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## Modulation of cutaneous reflexes in human upper limb muscles during arm cycling is independent of activity in the contralateral arm

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**Abstract** The amplitudes and signs of cutaneous reflexes are modulated during rhythmic movements of the arms and legs (during walking and arm or leg cycling for instance). This reflex modulation is frequently independent of the background muscle activity and may involve central pattern generator (CPG) circuits. The purpose of the present study was to investigate the nature and degree of coupling between the upper limbs during arm cycling, with regard to the regulation of cutaneous reflexes. Responses to electrical stimulations of the right, superficial radial nerve (five 1 ms pulses, 300 Hz) were recorded bilaterally in six arm muscles of eight participants during arm cycling involving only the limb ipsilateral to the stimulation, only the limb contralateral to the stimulation, and bilateral movement when the limbs were both in-phase and 180° out of phase. The pattern of cutaneous reflex modulation throughout the arm cycle was independent of the functional state of the limb contralateral to the recording site, irrespective of whether recordings were made ipsilateral or contralateral to the stimulation. Furthermore, cutaneous reflexes were significantly ( $p < 0.05$ ) modulated with arm position in only 8% of cases in which the limb containing the responding muscle

was either stationary or being moved passively by the experimenter. The results show that there is relatively weak coupling between the arms with regard to the regulation of cutaneous reflexes during rhythmic, cyclical arm movements. This suggests a loose connection between the CPGs for each arm that regulate muscle activity and reflex amplitude during rhythmic movement.

**Keywords** Cutaneous reflexes · Arm cycling · Central pattern generator · CPG · Bilateral movement · Reflex modulation

### Introduction

The organisation and function of cutaneous reflexes in the legs during rhythmic, cyclical movement has received considerable attention for tasks such as walking and leg cycling (for reviews, see Brooke et al. 1997; Zehr and Stein 1999). Less is known regarding the patterns of reflex modulation during rhythmic, cyclical movement performed with the arms. However, it has recently been demonstrated that some features of cutaneous reflex modulation observed during cyclical leg movements, such as task and phase dependency, are common to rhythmic arm movements, including arm cycling (Zehr and Kido 2001) and walking (Zehr and Haridas 2003). For example, in some muscles, the position of the limb during arm cycling influenced the size of the cutaneous reflex responses in a manner that was independent of the background EMG activity (premotorneural gating). There were also cases in which cutaneous stimulation resulted in an excitatory response at some points in the arm cycle, but inhibition at other points of the cycle (reflex reversals). Reflex reversals occurred in some muscles between static contractions and rhythmic movements (in other words task dependency; Zehr and Kido 2001).

The accumulating data support the hypothesis that the mechanisms of reflex modulation during rhythmic, cyclical movement are similar between the arms and legs, and may be due to interneuronal circuits that

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comprise central pattern generators (CPGs). The nature of coupling between CPGs for the arms is of significant interest as a basis for further comparison of the mechanisms of neural control between arm and leg movements. We recently found that some differences exist in the regulation of H-reflexes between the arms and legs, in that H-reflexes are not depressed in a stationary arm when the contralateral arm is passively moved in a rhythmic, cyclical manner (Zehr et al. 2003). Such weak contralateral effects may be indicative of a relatively “loose coupling” between the CPGs for each arm. This is in contrast to what has been observed for leg cycling tasks (Cheng et al. 1998; Collins et al. 1993; Misiaszek et al. 1998), and suggests that the strength of the neural coupling between the arms is weaker than between the legs, at least in terms of the regulation of muscle afferent reflexes. Tax et al. (1995) reported similarities in cutaneous reflexes at corresponding phases in the step cycle between the legs during running and suggested that cutaneous reflexes elicited during locomotion are determined by the functional context of the limb in which the responding muscles reside. In the present study, we examined cutaneous reflexes in both arms during bilateral and unilateral cycling tasks. Our purpose was to add to our understanding of the neural control of the arms during rhythmic, cyclical movements by using reflex modulation as a “neural probe” (Burke 1999). The working hypothesis in these experiments is that CPG elements are involved in regulating muscle activity and reflex amplitude during rhythmic arm cycling. The main objectives of this study were to further elucidate the strength of neural coupling between the arms during rhythmic movement, and to provide evidence regarding the sites of cutaneous reflex modulation. We systematically assessed how cutaneous reflexes in homologous arm muscles located both ipsilateral and contralateral to the stimulation were affected by movements of each arm. We hypothesized that if there is strong linkage in neural control between the arms, cutaneous reflexes in muscles both ipsilateral and contralateral to the stimulus should be influenced by movement of the opposite arm.

## Materials and methods

### Subjects

Eight individuals (six males, two females) with no documented neurological disease volunteered for this experiment. The participants ranged in age from 21 to 39 years old. The procedures conformed to the Declaration of Helsinki and were approved by the Human Research Ethics Board at the University of Alberta.

### Protocol

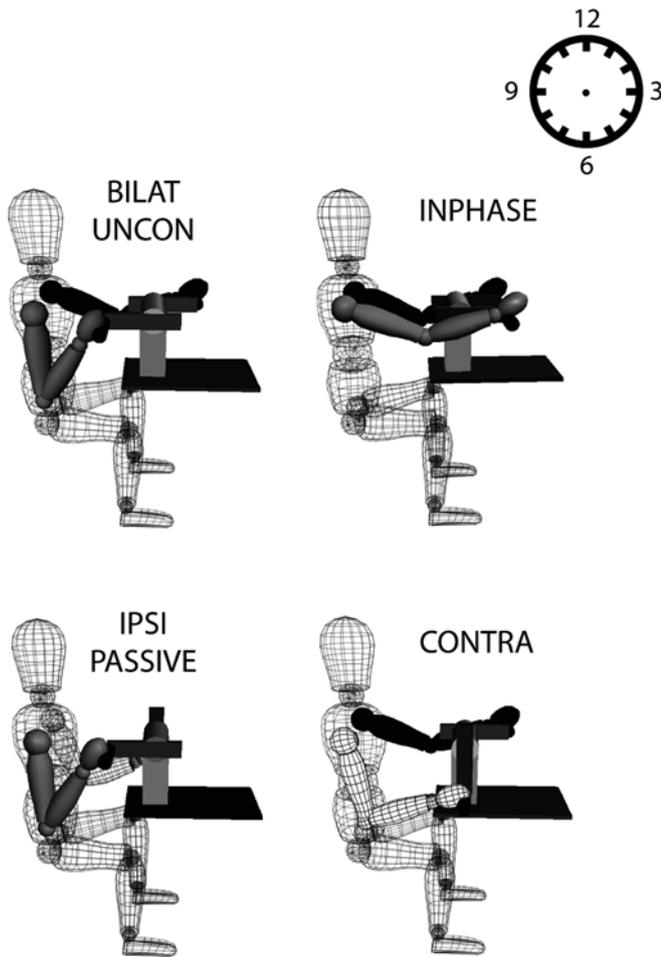
Participants performed rhythmic arm cycling with one or both limbs using a custom-built, hydraulic arm ergometer

