

Flexion reflex modulation during stepping in human spinal cord injury

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Abstract The flexion reflex modulation pattern was investigated in nine people with a chronic spinal cord injury during stepping using body weight support on a treadmill and manual assistance by therapists. Body weight support was provided by an upper body harness and was adjusted for each subject to promote the best stepping pattern with the least manual assistance required by the therapists. The flexion reflex was elicited by sural nerve stimulation with a 30 ms pulse train at 1.2–2 times the tibialis anterior reflex threshold. During stepping, stimuli were randomly dispersed across the gait cycle which was divided into 16 equal bins. A long latency (>110 ms) flexion reflex was present in all subjects, while a short (>30 ms) and a medium latency (>70 ms) flexion reflex were present only in three subjects. For each response, the non-stimulated EMG was subtracted from the stimulated EMG at identical

time windows and bins, normalized to the maximal corresponding EMG, and significant differences were established with a Wilcoxon rank-sum test. The long latency flexion reflex was facilitated at late stance and during the swing-to-stance transition phase. A reflex depression was present from heel strike until mid-stance and during the swing-to-stance transition phase. The short and medium latency flexion reflexes were depressed during mid-stance followed by facilitation during the stance-to-swing transition phase. Regardless of the latency, facilitatory flexion responses during the swing phase coincided with decreased activity of ipsilateral ankle extensors. The flexion reflex was modulated in a phase dependent manner, a behavior that was absent for the soleus H-reflex in most of these patients (Knikou et al. in *Exp Brain Res* 193:397–407, 2009). We propose that training should selectively target spinal reflex circuits in which extensor muscles and reflexes are involved in order to maximize sensorimotor recovery in these patients.

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Introduction

Excitation of group II and III muscle afferents, joint afferents, and cutaneous afferents evoke polysynaptic reflex actions characterized by the classical flexion and crossed extension reflexes. The actions of these afferents (flexor reflex afferents, FRA) (Eccles and Lundberg 1959), are manifested through alternative excitatory and inhibitory reflex pathways to flexor and extensor α motoneurons (Lundberg 1979; Lundberg et al. 1987). FRA pathways encompass interneurons associated with locomotion. Lundberg

and Jankowska et al. postulated in spinalized animals following L-Dopa (a precursor of dopamine and noradrenaline) administration that short latency FRA pathways were profoundly depressed, while long latency long-lasting reflex discharges of ipsilateral flexors and contralateral extensors were released (Anden et al. 1966a, b; Jankowska et al. 1967a, b; Fu et al. 1975). Because of the strong reciprocal organization and the alternating activity in flexors and extensors in spinalized animals following short FRA trains, the late-Dopa flexion reflex was related to stepping (Jankowska et al. 1967a, b; Lundberg 1979). A neuronal organization similar to that observed in spinalized animals treated with L-Dopa and Nialamide was postulated for the long latency flexion reflex in people with a spinal cord injury (SCI) (Roby-Brami and Bussel 1987, 1990, 1992). This comparison was largely based on observations that FRA volleys induced inhibition of the ipsilateral TA H-reflex via presynaptic inhibition of Ia afferents, depressed contralateral long-latency flexion reflexes (Roby-Brami and Bussel 1990, 1992), and modulated spontaneously occurring step-like movements (Calancie et al. 1994; Bussel et al. 1988, 1989).

Ongoing cyclic modulation of spinal reflexes during gait in humans suggests changes in spinal neuronal pathways at motoneuronal and/or interneuronal levels (Morin et al. 1982; Capaday and Stein 1986). Studying spinal reflexes during locomotion in people with a SCI can provide information on the physiological state of locomotor-related spinal neural circuits. The short latency reflexes, mediated largely by muscle spindle afferents, during the gait cycle in SCI subjects vary from a relatively normal pattern, when compared to non-injured subjects (Morin et al. 1982; Capaday and Stein 1986), to no modulation (Yang et al. 1991; Faist et al. 1999; Knikou et al. 2009).

Normalization of spinal locomotor-reflex circuits may contribute to locomotor recovery following repetitive step

training. This is supported by the recent findings reported for upper motoneuron lesions of cerebral origin in humans, where intensive step training on a treadmill contributed to the recovery of the soleus H-reflex depression during the swing phase of gait (Hodapp et al. 2009). Current available interventions for recovery of walking in people with a SCI are the Lokomat[®] Driven Gait Orthosis and locomotor training using body weight support on a treadmill (BWST) with therapists providing as needed external manual assistance (Barbeau et al. 1987; Dobkin et al. 1995; Behrman and Harkema 2000; Wernig and Müller 1992; Wirz et al. 2005). The objective of this study was to investigate the flexion reflex modulation pattern in people with a SCI during stepping.

Methods

Experiments were conducted after a full Institutional Review Board (IRB) approval of the experimental protocol (College of Staten Island and University of Louisville IRB committees), and in compliance with the Declaration of Helsinki. A written consent form was obtained from each subject before testing. Nine adults (two females, seven males) with spinal injury ranging from cervical 1 to thoracic 10 (neurological level) participated in the study (Table 1). Subjects participated in a previous study (Knikou et al. 2009) and are identified here with the same code.

