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RESEARCH ARTICLE

E. Paul Zehr · David F. Collins · Romeo Chua

Human interlimb reflexes evoked by electrical stimulation of cutaneous nerves innervating the hand and foot

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Abstract There is some discrepancy over the extent to which reflex pathways from different cutaneous nerves in the hand and foot link the cervical and lumbar spinal cord in neurologically intact humans. The present experiments were designed to determine whether stimulation of a cutaneous nerve in the foot or in the hand evoked reflexes in the non-stimulated limbs (interlimb reflexes). Reflexes were elicited by stimulating (5×1-ms pulses at 300 Hz) the superficial peroneal (SP; innervates the foot dorsum) or superficial radial (SR; innervates the dorsolateral portion of the hand) nerve while subjects (n=10) performed focused contractions of different upper and lower limb muscles. Reflex responses were divided into early (<75 ms), middle (75–120 ms), and late (>120 ms) epochs as determined from averages of 50 sweeps of stimulus-locked electromyographic activity. Significant interlimb reflexes were found at the early latency in 44/106 and 44/103 muscles sampled after SP and SR nerve stimulation, respectively. At the middle latency, significant interlimb reflexes were seen in 89/106 and 87/103 muscles sampled after SP and SR nerve stimulation, respectively. Interlimb reflexes were seen when stimulating at the wrist (i.e. SR nerve) and when stimulating at the ankle (i.e. SP nerve) with an equal probability. The results show that interlimb cutaneous reflexes are widely distributed in humans. The mean latency of the earliest response was quite short and may be mediated by a propriospinal pathway. Functionally, these pathways may provide a substrate for transferring information to coordinate movements between the limb segments.

Keywords Human interlimb reflexes · Electrical stimulation · Cutaneous nerves · Hand · Foot

Introduction

Sir Charles Sherrington (Sherrington and Laslett 1903) demonstrated reflex interconnections between the cervical and lumbar spinal cord in the cat. More detailed information on this issue was provided by Lloyd, who showed that stimulation of the brachial plexus exerted a propriospinal inhibition on lumbosacral motor pools (Lloyd 1942; Lloyd and McIntyre 1948). However, it was not until much later that the extensive propriospinal interlimb connections in the cat were revealed (Gernandt and Megirian 1961; Gernandt and Shimuamura 1961; Miller et al. 1973; Skinner et al. 1980). This work suggested that such reflexes could act to coordinate the fore- and hindlimbs of the cat during locomotion. Indeed, based upon studies of the coordination of all four limbs during swimming, walking, and air stepping, it has been suggested that propriospinal interlimb reflex pathways may be the primary locus of quadrupedal interlimb coordination (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 in quadrupeds.

In contrast to the work done in animal experiments, there is a discrepancy about the extent to which similar interlimb linkages are present in humans. Kearney and Chan (1979, 1981) demonstrated reflexes in arm muscles subsequent to both ankle displacement and cutaneous stimulation of the foot. Pieseiur-Strehlow and Meinck (1980) also observed reflexes in arm muscles after cutaneous stimulation in the leg. The first evidence of any reflex connection from the upper to lower limb in humans came when lumbosacral cord potentials were observed consequent to median nerve stimulation (Sarica and Ertekin 1985). However, this issue received little further attention until interlimb reflexes were examined in spinal cord injured persons (Calancie 1991; Calancie

E.P. Zehr (✉) · D.F. Collins
Neurophysiology Laboratory, E-401 VVC,
Faculty of Physical Education and Recreation,
University of Alberta, Edmonton, Alberta, Canada, T6G 2H9
e-mail: pzehr@ualberta.ca
Tel.: +1-780-4922004, Fax: +1-780-4922364

R. Chua
Perceptual-Motor Dynamics Laboratory, School of Human Kinetics,
University of British Columbia, Canada

et al. 1996). Stimulation of cutaneous nerves in the lower limb evoked reflexes in arm muscles of acute motor complete or chronic spinal cord injured individuals. In marked contrast to the earlier studies, no interlimb reflexes were observed in uninjured persons. Interestingly, such reflexes were also absent in those who had been injured but who had achieved a significant functional recovery. It was suggested that after spinal cord injury (SCI) a release of inhibition from descending centres may be responsible for the presence of interlimb reflexes. However, the reason for the discrepancy between those results and the previous work in neurologically intact subjects remains unclear. To clarify this issue we investigated interlimb reflexes in uninjured humans by examining and quantifying in detail responses to electrical stimulation of two cutaneous nerves, one in the hand and one in the foot. Portions of the present data have been communicated in abstract form (Zehr et al. 1999).

Materials and methods

Subjects and task

Ten subjects (age 21–36 years) participated with informed, written consent in a protocol approved by the Ethics Board at the University of Alberta. All subjects were healthy and free of documented neurological impairment. Subjects were seated comfortably in an armchair such that the elbow and knee joints were flexed to approximately 90°. Initially, subjects performed maximal voluntary isometric contractions (MVCs) of selected limb muscles. These maximum electromyographic (EMG) values were used to normalize values between subjects and to set the appropriate background EMG levels. During an experiment subjects performed focused contractions at ~50% of the maximal EMG value recorded for each muscle by viewing an oscilloscope record. These contractions were performed in separate trials for each muscle in random order within each nerve stimulation condition. The target level of 50% of the maximal EMG was selected such that a suitable background would be present to observe inhibition but that the motor pools would not be saturated so as to reduce the possibility of observing excitation.

Terminology

Muscles are described as ipsilateral (i) or contralateral (c) based on their relationship to the site of stimulation, which was always the right side. The term interlimb reflex is used to describe reflexes in muscles located in limbs other than that which was stimulated (e.g. a reflex in muscles of the left leg and both arms after stimulation of the foot).