that has been described previously (Zehr et al. 2003; Zehr and Kido 2001). The positions of the ergometer cranks were defined relative to a clock face, with the “top dead centre” position specified as 12 o’clock and the remaining positions following the conventions of a clock face when looking at the ergometer from the participant’s right (Fig. 1). The ergometer could be adjusted so that the two cranks were either coupled or allowed to rotate independently. The participants performed three bilateral and three unilateral arm cycling tasks. The bilateral tasks were arm cycling with: 1) the cranks coupled 180° out of phase (BILAT); 2) the cranks uncoupled but with instructions to maintain the arms 180° out of phase (UNCON); 3) the cranks uncoupled but with instructions to maintain the arms in phase (INPHASE). The unilateral tasks were arm cycling with: 1) the arm ipsilateral to the stimulation active and the contralateral limb held stationary at the six o’clock position (IPSI); 2) the arm ipsilateral to the stimulation passively rotated by an experimenter and the contralateral limb held stationary at the six o’clock position (PASSIVE); 3) the arm contralateral to the stimulation active and the ipsilateral limb held stationary at the six o’clock position (CONTRA). During the CONTRA condition, the participants maintained a tonic contraction in the ipsilateral wrist extensor muscles that was similar in magnitude to the average level of contraction observed during the BILAT condition.

The participants performed each of the arm cycling tasks for a total of eight minutes at a comfortable, self-selected rate between 60 and 80 revolutions per minute (rpm). Up to four short rest breaks were taken during trials. The order in which the tasks were performed was varied pseudo-randomly. Mean cycling rate varied from 67 ( $\pm 6$ ) rpm in the UNCON condition to 76 ( $\pm 9$ ) rpm in the IPSI and contra conditions. The mean rate of the BILAT ( $\pm 5$ ), passive ( $\pm 5$ ) and INPHASE ( $\pm 9$ ) conditions was approximately 70 rpm.

### Nerve stimulation

The superficial radial (SR) nerve, innervating the skin on the dorso-lateral surface of the hand, was stimulated with a train of five, 1 ms pulses at 300 Hz using self-adhesive, disposable stimulating electrodes placed on the dorsal surface of the right forearm just proximal to the radial head. A Grass S88 (Grass Instruments, AstroMed Inc., West Warwick, RI) stimulator, connected in series with a Grass SIU5 isolator and a Grass CCU1 constant current unit, delivered the stimuli at pseudorandom intervals of approximately 2.5–3.5 s during the arm cycling trials. The intensity of stimulation was set at approximately twice the radiating threshold (RT) for each subject and a brace was worn on the stimulated wrist to minimise electrode movement, as in previous studies (Zehr and Chua 2000; Zehr and Kido 2001). The participants were regularly asked to qualitatively rate the sensation induced by the nerve stimulation during the experiment to ensure that stimulus intensity was consistent.



**Fig. 1** Schematic illustration of the six arm-cycling tasks (*BILAT* arms constrained to move 180° out of phase, *IPSI* only the stimulated arm moved, *CONTRA* only the arm contralateral to the stimulation moved, *PASSIVE* only the stimulated arm moved passively, *INPHASE* uncoupled movement with arms moved together with identical orientation, *UNCON* uncoupled movement with arms 180° out of phase). A stationary limb is represented by a mesh outline. If the limb ipsilateral to the stimulation is moving, it is coloured grey, and if the limb contralateral to the stimulation is moving, it is coloured black. Electrical stimulation was delivered to the right arm in all tasks

## EMG

Surface EMG was recorded bilaterally from the flexor carpi radialis (FCR), extensor carpi radialis (ECR), biceps brachii (BB), and triceps brachii (Tri) muscles. The anterior deltoid (iAD), and posterior deltoid (iPD) muscles located ipsilateral to the stimulation were sampled from all eight participants and the PD and AD muscles in the limb contralateral to the stimulation (cAD and cPD respectively) were each sampled from four participants. EMG signals were preamplified (gain of 500–5000), band pass filtered (30–1000 Hz) and full wave rectified.

## Data acquisition and analysis

Data were sampled at 1000 Hz with a 12-bit National Instruments (Austin, TX) A/D board interfaced with a microcomputer running custom-written Labview (National Instruments, Austin, TX) software. Data analyses were performed off line using custom-written Matlab (The MathWorks Inc., Natick, MA) software. Trials were divided into individual cycles (consisting of one complete crank revolution) on the basis of crank position. For the remaining cycles, data were binned according to the position of the crank at the time of stimulation. Each revolution was divided into 12 equal bins defined relative to the clock face. That is, bin one contained all stimulations occurring when the crank was positioned between twelve and one o'clock, bin two contained all stimulations occurring when the crank was positioned between one and two o'clock, and so on. Data from all of the stimulated traces for each of the 12 bins were averaged from 100 ms before to 200 ms after the stimulus. For the trials in which the cranks were uncoupled (*INPHASE* and *UNCON*), data from individual cycles were only included if the phase relation between the two cranks was within  $\pm 45^\circ$  of the target value. The average number of responses averaged in each bin ranged from 10–14 across conditions.

The amplitude and latency of cutaneous reflexes were determined according to procedures described previously (Zehr and Kido 2001; Zehr and Chua 2000). Briefly, stimulated and unstimulated EMG traces from each bin were low pass filtered at 40 Hz, and the average unstimulated traces were subtracted from the average stimulated EMG. Reflexes were identified when the post-stimulus EMG escaped a threshold band defining  $\pm 2$  SD of the pre-stimulus EMG. The latency of the reflex responses was determined as the time at which the peak or valley with the greatest absolute value occurred during the period when the stimulated EMG escaped the 2 SD band. Reflex amplitudes for each subject were expressed as a percentage of the peak EMG observed during the averaged control cycles for the *BILAT* condition.

## Statistics

Wilcoxon matched pairs tests were conducted to detect significant differences between stimulated and unstimulated EMG traces at early (~50–80 ms) and middle (~90–120 ms) reflex latencies for the *BILAT* task in each muscle (to determine whether reflexes were statistically significant). Statistical significance was set at  $p < 0.05$ . Paired *t*-tests were also used to detect significant reflexes at individual bins. The Bonferroni correction was applied to avoid Type 1 error (critical  $p = 0.0042$ ). For the significant reflexes, Wilcoxon matched pairs tests were conducted to test whether pre-stimulus EMG amplitudes and reflex amplitudes differed between pairs of tasks. The Bonferroni correction was applied (critical  $p = 0.0033$ ). To determine whether there was significant modulation of reflex size at different phases in the movement cycle for particular tasks

and muscles, one-way ANOVAs were performed on reflex amplitudes across the 12 movement bins for each task. Statistical significance was set at  $p < 0.05$ . Pearson product moment correlation analysis was conducted on the relationship between reflex amplitudes and control EMG for each muscle to determine the extent to which variations in reflex size across movement phases were linearly related to changes in background muscle activation. For our sample size of eight, there were seven degrees of freedom, yielding a critical  $r$  of 0.666 at  $p < 0.05$ .

