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RESEARCH ARTICLES

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Induction of locomotor-like EMG activity in paraplegic persons by orthotic gait training

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Abstract This is, to our knowledge, the first report demonstrating the effects of orthotic gait training on the activity of the spinal locomotor neural networks. Three subjects with complete spinal cord injury (SCI) performed 1-h training with reciprocating gait orthosis 5 days/week for 12 weeks. The results showed that after 3 (n=1) or 6 weeks (n=2) of training, EMG activities synchronized with locomotor rhythm appeared in the soleus muscle (SOL) in all subjects, although very little EMG activity accompanied the orthotic gait at the early training stage. Our results suggest that the induced modulation in the SOL EMG waveforms might be attributable to changes in the orthotic gait movement pattern, and/or changes in the interneuronal activities of the spinal locomotor neural networks, as a result of orthotic gait training.

Keywords Spinal cord injury · Locomotion · Gait orthosis · Plasticity

Introduction

It has been well established that the human spinal cord has the potential to generate the basic locomotor pattern by interaction of the locomotor neural networks and peripheral sensory information concomitant with limb movements (Harkema et al. 2000). For example, several researchers have demonstrated that in severe spinal cord-injured (SCI) subjects, locomotor-like coordinated electromyographic (EMG) activity can be induced in paralyzed lower limb muscles by passive stepping on a moving treadmill with partial body-unloading (Dietz et al. 1994, 1995; Dobkin et al. 1994; Wernig et al. 1995). However, the nature of the neural networks involved in generation of locomotor EMG activities in SCI persons is not yet fully understood.

During a specific type of upright walking with gait orthosis called weight bearing control orthosis (WBCO) (Yano et al. 1997), modulation of lower leg-muscle activities that synchronize with that particular locomotor cycle can be induced (Kojima et al. 1998). Because the WBCO gait, like other reciprocating gait orthoses, is a "stiff-leg" gait, i.e., a gait with the knee locked in full extension and the ankle in a neutral position, the afferent information thought to primarily contribute to inducing the locomotor-like EMG activity would be associated with hip-joint movement and load on the leg (Dietz et al. 2002). This in turn might mean that use of the orthotic gait would allow us to investigate the contribution of the involvement of hip extension/flexion movement or load on the leg to generation of locomotor-like EMG modulation, specifically in the "lower leg" muscles, which are remote from the hip *joint*. However, in our experience, little EMG activity appears during the WBCO gait when the user is not well trained, whereas it has been demonstrated in a well-trained SCI subject that locomotor-like EMG is observed (Kojima et al. 1998). These empirical observations might be explained as follows: (1) afferent inputs concomitant with limb movements would not be sufficient to evoke locomotor EMGs during the untrained orthotic gait; and (2) the orthotic gait training induces an alteration in interneuronal activities in spinal neural networks, which would generate the locomotor EMG even when the pattern and amount of afferent inputs are the same. To test these possibilities, we first had to longitudinally evaluate changes in EMG activities in paralyzed muscles, and to relate these EMG changes with gait-motion changes during the time course of training. The purpose of this study, therefore, was to clarify: (1) whether alteration in the EMG activities in the lower leg muscles occurs during the time course of orthotic gait training, and (2) the relation between the EMG activities and kinetic/kinematic alteration of the gait motion due to the training.

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Materials and methods

Subjects and orthotic gait training

Three clinically complete paraplegic men (22–28 years; 60–68 kg; 173–177 cm) with traumatic spinal cord injuries (Th8–Th12) voluntarily participated in this study. The physical characteristics of the subjects are shown in Table 1. The American Spinal Injury Association (ASIA) impairment scale was used for the clinical assessment of subjects, and in each case the sensorimotor functions were classified as A, which means no motor or sensory function below the level of the lesion. The subjects gave their informed consent to the experimental procedures, which were conducted in accord with the Helsinki Declaration of 1975 and approved by the ethics committee of the National Rehabilitation Center for the Disabled, Tokorozawa, Japan. The long brace reciprocating gait orthosis, the WBCO, was used for the training. The subjects performed orthotic gait training with WBCO for 12 weeks, at 1 hour/d for 5 days/week. The mechanical features of the WBCO have been fully described elsewhere (Yano et al. 1997; Kojima et al. 1998). In short it has two specific features that the other existing gait orthoses do not have. The first one is a special gas-powered system to control the foot sole thickness. It can switch the sole thickness depending on the gait phase; when a leg is swinging forward, the sole of this particular leg is held at the thinner position; and just before the heel strikes, the sole gets changed to the thicker position. With this system a user can swing their legs easier without leaning the body sideward to make a clearance between a foot sole and floor. The second one is a special hip joint device. With this device a torque exerted by the right (left) hip joint is mechanically transmitted to the left (right) hip joint, resulting in the torque to the opposite direction exerted by the left (right) hip joint. This system assists each leg to reciprocally propel forward. As a whole these mechanical features enable a user ambulate at faster speed and with less energy expended (Kawashima et al. 2003).