Electrical stimulation

Cutaneous reflexes were evoked by trains (5×1.0-ms pulses @ 300 Hz) of isolated constant current stimulation (Grass S88 stimulator with SIU5 and CCU1 isolation and current units, AstroMed-Grass Inc.) applied to the superficial radial (SR) nerve at the wrist or to the superficial peroneal (SP) nerve at the ankle in separate trials. Stimulation intensities were set as multiples of the threshold at which clear and full radiating parasthesia (radiating threshold, RT) into the innervation areas for each nerve was perceived. This criterion is one we have used extensively in previous experiments as we have found it to be more stable throughout an experiment than is the perceptual threshold (Komiyama et al. 2000; Zehr et al. 1997; Zehr and Chua 2000). These nerves innervate anatomically similar regions of the hand and foot (SR, lateral portion of the dorsum of the hand, SP, dorsum of the foot) and were selected in part because during previous experiments of rhythmic human movement, electrical stimulation of both nerves evoked prominent and functionally relevant reflexes in muscles of the stimulated limb (Zehr et al. 1997; Zehr and Chua 2000). Further, interlimb reflexes have not been studied from these nerves. Stimulation levels were set to evoke a strong cutaneous sensation that was not considered to be noxious by the subjects. This level ranged from 1 to 6×RT, but 4×RT was most commonly used.

Electromyography (EMG)

Disposable surface EMG electrodes (H69-P, Jason-Kandell LTP, CA) were placed on the skin over selected muscles of the upper and lower limbs. Typically 8–16 muscles were sampled in a given experiment with a minimum of two muscles sampled from each of the four limbs. In total and across all subjects, 106 observations were made for interlimb muscles (i.e. muscles not located in the stimulated limb) from SP nerve stimulation, and 103 observations for interlimb muscles from SR stimulation. Upper limb muscles from which recordings were made included first dorsal interosseus (FDI), flexor carpi radialis (FCR), flexor digitorum superficialis (FDS), biceps and triceps brachii (BB, TB), and anterior and posterior deltoid (AD, PD). In the lower limb, recordings were made from tibialis anterior (TA), soleus (SOL), medial gastrocnemius (MG), vastus lateralis (VL), rectus femoris (RF) and biceps femoris (BF). Ipsilateral and contralateral FCR and TA were recorded in every subject. EMG signals were amplified (×500–5000), bandpass filtered from 30 to 300 Hz (GRASS P511, Astromed-Grass Inc.), and sampled at 1000 Hz by a microcomputer running custom-written LabView software (National Instruments, Austin, TX).

Reflex analysis

Reflexes were determined by analyzing averages of 50 sweeps of rectified EMG (50 ms pre- and 250 ms poststimulation) based upon visual inspection using an interactive custom-written software program (Matlab, The Mathworks, Natick, MA). Within a subject, a reflex was considered to be significant if it exceeded, for more than 5 ms, a 2-SD band centred about the prestimulus mean EMG level. The latency to the peak of the evoked response was used to separate the reflexes into three epochs. These comprised early (<75 ms), middle (75–120 ms), and late (>120 ms) responses. It should be noted that these epochs were set based upon visual inspection of superimposed data from all subjects and thus reflect the observed pattern of responses. That is, the response epochs were not determined a priori and then used to force responses into certain epochs. On the rare occasion that more than one significant response was found in an epoch, only the first response was selected. We were most interested in the early and middle latency responses as the former provided detail about possible pathways and the latter has been shown to be very sensitive to functional modulation during behaviour (Duysens and Tax 1994). Thus, detailed analysis and discussion are presented on only early and middle latency responses and the late responses are provided merely as reference for the use of future researchers. Onset latency was calculated by determining the time, immediately prior to the peak of the response, at which the EMG signal crossed the 2-SD band. Reflex amplitudes were normalized to the maximal voluntary activation levels for each muscle.

Statistics

Frequency of interlimb reflex responses was evaluated using chisquare analyses. Reflex amplitudes and onset latencies were evaluated using *t*-tests and repeated measures analysis of variance. Values are presented as means ± standard error of the mean (SEM). The level for statistical significance was set at $P<0.05$.