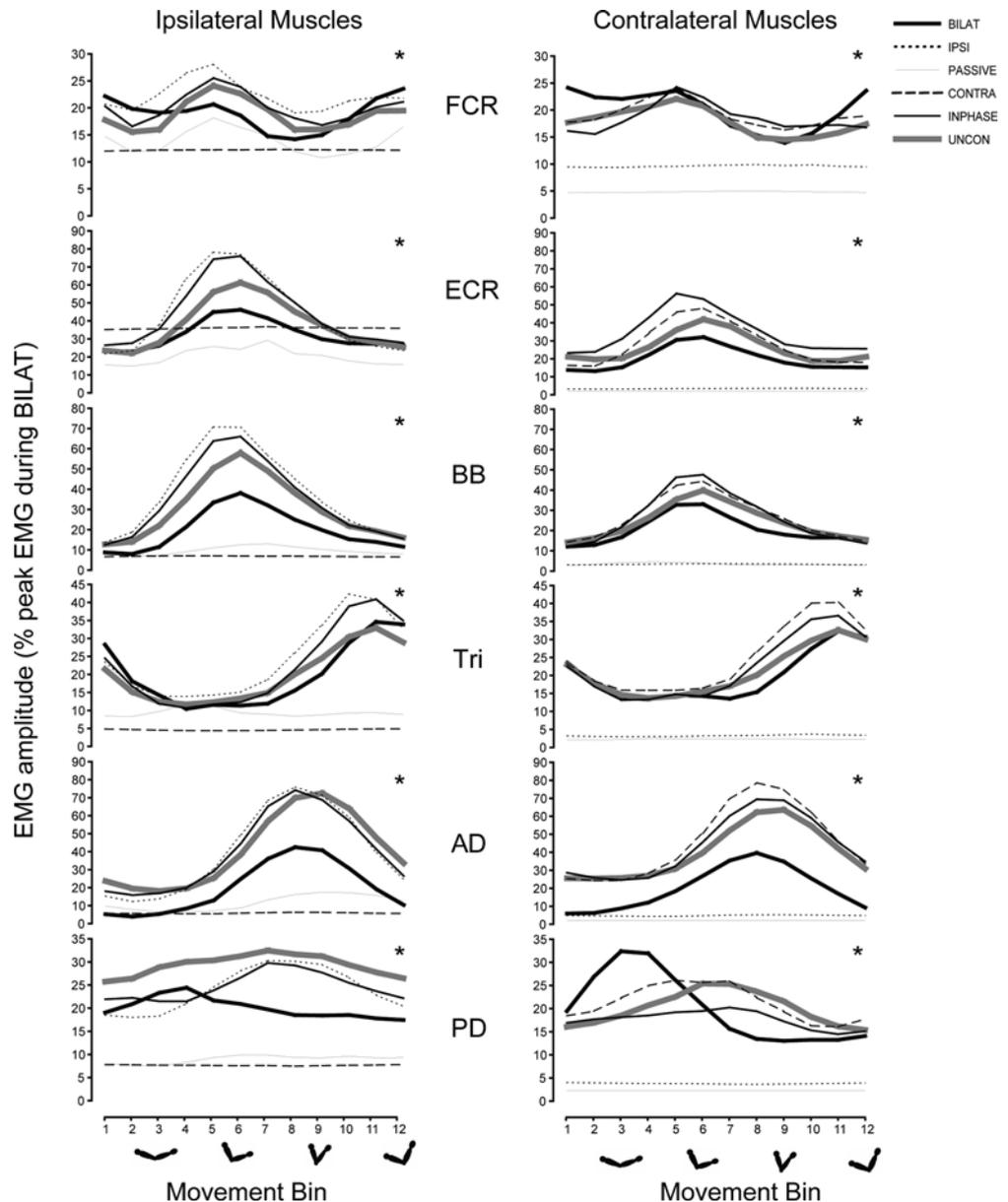
## Results

### Muscle activity during the different arm cycling tasks

The average background EMG activity from unstimulated sweeps for each of the 12 muscles and six tasks is shown

in Fig. 2. For Fig. 2, the phase of the movement cycle for a particular muscle is specified relative to the position of the limb in which that muscle resides. That is, data shown in bin 1 for all of the contralateral muscles was recorded when the limb contralateral to the stimulation was located between 12 o'clock and one o'clock. For cases in which muscles reside in a limb that did not move (the ipsilateral muscles for the CONTRA task, and contralateral muscles for the IPSI task), the phase is specified by the position of the opposite, moving limb. The general pattern of EMG activity across arm positions for the BILAT task was similar to that observed for the other tasks in which each muscle was actively involved in arm cycling (UNCON, INPHASE and IPSI for ipsilateral muscles, and UNCON, INPHASE and CONTRA for contralateral muscles). Exceptions to this generalization occurred in iPD and cPD, for which muscles the peak in EMG activity shifted from the transition point from shoulder extension to

**Fig. 2** Background EMG amplitude from unstimulated arm cycling (*FCR* flexor carpi radialis, *ECR* extensor carpi radialis, *Tri* triceps brachii, *BB* biceps brachii, *AD* anterior deltoid, *PD* posterior deltoid; task abbreviations as given in Fig. 1). Data are group means for each bin and each of the six tasks and 12 muscles. Amplitudes are expressed relative to the peak EMG amplitude measured in the BILAT task during movement cycles for which there were no stimulations. The approximate positions of each arm (ipsilateral and contralateral to the stimulus) at the 3, 6, 9 and 12 o'clock positions are illustrated schematically beneath the horizontal axis labels. Asterisks denote muscles in which there were significant differences in EMG activity between tasks ( $p < 0.05$ )



flexion in the BILAT task (bins three, four, and five) to approximately at the mid-point of the shoulder flexion (bins seven, eight and nine) in the other active tasks for each arm. Despite the general similarities in the pattern of EMG activity across the movement cycle, there were significant EMG amplitude differences between at least one pair of tasks for all muscles ( $p < 0.05$ ). There was significantly less EMG activity ( $p < 0.05$ ) during the BILAT condition compared with at least one of the other unconstrained, active tasks (IPSI, INPHASE, UNCON for ipsilateral muscles; CONTRA, INPHASE, UNCON for contralateral muscles) for iECR, cECR, iBB, cBB, iTri, cTri, iAD, cAD and iPD. Therefore, it appears that the pattern of muscle activity required to perform arm cycling movements for each arm independently is generally similar to the pattern required for constrained arm cycling, for all of the muscles sampled in this study other than PD. However, some of the unconstrained tasks involved significantly greater EMG activity than the BILAT task in ECR, BB, Tri, AD and PD.