Experiments

To evaluate the kinetic and kinematic changes in the orthotic gait motion during the course of training, the gait motion was measured with a three-dimensional motion-analysis system (VICON370, Oxford Metrics, UK). The motion-analysis system consists of a conventional video-analysis system with seven cameras and Kistler force plates. The force plates, sized 160×450 cm, consisted of two 80×200 cm plates and four 40×250 cm plates. These separate force plates enable us to measure ground reaction forces (GRF) under the feet and canes on both sides, separately. The orthotic gait motion was recorded along with electromyographic (EMG) activities in the right soleus (SOL) and tibialis anterior (TA) muscles. EMGs were recorded by two surface electrodes (Ag/AgCl, 0.8 cm diameter) attached along the muscle fibers over the belly of each muscle and set at an interelectrode distance of 0.5 cm. The EMG signal was detected by a bipolar differential amplifier with upper and lower cutoff frequencies of 50–3000 Hz. Very thin elastic nylon bandages were used to firmly hold both electrodes and lead lines to the body, preventing any small displacement of electrodes and lines that might cause artifacts. These measurements were carried out three times (after 1, 6, and 12 weeks) in subject A; six times (after 1, 2, 3, 4, 10, and 12 weeks of training) in subject B; and twice (after 1 and 6 weeks) in subject C during the training period. For the measurement, subjects ambulated along a 10-m walkway several times at comfortable cadences. They repeated the trials with short-time intermissions, usually a couple of minutes, until the minimum required number of data was obtained. We sampled at least six step cycles for the analysis. Many step cycles, for example more than ten cycles, could not be recorded in the measurements of this study, since high quality VICON data could be obtained only for one or two steps of around five steps in a trial. At the beginning of training, especially, the experimenter had to walk beside the subjects to prevent a fall. This disturbs the motion capture with the VICON system, and makes the space in which the motion capture is possible small. Due to this limitation it would have taken a relatively longer time for the subjects to record many step cycles. To reduce time for the experiment we decided to finish the measurement when at least six step cycles were obtained in good quality.

Changes in the following kinetic and kinematic variables were evaluated from the measured VICON data throughout the training period: kinetic variables, including the impulse and mean vertical GRF (mGRF) under the foot, and kinematic variables, including the stance time and swing time, velocity, cadence and step length, joint range of motion (ROM), and peak velocity during the stance phase of the hip and ankle joints. The digitized EMG signals were full wave-rectified after rejection of the DC component. Then, from the rectified EMG signals, mean values (mEMG) for the stance phase were calculated and normalized by those values at rest.

Stretch reflex test

The reflex EMG responses elicited by mechanical stretches at various velocities were tested to verify whether the stretch reflex mediated the induced EMG activity in the SOL during the orthotic gait. Stretch reflex responses were evoked by imposing a quick dorsiflexion with an amplitude of 10 deg to the SOL muscle, while the subjects were seated comfortably in a chair with the right leg fixed to a foot plate connected to a servo-controlled torque motor (Senoh Inc., Japan). The hip, knee and ankle joints were set at 80 deg, 60 deg flexed and 10 deg plantar-flexed positions (anatomical position is 0 deg), respectively. All of 25 perturbations, each consisting of various angular velocities (50–350 deg/s), were applied to the ankle joint in random order. In the present study, the short latency reflex component, M1, was evaluated, since only M1 component was induced in the three subjects. The onset of the first EMG response was defined as the moment when the rectified EMG activities reached levels higher than the average resting potential plus three times its standard deviation (BGA+3SD), and the response duration was defined as 30 ms from the response onset. The average rectified EMG value above the resting potential level over the response duration was considered as the M1 level, and the relation between the imposed stretch velocity and the M1 level was analyzed for each subject.