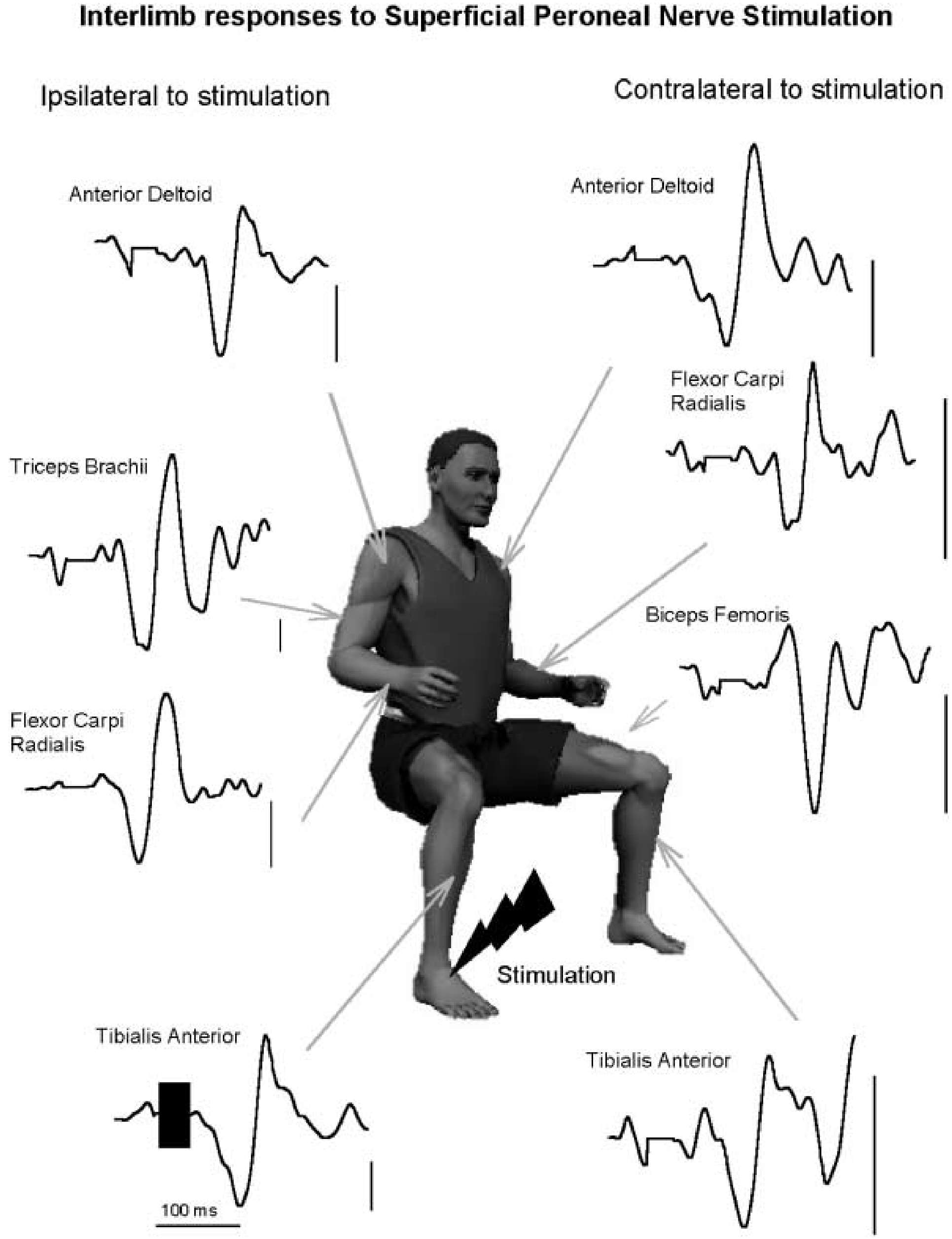

Fig. 1 Interlimb responses to superficial peroneal nerve stimulation. Shown are the mean EMG responses (n=50 sweeps) from different single subjects. Responses are shown for muscles ipsilateral (*left side of figure*) and contralateral (*right side*) to the site of stimulation. In each trace the stimulus artifact has been blanked during the interval shown by *the solid black rectangle* for ipsilateral tibialis anterior. *Arrows* indicate the approximate anatomical location for each muscle. *Individual calibration bars* represent 20% MVC for each muscle shown. Note that different scales are used to highlight the reflexes for each muscle as reflex amplitudes were of different sizes across muscles. It is due to this that the size of the calibration bar is different in each graph

Results

Individual subject analysis

Significant interlimb reflexes were evoked in all ten subjects studied. Examples of responses (averages of 50 sweeps) from representative muscles in each of the four limbs for individual subjects after stimulation of the SP and SR nerves are shown in Figs. 1 and 2, respectively. These figures show that stimulation of a cutaneous nerve in one limb evoked reflexes in muscles of all four limbs. The amplitude of interlimb reflexes could vary between muscles. In order to more clearly show the reflexes in each muscle, the scales and corresponding size of the 20% MVC calibration bars are different for each graph shown in Figs. 1 and 2. Reflexes were recorded from ipsilateral and contralateral TA and FCR in all ten subjects and average sweeps for each subject are shown by the grey lines in Figs. 3 (SP nerve) and 4 (SR nerve). The thick black lines in these figures represent the grand mean of all subjects. Data from each subject were normalized to the prestimulus EMG. The shaded vertical rectangle highlights the middle latency epoch. Interestingly, there was much greater between subject variability of the reflex sign (i.e. facilitation or suppression at a given latency) evoked in the stimulated limb as compared to the interlimb reflexes.

Table 1 summarizes the percentage occurrence of interlimb reflexes (regardless of sign) at early and middle latencies in all muscles examined. In Table 1, the total number of subjects in whom a given muscle was studied is indicated by “n” and thus the percentage occurrence is