Flexion reflex

Electromyographic (EMG) activity was recorded with bipolar surface electrodes of fixed inter-electrode distance of 2.5 cm (2DT2, Multi BioSensors, El Paso, TX, USA) from the ipsilateral (stimulated) and contralateral (non-stimulated) soleus (SOL), medial gastrocnemius (MG), and

Table 1 Characteristics of SCI subjects

Subject ID	Neurological level	ASIA score	Age (years)	Post-injury (years)	Gender	Anti-spasticity medication	BWS	m/s
A33	C3	A	52	2.4	M	None	60	0.89
B06	C5	B	38	1.8	F	None	40	1.07
D11	C5	D	39	1.1	M	None	30	0.98
D13	T10	D	60	2.5	F	Baclofen	40	0.98
D14	C7	D	22	3.2	M	Baclofen	40	1.07
D15	C1	D	67	46.0	M	None	50	0.49
D16	C3	D	44	6.5	M	Baclofen	20	0.80
D20	C3	D	63	2.0	M	None	30	0.98
C14	C3	C	41	1.0	M	Gabapentin	35	0.98

Body weight support (BWS) was provided at a level that knee and trunk buckling could be avoided during standing and stepping. The neurologic impairment is identified in column 3 based on the American Spinal Injury Association (ASIA) Impairment Scale (Maynard et al. 1997). Treadmill speed for each subject is indicated in the last column

C cervical, T thoracic, F female, M male

tibialis anterior (TA) muscles. All EMG signals were amplified, high pass filtered (cut-off frequency at 20 Hz), full-wave rectified and then low-pass filtered (cut-off frequency 500 Hz).

The flexion reflex was evoked according to methods previously employed in SCI subjects (Conway and Knikou 2008; Knikou and Conway 2005; Knikou 2007a, b). A pulse train of 30-ms duration (1-ms pulses at 300 Hz) was triggered from a computer (controlled by a customized Labview script) and delivered to the right (ipsilateral) sural nerve by a constant current stimulator (DS7A, Digitimer Ltd., Hertfordshire, UK). With subjects seated, a bipolar electrode was used as a probe to establish the site which elicited a response in the TA muscle at the lowest stimulus intensity. The bipolar electrode was then replaced by two monopolar electrodes (Medicotest, Ølstykke, Denmark) which were secured throughout the experiment. Each subject was then transferred to the treadmill (Biodex Medical Systems, NY, USA). While standing, subjects wore an upper body harness that was attached to pulleys controlled by a pneumatic closed-loop force body weight support (BWS) system (Innoventor Engineering Inc., Maryland Heights, MO, USA).

The stimulus intensity was increased progressively while subjects were standing with BWS, and the response was monitored to observe its sensitivity to the stimulus intensity strength. The stimulus intensity required to elicit an initial response in the ipsilateral TA muscle was identified as reflex threshold. During stepping, the sural nerve was stimulated between 1.2 and 2 times the reflex threshold and ranged from 6.3 to 29 mA across subjects. The criteria for selecting the stimulation intensity for each subject were constant/repetitive TA responses and absent limb movement. In addition, SCI subjects with preserved sensation reported no pain (but uncomfortable) and sensation within the cutaneous receptive field of the sural nerve e.g. lateral side of the foot towards the heel and the fifth to fourth metatarsal. Based on these criteria, stimulation excited primarily cutaneous and muscle afferents (Knikou and Conway 2005; Conway and Knikou 2008), but high-threshold afferents cannot be excluded. The intensity was checked several times during the course of the experiment to ensure its stability.

During stepping, a therapist positioned behind the subject assisted with pelvis and trunk stabilization, as well as appropriate weight shift. Therapists positioned at each limb provided manual assistance using a customized technique that promotes standing and toe clearance during swing (Barbeau et al. 1987; Behrman and Harkema 2000; Visintin and Barbeau 1994). Before data acquisition, each subject walked on the treadmill for one to three minutes to select the most appropriate BWS and treadmill speed. All therapists provided assistance only when needed.

In all subjects, sural nerve stimulation was triggered based on the signal from a foot switch (Noraxon USA Inc., Scottsdale, AZ, USA), and was delivered randomly every three to ten steps. Stimuli were randomly dispersed throughout the step cycle, which was divided into 16 equal bins. The step cycle phases of the contralateral leg were also identified by a foot switch. A custom written software program (Labview, National Instruments, Austin, TX, USA) was used to identify the 16 bins for the stimulated and non-stimulated steps. Bin 1 corresponds to heel strike. Bins 8, 9, and 16 correspond approximately to stance-to-swing transition, swing phase initiation, and swing-to-stance transition, respectively. At each bin, at least five reflexes were randomly recorded. Data were sampled at 2,000 Hz, band-pass filtered at 20–1,000 Hz (National Instruments, Austin, TX, USA) and stored on a personal computer for off-line analysis.

Data analysis

EMG signals during stepping (with and without sural nerve stimulation) were full-wave rectified, high-pass filtered at 20 Hz and low-pass filtered at 500 Hz. Off-line analysis started with identification of the responses in the ipsilateral TA muscle with a customized Labview script. To quantify the flexion reflex three analysis windows were defined. The first window started at 30 ms post-stimulus with 40-ms duration (short-latency), the second window started at 70 ms post-stimulus with 30-ms duration (medium-latency), and the third window started at 110 ms post-stimulus with 290-ms duration (long-latency) (Fig. 1).

