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The human spinal cord interprets velocity-dependent afferent input during stepping

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Summary

We studied the motor response to modifying the rate of application of sensory input to the human spinal cord during stepping. We measured the electromyographic (EMG), kinematic and kinetic patterns of the legs during manually assisted or unassisted stepping using body weight support on a treadmill (BWST) in eight individuals with spinal cord injury (SCI). At various treadmill speeds (0.27–1.52 m/s), we measured the EMG activity of the soleus (SOL), medial gastrocnemius (MG), tibialis anterior (TA), medial hamstrings (MH), vastus lateralis (VL), rectus femoris (RF) and iliopsoas (ILIO); the hip, knee and ankle joint angles; the amount of body weight support (BWS); and lower limb loading. The EMG amplitude and burst duration of the SOL, MG, TA, MH, VL, RF and ILIO were related to the step cycle duration during stepping using BWST. EMG mean amplitudes increased at faster treadmill speeds, and EMG burst durations shortened with decreased step cycle durations. Muscle stretch of an individual muscle could not account for the EMG amplitude modulation in response to stepping speed. The effects on the EMG amplitude and burst duration were similar in subjects with partial and no detectable supraspinal input. We propose that the human spinal cord can interpret complex step-related, velocity-dependent afferent information to contribute to the neural control of stepping.

Keywords: spinal cord injury; locomotion; sensory processing; speed; locomotor training

Abbreviations: ASIA = American Spinal Injury Association; BWL = body weight load; BWST = body weight support on a treadmill; EMG = electromyography; ILIO = iliopsoas; LL = limb load; MG = medial gastrocnemius; MH = medial hamstrings; MTL = muscle–tendon length; RF = rectus femoris; SCI = spinal cord injury; SL = shank length; SOL = soleus; TA = tibialis anterior; VL = vastus lateralis; VMTL = velocity of muscle–tendon length.

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Introduction

Peripheral feedback interacting with spinal neural centres allows spinalized animals to adapt to changes in treadmill speed during stepping and execute successful hindlimb stepping (Forssberg and Grillner, 1973; Forssberg *et al*., 1980*a*, *b*; Andersson *et al*., 1981; Pierotti *et al*., 1989; Roy *et al*., 1991; de Leon *et al*., 1998). The efferent patterns during these speed adaptations are similar to those observed in intact cats responding to changes in speed (Goslow *et al*., 1973; Halbertsma *et al*., 1976; Gardiner *et al*., 1982). Results similar to those of the animal studies have been observed during walking in humans at various speeds (Grillner *et al*., 1979; Dietz *et al*., 1994; Andersson *et al*., 1997). However, whether this response is mediated at the level of the spinal cord by afferent cues in humans is not known. Identifying the critical sensory cues that facilitate effective locomotor activity in humans may be important for designing more effective rehabilitative strategies for the recovery of walking after neurological injury.

The human nervous system can respond to specific sensory cues related to lower extremity weight-bearing and the kinematics of stepping when supraspinal input is severely compromised (Maegele *et al*., 2002). These results suggest that the recovery of walking after spinal cord injury (SCI) may be more dependent on sensory processing than previously considered in humans (Crozier *et al*., 1992; Waters *et al*., 1993).

During stepping, the human spinal cord may be able to generate effective activity in flexors and extensors by integrating complex afferent information related to stepping with remaining supraspinal input after injury. We have previously shown that step-associated proprioception related to alternating leg loading and kinematics can activate and coordinate spinal motor pools in an effective temporal sequence to generate stepping even when an individual is not able to voluntarily execute similar motor patterns in resting positions (Maegele *et al*., 2002). Presumably, manually assisted stepping provided an ensemble of sensory inputs derived from the legs that are associated with walking, which facilitated the ability of clinically complete and incomplete SCI subjects to activate leg muscles. For example, the level of limb load (Harkema *et al*., 1997) and information from the other leg (Ferris *et al*., 2004) were shown to modulate EMG amplitudes during stepping. These modulations were attributed to sensory processing by the human spinal cord.

The aim of this study was to assess whether velocity-dependent afferent input can modulate efferent patterns when supraspinal control is compromised or absent during manually assisted stepping in humans. We varied the stepping velocity by changing treadmill speed, and assessed the modulation of step cycle characteristics as well as leg muscle EMG burst durations and mean amplitudes from individuals with clinically complete and incomplete SCI. We studied these parameters to assess whether velocity-dependent afferent information from the legs during stepping can provide important information to facilitate the generation and modulation of locomotor efferent patterns by the human spinal cord.

Material and methods

Subject population

Eight healthy subjects with a thoracic-level SCI resulting from trauma or ischaemia volunteered for this study (Table 1). None of the subjects were taking any antispasticity medication during the study. A clinician assessed the level and extent of SCI according to the American Spinal Injury Association (ASIA) impairment scale (Maynard *et al*., 1997). Five subjects (A1, A6, A7, A8 and A14) were classified as having a clinically complete SCI, as they were graded as ASIA A (no motor or sensory function below the lesion, including the sacral segments S_4–S_5), and had an absent sensory evoked potential (SEP) response at the cortex during unilateral posterior tibial nerve electrical stimulation at the ankle. Two subjects (C1 and C7) were classified as ASIA C (motor preservation below the lesion, but little to no active movement against gravity) and one subject (C4) was classified as ASIA D (motor preservation below the lesion, with active movement against gravity in at least half the muscles below the lesion). All subjects had received locomotor training using body weight support on a treadmill (BWST). Injury level, years after injury, number of training sessions received and ASIA impairment scale leg motor scores for each subject are summarized in Table 1. The University of California, Los Angeles Institutional Review Board approved all experiments and each subject signed an informed consent form before participating in the study.

Experimental design

In all subjects we measured EMG activity, hip, knee and ankle joint angles, level of body weight support (BWS), and amount of lower leg loading during stepping at various treadmill speeds. All subjects wore a harness and were suspended by an overhead, motorized lift. Trainers provided manual assistance as necessary during stepping. Hand placement distal to the patella facilitated extension during the stance phase, and at the popliteal crease for flexion during swing. Hand placement proximal to the ankle assisted proper foot placement and foot clearance at lift-off. A trainer positioned behind the subject aided in hip stabilization and weight shifting between legs during stepping as needed. Data were recorded during stepping of SCI subjects at treadmill speeds between 0.27 and 1.52 m/s while at the same BWS. Speed trials were randomized and the treadmill belt was stopped between each trial.

Data acquisition

We collected EMG, joint angle, footswitch and BWS data at 1 kHz using a 24-channel hard-wired analogue-to-digital board and a custom-written Labview software acquisition program (National Instruments, Austin, TX, USA). EMG data were sampled and AC-coupled into a differential amplifier (Konigsberg Instruments, Pasedena, CA, USA). We measured EMG activity bilaterally from the soleus (SOL), medial gastrocnemius (MG), tibialis anterior (TA), medial hamstrings (MH), vastus lateralis (VL) and rectus femoris (RF) using bipolar surface electrodes. The electrode placements have been described previously (Harkema *et al*., 1997; Beres-Jones *et al*., 2003). We verified the efficacy of electrode placement in order to avoid contamination by crosstalk among muscles by eliciting and recording EMG activity in an individual muscle while recording inactivity in the agonists and antagonists. The iliopsoas (ILIO)

Table 1 *Subject characteristics*

Subject	Age (years)	After injury (years)	Injury level	Asia level	Motor score	SEP	No. of sessions
A1	39	4	T_8	A	0	Absent bilateral	18
A6	22	5	T_8	A	0	Absent bilateral	20
A7	44	8	T_4	A	0	Absent bilateral	74
A8	13	2	T_7	A	0	Absent bilateral	60
A14	33	0.75	T_6	A	0	Absent bilateral	61
C1	43	2	T_8	C	R = 8, L = 0	R: delayed L: absent	51
C4	19	0.5	T_6	D	R = 17, L =21	Not tested	53
C7	35	18	T_8	C	R = 5, L = 14	Not tested	60

ASIA, American Spinal Injury Association. Maximum motor score per limb is 25. L = left; R = right; SEP = sensory evoked potential at the cortex.

was recorded in five subjects (A1, A7, A8, C4 and C7) using a fine wire electrode placed medial to the anterior superior iliac spine. Eliciting a flexion response and recording EMG through the electrode verified accurate placement. Joint angles were measured using electrogoniometers placed bilaterally at the ankle, knee and hip. BWS was recorded from a loadcell in series with the cable attached to the harness.

Individual leg load was measured during each speed condition by recording pressure distribution of the foot's plantar surface using pressure sensor shoe inserts (Tekscan, Boston, MA, USA). We used Tekscan software to digitally sample the pressure data (50 Hz), which were then converted to vertical ground reaction force data. We dynamically calibrated the Tekscan shoe inserts with a force platform (Kistler, Amherst, NY, USA) using non-disabled subjects of comparable weight and shoe size to the SCI subjects. A previous study describes these procedures in more detail (Harkema *et al*., 1997). We used a customized Labview program to interpolate the ground reaction force data acquired from Tekscan software from 50 to 1000 Hz in order to continuously synchronize the load signal with the EMG signals. We also detected foot contact using the footswitch data acquired directly with the Labview acquisition system so we could confirm accurate synchronization of the ground reaction force data. The EMG data were rectified and high-pass filtered at 32 Hz using Labview software customized by our laboratory.