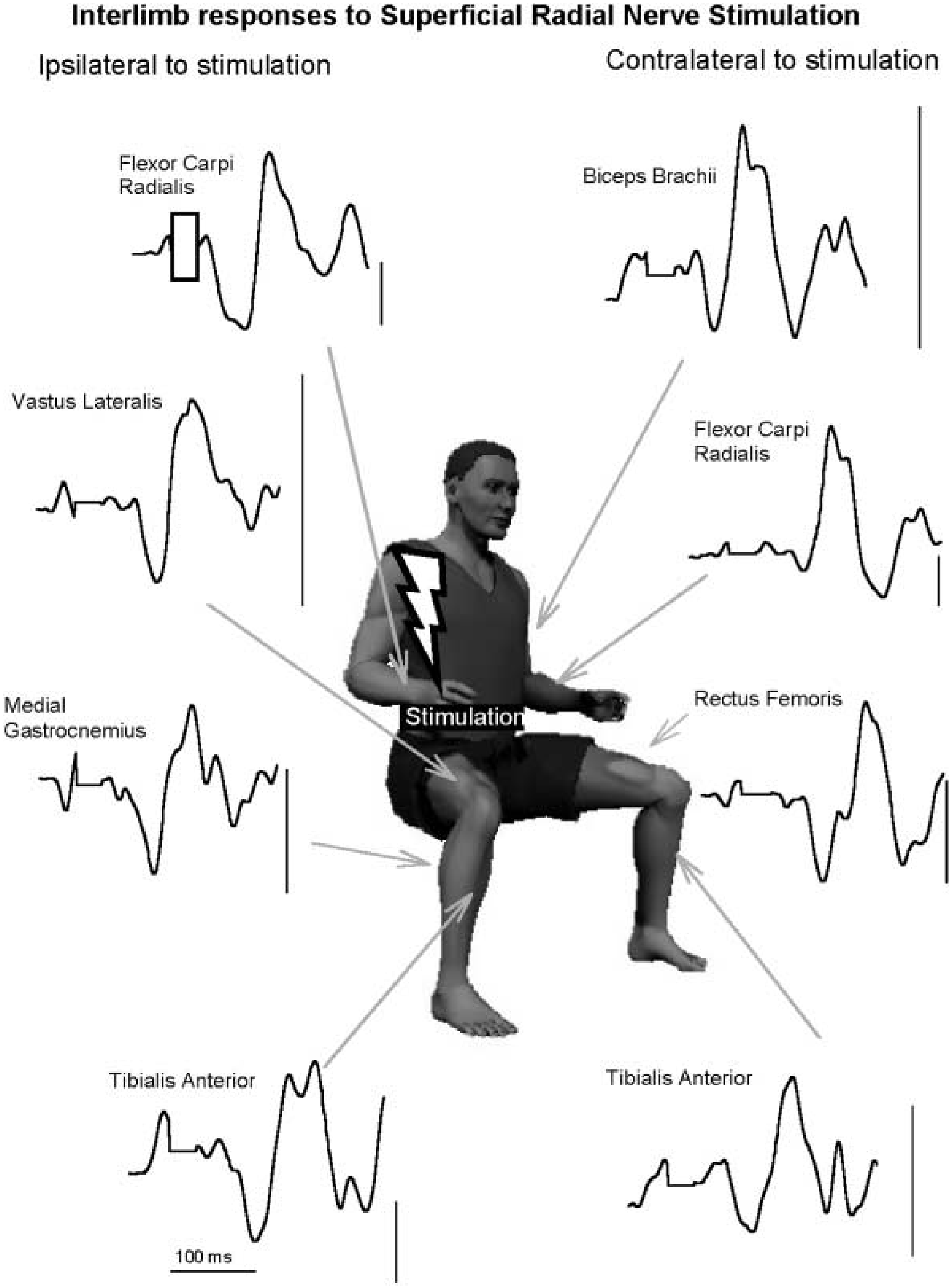

Fig. 2 Interlimb responses to superficial radial nerve stimulation. Mean EMG responses (*n*=50 sweeps) from different single subjects are shown for muscles ipsilateral (*left side of figure*) and contralateral (*right side*) to the stimulation location. *In each trace* the stimulus artifact has been blanked during the interval shown by *the open rectangle* for ipsilateral flexor carpi radialis. *Arrows* indicate the approximate anatomical location for each muscle. *Calibration bars* represent 20% MVC for each muscle shown. Note that different scales are used to highlight the reflexes for each muscle as reflex amplitudes were of different sizes across muscles. Due to this the size of the calibration bar is different in each graph

based upon this number. On average, early latency interlimb reflexes were found in 42% of muscles after SP and 41% of muscles after SR nerve stimulation. At the middle latency, interlimb reflexes were found in 83% of muscles for both SP and SR stimulation. Interestingly, as seen in Table 1, some muscles never showed an early latency interlimb reflex (e.g. iAD after SP and cMG after SR nerve stimulation). However, responses at the middle latency were more readily seen. Further, in no case did a subject fail to express an interlimb reflex in at least one muscle during the experiments.

Early interlimb responses were seen with greater frequency in arm muscles after SR stimulation, and in leg muscles after SP nerve stimulation (χ^2=12.236, *P*=0.0005). No significant differences in response frequency were observed for middle latency responses (*P*>0.1). There were also no differences in the frequencies with which responses were evoked in either the ipsilateral or contralateral limbs (*P*>0.8), or the frequencies with which SP and SR nerve stimulation elicited interlimb reflexes (*P*>0.1).

Reflex amplitudes

As described above (also see Table 1), not all subjects demonstrated significant reflex amplitudes at each latency. To determine the amplitude and sign of group responses

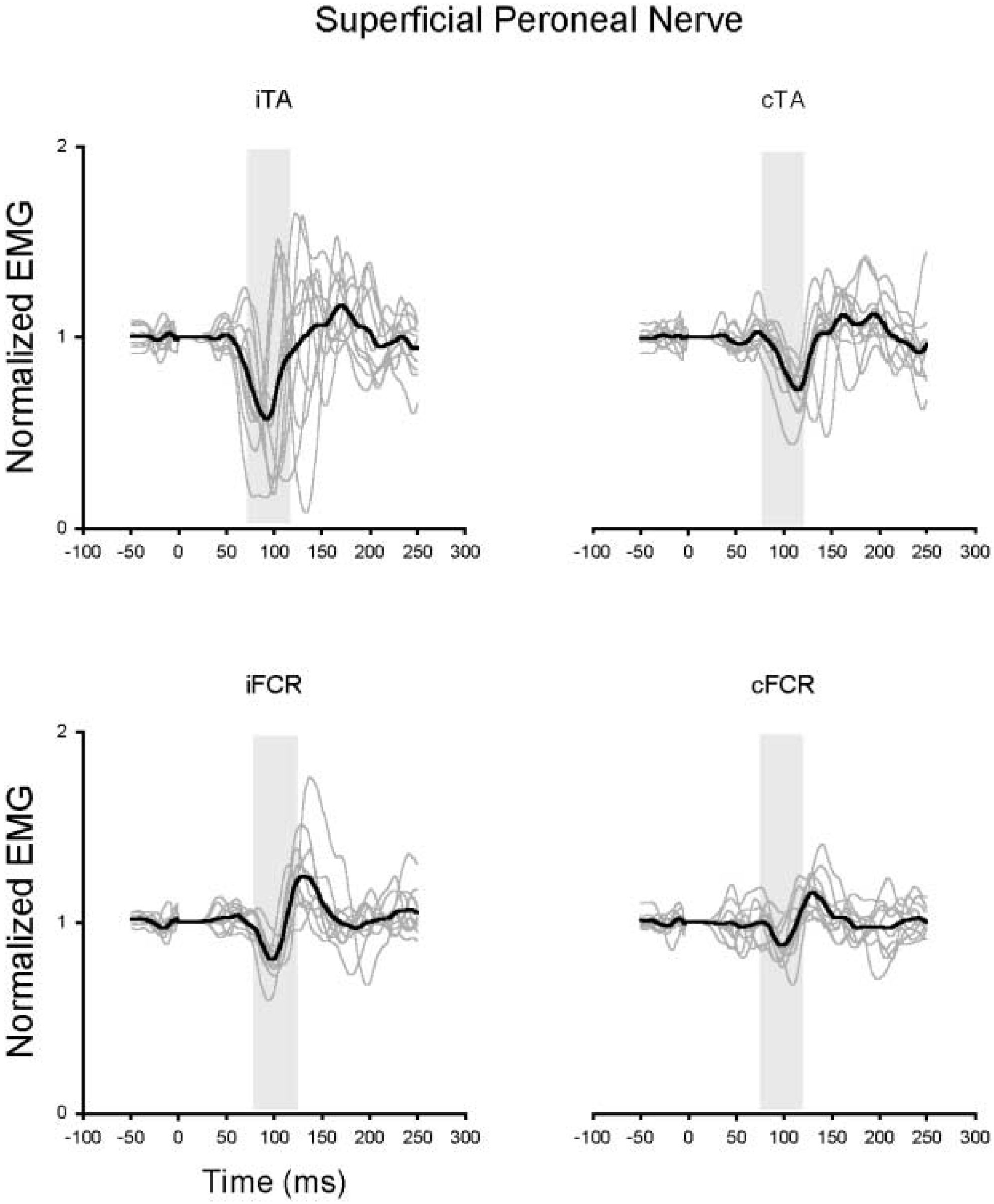

Fig. 3 Responses to superficial peroneal nerve stimulation for muscles recorded in all subjects. *The grey lines* show the mean responses (averaged across 50 sweeps) from each subject (*n*=10). *The thick black line* depicts the grand mean obtained by averaging together the mean responses from each subject. Data were normalized to the mean EMG activity over the prestimulus interval for each subject. *The shaded region* highlights the middle latency response (75–120 ms) in each panel. Stimulus artifacts have been blanked out and replaced by *flat lines* (*TA* tibialis anterior, *FCR* flexor carpi radialis). Ipsilateral and contralateral muscles are indicated by "*i*" and "*c*", respectively