For each bin of the step cycle, the full-wave rectified area for each response (short, medium, and long), were calculated and averaged separately for steps with and without sural nerve stimulation. For each subject and flexion reflex component, the average EMG of non-stimulated steps (control EMG) was subtracted from the average EMG of stimulated steps (reflex EMG) at identical time windows and bins to allow estimation of the flexion reflex modulation pattern during stepping (Zehr et al. 1997, 1998). This subtraction resulted in negative EMGs when the average reflex EMG was smaller than the control EMG and positive EMGs when the average reflex EMG was larger than the control EMG. For each bin, the average subtracted reflex EMG, non-subtracted reflex EMG, and control EMG were normalized to the maximal control EMG for comparison across subjects to be made possible. This was done separately for the responses of the ipsilateral and contralateral TA, MG, and SOL muscles corresponding to short, medium, and long latencies.

For each subject, statistical significance between the subtracted reflex and control EMGs at each bin was established with a Wilcoxon signed rank-sum test. The average

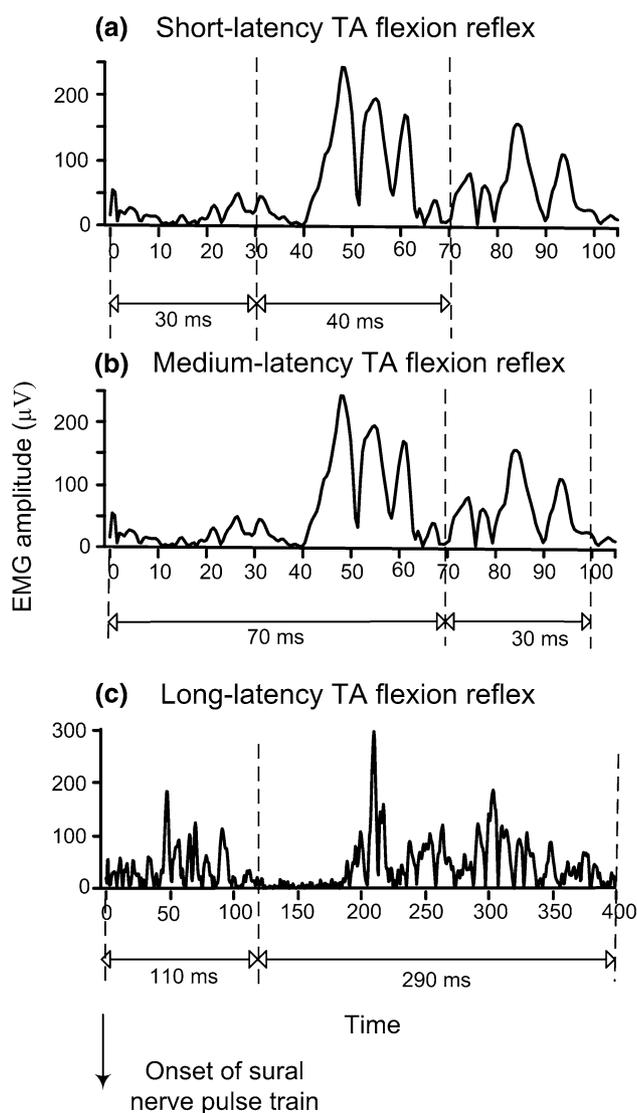


Fig. 1 Examples of short (a), medium (b), and long (c) latency ipsilateral tibialis anterior (TA) flexion reflexes from one subject (D20). For each response, the first time-window indicates the latency, and the second time-window indicates the duration for which the response was measured

subtracted reflex and control EMGs from each subject were then grouped by bin. Statistical significant differences were established with a Wilcoxon rank-sum test. This was done separately for ipsilateral and contralateral responses of short, medium, and long latencies.

The background EMG activity of the ipsilateral TA muscle for each bin was estimated from the mean value of the rectified and filtered EMG for a duration of 40-ms (high-pass filtered at 20 Hz, rectified, and low-pass filtered at 400 Hz), beginning 80 ms before sural nerve stimulation. The mean amplitude of the ipsilateral short, medium, and long latency TA flexion reflex was plotted on the y-axis versus the TA background activity (normalized to the maximal control EMG) on the x-axis, and a linear least-square

regression was fitted to the data. This analysis was conducted separately for each subject and for the pool data. In all statistical tests, significant differences were established at 95% of confidence level. Results are presented as mean values along with the standard error of the mean (SEM).