Additional experiments

Additional experiments were done for the subject A in order to ascertain whether: (1) the EMG activity was induced with another conventional gait orthosis (advanced reciprocating gait orthosis, ARGO), and (2) in order to compare how different gait velocities affected the induced EMG activity before and after the training. Because this subject continued the training for over half a year,

Table 1 Clinical characteristics of subjects studied

Subject	Sex	Age (years)	Height (cm)	Weight (kg)	Injury level (segment)	ASIA	Time postinjury (months)	Etiology
A	M	27	177	60	T10	A	10	Trauma
B	M	22	174	68	T12	A	8	Trauma
C	M	28	173	63	T8	A	12	Trauma

measurements could be taken at the 1st week (1-W), 4th week (4-W), and 20th week (20-W) of the training. In the measurements, the subject ambulated at various velocities, speeding up his pace on the basis of his comfort.

Statistics

The measured kinetic and kinematic variables during the training period were compared with the first measurement values using the Student's t-test. Data are presented as mean ± SD. Significance was accepted as $p<0.05$.

Results

All subjects could ambulate independently with the aid of canes in the 1st week of training. In subjects A and B, gait velocities were respectively increased from 7.7 to 13.2 m/min, and from 11.8 to 21.2 m/min after the 12-week training; these increases are concomitant with increases in step length, ROM, angular velocity of hip and ankle joints, and the mGRF during the stance phase. In subject C, however, both the hip and ankle-joint angular velocities were decreased; the hip joint's ROM was decreased; and the ankle joint's ROM was increased. These findings were likely due to the markedly faster gait velocity (22.4 m/min) of this subject, as compared to the other two subjects, at the beginning of the training. In none of the subjects was clear modulation in the EMG activities of either muscle observed at the beginning of the training. After three (subj. A) or six (subjs. B and C) weeks of training, however, synchronized EMG bursts with the stance phase commonly appeared in the SOL in all three subjects, whereas no clear modulation was observed in any of the TA EMG waveforms (Fig. 1A). Figure 2 shows changes in the walking velocities, hip and ankle joint angular velocities, mGRFs, and SOL EMGs during the time course of training in the three subjects. As mentioned above, the SOL EMG activities increased during the training period in all subjects, and this increasing time course was qualitatively most similar to the gait velocity and mGRF. The increasing patterns in the SOL EMGs were not necessarily in parallel with those in the hip and ankle joint velocities. In subject C, specifically, the hip joint and ankle joint velocities demonstrated a tendency to decrease, though the SOL EMG increased.