in those who had significant reflexes in an epoch, reflexes observed in these subjects were averaged for each latency epoch. Mean reflex amplitudes for ipsilateral and contralateral TA and FCR are plotted in Fig. 5 for SP (top) and SR (bottom) nerve stimulation. The values are expressed as a ratio of the background EMG level. To more clearly indicate facilitation or suppression, a value of 1 has been subtracted from each ratio. Thus, facilitation is shown as bars greater than zero and suppression as bars less than zero (zero representing no effect of stimulation). Analyses of reflex amplitudes using independent *t*-tests revealed significant amplitudes in all three interlimb muscles after stimulation of either nerve (Fig. 5, $P<0.05$). In TA the prominent mean response was suppression at the middle latency regardless of the nerve stimulated. In contrast, FCR showed mixed responses of facilitation and suppression after stimulation of both nerves. The variability of the responses in the stimulated limb can be seen here as the larger error bars in iTA after SP and iFCR after SR nerve stimulation.

Reflex latencies

To determine the average time taken for the afferent volley from the foot (i.e. SP nerve) and hand (i.e. SR nerve) significantly after the EMG of the arm and leg muscles, we evaluated the latency to the first significant reflex, regardless of its epoch, in all ten subjects (see Fig. 6A). Latencies from subjects who did not show an early reflex were averaged together with those who did for this analysis. Data for FCR and TA were analysed using a 2 Nerve (SP, SR) × 2 Side (ipsilateral, contralateral) × 2 Muscle (FCR, TA) repeated measures analysis of

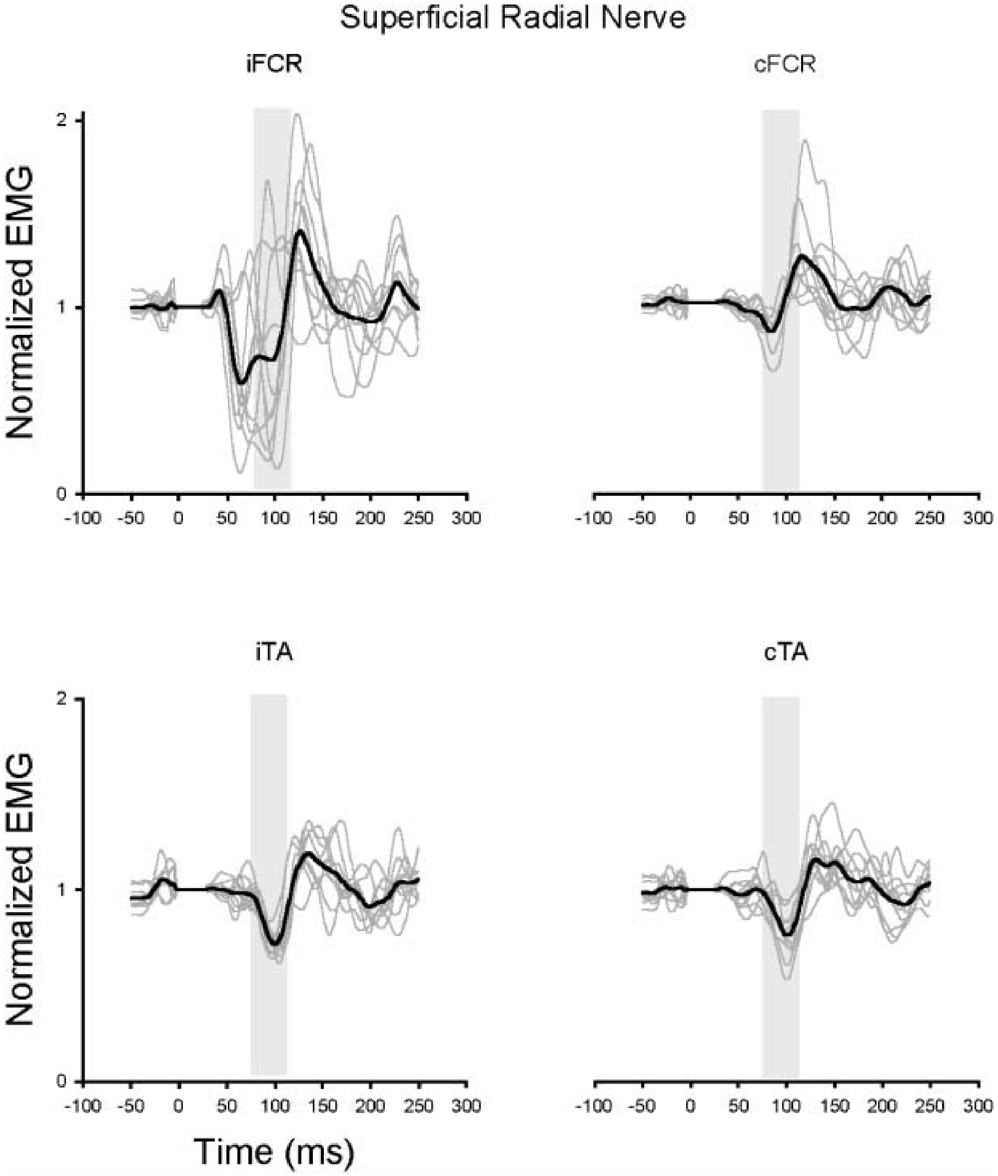

Fig. 4 Responses to superficial radial nerve stimulation in muscles recorded in all subjects. *The grey lines* show the mean responses (averaged across 50 sweeps) from each subject (*n*=10). *The thick black line* depicts the grand mean obtained by averaging together the mean responses from each subject. Data were normalized to the mean EMG activity over the prestimulus interval for each subject. *The shaded region* highlights the middle latency response (75–120 ms) in each panel. Stimulus artifacts have been blanked out and replaced by *flat lines* (*TA* tibialis anterior, *FCR* flexor carpi radialis). Ipsilateral and contralateral muscles are indicated by "*i*" and "*c*", respectively

variance. This analysis revealed that responses in FCR muscles occurred earlier than responses in TA muscles after SR stimulation, $F_{(1,9)}=8.561$, $P<0.025$. No difference in latencies was evident after SP nerve stimulation. This is not surprising, as the conduction velocity of cutaneous afferents is known to be greater in the upper limb as compared to the human lower limb (Macefield et al. 1989). There were no other significant effects.