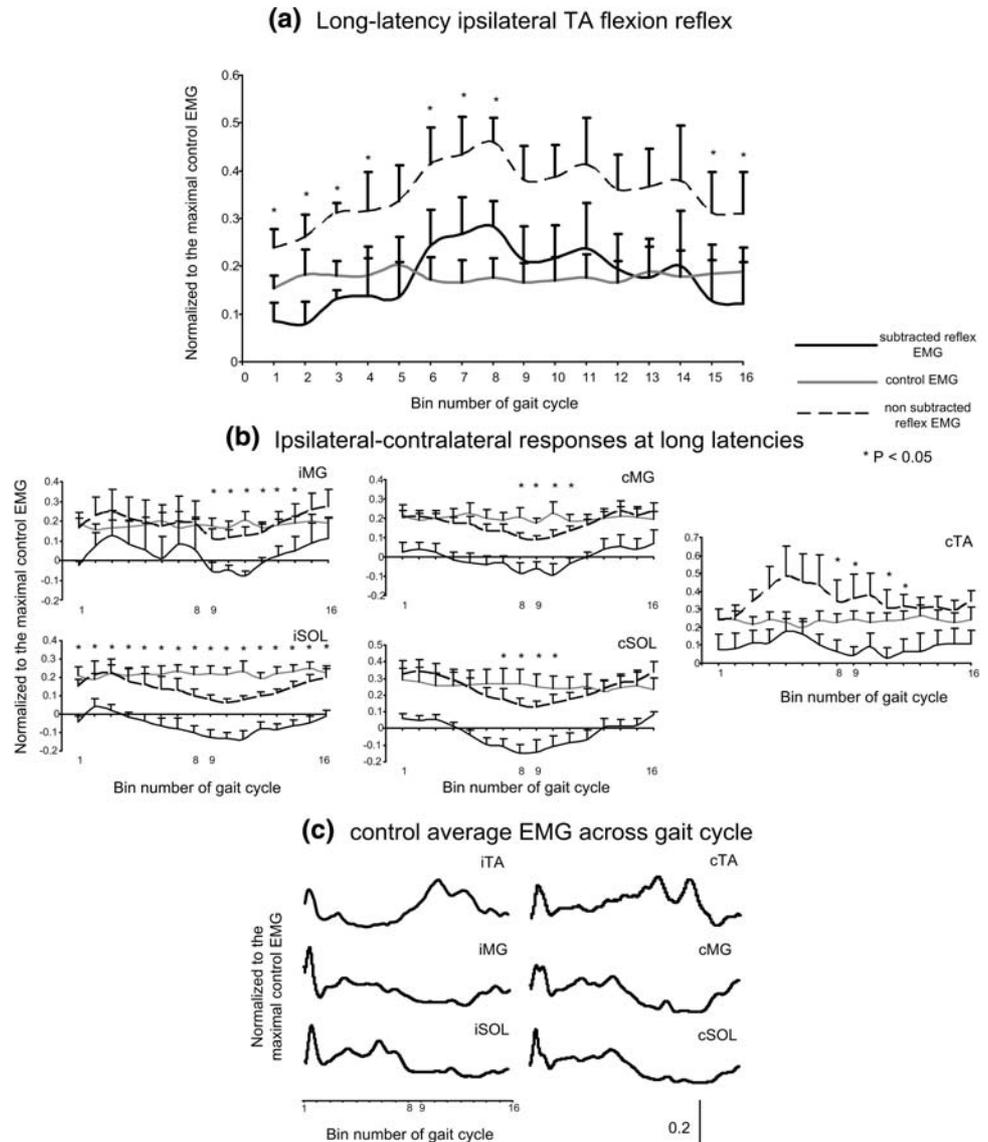
Results

The average walking speed was 0.91 ± 0.18 m/s. The step cycle duration was not significantly different between the right and left legs with a mean duration of $1,160 \pm 40$ and $1,185 \pm 39$ ms ($P = 0.32$), respectively. The long latency TA flexion reflex was consistently observed in all SCI subjects, being significantly depressed ($P < 0.05$) compared to the control EMG from heel strike until mid stance (bins 1–4), and facilitated during late stance (bins 6 and 7) and during stance-to-swing transition phase (bin 8) (Fig. 2a). The long latency TA flexion reflex was significantly ($P < 0.05$) depressed during the swing-to-stance transition (bins 15 and 16).

At long latencies, sural nerve stimulation induced a significant depression of the ipsilateral MG muscle from bins 9–14, while the ipsilateral SOL muscle was depressed throughout the step cycle (Fig. 2b). In the contralateral muscles (MG, SOL, and TA, USA), a depression of the reflex EMG was evident during the swing phase (Fig. 2b). The average (from all subjects) control EMG as a function of the step cycle is indicated in Fig. 2c. Similar to previous observations, ipsilateral and contralateral MG and SOL activity occurred during stance with some activity also observed during swing (Fig. 2c). Ipsilateral and contralateral TA activity generally increased during swing, with activity also observed during stance.

The medium and short latency TA flexion reflexes were present in three out of nine SCI subjects (D13, D15, and D20). The presence of these responses in these subjects was not correlated to a physiological soleus H-reflex modulation pattern during stepping (Knikou et al. 2009). Figure 3a shows the average medium latency TA flexion reflex during stepping from these three SCI subjects. The medium latency TA flexion reflex was depressed at mid-stance (bin 5) followed by a strong facilitation during stance-to-swing transition phase (bin 8). The reflex EMG facilitation remained during early swing reaching maximal amplitude at bin 11 (Fig. 3a), and re-appeared at late swing (bin 14) ($P < 0.05$). Sural nerve stimulation decreased the subtracted reflex EMG amplitude of the ipsilateral MG and SOL muscles during swing phase (Fig. 3b). Similar to that previously reported for the long latency muscle responses, FRA excitation during stepping resulted in depression of the subtracted reflex EMG amplitude of the contralateral ankle extensor muscles (MG, SOL) primarily during swing. The contralateral