### Cutaneous reflexes

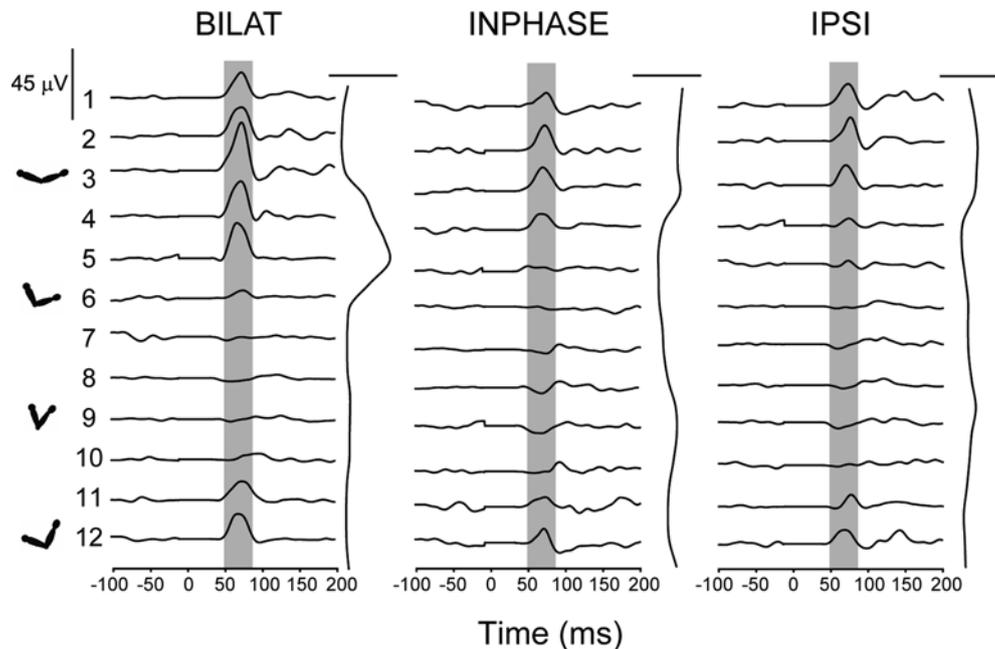
The first two reflex latencies were analysed in detail in this study and termed early (~50–80 ms) and middle (~90–120 ms). The peak latencies of these responses are comparable to those that we have reported previously (Zehr and Kido 2001; Zehr and Chua 2000), and are similar across tasks. Reflexes were statistically significant ( $p < 0.05$ ) in all

muscles except for cPD (early latency), iECR (middle latency), cFCR (middle latency) and iPD (middle latency). Therefore, electrical stimulation of the SR nerve elicited significant cutaneous reflexes in 20 out of 24 cases (12 muscles by two latencies).

Plots of the average, subtracted EMG (stimulated sweeps with control subtracted) in the BILAT, INPHASE and IPSI tasks for iPD from an individual participant are displayed in Fig. 3. It is apparent that the pattern of reflex modulation across the movement cycle is similar in the three tasks despite differences in the background EMG activity and the activity state of the contralateral limb. Across all subjects, this general similarity in the pattern of reflex modulation across the movement cycle was evident for most muscles for both the early (Fig. 4) and middle (Fig. 5) latency responses. In each muscle for which there was an obvious phase modulation of reflexes in the BILAT task (thick black traces in the figures), there was an almost identical pattern of reflex facilitation or inhibition throughout the cycle for the other tasks in which that muscle was active. A systematic description of these results for all muscles and tasks will follow.

### Amplitude of cutaneous reflexes in the BILAT and UNCON tasks

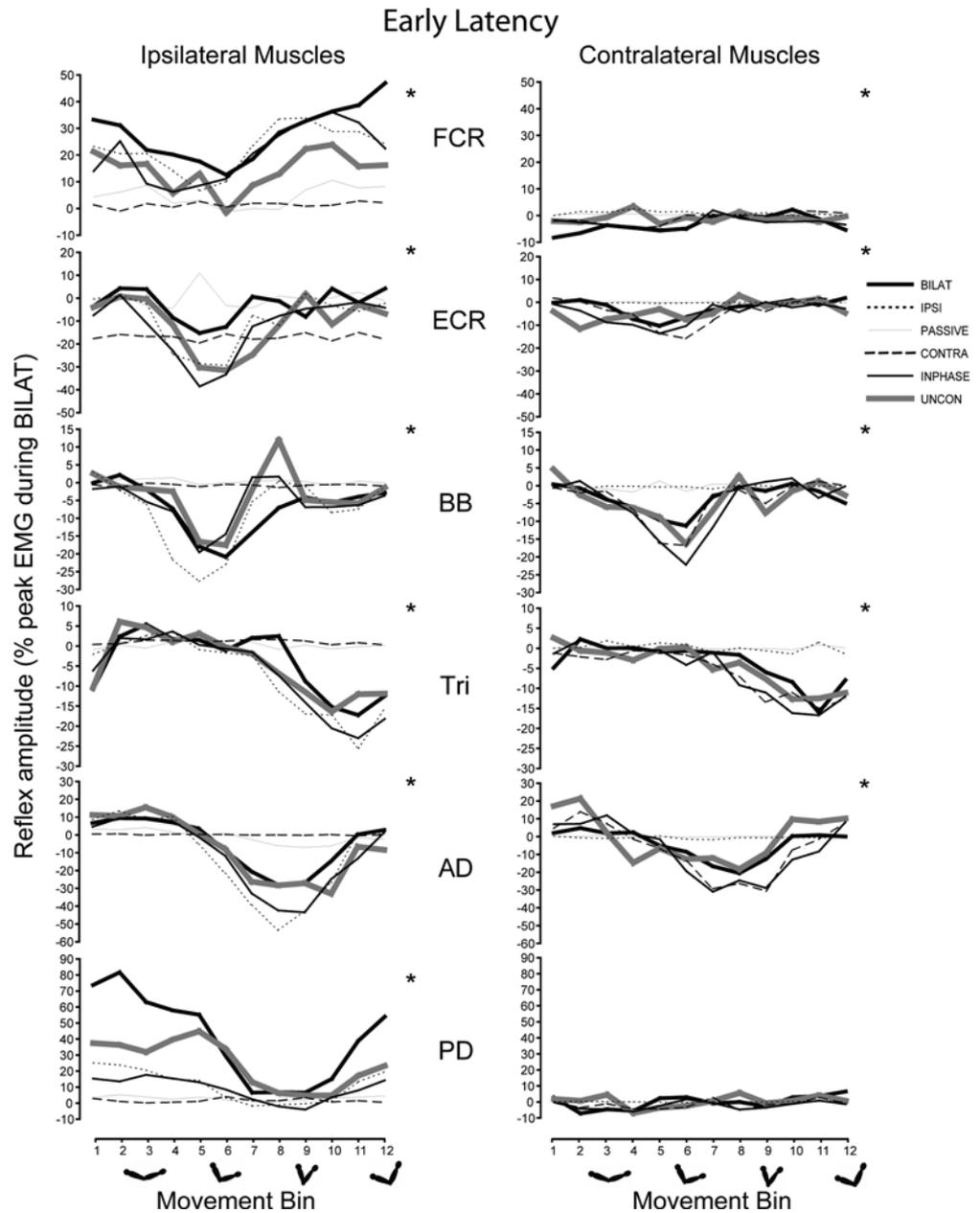
For the BILAT task, the general patterns of reflex modulation across the movement cycle were similar to those we reported previously (Zehr and Kido 2001; Zehr