Data analyses

We manipulated the treadmill speed (0.27–1.52 m/s) to alter the step cycle characteristics, and thus the rate of the kinematics and kinetics during stepping. Figure 1A and B illustrates a typical recording of BWS (top panel) and left and right limb loading calculated from the vertical ground reaction force data (middle and bottom panels) during stepping using BWST and manual assistance. BWS was calculated as the mean force from the loadcell during the series of steps. Step cycle characteristics were determined from the vertical ground reaction force data: step cycle duration (s) as the time from foot contact to next foot contact; stance duration (s) as the time from foot contact to lift-off; and swing duration (s) as the time from lift-off to the subsequent foot contact. The step cycle characteristics were consistently modulated by changing treadmill speeds, as evidenced by exemplary data from these two SCI subjects (Fig. 1C and D).

Data from approximately 7–13 steps from the eight subjects were analysed. Onset of an EMG burst was defined as the time when the signal amplitude remained above the threshold (mean of the baseline + 3 standard deviations) for 30 ms. The end of the EMG burst was defined as the time when the signal amplitude remained below the threshold level for 50 ms. Burst duration was calculated as the time between the onset and the end of the EMG burst. Mean EMG amplitude was calculated by dividing the sum of the amplitudes of each burst by the burst duration.

To understand whether the EMG activity modulation was the result of changes in the level of leg loading or immediate afferent feedback from biomechanical events, we assessed the relationships among the EMG activity, limb load (LL), and changes in muscle–tendon length (MTL) for each muscle. LL was calculated for each leg as the mean ground reaction force during stance. Percentage body weight load (% BWL) was LL divided by the total body weight. MTL was calculated with the acquired joint angle measurements using regression equations that were derived from correlations of joint angle and direct muscle–tendon complex length measurements from anthropometric specimens (Hawkins and Hull, 1990). The velocity of muscle–tendon length change (VMTL) was the derivation of the MTL curve. These values were normalized to the shank length (SL). The relationship among mean EMG activity, MTL and VTML was compared in two ways. First, the mean EMG amplitude was correlated with the muscle–tendon stretch, defined as the maximum increase in MTL during the entire step cycle. Secondly, to assess the immediate response of the EMG activity to muscle–tendon stretch, the mean EMG amplitude was correlated to the muscle–tendon stretch coinciding with the EMG activity, incorporating a 70 ms delay for signal conduction velocity. Onset latencies of EMG activity from biomechanical events (LL, muscle–tendon stretch) were calculated as the time from the onset of the event to the onset of EMG activity. End latencies of EMG activity from biomechanical events (LL, muscle–tendon stretch) were calculated as the time from the end of the event to the end of the EMG activity.

Statistical analyses

We used the statistical method for repeated measures for the following relationships for each leg of eight subjects: (i) step cycle duration, stance duration, swing duration and LL versus treadmill speed; (ii) EMG amplitude and burst duration for each muscle versus step cycle duration (load and leg were included in the model below as covariates); and (iii) MTL and VMTL for each muscle versus EMG amplitude. Group analyses (all SCI subjects) and subgroup analyses (clinically complete and incomplete SCI subjects analysed separately) were also performed for each muscle EMG amplitude and burst duration. Stepping tests were carried out 7–13 times at four to eight different speeds. These variables were repeatedly measured for 6–10 steps for the seven muscles on both legs for each test and subject. We used a mixed linear model method as a statistical method that incorporates analyses for random effects, repeated measurements, random coefficients, and other statistical problems. For the same muscle, several statistical tests were performed, each with a different treadmill speed. There are several factors that may have influenced the outcome: load, stepping rate, muscle and/or leg. These factors are included in the model as fixed effects. The sequences of the tests were considered as random effects to allow the variation among the tests on the same muscle of a subject. In addition, during each test, the outcome was repeatedly measured for 6–12 steps; thus, the measurements for the steps in a test might be correlated (e.g. not independent). Therefore, we assume that the error terms are correlated and the covariance matrix of the error term is block diagonal, with each block corresponding to a single test. The structure for the block is assumed to be first-order autoregressive:

$$\begin{bmatrix} 1\rho\rho^2\rho^3 \ldots \rho^k \\ \rho 1\rho\rho^2 \ldots \rho^{k-1} \\ \rho^2\rho 1\rho \ldots \rho^{k-2} \\ \rho^2\rho^3\rho^2\rho 1 \ldots .\rho^{k-3} \\ \rho^k\rho^{k-1} \ldots \ldots \ldots \ldots 1 \end{bmatrix}$$

where k is the number of steps in a test. In a test, the closer the steps are in sequence, the higher the correlations.

For all subjects, the model is:

$$Y_{ijk} = \alpha + \mathbf{X}_{ijk}\beta + t_{ij} + \varepsilon_{ijk}$$
$$i = 1, 2, \ldots 8, j = 1, 2, \ldots j_i, \; k = 1, 2, \ldots k_{ij}$$

where Y_{ijk} is the measurement obtained from the kth step in the jth test for subject i, α is the intercept, $\mathbf{X}_{ijk}$ is the vector of fixed

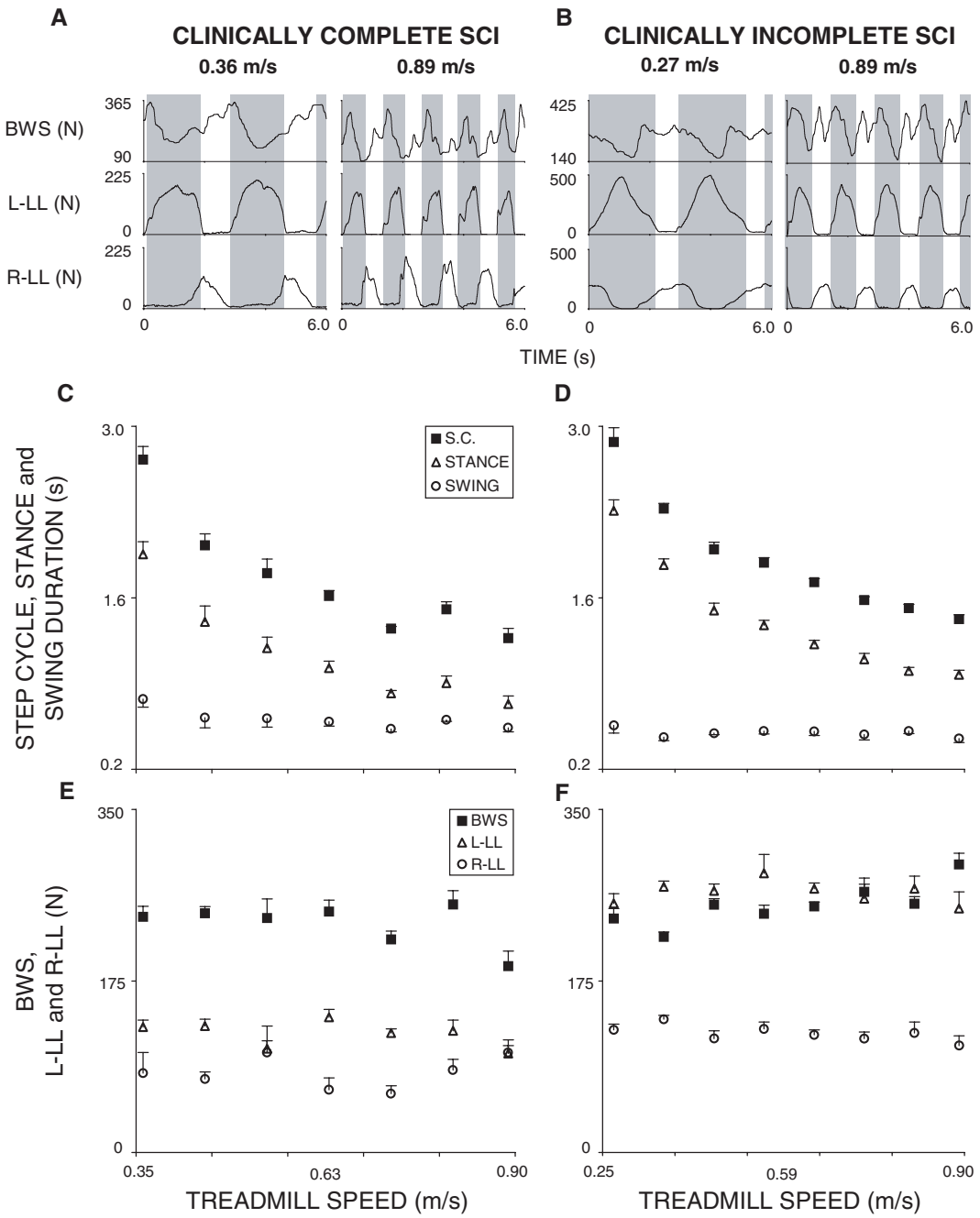

Fig. 1 Step cycle, stance and swing durations decreased at faster treadmill speeds at the same body weight support in a clinically complete and incomplete spinal cord-injured individual. (**A** and **B**) Body weight support (BWS; newtons, N) and left (L-) and right (R-) limb loads (LL) during 6 s of stepping with (**A**) a clinically complete SCI (subject A8, left panel 0.36 m/s, right panel 0.89 m/s) and (**B**) a clinically incomplete SCI (subject C4, left panel 0.27 m/s, right panel 0.89 m/s). Shaded bars indicate left leg stance phase. (**C** and **D**) Average and standard error values for step cycle (S.C.; squares), stance (triangles) and swing (circles) durations (s) versus treadmill speed (m/s) for the left leg of the subjects depicted in **A** and **B**. (**E** and **F**) Averages and standard errors for BWS (squares; N), left limb load (L-LL; triangles; N) and right limb load (R-LL; circles; N) are plotted against treadmill speed (m/s) for the subjects depicted in **A**–**D**.

effects, such as speed, load, side and step cycle duration, β is the vector of the regression coefficients for the fixed effects, t_{ij} is a random effect of the jth test for subject i; $t_{ij} \sim$ iid N(0, σ_t^2), and ϵ_{ijk} is the error term. The covariance matrix of the error term is block diagonal, each block corresponding to a single test for subject i. The structure for the block is assumed to be autoregressive order 1.