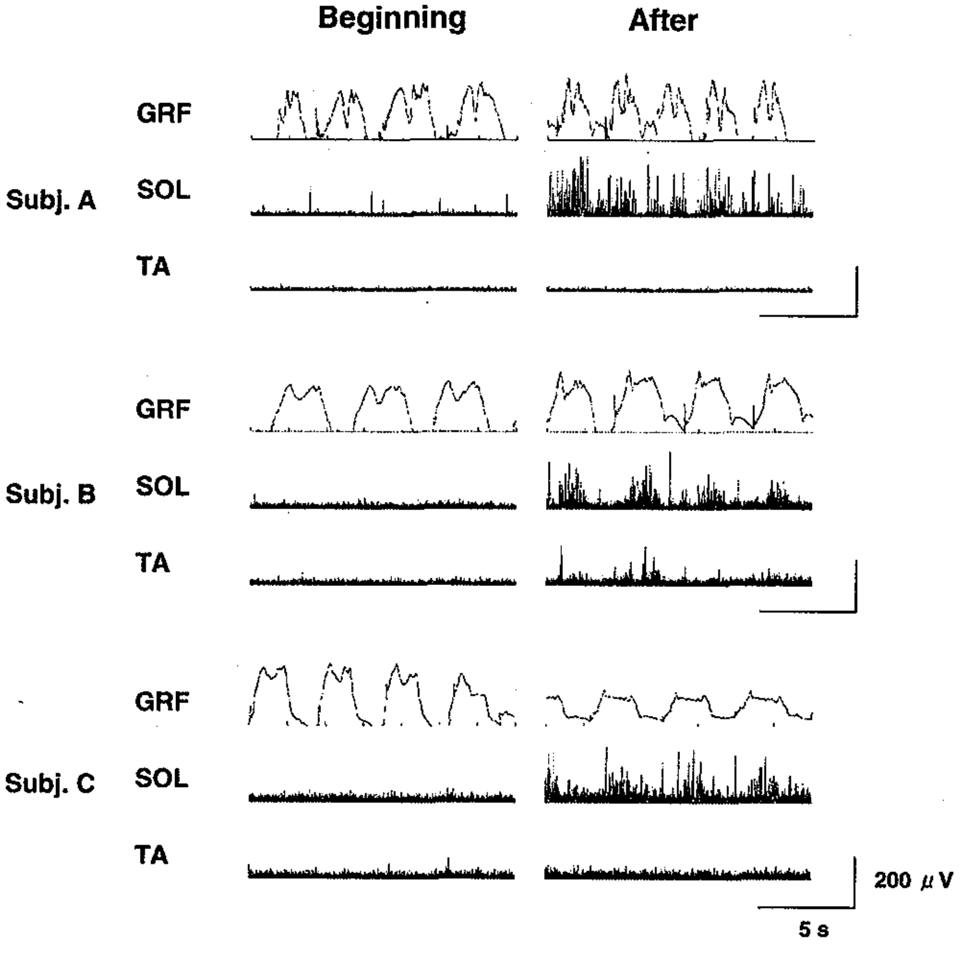

Fig. 1 Changes in EMG activities in the lower leg muscles during orthotic gait before and after the training. Results from the three subjects are shown (*GRF* the vertical ground reaction force, *SOL*, *TA* rectified EMGs from the soleus and tibialis anterior muscles, respectively)