Further analysis of reflex latencies was conducted to determine the shortest latency and, hence, shortest possible pathway for interlimb reflexes evoked by SP and SR nerve stimulation. For this analysis, only responses at the early latency were included. Results from this analysis are shown in Fig. 6B. The numbers superimposed on the bars indicate the number of subjects who showed an early latency response for each condition. In this figure, the horizontal grey line at 70 ms indicates the earliest possible latency for a transcortical reflex (Nielsen et al. 1997). The early reflex latencies were tested against this value to see if they were significantly different from 70 ms and thus not likely to be mediated by a transcortical pathway. With the exception of the contralateral FCR after SP and SR nerve stimulation, independent *t*-tests revealed that the remaining nerve-muscle combinations exhibited early latency responses that were significantly shorter than the 70-ms criterion ($P<0.05$).

Reflex threshold

In four subjects we explored the relationship between reflex amplitude and stimulus intensity. Typically the minimal threshold at which an interlimb reflex could be evoked was 2–2.5×RT. This can be seen in Fig. 7 for ipsilateral AD subsequent to SP nerve stimulation (refer to the shaded middle latency epoch). When the intensity

Table 1 Percentage of muscles with significant interlimb responses at the early (<75 ms) and middle (75–120 ms) latencies. Shown is a summary of the results of the analysis of data from single subjects. The percentage of observations of interlimb reflexes at early and middle latency are shown in each column for each nerve stimulated (*AD* anterior deltoid, *PD* posterior deltoid, *TB* triceps brachii, *BB* biceps brachii, *FCR* flexor carpi radialis, *FDS* flexor digitorum superficialis, *FDI* first dorsal interosseus, *BF* biceps femoris, *VL* vastus lateralis, *RF* rectus femoris, *SOL* soleus, *TA* tibialis anterior). Ipsilateral and contralateral muscles (relative to site of nerve stimulation) are indicated with "*i*" and "*c*", respectively (*n* indicates the number of subjects studied)

Superficial peroneal nerve stimulation (right foot)				
Muscle location	Muscle	Early	Middle	*n*
Contralateral leg	cBF	60	90	10
	cMG	60	80	5
	cRF	50	100	6
	cSol	75	100	4
	cTA	30	100	10
	cVL	50	100	4
Contralateral arm	cAD	40	80	5
	cBB	20	80	5
	cFCR	40	90	10
	cFDS	33	33	3
	cPD	0	100	2
	cTB	20	40	5
Ipsilateral arm	iAD	0	67	6
	iBB	40	100	5
	iFCR	0	100	10
	iFDI	0	33	3
	iFDS	20	80	5
	iPD	67	67	3
	iTB	20	100	5
	Mean	33	81	

Superficial radial nerve stimulation (right hand)				
Muscle location	Muscle	Early	Middle	*n*
Contralateral arm	cAD	100	80	5
	cBB	80	80	5
	cFCR	70	70	10
	cFDI	100	100	2
	cFDS	80	60	5
	cPD	25	100	4
	cTB	67	100	3
Contralateral leg	cBF	43	86	7
	cMG	0	100	5
	cRF	40	80	5
	cSol	0	67	3
	cTA	30	90	10
	cVL	0	50	2
Ipsilateral leg	iBF	20	90	10
	iMG	0	40	5
	iRF	80	80	5
	iSOL	100	100	3
	iVL	75	50	4
	iTA	0	100	10
		48	80	

of stimulation was increased, the response in AD increased in amplitude and became more pronounced. However, the response was evident at 2×RT and was clearly expressed at 4×RT (the stimulation amplitude commonly used in these experiments). The interlimb reflexes did not typically increase in size with the stimulus intensity above 4×RT (Fig. 7). Please note that in this particular subject we determined that the threshold for perception of noxious input occurred at between 5 and 6×RT.

Discussion

The major purpose of these experiments was to determine the extent to which interlimb cutaneous reflexes are present in humans free of neurological injury. We found