For an individual leg, the same model is used except that there is no i in the subscript. The statistical software SAS was used to carry out all analyses. All tests were two-sided with significance level 0.05.

Results

In this study we will present results relating the speed of stepping to step cycle and EMG burst characteristics, including the effect of stepping velocity on step cycle, stance and swing durations and level of loading; the effect of stepping velocity on leg EMG mean amplitudes and burst durations; and the characteristics of the EMG burst pattern in relation to the dynamics of the step cycle.

Stepping speed modulated step cycle, stance and swing durations

Step cycle durations were lower at higher stepping speeds, primarily attributed to a decrease in the duration of the stance phase (Fig. 1A–D). Step cycle duration and stance duration decreased in the clinically complete (Fig. 1A and C) and incomplete (Fig. 1B and D) SCI subjects with increasing treadmill speeds. In all SCI subjects, step cycle and stance duration decreased significantly ($P < 0.05$) in both legs, and swing duration ($P < 0.05$) decreased significantly in 14/16 legs with higher treadmill speeds (Fig. 2A). However, in all subjects, the reduction in swing duration (-0.70 ± 0.40 s) was considerably less than the reduction in stance duration (-1.33 ± 0.40 s). Stance duration was longer than swing duration in all SCI subjects except in one clinically complete SCI subject (A14). Step cycle, stance and swing durations were similar between the left and right legs.

There was no predictable or consistent trend between load and speed in the SCI subjects. Exemplary data from a clinically complete (Fig. 1E) and incomplete (Fig. 1F) SCI subject show the variation in leg load across the treadmill speeds and also illustrate that while changes may occur from speed to speed, there was no predictable or consistent trend between load and speed. The correlation between leg load and treadmill speed was significant in only 6/16 legs. Furthermore, the leg load changed by less than 13% in 14/16 legs from the slowest to fastest treadmill speeds and actually decreased in 11/16 legs (Fig. 2B). In one subject, there was a significant decrease of leg load (21%) with higher treadmill speeds. We have previously shown that increasing leg loading during stepping can increase EMG mean amplitudes when stepping at a constant speed (Harkema *et al*., 1997); however, in this study higher rates of stepping did not result in consistent increases in leg loading.

Stepping velocity modulated leg EMG mean amplitudes and burst durations

Faster stepping speeds resulted in higher motor pool output and shorter burst durations (Table 2). The percentage change in EMG burst duration ranged from 41 to 60% and EMG mean amplitude ranged from 28 to 70% in muscles from the slowest to fastest stepping speed in all SCI subjects. EMG burst durations were significantly ($P < 0.05$) shorter and EMG mean amplitudes were significantly ($P < 0.05$) higher in all muscles by group analyses in all SCI subjects. In subgroup analyses (clinically complete and incomplete SCI subjects analysed separately) similar results were found (Table 2). In both SCI groups, EMG burst durations were significantly ($P < 0.05$) shorter at faster speeds in all muscles. EMG amplitudes were higher in the clinically incomplete than in the complete SCI subjects in all muscles except the ILIO. In clinically complete SCI subjects ($n = 5$), SOL, MG, TA, MH and ILIO EMG amplitudes were significantly higher at the faster speeds ($P < 0.05$); however, VL and RF were not. In clinically incomplete SCI subjects ($n = 3$), SOL, MG, MH, VL and RF were significantly higher at the faster speeds ($P < 0.05$), but the TA was not. In individual legs analyses, significance in the increase of EMG amplitudes at faster speeds was observed from clinically complete SCI subjects of VL (4/9 legs) and RF (5/9 legs) and from clinically incomplete SCI subjects from the TA (4/6 legs). Thus, non-significant results of the subgroup analyses are probably attributable to individual subject amplitude differences and the lower number of subjects within each group, rather than to subgroup differences.

This increase in EMG activity was reflected in a variety of ways. For example, in muscles that displayed little or no EMG burst activity at the slowest speeds, activity often emerged at faster stepping speeds (Fig. 3A, TA and VL muscles; 0.27 and 0.54 m/s). Furthermore, in muscles in which EMG burst activity was already present at a lower speed, amplitudes were even greater at faster velocities (Fig. 3A). This finding of higher EMG amplitude at faster speeds is consistent across steps, as shown by comparing the average EMG mean amplitude from approximately ten steps taken at each speed (Fig. 3B). Burst durations were shorter at faster stepping speeds, as shown by the difference in duration of the EMG burst activity at the three speeds (Fig. 3A–C). For example, at 0.27 m/s only one burst of activity occurred in 4 s, whereas two bursts were present at 0.54 m/s and three occurred at 0.89 m/s (Fig. 3A). The increase in EMG amplitude was not attributed to an increase in leg load since there was little change in loading, with even a small decrease at the fastest speed (Fig. 3D). Representative data from six clinically complete and incomplete SCI subjects show the relationships among EMG burst duration (Fig. 4), EMG mean amplitude (Fig. 5) and step cycle duration across the treadmill speeds.

Characteristics of the EMG burst pattern in relation to afferent feedback

The EMG amplitude changes could not be solely attributed to the immediate afferent feedback from stretching and the rate of stretching of the muscle–tendon complex. As stepping velocity increases, presumably so too does the changes in length of the muscle–tendon complex, and the velocity at which it lengthens. However, the relationship between EMG amplitude and step cycle duration remained significant ($P < 0.05$) in all muscles when including the effect of muscle–tendon length (MTL) and velocity of muscle–tendon length