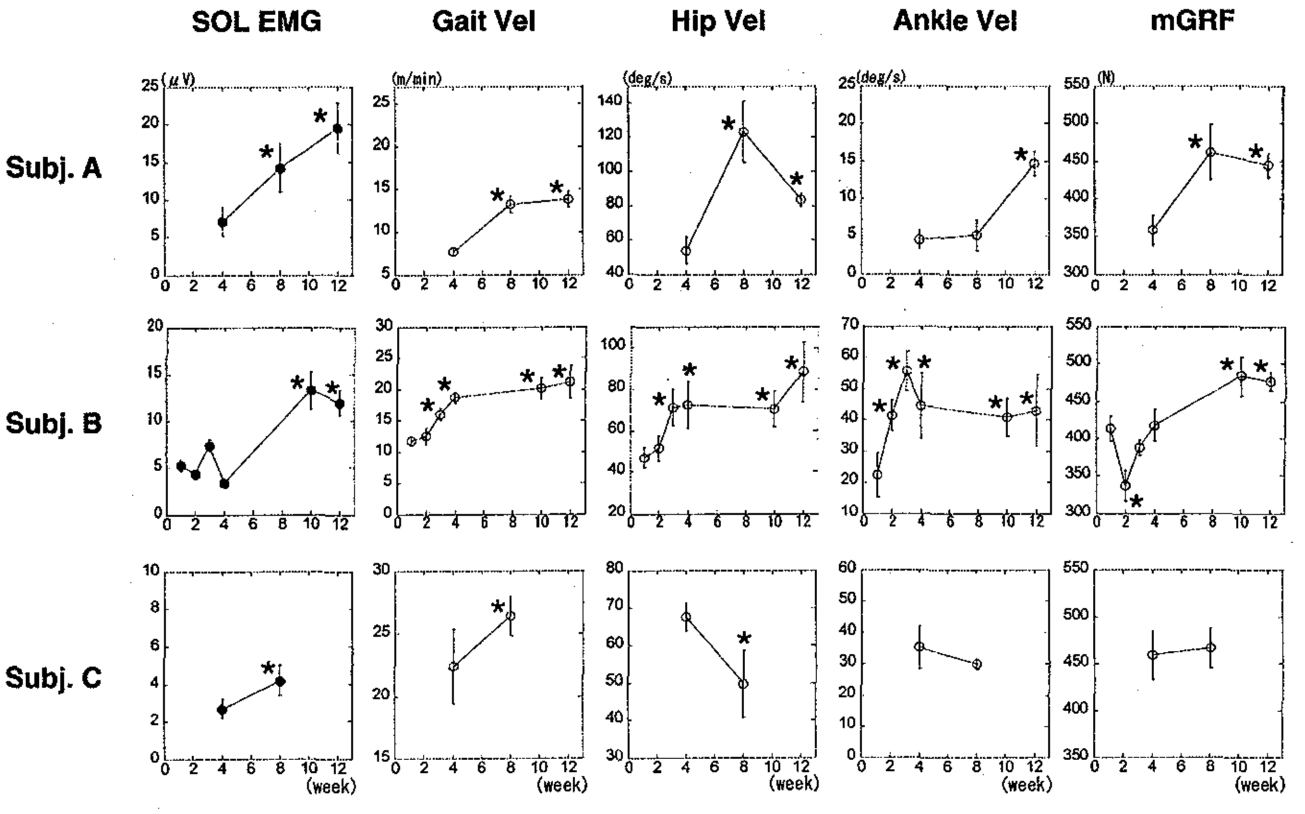

Fig. 2 Changes in the SOL EMGs, the gait velocities, the hip and ankle joint angular velocities, and the ground reaction forces over the training period for the three subjects

Additional experiment

Figure 3 shows the SOL EMG activities during the orthotic gait at three different gait velocities at the 1-W and 4-W measurements. It was demonstrated that the synchronized EMG burst with the stance phase increased drastically with the ambulation velocity after 4 weeks of training; no such clear modulation was observed at the 1st week measurement.

Relationships of the SOL EMGs during the stance phase with the gait velocity, hip velocity, ankle velocity, and ground reaction force, respectively, in each measurement are demonstrated in Fig. 4. In the 1-W measurement, the SOL EMG did not clearly increase with the gait velocity or the other kinetic and kinematic variables; the measurement reflected no qualitatively clear modulation. In the 4-W and 20-W measurements, however, the SOL EMGs covaried with the gait velocity and the other variables. It should be noted that the levels of SOL EMGs in the 4-W and 20-W measurements were greater than those in the 1-W measurement, even though the kinetic and kinematic variables were in similar ranges. This result suggests that the observed increase in the SOL EMG during the time course of training was not merely dependent on the kinetic and kinematic factors; neurological factors were to some degree involved.

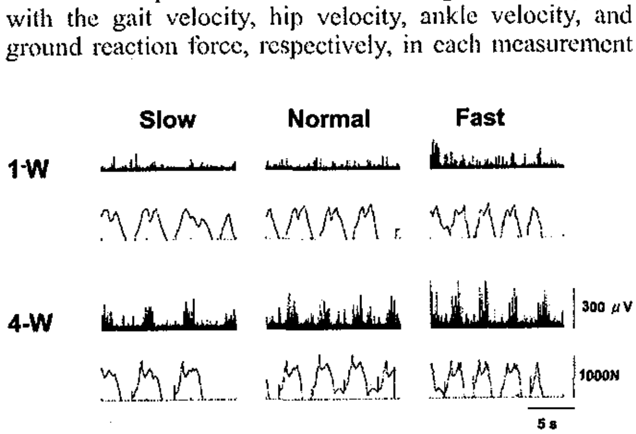

Fig. 3 A comparison of the velocity dependent changes in the SOL EMGs during orthotic gait before and after the 4-week training with the other gait orthosis

Stretch reflex test

Figure 5 demonstrates the relationships between stretch velocity and the reflex EMG responses in the SOL for the three subjects. It was indicated that in all three subjects, the stretch reflex EMG response was induced when the applied stretch velocity was faster than 100 deg/s, meaning the threshold velocity of the reflex was around 100 deg/s. These threshold velocities were well above the peak ankle dorsiflexion velocities observed during the orthotic gait in the three subjects, suggesting that the SOL EMGs