Fig. 2 Long-latency flexion reflex modulation during stepping in SCI. **a** The mean (+SEM) subtracted long-latency tibialis anterior (TA) flexion reflex amplitude, control TA EMG, and non-subtracted TA reflex EMG normalized to the maximum locomotor control TA activity is indicated as a function of the step cycle. **b** The mean (+SEM) long-latency subtracted responses, non-subtracted reflex and control EMGs of the ipsilateral and contralateral soleus (SOL), medial gastrocnemius (MG), and contralateral TA muscles are indicated as a function of the step cycle. **c** The mean (+SEM) normalized control EMG activity (non stimulated steps) as a function of the step cycle. *Asterisks* indicate suppressive and facilitatory subtracted reflex EMGs compared to the control EMG based on the *P* value of the Wilcoxon signed rank-sum test. *i* ipsilateral, *c* contralateral



TA reflex EMG amplitude was significantly ($P < 0.05$) decreased compared to control EMG during early stance and late swing (Fig. 3b).

The short latency TA flexion reflex was modulated in a phase dependent manner similar to that observed for the medium latency TA flexion reflex. This reflex was facilitated during stance-to-swing transition phase (bin 8) and remained facilitated during early swing ($P < 0.05$). The reflex was significantly decreased compared to the control EMG during mid-stance ($P < 0.05$) (Fig. 4a). Ipsilateral and contralateral ankle subtracted reflex EMG responses (Fig. 4b) at short latencies were similar to those previously reported for the medium latency responses.

The background EMG amplitude of the ipsilateral TA muscle as a function of the gait cycle is illustrated in Fig. 5a. The relationship between TA flexion reflex amplitude for the medium and short latencies were linearly

related to the TA background activity during stepping ($R^2 = 0.65$ and $R^2 = 0.7$, respectively). The long-latency TA flexion reflex was not linearly related to the TA EMG background activity ($R^2 = 0.075$).

Discussion

This study provides evidence of modulation of the flexion reflex during stepping in people with a chronic SCI. Our study showed that the flexion reflex, regardless of latency, could be modulated in a phase-dependent manner. The onset of the long latency flexion reflex facilitation consistently occurred during late stance, while short and medium latency flexion reflexes onset facilitation occurred during the stance-to-swing transition. Long latency flexion reflex inhibition was evident primarily during stance or late

Fig. 3 Medium-latency flexion reflex modulation during stepping in SCI. **a** The mean (+SEM) ($n = 3$; subjects D13, D15, and D20) subtracted medium-latency tibialis anterior (TA) flexion reflex, control TA EMG, and non-subtracted reflex TA EMG normalized to the maximum locomotor control TA activity is indicated as a function of the step cycle. **b** The mean (+SEM) ($n = 3$; subjects D13, D15, and D20) medium-latency subtracted responses, non-subtracted reflex and control EMGs of the ipsilateral and contralateral soleus (SOL), medialis gastrocnemius (MG), and contralateral TA muscles are indicated as a function of the step cycle. Asterisks indicate suppressive and facilitatory subtracted reflex EMGs compared to the control EMG based on the P value of the Wilcoxon signed rank-sum test. *i* ipsilateral, *c* contralateral