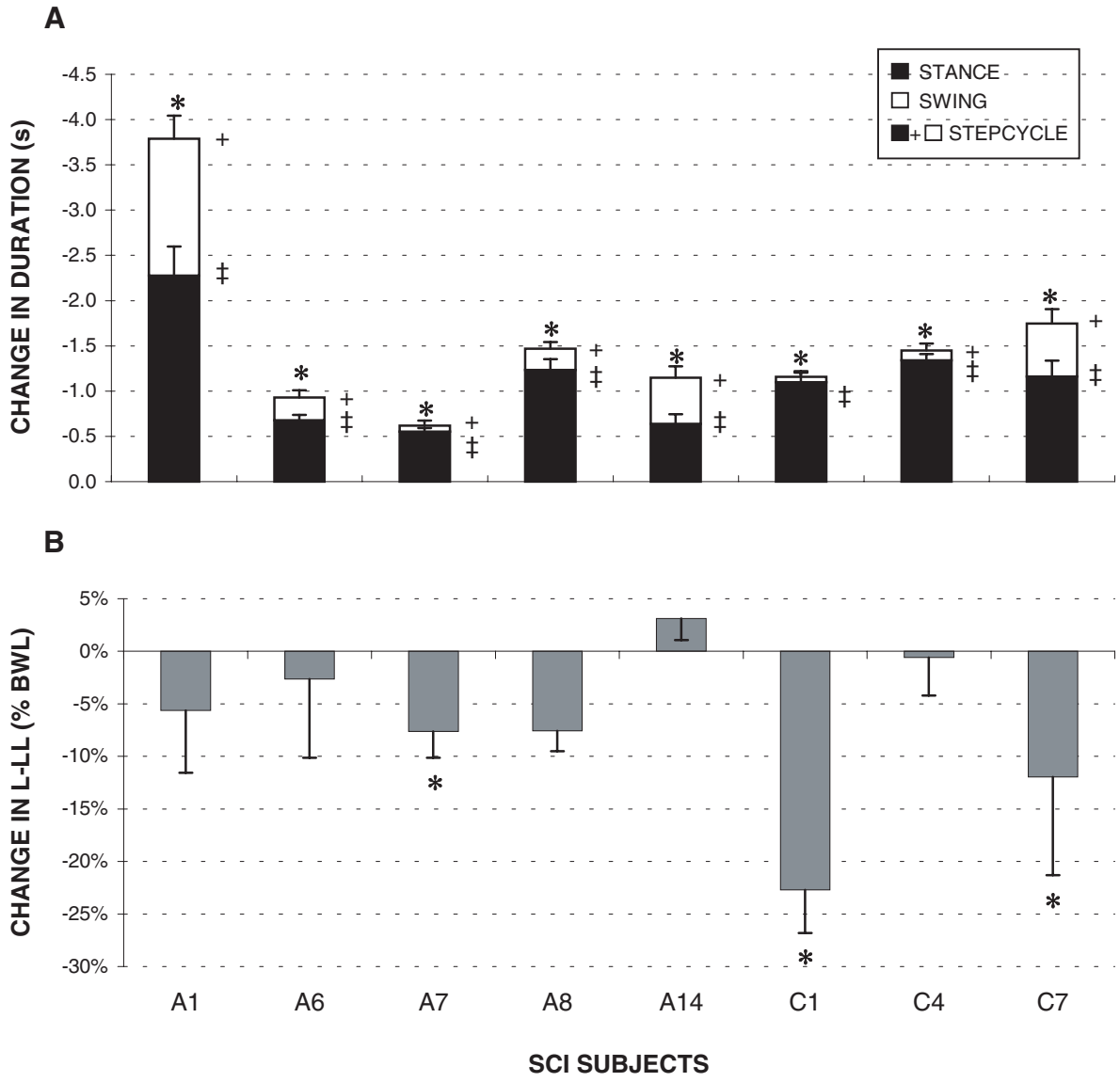

Fig. 2 Step cycle, stance and swing durations decreased with no change or decreases in leg load at faster stepping speeds in all spinal cord-injured individuals stepping on a treadmill using body weight support. (**A**) Averages and standard errors for the difference in duration from the highest to the lowest treadmill speed of step cycle (sum of black bar + white bar), stance (black bar) and swing (white bar) for all clinically complete SCI subjects (A1, A6, A7, A8, A14) and incomplete SCI subjects (C1 C4, C7). Statistically significant ($P < 0.05$) differences are indicated for step cycle (stars), stance (double crosses) and swing (single crosses) durations versus treadmill speed for all speeds studied. (**B**) Averages and standard errors for the difference in left limb load (L-LL, % body weight load, BWL) from the highest to the lowest treadmill speed for all clinically complete SCI subjects (A1, A6, A7, A8, A14) and incomplete SCI subjects (C1 C4, C7). Statistically significant ($P < 0.05$) differences are indicated (stars) for limb load versus treadmill speed.

(VMTL) as covariates with group analyses and subgroup analyses, both when considering muscle stretch during the entire step cycle and only during muscle activation (for details of analyses see Material and methods, and Harkema *et al*., 1997).

The muscle stretch during the entire step cycle could not account for EMG amplitude changes, as it did not increase at the faster stepping speeds. In fact, in all muscles the MTL significantly ($P < 0.05$) decreased both with group and subgroup analyses. This can be illustrated by examining the changes in EMG amplitude and SOL MTL from a clinically complete SCI subject at three stepping speeds (Fig. 6). The EMG amplitude is higher at the faster stepping speeds (Fig. 6A and D). However, the absolute length change is greater at the slowest speed (0.36 m/s) than at the two faster speeds (0.63 and 0.89 m/s; Fig. 6B). This is also reflected when examining the relationship between EMG amplitude and the extent of SOL muscle stretch at all the stepping speeds; the greater the EMG amplitude the lower the SOL MTL (Fig. 6E). The rate of muscle stretch during the entire

Table 2 *Average percentage change in EMG burst duration and EMG mean amplitude between the slowest and fastest stepping speeds*

Muscle	Change from slowest to fastest speed (%)			
	Burst duration		Mean amplitude	
	ASIA A	ASIA C/D	ASIA A	ASIA C/D
SOL	**−66 ± 7**	**−50 ± 4**	**48 ± 14**	**48 ± 7**
MG	**−57 ± 6**	**−41 ± 2**	**37 ± 9**	**54 ± 18**
VL	−42 ± 8	**−43 ± 5**	48 ± 16	**89 ± 34**
RF	**−48 ± 7**	**−35 ± 5**	33 ± 9	**98 ± 12**
MH	**−66 ± 5**	**−45 ± 8**	**25 ± 8**	**32 ± 7**
TA	**−55 ± 9**	−43 ± 6	**55 ± 14**	57 ± 9
ILIO	**−50 ± 5**	**−51 ± 6**	**68 ± 27**	**17 ± 5**

ASIA = American Spinal Injury Association; ASIA A = clinically complete; ASIA C/D = clinically incomplete; SOL = soleus; MG = medial gastrocnemius; VL = vastus lateralis; RF = rectus femoris; MH = medial hamstrings; TA = tibialis anterior; ILIO = iliopsoas. Bold values denote significance at $P < 0.05$. Statistical analysis was performed on the entire data set as described in the Material and methods section.

step cycle was higher at the faster stepping speed, as expected (Fig. 6C and F); however the correlation between EMG amplitude and VTML was much lower (Fig. 6F; $r^2 = 0.04$) than the correlation between EMG amplitude and step cycle duration (Fig. 6D; $r^2 = 0.30$).

The muscle stretch that occurred during the EMG activity could not account for the EMG amplitude modulation with changes in step cycle duration. Several muscles (TA, VL, RF and ILIO) would routinely shorten during EMG activation; thus, it is unlikely that immediate afferent input from muscle stretch solely contributed to the EMG amplitude modulation with speed of stepping. Even in those muscles that primarily lengthened during EMG activation, muscle stretch did not solely account for the EMG modulation with stepping speed. This can be shown by examining these relationships in the SOL muscle, where it has been demonstrated that homonymous muscle stretch can influence the EMG amplitude during stepping (Yang *et al*., 1991). The correlation between EMG amplitude and step cycle duration (Fig. 6D; $r^2 = 0.30$) was much higher than that between EMG amplitude and synch MTL (Fig. 6G; $r^2 = 0.001$) and synch VTML (Fig. 6 H; $r^2 = 0.04$).

In addition the SOL muscle burst activity was not phase-locked to either the stretch of the muscle–tendon complex or the leg loading, indicating that the activity was not dependent only on immediate afferent input related to loading during stance or muscle stretch (Fig. 7). The SOL burst should occur immediately after loading if this stimulus were the primary afferent input generating the activity. However the SOL onset always preceded the onset of the loading in this subject (Fig. 7A, C, D). Furthermore, the end of the SOL burst preceded the end of the loading at all speeds studied (Fig. 7A, C, D). We also measured these latencies of the burst onset and end of loading across all eight subjects in all muscles (15 legs). The timing of the burst pattern in relation to loading did not show that the immediate feedback from loading consistently resulted in the muscle activity. Likewise, if SOL burst activity was dependent only on immediate afferent input related to muscle–tendon stretch, then the onset of the SOL burst should always have occurred after the initiation of stretch. However, the SOL burst onset preceded the initiation of stretch in the SOL muscle across all speeds (Fig. 7A, B, E). When we measured the latency of the SOL burst onset to the onset of muscle–tendon stretch in all eight subjects (15 legs) during EMG activity, the timing of the burst pattern in relation to the onset of muscle–tendon stretch did not support the idea that immediate feedback from stretch consistently resulted in the muscle activity.

We also compared the relationships among step cycle duration, EMG amplitude, hip extension position and hip extension velocity (Fig. 8). As exemplified by data from a clinically complete SCI subject, there were significant correlations between hip extension velocity and step cycle duration ($r^2 = 0.77$), EMG amplitude and hip extension velocity ($r^2 = 0.61$), and EMG amplitude and hip extension position ($r^2 = 0.15$) across stepping speeds.

Discussion

The present data demonstrate that the rate of application of afferent input provides important sensory information that modulates leg motor pool activity in humans with compromised or no detectable supraspinal input during stepping. This efferent modulation cannot be explained by the response to immediate afferent stimuli from a specific stimulus, but rather is the result of an ensemble of stimuli dependent on the rate of application of the sensory input.

Sensory processing by the human spinal cord

We have demonstrated that velocity-dependent modulation of locomotor activity during stepping in human subjects occurs without detectable supraspinal input. In subjects with clinically complete SCI, step cycle and stance phase durations shortened at faster stepping velocities, while swing phase duration showed less modulation (Figs 1 and 2). EMG mean amplitudes were higher and burst durations were shorter at faster stepping velocities in the muscles studied in all SCI subjects (Figs 3–5; Table 2). Since these modulations occurred with no or compromised supraspinal input available, a significant level of neural control of stepping can be attributed to the interpretation of particular patterns of afferent information by the human spinal cord. These data support the idea that the human spinal cord can interpret complex velocity-dependent afferent information during stepping to facilitate the generation and modulation of locomotor efferent patterns.