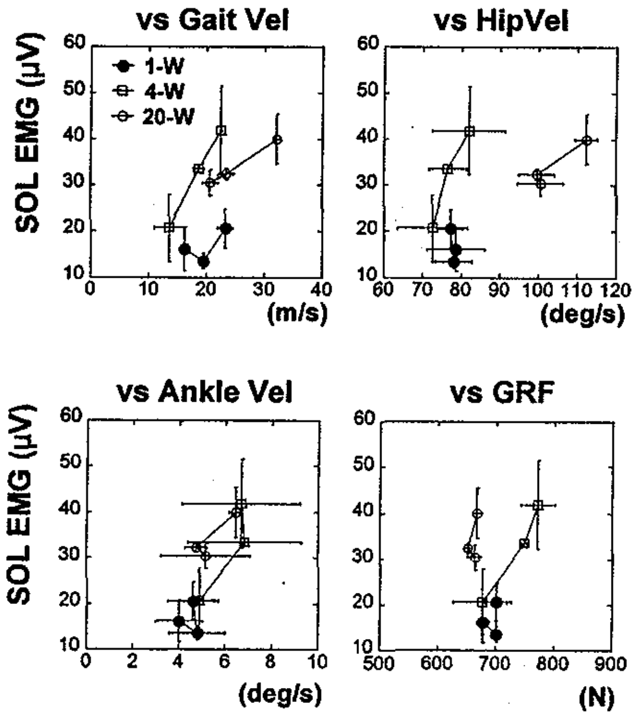

Fig. 4 Comparisons of the relationships of the SOL EMGs to the kinetic and kinematic variables before and after 1 month and 5 months of training. Abbreviations: *vs Gait Vel*, *vs Hip Vel*, *vs Ankle Vel*, and *vs GRF* refer to the relationships between the SOL EMG and the gait velocity, hip joint angular velocity, ankle joint angular velocity, and ground reaction force, respectively

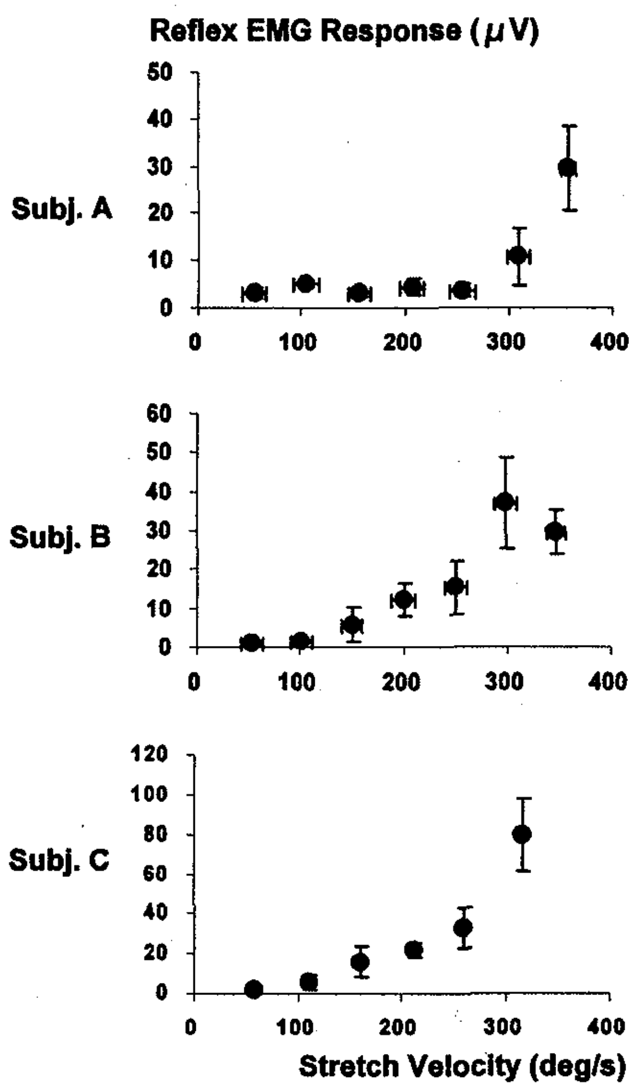

Fig. 5 Relationships between the stretch reflex EMG activities in the SOL and the applied stretch velocity for the three subjects. Note that the estimated threshold velocity to elicit the reflex is over 100 deg/s, which is far faster than the peak ankle joint velocity during the orthotic gait in any of the three subjects

observed were not merely mediated by the stretch reflex pathway.

Discussion

The results in the present study demonstrated that intense orthotic gait training induced modulation of EMG activities in the ankle extensor SOL muscle in individuals with clinically complete SCI. These results constitute neurologically significant indirect evidence that knee (and to some degree ankle) movements are far less important than hip movement and loading for the induction of locomotor EMG activity, at least in the SOL. Further, these results have great clinical significance especially in terms of gait rehabilitation of patients with incomplete spinal cord injury. It is worth noting that the results must be carefully interpreted, given that many factors may contribute the observed phenomena. Considering that possibility, we divided the various factors into two different types: (1) kinetic and/or kinematic, related to changes in the orthotic gait movement itself, and (2) neurological factors, namely, supposed changes in the interneuronal activities of the spinal locomotor networks as a result of training. We believe that neither the kinetic/kinematic nor the neurological factors alone can fully explain the observed results

Effects of the orthotic gait motion on modulation of EMG activity

The results of the stretch reflex test in the SOL indicated that the threshold velocities of stretch reflex in the SOL were far higher than the observed ankle dorsiflexion velocity during the orthotic gait. This result strongly suggests that the observed SOL EMGs during the orthotic gait were not induced merely by the spinal stretch reflex. Rather, in the present study, supposed spinal locomotor networks appeared to play a role in the induction of SOL EMGs during orthotic gait.