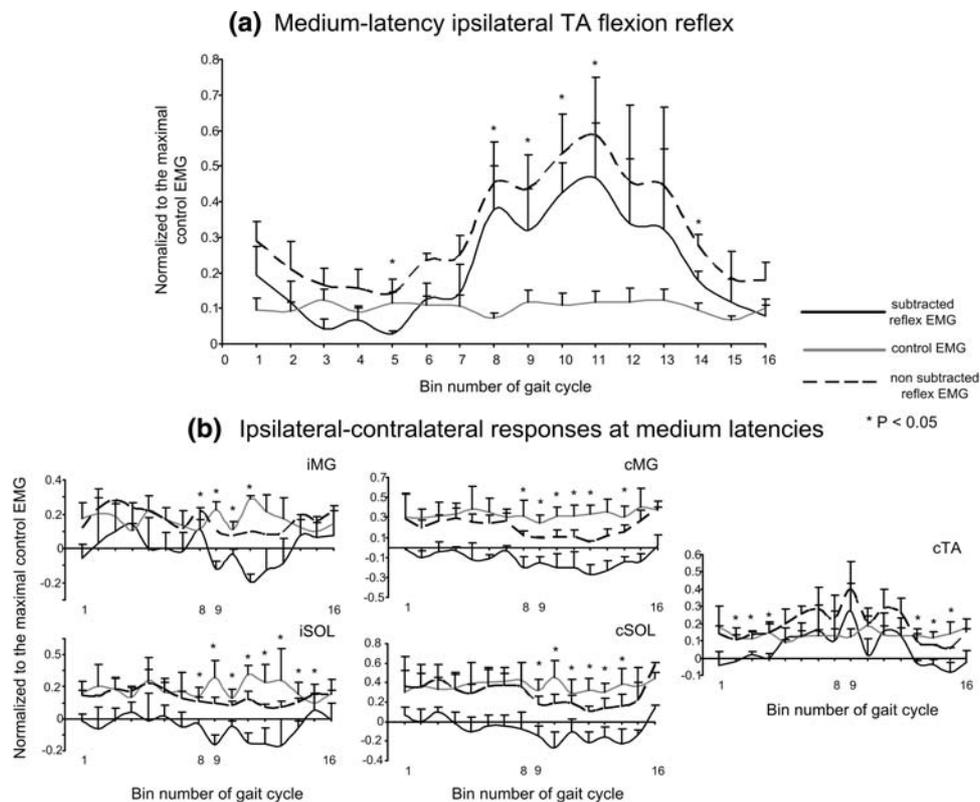


Fig. 4 Short-latency flexion reflex modulation during stepping in SCI. **a** The mean (+SEM) ($n = 3$; subjects D13, D15, and D20) subtracted short-latency tibialis anterior (TA) flexion reflex, control TA EMG, and non-subtracted reflex TA EMG amplitudes normalized to the maximum control TA activity is indicated as a function of the step cycle. **b** The mean (+SEM) ($n = 3$; subjects D13, D15, and D20) short latency subtracted responses, non-subtracted reflex and control EMGs of the ipsilateral and contralateral soleus (SOL), medialis gastrocnemius (MG), and contralateral TA muscles are indicated as a function of the step cycle. Asterisks indicate suppressive and facilitatory subtracted reflex EMGs compared to the control EMG based on the P value of the Wilcoxon signed rank-sum test. *i* ipsilateral, *c* contralateral

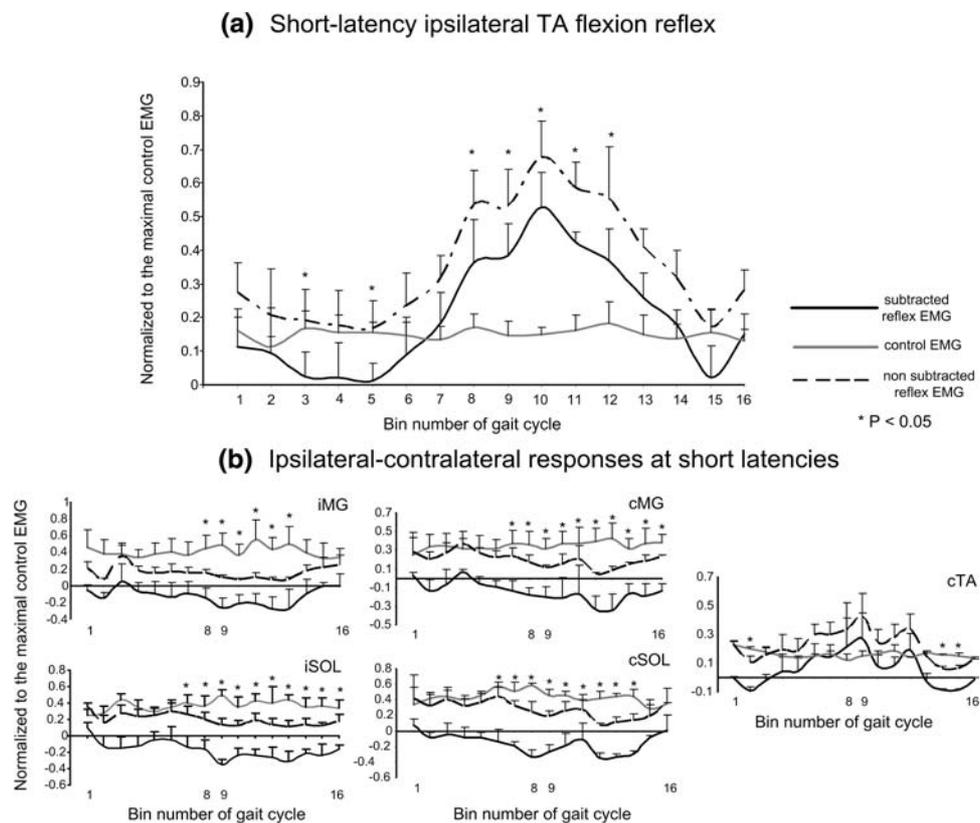
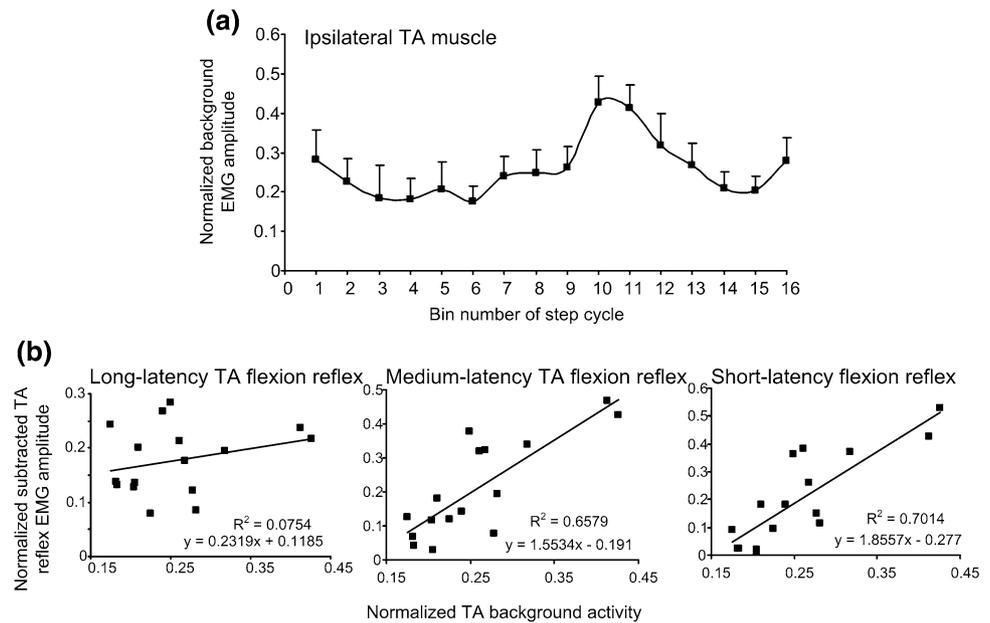