Spinal neural centres responding to peripheral feedback are essential for spinalized animals to adapt to changes in treadmill speed during stepping (Forssberg and Grillner, 1973; Forssberg *et al*., 1980*a*; Andersson *et al*., 1981; Pierotti

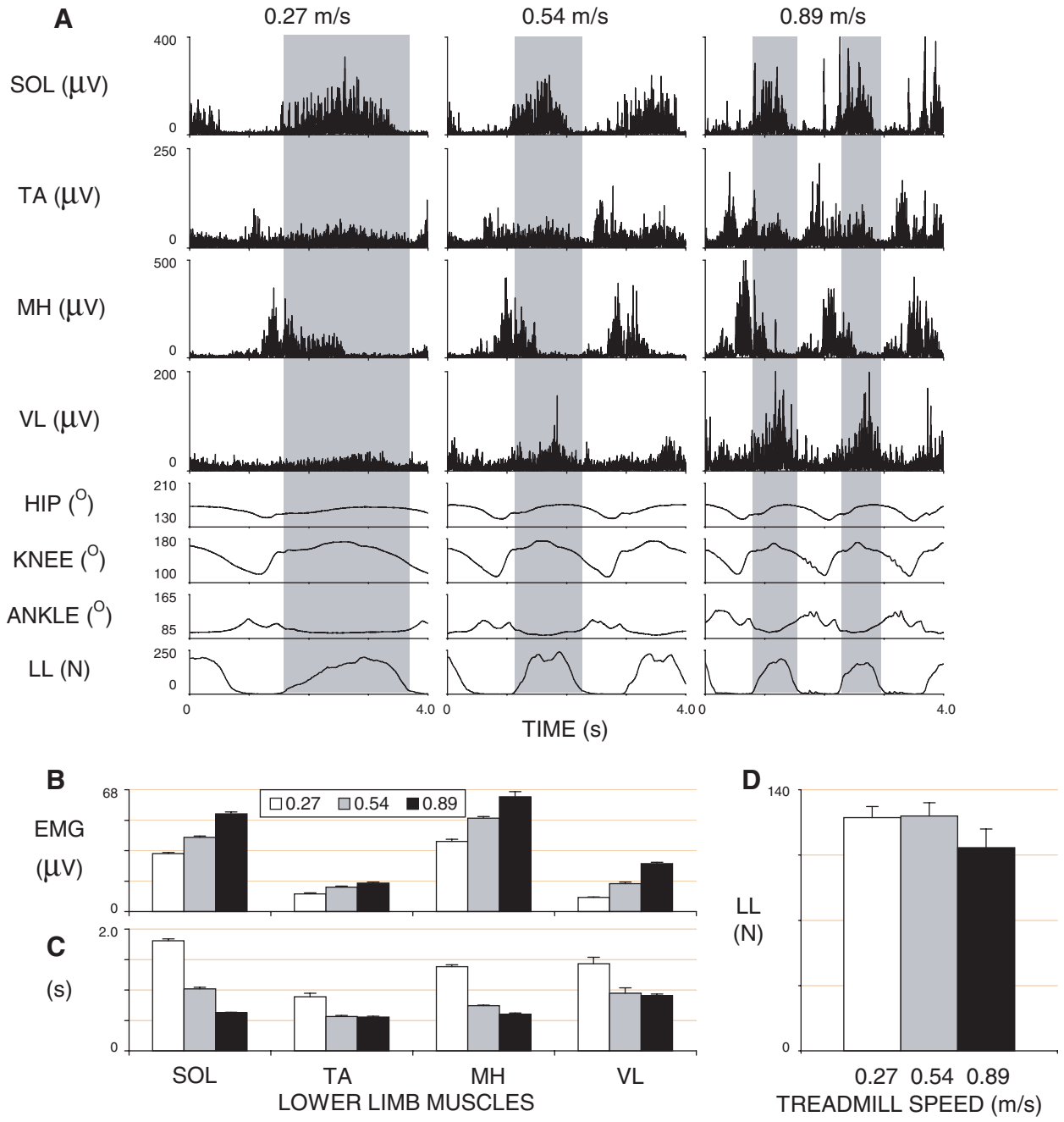

Fig. 3 Lower leg electromyographic activity increased at faster stepping speeds during stepping on a treadmill using body weight support in a clinically incomplete spinal cord injured individual. (**A**) Soleus (SOL), tibialis anterior (TA), medial hamstring (MH) and vastus lateralis (VL) EMG activity (μV; rectified and high pass filtered at 32 Hz); hip, knee and ankle angles (degrees); and vertical ground reaction force (newtons, N) are shown for the right leg of subject C4 during stepping at 0.27 m/s (left column), 0.54 m/s (middle column) and 0.89 m/s (right column). The stance phase of the step cycle is evidenced by the elevation in the ground reaction force trace and indicated by the shaded region, and the unshaded portion of the graph represents the swing phase. (**B** and **C**) Average plus standard error values for SOL, TA, MH and VL EMG mean amplitude (**B**) and for burst duration (**C**) at 0.27 m/s (white), 0.54 m/s (grey) and 0.89 m/s (black) respectively. (**D**) Average plus standard error values for the limb load (LL) at 0.27 m/s (white), 0.54 m/s (grey) and 0.89 m/s (black).

et al., 1989; de Guzman *et al*., 1991; Roy *et al*., 1991; de Leon *et al*., 1998). These locomotor patterns observed at various stepping speeds are similar to those observed in intact cats (Goslow *et al*., 1973; Halbertsma *et al*., 1976). Furthermore, studies of fictive locomotion report that cycle period modulates burst duration to a greater degree in extensors than flexors (Andersson and Grillner, 1983; Pearson and Rossignol, 1991) and more consistently after repetitive step training (Baker *et al*., 1984). In our study, the extensor muscles SOL, MG and VL showed the most consistent burst duration response to stepping velocity, as burst durations were shorter at faster speeds in nearly every case (Fig. 4). The changes in

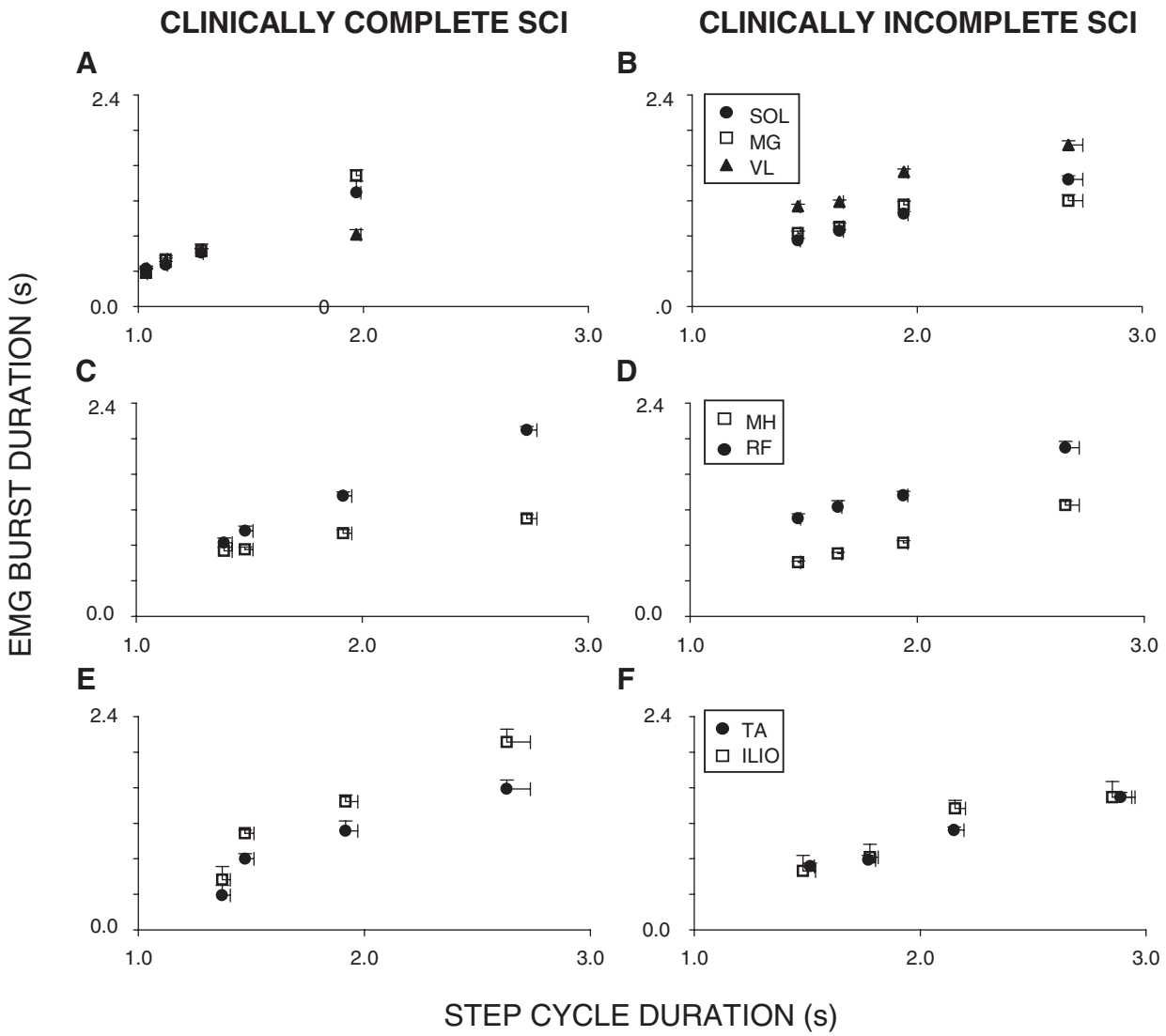

Fig. 4 Lower leg muscle electromyography burst duration decreased as step cycle duration decreased in subjects with clinically complete and incomplete spinal cord injury. EMG burst duration (s) versus step cycle duration (s) are presented for either the right or left leg from extensor muscles: soleus (SOL, circles), medial gastrocnemius (MG, squares) and vastus lateralis (VL, triangles) of (**A**) clinically complete SCI subject A6 and (**B**) clinically incomplete SCI subject C4; from bifunctional muscles: medial hamstrings (MH, squares) and rectus femoris (RF, circles) of (**C**) clinically complete SCI subject A8 and (**D**) clinically incomplete SCI subject C4; and flexor muscles: tibialis anterior (TA, circles) and iliopsoas (ILIO, squares) of (**E**) clinically complete SCI subject A8 and (**F**) clinically incomplete SCI subject C7. Each point represents the average (+ standard error) of EMG burst durations and step cycle durations within each trial at each treadmill speed, where the data were binned in 10 ms intervals.

step cycle characteristics in SCI subjects observed in this study are also similar to reports from intact animals (Gardiner *et al*., 1982; Pierotti *et al*., 1989; Roy *et al*., 1991), non-disabled humans during walking (Murray *et al*., 1966; Grillner *et al*., 1979; Shiavi *et al*., 1981, 1987; Nilsson *et al*., 1985; Nilsson and Thorstensson, 1987; Dietz *et al*., 1994; Andersson *et al*., 1997) and ambulatory clinically incomplete SCI subjects (Pepin *et al*., 2003*a*, *b*). However, in these SCI subjects stepping independently on a treadmill, hip, knee and ankle angles and stride length were significantly different from non-disabled subjects during similar slower walking speeds (Visintin and Barbeau, 1994; Pepin *et al*., 2003*a*, *b*).

