foot to hand. Additionally, interlimb cutaneous reflex responses are task-modulated.
The implications of these observations, suggested pathways and mechanisms mediating these reflexes, and a functional interpretation of the kinematic outcomes are discussed in the following text.

**Functional relevance**

It was speculated that interlimb reflex responses could assist in the coordination of locomotor movements by transferring exteroceptive information between the arms and legs (Zehr et al. 2001a). We observed kinematic changes at the ankle during SP and SR nerve stimulation. These are summarized in Fig. 6. The figure shows an opposite response in the ipsilateral ankle to SP (plantar flexion) and SR (dorsiflexion) nerve stimulation. In contrast, the contralateral ankle showed the same response to both SP and SR stimulation (dorsiflexion).

With SP nerve stimulation, an increase in plantar flexion was
observed during the stance-swing transition for the ipsilateral ankle (Fig. 2, middle left, portions 9–10), and an increase in ipsilateral knee flexion was noted during swing (Fig. 2, bottom left, portion 13). Altogether, the responses in the ipsilateral lower leg with SP nerve stimulation are typical of a stumbling corrective response (Van Wezel et al. 1997; Zehr et al. 1997). This finding has also been observed in studies focusing on the control strategies that humans utilize when recovering from a trip during walking (Eng et al. 1994; Rietdyk and Patla 1998). It is challenging to interpret the responses in the contralateral leg in a functional manner. A facilitation response in cMG during stance (i.e., ipsilateral leg is in swing) during SP nerve...
stimulation might be able to assist a stumbling corrective response, which is seen in the ipsilateral leg. This facilitation could assist toe-off of the contralateral foot in response to an obstacle encountered by the ipsilateral foot. Combined with the ipsilateral stumbling corrective response, this could allow for the ipsilateral leg to be moved through the swing phase of the step cycle quicker than normal, thus allowing for it to contact the ground sooner to regain a more stable base of balance. The inhibitory response in cBF during the latter portion of swing (i.e., as the contralateral leg is swinging forward) may allow for the knee to be extended easily, thus allowing the foot to quickly contact the ground. However, there were no significant kinematic responses for the contralateral knee to corroborate this assertion.

The increased dorsiflexion in the contralateral ankle near the stance-swing transition (Fig. 2, middle right) is opposite to that seen ipsilaterally. The increase in dorsiflexion in the contralateral ankle near the stance-swing transition could be interpreted as a stumble-avoidance response. This response would retard the forward progression of gait by making contralateral toe-off (i.e., plantar flexion) more difficult.

In the introduction, it was suggested that responses in arm muscles should be expected after SP nerve stimulation as part of a global stumble correction in preparation for a possible fall. Although significant reflex responses were noted in arm muscles (e.g., Figs. 1 and 3), it is somewhat perplexing that changes in upper limb kinematics were not observed in concert with the changes in EMG. McIlroy and Maki (1995) showed quite clearly that early arm-muscle activation occurred in concert with overt kinematic changes after platform perturbations during standing. Recently, the arms were shown to be strongly active in reactive balance recovery to unexpected slips during walking (Marigold et al. 2003). However, significant reflex responses have been induced by either treadmill acceleration/deceleration or cutaneous (distal tibial) nerve stimulation with negligible effects on arm kinematics during walking (Dietz et al. 2001). It may be that the type of stimulation applied in our study was sufficient to demonstrate a pathway linking inputs from the foot to the arm musculature but may have been subthreshold for evoking a significant kinematic effect. Possibly, convergent input from other sensory modalities (e.g., vestibular) and other receptors (e.g., muscle spindles) would be needed for a larger response. It is also possible that the duration of our electrical stimulation pulse train may have been too brief to evoke responses in the arm muscles sufficiently large to alter kinematic trajectories in the upper limb.

With SR nerve stimulation, there was an increase in dorsiflexion bilaterally at the stance-swing transition (Figs. 5 and 6, bottom). At the stance-swing transition, the hand is positioned forward and away from the torso, while the foot is ready to enter the swing phase. In this position, the innervation area of the SR nerve would contact an obstacle during walking. If the hand was to hit an object while away from the body, an increase in dorsiflexion of the ankle near the stance-swing transition could help prevent forward progression by acting against toe-off as also seen in the ipsilateral ankle during SP nerve stimulation. This in turn could serve to help stop forward locomotion, thereby preventing the body from colliding with an object. Thus our results here extend the earlier suggestion that reflex responses within the legs can be utilized to alter limb mechanics in a functional manner during walking and highlight the integrated functional nature of reflex modulation during human walking (Zehr and Stein 1999).

Phase-dependent modulation of interlimb cutaneous reflex responses during walking

Phase-dependent modulation of interlimb cutaneous reflex responses was commonly found here. Within the legs, Van Wezel et al. (1997) showed that cutaneous stimulation of the foot generated contralateral reflex responses of smaller amplitude than the ipsilateral ones. Contralateral reflex responses seem to follow the movement phase of the contralateral limb, not the stimulated one (Duyens et al. 1990; Tax et al. 1995). Corrective responses during treadmill acceleration and deceleration have characteristics of bilateral control of reflex pathways (Berger et al. 1984) that also depend on movement phase. Interestingly, the sign of the reflex may be different on the contralateral side implying the presence of polysynaptic pathways across the spinal cord (Van Wezel et al. 1997). Here, middle-latency reflex responses in all lower limb muscles (Fig. 2) showed phase-dependent modulation after SP stimulation. In TA, inhibition was seen bilaterally during late swing. However, a reciprocal crossed effect was noted for MG and BF. In stance, inhibition was observed for iMG, but cMG displayed facilitation. For iBF, significant facilitation was seen during swing with inhibition in cBF during contralateral swing. Observations in TA and BF correspond with previous studies on ipsilateral (Zehr et al. 1997) and contralateral (Van Wezel et al. 1997) reflex responses while data on iMG and cMG represent new observations. In the arms, a reciprocal crossed effect was also observed in PD during SP nerve stimulation (Fig. 3).