**Fig. 3** Average EMG traces of all stimulated sweeps in each movement bin from 100 ms prior to stimulation to 200 ms after stimulation for an individual participant. Data are from iPD for the BILAT, INPHASE, and IPSI cycling tasks. Early latency reflexes (~50–80 ms after stimulation) are highlighted with a grey bar in each task. The average EMG recorded during unstimulated movement cycles is displayed vertically to the right of the raster plots for each

task. Each trace is scaled to the peak EMG amplitude measured in the BILAT task during movement cycles for which there were no stimulations (0=far left of axes). The stimulus artefacts are replaced by flat lines at the average pre-stimulus EMG amplitudes. The approximate positions of the arms at the 3, 6, 9 and 12 o'clock positions are illustrated schematically on the left side of the figure

**Fig. 4** Mean amplitudes of early latency cutaneous reflexes (~50–80 ms post stimulus) elicited in each movement bin for the six tasks and 12 muscles (abbreviations as given in Figs. 1 and 2). Reflex amplitudes are expressed relative to the peak EMG amplitude measured in the BILAT task during movement cycles for which there were no stimulations. The approximate positions of each arm at each movement bin are illustrated schematically beneath the horizontal axis labels. Asterisks denote muscles in which significant reflexes were observed

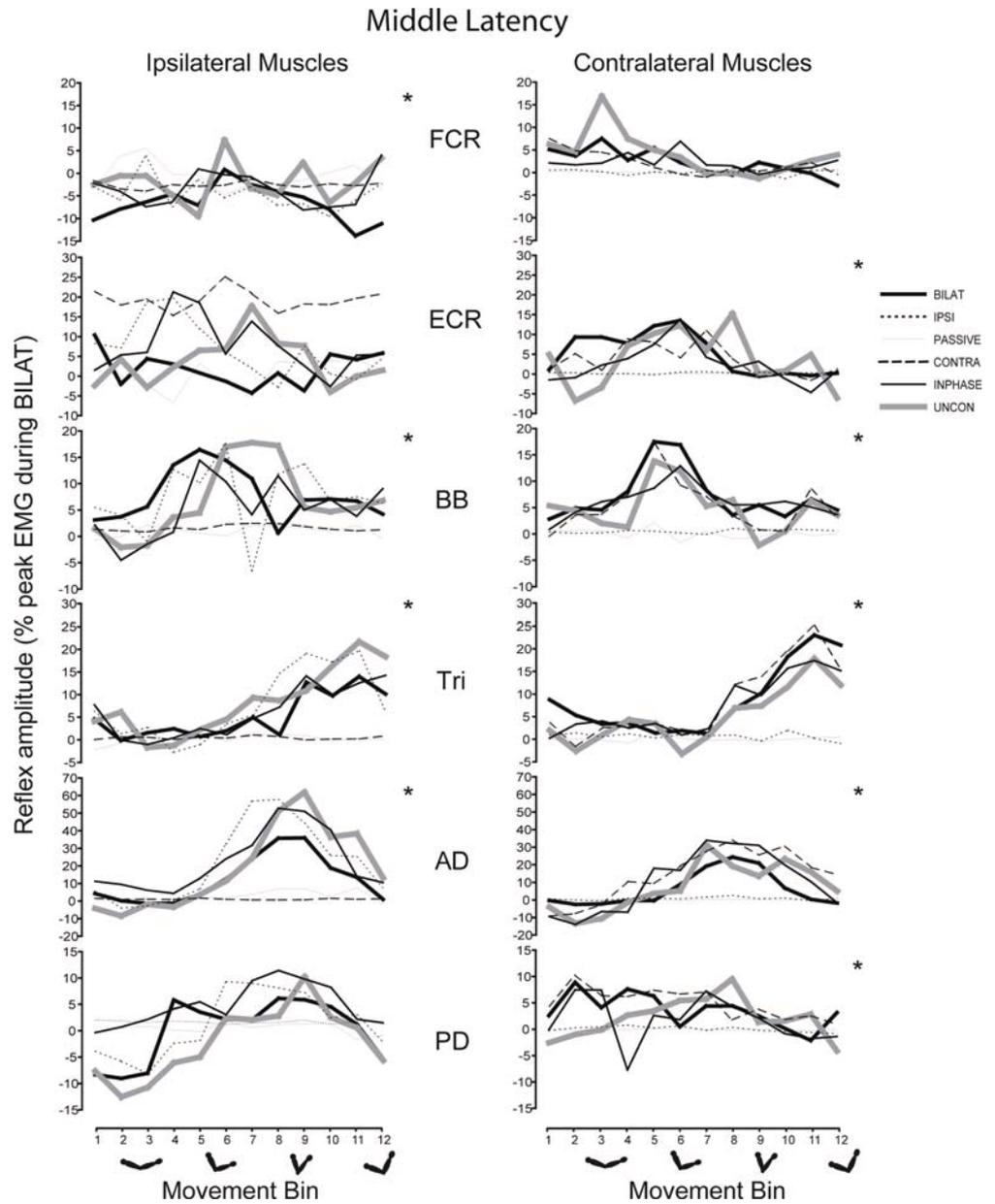


and Chua 2000) for the ipsilateral muscles and for cAD (Figs. 4 and 5). Reflexes in cPD were either small (middle latency) or non-significant (early latency), and showed little relationship to the pattern of modulation evident in iPD. For the contralateral BB and Tri muscles, which had not previously been studied, cutaneous reflexes were similar to those for the homologous ipsilateral muscles at the same phase of the movement cycle. Cutaneous reflexes for cFCR and cECR were small and showed no significant modulation across the movement cycle. Therefore, there was no consistent cutaneous reflex modulation in three of the six muscles contralateral to the stimulus during constrained, bilateral arm cycling. For the other three muscles contralateral to the stimulus, the amplitudes of cutaneous reflexes at each point in the movement cycle

were strikingly similar to those of the ipsilateral muscles (Figs. 4 and 5).

The amplitudes of cutaneous reflexes were similar between the BILAT and UNCON tasks at equivalent points in the movement cycle. There were significant differences in reflex amplitude ( $p < 0.05$ ) between the two tasks in only 5 of 20 cases (the 20 significant cases from the 12 muscles and two latencies). This suggests that any differences in motor pattern associated with the independent control of each arm had a minor effect on the modulation of cutaneous reflexes.