Afferent modulation of locomotor patterns

Load-related sensory pathways have been shown to modulate the locomotor networks in spinalized animals. The locomotor rhythm can be entrained by stimulation of group I afferents (Conway *et al*., 1987; Pearson *et al*., 1992) and limb loading during stance activates positive feedback pathways that contribute to ipsilateral extensor muscle activation in animals (Duysens and Pearson, 1980; Gossard *et al*., 1994; Guertin *et al*., 1995; McCrea *et al*., 1995; Whelan *et al*., 1995; Whelan and Pearson, 1997). Leg loading during the stance phase has also been shown to modulate extensor efferent output during walking in humans (Bastiaanse *et al*., 2000; Sinkjaer *et al*.,

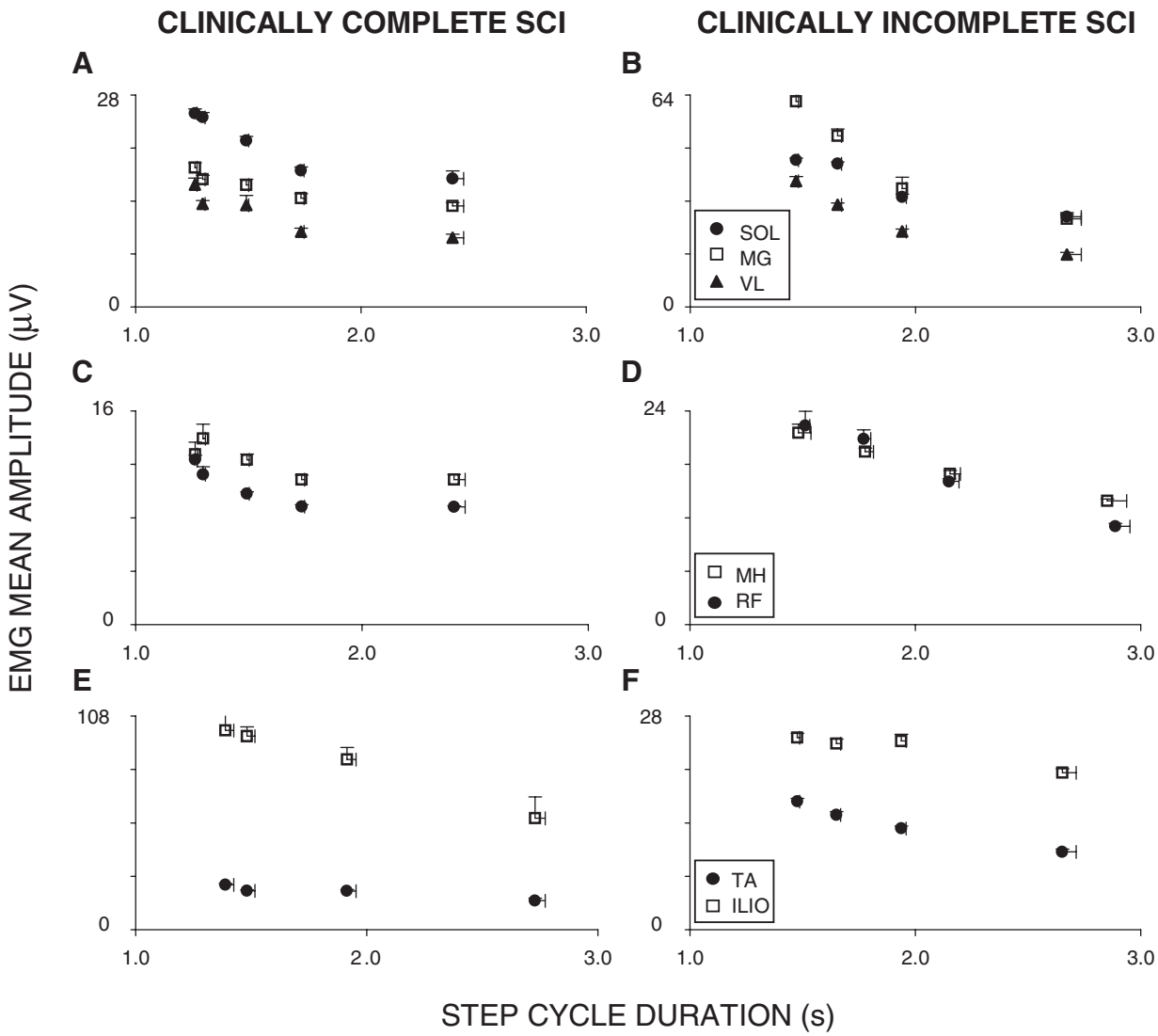

Fig. 5 Lower leg muscle electromyographic mean amplitude increased as step cycle duration decreased in subjects with clinically complete and incomplete spinal cord injury. EMG mean amplitudes (μV) versus step cycle duration (s) are presented for either the right or left leg from extensor muscles: soleus (SOL, circles), medial gastrocnemius (MG, squares) and vastus lateralis (VL, triangles) of (**A**) clinically complete subject A14 and (**B**) clinically incomplete subject C4; from bifunctional muscles: medial hamstrings (MH, squares) and rectus femoris (RF, circles) of (**C**) clinically complete SCI subject A14 and (**D**) clinically incomplete SCI subject C7; and flexor muscles tibialis anterior (TA, circles) and iliopsoas (ILIO, squares) of (**E**) clinically complete SCI subject A8 and (**F**) clinically incomplete SCI subject C4. Each point represents the average (+ standard error) of EMG mean amplitudes and step cycle durations within each trial at each treadmill speed, where the data were binned in 10 ms intervals.

2000; Stephens and Yang, 1999) and to be mediated at the level of the human spinal cord (Harkema *et al*., 1997). Furthermore, it has been reported in humans (Sinkjaer *et al*., 2000; Stephens and Yang, 1999) and animals (Hiebert and Pearson, 1999) that extensor muscle group I afferent feedback comprises more than 50% of the extensor output during walking. In this study there was either no significant change or a decrease in the amount of weight-bearing at faster speeds; thus, the EMG amplitude modulation with step cycle duration could not be attributed to changes in the level of loading (Figs 1 and 2). In some subjects EMG activity emerged only at the highest stepping speeds even with a lower level of load (Fig. 3). Although the amount of load did not account for the EMG amplitude modulations with stepping speed, the rate of the Ib afferent input could have contributed to the modulation. In addition, the length of time during which load-related information was presented to the spinal networks may have been an important factor in determining the EMG burst durations (Andersson *et al*., 1981; Kriellaars *et al*., 1994; Whelan and Pearson, 1997).

Stretch-related afferent information has been demonstrated to contribute 30–60% of SOL EMG amplitude during human walking (Yang *et al*., 1991). In our study, when MTL and VMTL were considered as covariates, the relationship