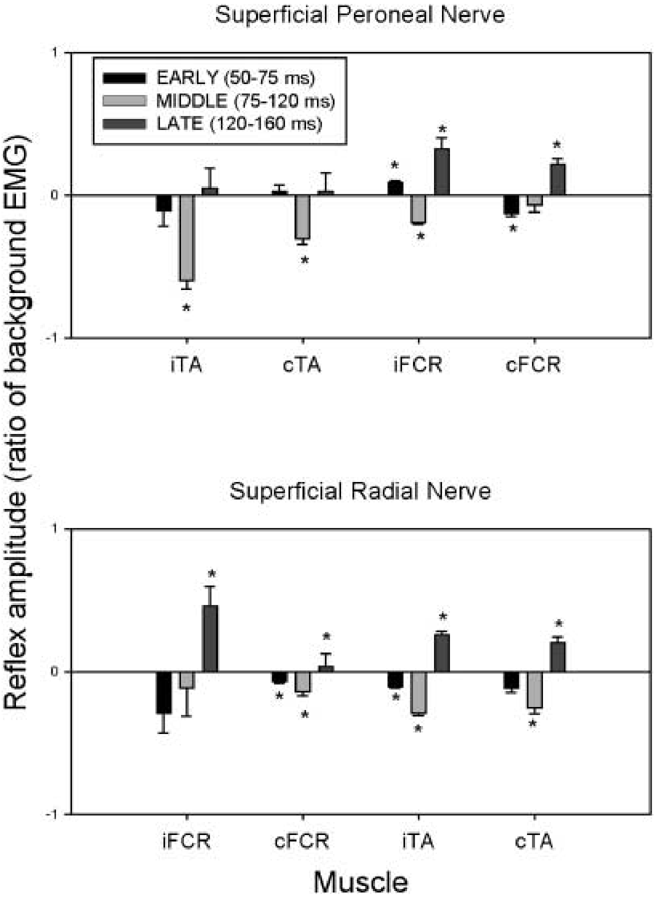

Fig. 5 Quantified peak reflex amplitudes at each latency averaged across all subjects. Shown are the responses recorded during stimulation at the foot (*top panel* superficial peroneal nerve) and hand (*bottom panel* superficial radial nerve). Responses observed at three epochs (early, middle, and late) are shown separately. Data from individual subjects are included for the mean calculation only when a significant response was found at that latency for that subject. Values are expressed as a ratio of the mean EMG activity during the prestimulus 50 ms for each subject. *Asterisks* denote significant responses across the group at $P<0.05$. *Error bars* represent the SEM (*TA* tibialis anterior, *FCR* flexor carpi radialis). Ipsilateral and contralateral muscles are indicated by "*i*" and "*c*", respectively

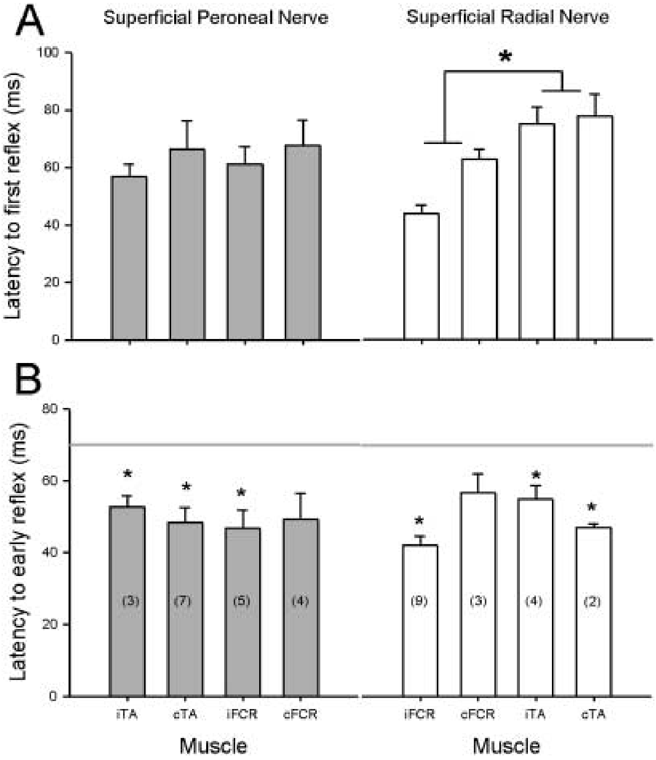

Fig. 6A, B Mean latencies for muscles recorded in all subjects. **A** Time to the first significant response, regardless of latency, across all subjects. Latencies are shown only for muscles that were recorded from all subjects (n=10) and were defined as that point at which the mean EMG broke out of 2 SD of the prestimulus EMG activity (see “Materials and methods”). *Asterisks* indicate a significant difference between FCR and TA responses after SR nerve stimulation. Each *mean value* represents the mean of ten observations and *the error bars* depict SEMs. **B** Latency for subjects in whom there was a significant early response. Data are included only when a significant early response was recorded from a given subject. The number of subjects included in each mean is denoted by *the bracketed numbers on each bar*. *The horizontal grey line* indicates the estimated time required for a transcortical pathway. *Asterisks* denote significant differences from 70 ms (*horizontal line*). *Error bars* depict SEMs

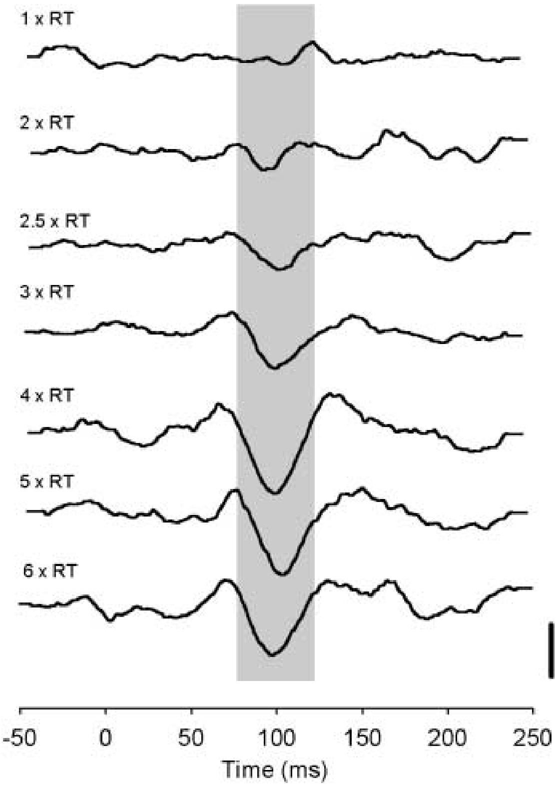

Fig. 7 Interlimb responses from a single subject across a range of superficial peroneal nerve stimulation intensities. Shown are the mean data sweeps showing responses in the ipsilateral anterior deltoid muscle (n=50 sweeps each) while the subject maintained a ~50% maximal contraction of that muscle. *The shaded region* highlights the middle latency response (*vertical calibration bar* 20% MVC)

that electrical stimulation of a cutaneous nerve in the foot (SP nerve) evoked large and reproducible reflexes in the arm musculature and the contralateral leg. Further, by studying the same subjects in the same paradigm we also demonstrated that stimulation of a cutaneous nerve in the hand (SR nerve) evoked large reflexes in the legs and the contralateral arm. Hence, there are strong interlimb cutaneous reflex projections observed bilaterally and between the human lumbar and cervical spinal cord in neurologically uninjured humans. This is the first paper to quantify and examine in detail interlimb reflexes evoked by stimulation of the SR and SP nerves.

Human interlimb cutaneous reflexes?