**Fig. 5** Mean amplitudes of middle latency cutaneous reflexes (~90–120 ms post stimulus) elicited in each movement bin for the six tasks and 12 muscles (abbreviations as given in Figs. 1 and 2). Reflex amplitudes are expressed relative to the peak EMG amplitude measured in the BILAT task during movement cycles for which there were no stimulations. The approximate positions of each arm at each movement bin are illustrated schematically beneath the horizontal axis labels. Asterisks denote muscles in which significant reflexes were observed



**Amplitude of cutaneous reflexes in the unilateral cycling tasks**

The amplitude of cutaneous reflexes at each arm position (or the pattern of reflex modulation across the cycle) was similar between the IPSI task and the BILAT task for muscles located ipsilateral to the stimulus, and between the CONTRA task and the BILAT task for muscles located contralateral to the stimulus (Figs. 4 and 5). These similarities were partially supported by statistical analyses, in that the only significant difference in reflex amplitude between BILAT and CONTRA tasks for a contralateral muscle occurred in cAD (middle latency). However, reflex amplitudes were significantly smaller in the IPSI task than the BILAT task for the iPD (early latency), but larger in the IPSI task in the iAD (early and middle latency) and iTri (early latency) muscles ( $p < 0.05$ ).

There was only one case of significant reflex modulation occurring across the cycle for the muscles located ipsilateral to the stimulus in the CONTRA task, and contralateral to the stimulus in the IPSI task (in a limb that was stationary while the other limb performed arm cycling; Figs. 4 and 5). Reflex amplitude was significantly modulated across movement phases in iFCR (middle latency;  $p < 0.05$ ). A lack of phase modulation was apparent even for the iECR muscle during the CONTRA task (see Figs. 4 and 5). In this case, a tonic contraction was maintained in the stationary limb (which received the stimulation), while the contralateral limb performed active cycling. This suggests that the lack of phase modulation evident in muscles residing in stationary limbs is not caused merely by an absence of discernible reflexes due to minimal muscle activity. The degree of coupling between the arms is therefore not sufficiently strong to cause phase

modulation of cutaneous reflexes in a stationary limb that is contralateral to a moving arm, irrespective of whether this arm is on the same or the opposite side of the body to the stimulation.

#### Amplitude of cutaneous reflexes in the PASSIVE cycling task

Cutaneous reflexes during the PASSIVE condition were small and showed little phase modulation for both the early and middle latency responses (Fig. 4 and 5). There was significant modulation of reflex amplitude ( $p < 0.05$ ) across the cycle in only 2 of 20 cases (early and middle latency reflexes for iAD). In summary, for the inactive limbs in these three tasks, there was significant reflex modulation across the cycle in only 3 of 40 cases (8%; 2 tasks by 20 significant reflex latencies).

#### Amplitude of cutaneous reflexes in the INPHASE cycling task

The amplitudes of cutaneous reflexes at each arm position during the INPHASE task were similar to those during the BILAT task for both limbs, although reflexes were significantly larger in the BILAT task for iPD (early latency) and iECR (early latency) and significantly smaller in the BILAT task for iAD (early and middle latency;  $p < 0.05$ ). Importantly, there were no significant differences

in reflex amplitude between these tasks in any of the muscles located contralateral to the stimulation. In this case, the position of the limb opposite to the stimulus was identical, but the limb that was stimulated was 180° out of phase between the two conditions.

#### Pattern of reflex modulation across the movement cycle

The general similarity in the pattern of cutaneous reflex regulation among all of the tasks that involved active arm cycling, that has been illustrated across a range of muscles in the upper limbs, can be further appreciated by considering the results for individual muscles in detail. For example, in iAD, there were small excitatory early latency reflexes in bins one to five, and larger inhibitory reflexes in bins six to ten for the BILAT, IPSI, INPHASE, and UNCON tasks (Fig. 4). Therefore, the pattern of cutaneous reflex modulation across the movement cycle was identical in all of these tasks, even though the limb contralateral to the stimulation was either stationary, constrained to move out of phase with the ipsilateral limb, or moving in or out of phase with the ipsilateral limb by volitional control. In contrast, there was much less modulation of the early reflexes for the PASSIVE and CONTRA tasks (thin and dashed lines in Fig. 4), although there was reflex modulation that achieved statistical significance for the PASSIVE task ( $p < 0.05$ ). In these tasks, the limb in which iAD resides was either stationary

**Table 1** Pearson correlation coefficients ( $r$ ) for regressions between reflex amplitude and background EMG

Muscles	$r$ values for cycling task							
	BILAT	UNCON	INPHASE	IPSI	PASSIVE	CONTRA		
Early latency	iFCR	0.30	0.17	0.13	0.21	0.06	0.06	
	iECR	-0.02	0.01	-0.19	0.03	-0.27	-0.11	
	iBB	-0.76*	-0.29	-0.16	-0.28	0.28	-0.52	
	iTri	-0.48	-0.60	-0.73*	-0.54	0.23	0.69*	
	iAD	-0.58	-0.47	-0.65	-0.72*	-0.42	-0.46	
	iPD	0.46	0.52	0.03	-0.16	0.35	-0.37	
	cFCR	-0.33	0.03	-0.24	0.03	0.35	0.06	
	cECR	-0.10	0.00	-0.04	-0.11	0.03	-0.26	
	cBB	-0.63	-0.69*	-0.67*	-0.46	-0.40	-0.48	
	cTri	-0.82*	-0.82*	-0.87*	-0.58	-0.21	-0.91*	
	cAD	-0.83*	-0.38	-0.53	-0.63	0.13	-0.56	
	cPD	-0.01	0.09	-0.44	0.65	0.03	-0.49	
	Middle latency	iFCR	-0.47	0.39	0.20	-0.31	-0.24	-0.81*
		iECR	0.13	0.11	0.00	0.20	0.05	0.25
iBB		0.40	0.29	0.13	0.01	0.27	0.76*	
iTri		-0.22	0.58	0.02	0.01	0.03	-0.64	
iAD		0.67*	0.52	0.57	0.60	0.46	0.80	
iPD		-0.24	-0.42	0.28	0.22	0.15	0.60*	
cFCR		-0.14	0.11	0.14	-0.32	0.11	-0.10	
cECR		0.04	0.04	-0.09	0.12	0.09	0.20	
cBB		0.65	0.65	0.60	0.11	0.11	0.60	
cTri		0.83*	0.81*	0.80*	0.66	0.10	0.87*	
cAD	0.85*	0.61	0.63	0.52	0.11	0.60		
cPD	-0.06	0.44	0.38	-0.13	-0.13	0.77*		

Statistically significant ( $p < 0.05$ ) correlations are indicated by \*. Abbreviations: BILAT (arms constrained to move 180° out of phase), IPSI (only the stimulated arm moved), CONTRA (only the arm contralateral to the stimulation moved), PASSIVE (only the stimulated arm moved passively), INPHASE (uncoupled movement with arms moved together with identical orientation), UNCON (uncoupled movement with arms 180° out of phase). “i” and “c” denote ipsilateral and contralateral respectively. FCR=flexor carpi radialis, ECR=extensor carpi radialis, Tri=triceps brachii, BB=biceps brachii, AD=anterior deltoid, PD=posterior deltoid

or being passively moved by the experimenter. A similar trend was also observed in some muscles contralateral to the stimulated arm. For example, in cTri, there was little early latency reflex activation in bins one to eight, and a large reflex inhibition of the ongoing EMG in bins 8 to 12 for the BILAT, UNCON, INPHASE, and CONTRA tasks (Fig. 4). Once again, the pattern was identical in these conditions regardless of the functional state of the limb ipsilateral to the stimulation. There was no significant reflex modulation across the cycle for the IPSI and PASSIVE conditions, in which cases the arm in which cTri resides was stationary.