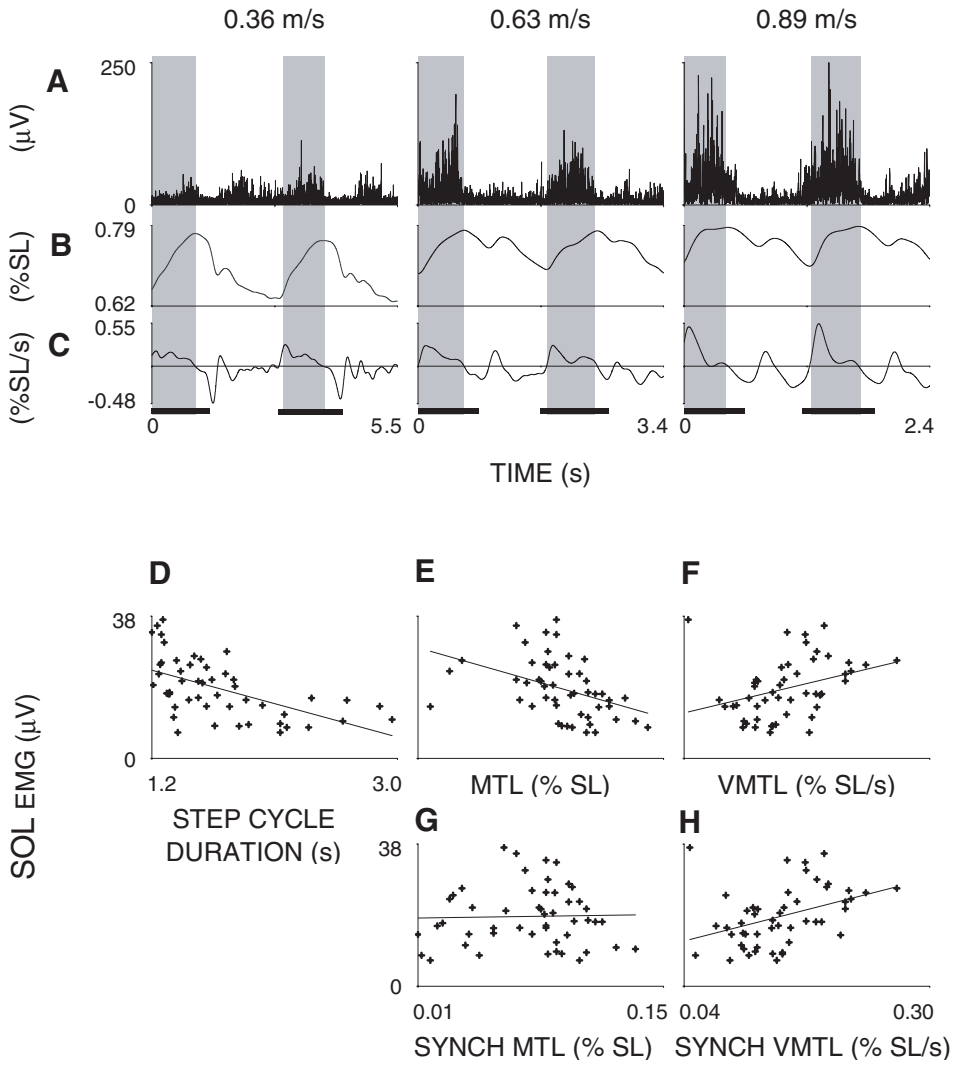

Fig. 6 Soleus electromyography activity is correlated to step cycle duration but not to soleus muscle–tendon stretch or rate of stretch in a clinically complete SCI subject. (**A**) SOL EMG activity (μV; rectified and high pass filtered at 32 Hz), (**B**) SOL muscle–tendon length (MTL; % shank length, % SL) and (**C**) SOL velocity of muscle–tendon length (VMTL; % SL/s) from a subject with clinically complete SCI subject (A8) during stepping on a treadmill with body weight support (BWS) and manual assistance at 0.27 m/s (left panels), 0.63 m/s (middle panels) and 0.89 m/s (right panels) and 45% BWS. Black horizontal bars indicate the stance phase and open spaces indicate the swing phase. The first shaded vertical bar in each panel indicates the period of increasing MTL (stretch) occurring during the whole step cycle, and the second shaded vertical bar indicates the period of increasing MTL (stretch) occurring with EMG activity. (**D**–**F**) SOL EMG mean amplitude (μV) versus (**D**) step cycle duration (s; $r^2 = 0.30$); (**E**) muscle–tendon stretch over the entire step cycle (MTL; % SL; $r^2 = 0.15$), (**F**) velocity of muscle–tendon stretch over the entire step cycle (VMTL; % SL/s; $r^2 = 0.04$) (**G**) muscle–tendon stretch occurring simultaneously with EMG activity (SYNCH MTL; % SL; $r^2 = 0.001$); and (**H**) velocity of muscle–tendon stretch occurring simultaneous with EMG activity (SYNCH VMTL; % SL/s; $r^2 = 0.04$). Only the relationship between SOL EMG amplitude with step cycle duration was statistically significant.

between SOL EMG amplitude and step cycle remained significant. Furthermore, the onset and end of the SOL burst could precede the onset and end of either the stance phase or the stretch of the SOL muscle–tendon complex (Fig. 7). In all muscles, the increase in EMG mean amplitude was not highly correlated to the amplitude of muscle–tendon stretch or rate of stretch in SCI subjects (Fig. 6). Although stretch-related afferent information is likely to be important (Duysens *et al*., 1991), especially in the triceps surae, in generating EMG activity, this afferent feedback alone cannot explain the EMG amplitude modulations observed at different stepping velocities in these studies. These results indicate that the additional sensory input derived from stepping at faster velocities also modulates EMG amplitude and cannot be attributed only to immediate input from just one afferent to the same muscle.

Evidence that hip-associated velocity-dependent sensory information can influence central spinal locomotor networks includes the entraining of the bursting cycle by the frequency of hip movements in the fictive cat preparation, which could

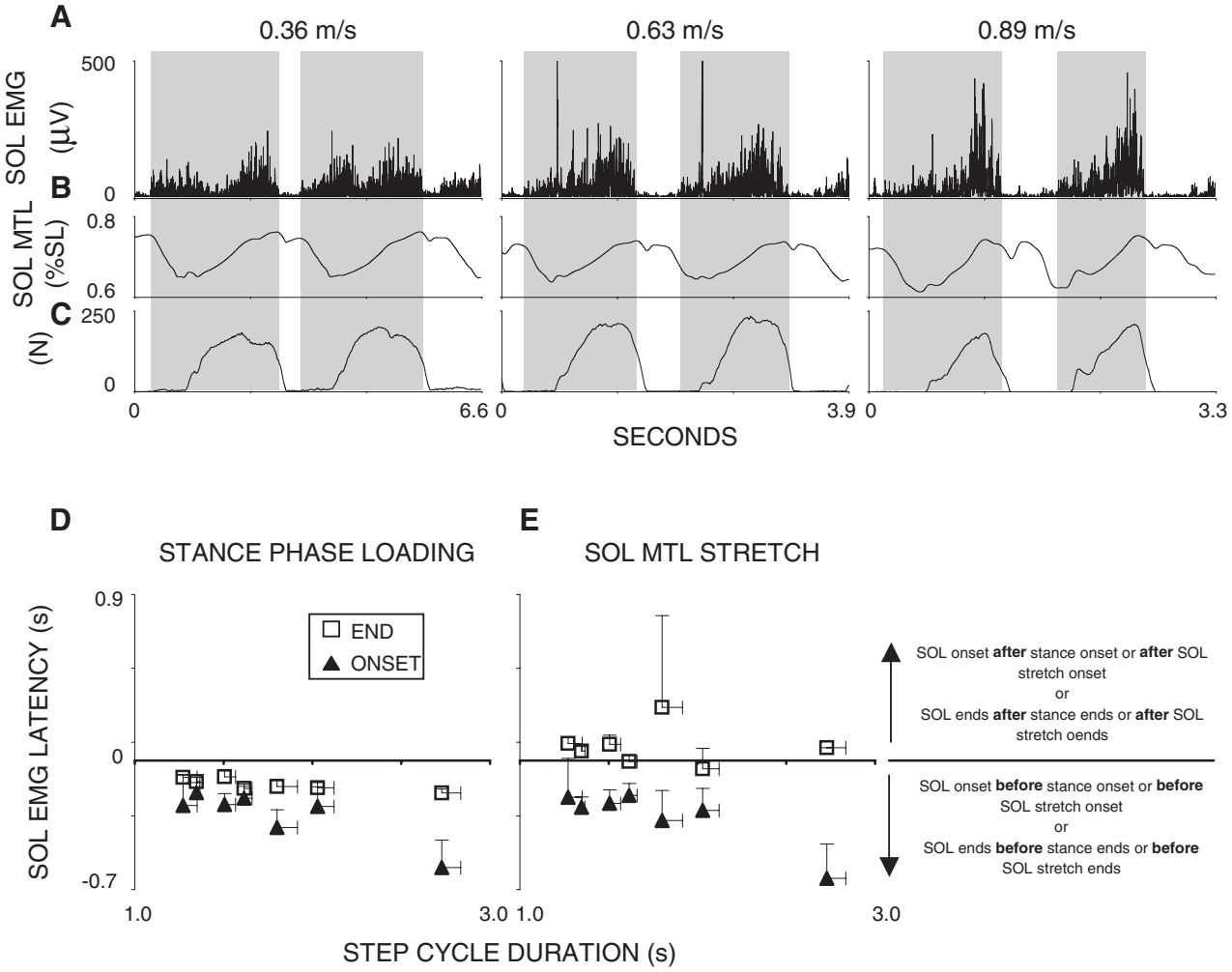

Fig. 7 Soleus electromyography activity was not the result of immediate biomechanical feedback from leg load or muscle–tendon stretch during stepping on a treadmill using body weight support and manual assistance in spinal cord-injured individuals. (**A**) SOL EMG activity (μV; rectified and high pass filtered at 32 Hz), (**B**) SOL muscle–tendon length (MTL; % shank length, SL) and (**C**) vertical ground reaction force from a subject with clinically complete spinal cord injury (A8) during stepping at 0.36 m/s (left), 0.63 m/s (middle) and 0.89 m/s (right) and 33% BWL on a treadmill with body weight support and manual assistance. Vertical shaded bars indicate the period of SOL EMG activation. (**D**–**E**) Average plus standard deviation values for latency (s) of SOL burst onset to onset (triangles) and offset (squares) of stance phase loading (**D**) and SOL MTL stretch (**E**) are plotted versus average plus standard deviation values for step cycle duration (s) for one representative subject with clinically complete spinal cord injury (A8). Negative values for onset latencies indicate that the SOL burst started before the stance phase started or before stretch of the SOL MTL occurred. Similarly, negative values for offset latencies indicate that the SOL burst ended before the end of the stance phase or before the end of the SOL MTL stretch. Positive values for onset latencies indicate that the SOL burst started after the stance phase started or after stretch of the SOL MTL occurred. Similarly, positive values for offset latencies indicate that the SOL burst ended after the end of the stance phase or after the end of the SOL MTL stretch.