The observed modulation in the SOL EMG activities synchronized with gait phase confirmed our previous observation that even the knee-locked "stiff-legged" gait with a gait orthosis is effective to induce locomotor-like

EMG activity in lower limb muscles (Kojima et al. 1999). Because the stiff-legged gait is a gait with the knee locked in full extension and the ankle in a neutral position, the afferent information thought to primarily contribute to inducing the observed modulation in the EMG activity would be associated with the hip-joint movement and load on the leg. This result is consistent with recent observations from infant stepping experiments (Pang and Yang 2000) and experiments using a driven gait orthosis for paraplegic subjects (Dietz et al. 2002). Dietz et al. (2002), on the basis of their elegant series of studies on locomotor capacity of human spinal cord and relevant animal and human studies, concluded that "afferent input from hip joints, in combination with that from load receptors, plays a crucial role in the generation of locomotor activity in the isolated human spinal cord". The result in the current study would constitute indirect evidence to support this notion. With respect to afferent input from the hip joint, further, Schimit and Benz (2002) recently demonstrated that imposed hip joint extension/flexion movements in spinal cord-injured subjects induce a unique, stereotypical reflex response in hip, knee, and ankle joints, suggesting that hip movement would activate spinal interneuronal pathways associated with coordinated motor behaviors such as posture and locomotion. Given this notion, the results in the current study suggest that afferent information associated with hip extension during the orthotic gait might activate the spinal neural network responsible, at least in part, for the synchronized EMG activity in the SOL, which may be the common network generating the extensor reflex. With regard to the effect of limb loading on the locomotor activity in the paraplegic human, a growing body of indirect evidence from studies on humans has indicated that load-related afferent inputs play an essential role in the generation of locomotor-like efferent patterns by the human spinal cord (Harkema et al. 1997; Pang and Yang 2000, 2001; Dietz et al. 2002). The observed close relationship between the SOL EMG levels and mGRF during the training period (Fig. 2) and within a single experiment (Fig. 4) in the current study is consistent with that found in previous reports and our previous study (Kojima et al. 1999), in which we demonstrated that the levels of lower limb muscle EMGs during orthotic gait were well correlated to the level of limb loading.

Alteration of the intrinsic property of spinal neural networks due to training

The observed EMG alteration in the SOL might not solely depend on gait-motion changes due to training, but also on alterations in the intrinsic properties of neural networks. This hypothesis is supported by the result of an additional experiment, in which the EMG modulation occurred even under kinematic and kinetic profiles of orthotic gait similar to those of the pre-training gait after 4 weeks of training (Fig. 4). In addition, the effect of changing gait velocity was obviously different before and after several weeks of training, suggesting that the input and output properties in the spinal neural networks during orthotic gait were altered due to the training. Another observation that supports this hypothesis might be the observed EMG changes in subject C, whose orthotic gait motion was at a higher level (i.e., faster velocity and larger ROM, etc.) at the first stage of training and did not largely change during the training period. Nevertheless, modulation of the SOL EMG was induced in this subject, despite rather reduced angular velocities of hip and ankle joints after 8 weeks of training.

Use-dependent plasticity is now a well-known property of spinal neural networks (Hodgson et al. 1994; Muri and Steeves 1997; Raineteau and Schwab 2001). Repeated afferent input accompanying gait training might result in improvement in the transmission efficacy within the neural network responsible for the SOL EMG activity during orthotic gait. This possibility is extremely important with regard to rehabilitation strategy for SCI patients (Field-Fote 2001; Protas et al. 2001). If the act ambulation with an orthosis itself has the potential to improve neuronal activity in the spinal locomotor neuronal networks, a specific gait orthosis one could be designed and developed for locomotor training. Future studies should explore the optimal design for a gait orthosis that can effectively activate the spinal locomotor neural network, using the findings in the current study as the first step in such a series of investigations.