#### Relationship between reflex amplitude and background muscle activity

Before interpretations regarding the mechanisms of cutaneous reflex modulation could be made, it was important to establish that the modulation of reflex amplitudes observed across the movement cycle was not simply due to a scaling of reflex size to the background EMG. Qualitative comparison between background EMG amplitudes (Fig. 2) and reflex amplitudes (Figs. 4 and 5) reveal similarities in the general pattern of phase modulation in BB, Tri and AD. These similarities were reflected in significant linear relationships between background EMG amplitude and cutaneous reflex amplitude for some of the tasks in which these muscles were actively involved in cycling (Table 1). Overall, this analysis revealed that only 15% (21/144) of correlations showed significant relationships between EMG level and reflex amplitude. Furthermore, for the FCR, ECR and PD muscles, there was only one case of a significant linear relationship between background EMG and reflex amplitude when a muscle actively contributed to arm cycling (cPD in the CONTRA task). Therefore, in these three muscles, there was modulation of cutaneous reflex magnitude that was not strongly related to the ongoing muscle activity, which provides evidence of pre-motoneuronal gating. There were also examples of changes in the sign of reflexes from excitatory to inhibitory throughout the cycle for iAD (early latency response; Fig. 4), and cAD (middle latency response; Fig. 5).

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## Discussion

In this study we first compared reflex modulation during bilateral arm cycling with the limbs constrained to move 180° out of phase, which we have previously described (Zehr and Kido 2001), with reflex modulation during arm cycling when the arms were free to move independently, but the participants intended to keep a 180° phase relationship between the limbs. This “unconstrained” cycling task was necessary to ensure that any differences in reflex modulation between the constrained task and the other unconstrained tasks were not due to differences in the motor pattern required to independently rotate each

limb through the entire range of motion (without assistance from the contralateral limb; see Ting et al. 1998). We then compared cutaneous reflexes during these two bilateral, out of phase tasks with reflexes during arm cycling involving only the limb ipsilateral to the stimulation, only the limb contralateral to the stimulation, and during passive cycling of the ipsilateral limb. Finally, we measured reflex responses in both arms during bilateral arm cycling when the limbs were in phase. If the pattern of reflex responses in the arm contralateral to the stimulation was phase-locked to the position of the stimulated limb in both the in-phase and out-of-phase tasks, it would suggest that the regulation of cutaneous reflexes depends primarily on the functional state (afferent and/or efferent activity) of the stimulated limb. Conversely, if cutaneous reflexes in the limb contralateral to the stimulation were modulated according to the position of that arm in both tasks, it would indicate that the sign and amplitude of cutaneous reflexes is determined according to the functional state of the limb in which a reflex is expressed, regardless of the site of stimulation. The most striking feature of our results is that the pattern of cutaneous reflex modulation in each arm during rhythmic arm cycling is relatively independent of the activity of the contralateral limb. That is, the modulation of cutaneous reflexes depends mainly on the movement context of the limb in which the reflex is expressed. This was the case for reflexes in muscles both ipsilateral and contralateral to the stimulation, and occurred despite differences between tasks in the rate of cycling and background EMG activity. Furthermore, when reflexes were recorded from a muscle in a limb that was either stationary, or being moved passively, there was significant phase modulation of cutaneous reflexes in only 3 out of 40 cases (8%).

#### Effect of task constraints on cutaneous reflex modulation during arm cycling

An important aspect of the present study was the examination of reflex modulation in both limbs while the opposite limb was in various functional states. There were no consistent differences in the amplitudes of cutaneous reflexes between the four active cycling tasks involving each arm, despite fundamental differences in position, movement and muscle activity of the opposite limb in each of these tasks. Therefore, for most muscles, the amplitude of cutaneous reflexes was not dependent on the functional state of the opposite limb, or whether the phase relationship between the limbs was mechanically constrained or not. The magnitude and sign of cutaneous reflexes elicited in a particular muscle during arm cycling appears to be determined by the functional state of the limb in which that muscle resides, irrespective of whether the stimulation is ipsilateral or contralateral to the muscle. This suggests that cutaneous reflexes elicited in a particular muscle are mostly influenced by neural circuits that are directly involved in controlling the limb in which that muscle resides (e.g. the CPG for that arm), rather than

determined by circuits specifically involved in controlling the limb in which the afferent volley to electrical stimulation arises.

Changes in the level of EMG activity across the movement cycle are likely involved in the expression of phase-dependent modulation during arm cycling, since there was an association between EMG amplitude and reflex amplitude in some muscles in this study and previously (Zehr and Chua 2000; Zehr and Kido 2001). The magnitude of cutaneous reflexes is also related to the EMG activity in upper limb muscles under static conditions, but not while walking (Zehr and Haridas 2003). Changes in background EMG probably make small contributions to the reflex effects in the present study, however, because we observed reflex reversals or changes in reflex amplitude that were independent of the ongoing EMG in four of the six muscles studied. Overall, only 15% of reflexes were significantly related to background EMG activity. Importantly, the similarities between tasks in the pattern of reflex modulation across the cycle were evident even in muscles in which there was no strong relationship between background EMG and cutaneous reflex size (iPD for example). This suggests that the circuits that determine cutaneous reflex sign and amplitude for each limb are not simply related to the activation of the motoneuron pool.

#### Comparisons between ipsilateral and contralateral cutaneous reflexes

We have previously described responses evoked in arm muscles by stimulation of cutaneous nerves in the contralateral arm (Zehr and Haridas 2003; Zehr and Kido 2001) and leg (Haridas and Zehr 2003). Similarly, Van Wezel et al. (1997) and Tax et al. (1995) studied reflexes in leg muscles contralateral to electrical stimulation of cutaneous nerves during walking and running respectively. In these studies, significant phase-dependent reflex modulation was evident in most of the contralateral muscles sampled, although the contralateral responses were often smaller than the ipsilateral reflexes. In our present study, there was significant phase modulation in half of the muscles contralateral to the stimulus. The amplitude and sign of the responses at equivalent positions in the movement cycle were similar for the two arms for these muscles. However, during walking, completely different patterns of cutaneous reflexes were expressed in homologous, contralateral, arm muscles at equivalent points in the arm-swing cycle (Haridas and Zehr 2003; Zehr and Haridas 2003). These differences in the ways that reflexes are modulated for each arm between walking and arm cycling may be due to the involvement of the legs during walking. Recent data showing the effects of arm cycling on soleus H-reflexes (Frigon et al. 2004), as well as modulation in arm muscles of cutaneous reflexes evoked by stimulation at the ankle (Haridas and Zehr 2003) suggest that there are important functional links between the neural circuits underlying reflex organisation for the legs and the arms.