not be explained by simple immediate afferent reflex (Andersson and Grillner, 1983). In this preparation, fictive locomotion was pharmacologically induced in a paralysed and spinalized cat that had been completely deafferented except for the hip joint and the surrounding small muscles. They found that varying the frequency of passive sinusoidal hip movement could entrain the fictive locomotor rhythm in both the ipsilateral and contralateral limb in hip, knee and ankle muscles. EMG burst durations shortened and EMG mean amplitudes increased, with extensor burst durations more affected than flexor burst durations. The increase in amplitude was attributed to velocity-dependent response of hip joint and muscle receptors since total angular excursion was the same across frequencies and there was no loading or stance phase. In this study, there was a significant correlation between hip extension velocity and EMG amplitude; however, based on these experiments alone we cannot tell whether the rate of hip extension is the primary afferent stimulus that resulted in the EMG modulation. For example, flexor afferents from other muscles may have contributed to shortening of the extensor phase and onset of flexion phase, as observed in animal studies (Hiebert *et al*., 1996), or the rate of load

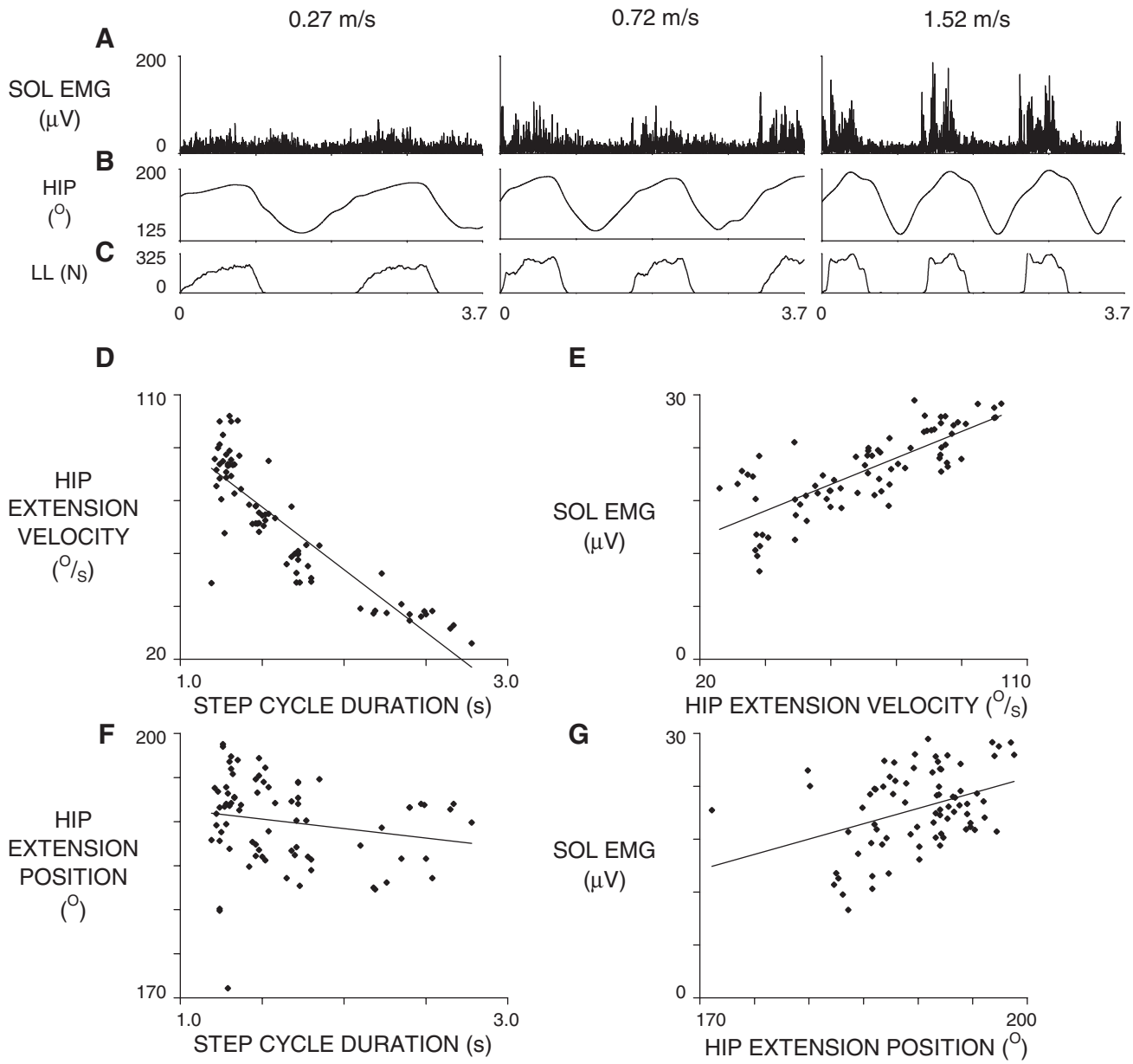

Fig. 8 Soleus electromyography activity was correlated to hip extension velocity but not position during stepping on a treadmill using body weight support and manual assistance in a clinically complete spinal cord injured individual. (**A**) SOL EMG activity (μV; rectified and high pass filtered at 32 Hz), (**B**) hip position (degrees) and (**C**) vertical ground reaction force from a subject with clinically complete spinal cord injury (A14) during stepping at 0.27 m/s (left), 0.72 m/s (middle) and 1.52 m/s (right) and 27% BWL on a treadmill with body weight support and manual assistance. (**D**) Hip extension velocity (degrees/s) versus step cycle duration ($r^2 = 0.77$); (**E**) SOL EMG activity (μV) versus hip extension velocity (degrees/s; $r^2 = 0.60$); (**F**) Hip extension position (degrees) versus step cycle duration ($r^2 = 0.03$); and (**G**) SOL EMG activity (μV) versus hip extension position (degrees; $r^2 = 0.15$).

and stretch-related information may also contribute (Yang *et al*., 1991).

Other studies have also shown that sensory pathways related to the hip joint and flexor muscles can effectively modulate locomotor patterns (Kriellaars *et al*., 1994; Hiebert *et al*., 1996; Lam and Pearson, 2001). Furthermore, the combination of hip extension (Grillner and Rossignol, 1978; Andersson and Grillner, 1981) and unloading of one limb at terminal stance was shown to be closely linked to the initiation of swing in the spinal cat (Duysens and Pearson, 1980; Conway *et al*., 1987). Human studies have also identified hip extension as an important sensory cue in infant stepping (Pang and Yang, 2000) and after human spinal cord injury (Dietz *et al*., 2002). In this study, hip extension position was not significantly different across stepping speeds. However, it is interesting to note that at the same hip position, at the slower rates flexor EMG activity was not elicited as it was at the higher rates (Fig. 8). Future studies should be designed to

individually manipulate the rate of joint kinematics independent of stepping rate and levels of loading to distinguish the relative contributions of velocity components of hip and other flexor afferents in generating human locomotion.

Response to the rate of application of sensory input in SCI subjects

We propose that the functionally isolated human spinal cord does not just respond to one simple afferent signal, but that it can process and interpret an ensemble of velocity- and load-dependent afferent information during stepping to effectively modulate locomotor EMG patterns. Immediate group I afferent responses (e.g. from rate of stretch or from increased limb load amplitude at faster speeds) may not be solely responsible for the efferent modulations observed in this study, but that is not to say that these afferents do not play a role in modulation of EMG activity during locomotion. However, the rate at which afferent input is delivered to the CNS may be important in more complex regulation of efferent patterns. These results support the idea that the human spinal cord plays a key role in the complex neural control of locomotion, as described in other mammals, incorporating a myriad of sensory input into coherent locomotor output.

Clinical implications

During conventional gait rehabilitation (Ford and Duckworth, 1974; Somers, 1992), locomotor training for recovery of walking (Stewart *et al*., 1991; Wernig and Müller, 1991; Barbeau and Fung, 1992; Dietz *et al*., 1995; Wernig *et al*., 1995; Colombo *et al*., 1998; Field-Fote, 2001) and studies of locomotion after SCI (Fung and Barbeau, 1994; Visintin and Barbeau, 1994; Harkema *et al*., 1997; Maegele *et al*., 2002), slower than normal walking speeds are primarily used. Furthermore, normative speeds of stepping have been unattainable in ambulatory SCI individuals during independent stepping on a treadmill (Pepin *et al*., 2003*a*, *b*).

The results from this study demonstrate that stepping at more normative treadmill speeds results in higher leg EMG output during stepping when compromised or when no supraspinal input is available to the spinal cord. The level of leg loading has also been shown to modulate EMG amplitude in SCI subjects stepping at a constant treadmill speed. From a clinical perspective it will be important in future studies to assess the interactive effect of the level of loading and stepping speed in generating the most effective locomotor patterns in individuals following SCI. Furthermore, to maximize recovery of walking after neurological injury, rehabilitative strategies should include approaches that repetitively provide the appropriate sensory cues associated with locomotion by including normative stepping speeds while maximizing loading on the legs.

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