Prior to the present study, some inconsistency remained concerning the presence of interlimb reflexes in neurologically intact human subjects. By examining H-reflex modulation, Delwaide and Crenna (1984) had shown that stimulation of tactile afferents in the human median and sural nerves could evoke reflex changes in the upper and lower limbs. Median nerve stimulation caused a large facilitation of the SOL H-reflex at ~70 ms latency. A similar facilitation of the BB tendon jerk was found at ~90 ms in concert with a suppression of TB tendon jerk after sural nerve stimulation. Piesiur-Strehlow and Meinck (Meinck and Piesiur-Strehlow (1981, Piesiur-Strehlow and Meinck 1980) also demonstrated propriospinally mediated reflex conditioning of muscles in the lower limb after painful cutaneous stimulation of arm nerves using H-reflex and measurement of changes in tonic EMG. Kearney and Chan (1979, 1981) showed that large reflexes could be evoked in upper limb flexor and extensor muscles after activation of both cutaneous and muscle afferents from the foot and leg. A descending connection from brachial to lumbosacral muscles was also demonstrated by the intrathecal measurement of lumbosacral cord potentials (Sarica and Ertekin 1985). Thus, the results described in this paper support the earlier descriptions of interlimb reflexes and extend them to the SP and SR nerves, thus identifying an extensive pattern of interlimb reflex connections in the neurologically intact human.

In marked contrast to earlier observations and those of this study, Calancie (1991) suggested there were no interlimb reflex connections in neurologically intact humans but that interlimb reflexes were present only in those who had suffered a SCI. This group stimulated the distal tibial nerve and observed interlimb responses in FCR (and other muscles) only in spinal cord injured subjects. However, they did not observe any responses in wrist flexor (FCR) or extensor (ECR) muscles nor thenar muscles of neurologically intact subjects after distal tibial and posterior tibial nerve stimulation (Calancie 1991). This observation was in disagreement with the earlier work done by other researchers as described above. Here, we observed strong interlimb reflexes in many muscles on both the ipsi- and contralateral sides after SP and SR nerve stimulation in neurologically intact subjects. There are several possible explanations as to why interlimb reflexes were not seen in neurologically intact subjects in the previous studies by Calancie et al. (Calancie 1991; Calancie et al. 1996). Firstly, we stimulated two cutaneous nerves that had not been examined previously. It is possible that the cutaneous projections from SP and SR nerves may involve interlimb pathways whereas tibial nerve projections do not. It is likely that our stimulation of the cutaneous SP and SR nerves will have evoked a qualitatively different afferent volley than did distal tibial nerve (a mixed nerve) stimulation. At present we cannot state exclusively if the choice of nerve type (i.e. mixed or cutaneous) was the determining factor in generating different observations. However, it is interesting to note that we observed prominent interlimb reflexes in this study after stimulation of two predominately cutaneous nerves, suggesting that the nature of the afferent volley is important in evoking the interlimb reflexes. Secondly, we measured EMG exclusively with surface electrodes, whereas Calancie (1991) used mainly indwelling and some surface electrodes. It is not clear in which muscles either method was used. Since indwelling electrodes sample a much smaller portion of the muscle than surface electrodes, it is possible that an overall change of muscle activity (such as observed in this paper) may not be seen at the single motor unit level. Thirdly, as clearly stated by Calancie (1991), studies of control subjects were far less detailed than those conducted in SCI subjects. That is, there is very little information on the procedures and observations of responses seen in the neurologically intact subjects in that study. In particular, the background EMG level and the intensity of stimulation are not clear for either SCI or neurologically intact subjects, thus further hindering direct comparison with the observations detailed in this paper.

Pathways

These cutaneous reflexes that interconnect the four limbs probably involve a propriospinal pathway. Indeed, it has been suggested that interlimb cutaneous reflexes from lumbosacral to the cervical cord in SCI subjects were mediated by such linkages (Calancie 1991; Calancie et al. 1996). We found that the interlimb reflex latencies between the pairings of SP-iFCR nerve and SR-iTA nerve are not significantly different. For these pairings the distance from the stimulating (e.g. at the wrist or ankle) to recording (e.g. midway up the tibia or close to the elbow) electrodes was relatively similar. That is, the physical distance travelled by afferent and efferent signals would be similar in both cases. Since the latencies are similar, this may suggest a similar pathway, but we cannot state this unequivocally. The early latency reflex gives the most valid but still tenuous information about possible pathways mediating the interlimb reflexes. When we examined the latency to the early reflex (see Fig. 7, FCR vs TA after SR nerve stimulation), the interlimb responses were typically much shorter than 70 ms. On the basis of somatosensory evoked potential and motor evoked potential measurements, 70 ms has been suggested as the earliest possible latency for a transcortical effect (Nielsen et al. 1997). Thus, while we cannot completely exclude subcortical brain regions, the latencies here are suggestive of a propriospinally mediated early interlimb reflex response.

Functional implications

The presence of prominent interlimb reflexes mediated via propriospinal connections has been documented in the cat (Miller et al. 1973). The function of the interlimb connections has been typically ascribed to coordination of the fore- and hindlimbs of the animal during locomotor behaviours (Miller and van der Meche 1976). While humans are not quadrupedal, we do certainly have to coordinate the movements of our arms and legs during behaviours such as walking, running, swimming, opening a door, and overcoming obstacles. Interestingly, stretch reflexes of SOL, quadriceps, and BF muscles were affected by alterations in arm postures of intact human subjects (Delwaide et al. 1977). This suggests that there may be interlimb reflex modulation with movement. Currently, the extent and function of these interconnections and the possible modulation with posture and movement in humans is uncertain. Our present demonstration of both ascending and descending interlimb reflex linkages in the intact human suggests that there may be similar mechanisms across species to control the movement and coordination between the limbs. As such, interlimb reflex pathways connecting distant cutaneous receptive fields could be important in directly relaying exteroceptive information important for the reflex coordination of movement.

In conclusion, we have demonstrated a widespread distribution of cutaneous reflexes in neurologically intact human subjects. These interlimb reflexes were evoked by stimulating a nerve in the hand or in the foot. The extent to which interlimb reflex connections can be observed after stimulation of different nerves, and the nature of their modulation during movement, remains to be determined in future investigations.

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