Fig. 5 a Mean (+SEM) normalized tibialis anterior (TA) EMG background activity from all subjects as a function of the step cycle. **b** The relationship between the TA long (*left panel*), medium (*middle panel*), and short (*right panel*) latency average TA reflex amplitude normalized to the maximum control TA activity is indicated as a function of normalized TA EMG background activity from all subjects. In each graph, the 16 points correspond to the 16 bins of the gait cycle



swing. Our findings denote that in people with a SCI, the long latency flexion reflex is modulated in a physiological manner during stepping, and that the short and medium latency flexion reflexes were preserved in three out of nine subjects.

Expression of the flexion reflex during stepping in human SCI

The long latency TA flexion reflex was modulated in a phase dependent manner during stepping regardless of the neurologic injury level or ASIA score. Specifically, the reflex was facilitated during late stance reaching maximal amplitude before swing phase initiation, and was depressed at heel-strike, and during early stance and swing-to-stance transition (Fig. 2a). This denotes a shift between facilitatory and inhibitory interneuronal circuits that is consistent with a meaningful behavior of the flexion reflex during stepping. Further, flexion reflex facilitation coincided with reduced activity of the ipsilateral ankle extensor muscles (MG, SOL) (Fig. 2b), that occurred largely during the swing.

Ipsilateral and contralateral sural nerve stimulation has been reported to decrease presynaptic inhibition of soleus Ia afferent terminals in non-injured subjects (Delwaide et al. 1981; Iles 1996), a phenomenon that has been described for people with a motor complete SCI (Roby-Brami and Bussel 1992). Most likely, phasic modulation of presynaptic inhibition was involved in modifying the flexion reflex during stepping since the long latency TA flexion reflex amplitude was not directly related to the TA background EMG activity (Fig. 5b), and the reflex was phasically modulated regardless of an incomplete or complete spinal lesion. It has clearly been demonstrated in spinalized

animals through direct recordings that FRA evoke primary afferent inhibition in their own terminals (Eccles et al. 1962). However, because brain influences FRA transmission, and FRA interact with group I inhibitory interneurons (Lundberg and Voorhoeve 1962), postsynaptic mechanisms cannot be excluded.

The spinal interneuronal circuits engaged in the long latency flexion reflex have been correlated to the interneuronal circuitry generating stepping (Sherrington 1910; Jankowska et al. 1967b). This is substantiated by recent studies which showed that FRA volleys reset the locomotor rhythm by terminating the ongoing extensor activity and initiating a new flexor burst (Perreault et al. 1995; Schomburg et al. 1998; Stecina et al. 2005). If we assume that spinal interneuronal networks for locomotion exist in humans, we can suggest that the flexor pattern generator was engaged in a functional way in people with SCI during stepping.

The phase dependent flexion reflex modulation we observed might have been driven by movement related afferent feedback interacting with spinal neuronal circuits that mediated the shift between facilitatory and inhibitory interneuronal circuits within the FRA pathway. Plantar pressure, muscle contraction, and hip position modulate the long latency flexion reflex in motor complete and incomplete SCI subjects at rest (Conway and Knikou 2008; Knikou and Conway 2005; Knikou 2007b). Recent studies have shown that changes in hip position entrain the step cycle presumably via activity of hip flexor group II muscle afferents (Kriellaars et al. 1994; McVea et al. 2005; Perreault et al. 1995), which are a part of the FRA system. Our current observations are consistent with the modulation pattern of the long latency flexion reflex in SCI subjects by hip stretches, which is facilitated during hip extension and

depressed during hip flexion (Knikou et al. 2006, 2007; Knikou 2007a). In this study, flexion reflexes were facilitated at the step cycle phases at which the hip was extended and depressed when the hip was flexed as occurs during the swing-to-stance transition. Further research is needed, however, to understand the role of sensory feedback on the phase dependent modulation of spinal reflexes in both SCI and non-injured subjects.

The long latency flexion reflex was present despite the presence or absence of short and medium latency flexion reflexes. These responses were observed in three (D13, D15, and D20) motor incomplete (ASIA D) SCI subjects, with injuries at cervical and thoracic levels (Table 1). Flexion reflexes at latencies shorter than 100 ms are not commonly observed in complete or incomplete SCI subjects (Roby-Brami and Bussel 1987; Knikou and Conway 2005; Knikou 2007b). This may be related to the stimulation intensity being sub-threshold for these responses (Meinck et al. 1985), the need for presence of descending input, and engagement of different interneuronal pathways. The flexion reflex at short and medium latencies was facilitated during the stance-to-swing transition phase (Figs. 3, 4), and depressed during mid-stance. Jones and Yang (1994) postulated that in people with an incomplete SCI the medium latency TA flexion reflex was facilitated during swing and occasionally during stance. The difference between our study and that of Jones and Yang (1994) may be attributed to excitation of different afferent groups based on different stimulation sites (posterior tibial nerve at the medial malleolus vs. sural nerve) and intensities.