#### Passive arm cycling and cutaneous reflexes

We found that passive movement of the arm did not cause phase modulation of cutaneous reflexes in the limb contralateral to the stimulation, or in four of the six muscles ipsilateral to the stimulation. A lack of phase modulation with passive arm cycling is consistent with the data of Brooke et al. (1999), who found that passive cycling movements of the leg did not cause phase modulation of cutaneous reflexes. It appears that cutaneous reflexes, elicited during rhythmic, cyclical movement of either the arms or the legs, are not directly modulated by feedback from peripheral afferents. Rather, our data suggest that the central processes associated with active production of rhythmic movement (CPGs for instance) are required to modulate cutaneous reflexes in both arms and legs. However, previous work indicates that reflex organization differs in other respects between the arms and legs. Active (McIlroy et al. 1992) and passive (Cheng et al. 1998; Collins et al. 1993; Misiasek et al. 1998) cycling of the contralateral leg have both been shown to dramatically inhibit the soleus H-reflex in the stationary leg (for a review, see Brooke et al. 1997). In contrast, we found that active, but not passive, contralateral arm cycling inhibited ipsilateral forearm H-reflexes in the stationary arm (Zehr et al. 2003). Our current data regarding the regulation of cutaneous reflexes in the upper limb are also indicative of a relatively weak coupling between the arms. Therefore, it appears that the strength of coupling in the neural control of rhythmic cyclical movements is weaker between the arms than between the legs. We have speculated that this reduction in coupling strength may be associated with the more frequent independent usage of the arms (Zehr et al. 2003).

It is important to discuss the extent to which movements in the PASSIVE condition were truly “passive”, since there was significant phase modulation of background EMG in five of the six muscles in the moving limb for the PASSIVE task (all except iTri). Although the origin of this EMG is unclear, we are confident that it was not generated by volitional control, because the participants were repeatedly reminded to relax their arms during the task, and verbally confirmed that their arms were relaxed. It is possible that the involuntary EMG was brought about by reflex or CPG mechanisms. Nevertheless, the amplitude of background EMG was significantly greater in all of the tasks involving active arm cycling than in the PASSIVE task for all muscles. Importantly, there was little phase modulation of cutaneous reflexes in the PASSIVE task, even in most cases in which there was some involuntary EMG. It therefore seems clear that the afferent information alone that is derived from passive, rhythmic movements is insufficient to cause modulation of cutaneous reflexes.

#### Modulation of early and middle latency responses

The general nature and pattern of reflex modulation discussed above was quite similar whether the early or

middle latency reflexes were examined. Furthermore, both early and middle latency reflexes were usually observed in all subjects. The sign of the response is typically inverted when contrasting one latency with another (for instance early latency inhibition followed by middle latency facilitation). This has been shown before in other work on arm cycling and cutaneous reflexes (Haridas and Zehr 2003; Zehr and Chua 2000; Zehr and Kido 2001; Zehr and Haridas 2003). This contrasts with data from the leg muscles during walking in which early latency reflexes are not ubiquitous (for example, see Haridas and Zehr 2003; Duysens et al. 1990; Van de Crommert et al. 2003; Van Wezel et al. 1997) and are not as “stable” as those in arm muscles. Interestingly, the observation that both early and middle latency responses are typically evident and phase modulated in the arm parallels data from the cat hindlimb (Abraham et al. 1985; Duysens and Loeb 1980). The explanation and implication for these observations during rhythmic arm movement is presently unclear.

#### Neural mechanisms controlling rhythmic human movement

Tax et al. (1995) suggested that the pattern of cutaneous reflex modulation in leg muscles during running is determined by the functional state of the limb in which a muscle resides, although they were unable to exclude the possibility that a reciprocal pattern reflex organisation exists for opposite limbs that depends on the position and activation of the limb that receives the stimulation. Because we tested the regulation of cutaneous reflexes in tasks involving a number of functional relationships between the two limbs, we can confirm that, at least within the context of arm cycling, that reflex amplitude during rhythmic movement is largely determined according to the position and activity of the arm in which the response occurs. The data here support the concept that there are separate CPGs for each arm that can be flexibly coupled depending upon the functional relationship between the arms. This form of neural control seems widespread and crosses boundaries separating many species. For example, bilateral coordination of the feline hindlimbs has been well established. During split-belt treadmill walking in the low spinal cat it was clearly shown that the two hindlimbs could maintain coordinated bilateral rhythms even when one limb was driven at four times the rate of the other limb (Forssberg et al. 1980). This suggests that the feline spinal cord contains the necessary circuitry for coordination both within a hindlimb and between the hindlimbs (Grillner and Dubuc 1988). Stride cycle reorganization and bilateral timing compensation has also been shown between the legs in infant (Thelen et al. 1987) and adult (Dietz et al. 1994; Dietz et al. 1989; Dietz et al. 1995) humans walking on split-belt treadmills.

Although our data are consistent with the proposal from Tax et al. (1995) that the circuits responsible for cutaneous reflex modulation during rhythmic movement are located on the same side of the spinal cord as the responding

muscles, the available data are insufficient to allow identification of the circuits responsible for this reflex modulation. It is clear in neonatal mice that some CPG neurons project from one side of the ventro-medial spinal cord to influence the activity of the contralateral motor pools (Butt et al. 2002). Furthermore, in neonatal *Xenopus* tadpoles, interneurons on one side of the spinal cord can inhibit the activity of contralaterally-projecting sensory pathway interneurons (Li et al. 2002). Therefore, despite the fact that our current data suggest that the modulating circuits for cutaneous reflexes are specifically involved in controlling the responding limb, the locus of cutaneous reflex modulation may be ipsilateral to the cutaneous stimulation. It is also possible that cutaneous reflex modulation occurs in sensory pathway interneurons (if the activity of these neurons can be independently influenced by the activity state of the limb to which they project). Although these possibilities cannot be discounted, the recent description of the precise neuronal pathway for a cutaneous flexion reflex in the frog tadpole presented by Li et al. (2003) indicates that more likely sites of reflex modulation lie ipsilateral to the motor pool. Li et al. (2003) showed that dorso-lateral commissural interneurons receive connections from sensory pathway neurons before crossing the midline and synapsing with both motoneurons and a range of ascending and descending interneurons. We therefore suggest that the simplest explanation for our results is that, during rhythmic, cyclical movements, cutaneous reflexes for a particular muscle are modulated by CPG circuits located on the same side of the spinal cord as its motor pool.

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