Inhibition was seen in iPD during stance while facilitation was seen in cPD during contralateral stance. These crossed effects occurred in the same part of the step cycle for the respective leg just as described for responses within the legs.

Cutaneous reflex responses in leg muscles are phase- and task-modulated during leg cycling and walking (Brooke et al. 1997). Previously we documented that cutaneous reflex responses within the arms are also phase- and task-modulated during both arm cycling (Zehr and Kido 2001) and walking (Zehr and Haridas 2003). Therefore there is a similar pattern of reflex modulation for the arms and legs during rhythmic movement. The data in the current study extend this comparative organization of reflex pathways to patterns seen between the arms and legs. In comparing the sign of responses in arm muscles after SP nerve stimulation (Fig. 3) to those in leg muscles after SR nerve stimulation (Fig. 5), some similarities and differences can be seen. For example, with SR stimulation, inhibition was observed in iTA and cTA during late swing, consistent with SP nerve stimulation. However, a reversal in sign was observed in cMG between the two different nerve stimulation protocols. During SR stimulation, inhibition was seen in cMG during stance. With SP stimulation, however, facilitation was seen in the same muscle during the same part of the step cycle. This suggests a different form of reflex organization from the SR and SP nerves onto motoneurons innervating muscles in the upper and lower limbs.

Task dependency of interlimb reflex responses

Association between EMG and reflex amplitudes was tested by linear regression. The lack of a significant relationship...
during rhythmic movement has been previously ascribed to the activity of CPG circuitry (Duyens and Tax 1994; Komiyama et al. 2000; Van de Crommert et al. 1998; Van Wezel et al. 1997; Zehr and Haridas 2003; Zehr and Kido 2001; Zehr et al. 2001b). With SP nerve stimulation, most of the muscles showed strong linear relations between reflex amplitude and background EMG during static contraction, whereas this relationship was mostly absent during walking (see Table 1) (for comparable data in arm muscles after SR nerve stimulation, please refer to Table 1 in Zehr and Haridas 2003). Taken together with the preceding description of phase-dependent modulation of reflex amplitude, the current observations suggest a role for CPGs in contributing to the control of rhythmic arm and leg movements. This corresponds with the contention advanced by Dietz (Dietz 2002a,b; Dietz et al. 2001). Interestingly, the projections from SR nerve onto leg muscles evoke relatively weaker responses than reflex responses evoked in arm muscles by SP nerve stimulation. We observed little relation between reflex and EMG amplitude in leg muscles after SR stimulation even during static contraction. In contrast, it was recently shown that SR reflex responses within the arms are strongly associated with background EMG during static contraction but dissociated during walking (Zehr and Haridas 2003). Additionally, the reflex responses observed in upper and lower extremity muscles on both the ipsilateral and contralateral sides of the body at the same portion of the step cycle suggests that a segmental CPG may be the mechanism allowing for the control of the cutaneous reflex responses observed.

**Putative pathways mediating interlimb cutaneous reflexes**

It has been suggested that in neurologically intact subjects, the transmission of interlimb cutaneous reflex responses may at least partially be mediated propriospinally (Zehr et al. 2001a). Major evidence for this was the short-latency values (<60 ms) noted for these responses. While responses at these short latencies could be seen as at a reasonable propriospinal latency, middle-latency (80–120 ms) responses are not necessarily excluded from a propriospinal locus, but the evidence to support them as such is much weaker. Furthermore, data on interlimb reflex responses obtained in persons with spinal cord injury suggest propriospinal linkages between the arms and legs (Calancie 1991; Calancie et al. 1996). Propriospinal coupling between the cervical and lumbar spinal cord has been observed in primates, including humans (Molenaar and Kuypers 1978; Nathan et al. 1996; Skinner et al. 1979). The organization of the long descending propriospinal tract seems to be similar between the monkey and the cat, although the distribution of neurons differs (Skinner et al. 1979). Despite the focus here on responses at middle latency (80–120 ms), the mere presence of long propriospinal connections may still be considered relevant to the current data. Long descending propriospinal neurons could convey cutaneous information from the arms to evoke reflex responses in leg muscles (Skinner et al. 1979). Recent data from the *Xenopus* tadpole model also show that ascending interneurons fire rhythmically during swimming and may contribute significantly to cutaneous reflex modulation during rhythmic movement (Li et al. 2002). Also, it has been demonstrated that reticulospinal projections can have potent direct and indirect effects on ipsilateral and contralateral hindlimb motoneurons of the cat (Jankowska et al. 2003). Similar projections, if present in the human, would be well suited to produce the interlimb cutaneous reflex modulation observed here. This remains to be substantiated, however. Additionally, the middle-latency interlimb cutaneous reflex seen in this study was within the earliest latency suggested by Nielsen et al. (1997) for a transcortical effect. Thus we cannot exclude the role of other supraspinal effects in contributing to the modulation observed here.

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