The flexion reflex depends largely on the stimulus strength and site of stimulation (Kugelberg 1948; Andersen et al. 1999, 2001; Spaich et al. 2004). This dependency has resulted in nociceptive flexion reflexes observed at latencies of 40–60 and 110–400 ms (Shahani and Young 1971; Hagbarth and Finer 1963), and even beyond 2,000 ms (Kugelberg 1948) in non-injured subjects at rest. Regardless the latency, the nociceptive flexion reflex is modulated in a phase-dependent manner in non-injured subjects (Crenna and Frigo 1984; Spaich et al. 2004, 2009), similar to our observations.

Sural nerve stimulation at non-nociceptive levels in non-injured subjects at rest does not evoke long latency responses (Knikou 2007b). The long latency flexion reflex we observed here appears to be related to the patient population, and our findings are in line with those reported in chronic spinal cats (Forssberg et al. 1977). The responses observed in non-injured subjects following non-nociceptive stimulation of skin, sensory or mixed peripheral nerves are also modulated in a phase-dependent manner during walking (Duysens et al. 1993; Tax et al. 1995; Zehr et al. 1997, 1998; Van Wezel et al. 1997). However, foot innocuous stimulation induced responses were reported to be phase

independently modulated for the TA and phase dependently modulated for other ipsilateral and contralateral muscles (Belanger and Patla 1987). A cyclic modulation in the TA responses was observed during running and cycling (Patla and Belanger 1987). This suggests that the task-dependent regulation of these responses occurs independently of the muscle activity during movement (Belanger and Patla 1987; Patla and Belanger 1987).

The role of sensory feedback and excitation threshold after a SCI in humans may be shifted. Further, because the proportion of afferents (largely $A\beta$ and $A\delta$) activated by the stimulus train play a significant role in the expression of the long latency flexion reflex (Conway et al. 1995), a comparison of flexion reflexes evoked in SCI and non-injured subjects cannot be made. It should be noted that cutaneous, nociceptive, and non-nociceptive flexion reflexes may share common spinal interneuronal circuits and neuronal pathways.

Last, TA impaired function during walking in neurological disorders has been strongly correlated to an absent or reduced corticospinal drive to TA motoneurons on the basis of absent short-term TA motor unit synchronization during the swing phase (Hansen et al. 2005; Nielsen et al. 2008). Despite the impaired TA function due to supraspinal deficits after neurologic injury and the supraspinal control of the flexion reflex (Holmqvist and Lundberg 1961; Lundberg and Voorhoeve 1962; Hongo et al. 1969), the electrically induced flexion reflexes in SCI subjects were modulated in a phase dependent manner during stepping.

Study limitations

Spinal cord injury was characterized as ASIA D in six out of nine subjects, while people with ASIA A, B, and C participated in the study increasing the variability of the lesion type within the SCI group. A challenge of studying individuals with SCI is their availability at individual rehabilitation and research centers. Our understanding of spinal reflex circuitry and neuronal pathways during stepping would be greatly enhanced by collaborations across centers to increase the numbers of subjects representing different levels and completeness of SCI. Three subjects were also taking anti-spasticity medication at the time of the study. Baclofen enhances the levels of presynaptic inhibition (Abbruzzese 2002), a mechanism that accounts largely for the phase dependent modulation of monosynaptic spinal reflexes during walking in humans (Morin et al. 1982; Yang and Whelan 1993; Faist et al. 1996). However, the TA flexion reflex was modulated during stepping in all SCI subjects, including those under medication.

During stepping using BWST, external manual assistance is provided by therapists so appropriate kinematics and kinetics of walking to be generated (Wernig and Müller

1992; Behrman and Harkema 2000; Field-Fote et al. 2005). This manual assistance may have resulted in excitation of different types of afferents, including cutaneous afferents, which modulate and mediate flexion reflexes in SCI subjects (Knikou et al. 2007; Knikou 2007b). However, understanding the interaction of spinal interneuronal circuits and sensory feedback related to cutaneous input, stretch, and load after neurologic injury with rehabilitative interventions is important for optimizing strategies so to improve recovery of walking after SCI.

Conclusion

The flexion reflex, regardless of latency, could be modulated in a phase dependent manner during stepping using BWST and manual assistance in people with a chronic SCI. Flexion reflex facilitation coincided with decreased activity of ipsilateral ankle extensors, supporting a reciprocal organization of the FRA interneuronal circuits during stepping. Our results suggest that the mechanisms underlying phase dependent TA flexion reflex modulation are preserved in SCI subjects and may have been triggered or potentiated from the intervention utilized in this study. Based on our current findings and on the abnormal modulation pattern of the soleus H-reflex observed in the majority of these patients (Knikou et al. 2009), we suggest that training should selectively target spinal reflex circuits in which extensor muscles are involved so sensorimotor recovery in these patients can be maximized.

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