Finally, almost no EMG modulation appeared in the TA in the current study. This might be explained by the following: (1) because the correlation between the load on a limb and EMG activity is less in the TA than in the SOL (Harkema et al. 1997; Kojima et al. 1999), load-related afferent information during the orthotic gait in our study might not have been sufficient to evoke TA activity; and (2) although an imposed hip flexion can induce the ankle flexor response (Schmit and Benz 2002), the flexion amplitude or velocity during the orthotic gait was not sufficient to induce the TA activity. Further, the ankle joint was mechanically immobilized in the orthosis in our study, and the absence of ankle motion might have prevented the elicitation of TA activity. However, further training might induce modulation in TA EMG activity, based on the fact that we observed a reciprocal EMG activity pattern between the ankle extensor and flexor muscles during the orthotic gait in a well-trained SCI subject (Kojima et al. 1998). Further studies are needed to clarify this issue.

References

Dietz V, Colombo G, Jensen L (1994) Locomotor activity in spinal man. Lancet 344:1260–1263

Dietz V, Colombo G, Jensen L, Baumgartner L (1995) Locomotor capacity of spinal cord in paraplegic patients. Ann Neurol 37:574–582

Dietz V, Muller R, Colombo G (2002) Locomotor activity in spinal man: significance of afferent input from joint and load receptors. Brain 125:2626–2634

Dobkin BH, Harkema SJ, Requejo PS, Edgerton R (1995) Modulation of locomotor-like EMG activity in subjects with complete and incomplete spinal cord injury. J Neurol Rehabil 183–190

Field-Fote EC (2001) Combined use of body weight support, functional electric stimulation, and treadmill training to improve walking ability in individuals with chronic incomplete spinal cord injury. Arch Phys Med Rehabil 82:818–824
Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, Edgerton VR (1997) Human lumbosacral spinal cord interprets loading during stepping. J Neurophysiol 77:797–811
Harkema SJ, Dobkin BH, Edgerton VR (2000) Pattern generators in locomotion: implications for recovery of walking after spinal cord injury. Top Spinal Cord Rehabil: 82–96
Hodgson JA, Roy RR, deLeon R, Dobkin B, Edgerton R (1994) Can the mammalian lumbar spinal cord learn a motor task? Med Sci Sports Exerc 26:1491–1497
Kawashima N, Sone Y, Nakazawa K, Akai M, Yano H (2003) Energy expenditure during walking with weight bearing control orthosis (WBC) in thoracic level of paraplegic patients. Spinal Cord 41:506–510
Kojima N, Nakazawa K, Yamamoto S-I, Yano H (1998) Phase-dependent electromyographic activity of the lower-limb muscles of a patient with clinically complete spinal cord injury during orthotic gait. Exp Brain Res 120:139–142
Kojima N, Nakazawa K, Yano H (1999) Effects of limb loading on the lower-limb electromyographic activity during orthotic locomotion in a paraplegic patient. Neurosci Lett 274:211–213
Muri GD, Steeves JD (1997) Sensorimotor stimulation to improve locomotor recovery after spinal cord injury. TINS 20:72–77
Pang MY, Yang J (2000) The initiation of the swing phase in human infant stepping: importance of hip position and leg loading. J Physiol (Lond) 528:389–404
Pang MY, Yang J (2001) Interlimb co-ordination in human infant stepping. J Physiol (Lond) 533:617–625
Protas EJ, Holmes SA, Qureshy CSH, Johnson A, Lee D, Sherwood AM (2001) Supported treadmill ambulation training after spinal cord injury: a pilot study. Arch Phys Med Rehabil 82:825–831
Raineteau O, Schwab ME (2001) Plasticity of motor systems after incomplete spinal cord injury. Nature Rev Neurosci 2:263–273
Schmit BD, Benz EN (2002) Extensor reflexes in human spinal cord injury: activation by hip proprioceptors. Exp Brain Res 145:520–527
Wernig A, Muller S, Nanassy A, Cagol E (1995) Laufband therapy based on "rules of spinal locomotion" is effective in spinal cord injured persons. Eur J Neurosci 7:823–829
Yano H, Kaneko S, Nakazawa K, Yamamoto S, Bettoh A (1997) A new concept of dynamic orthosis for paraplegia: the weight bearing control (WBC) orthosis. Prost Orthot Int 21:222–228

J Neurophysiol 93: 777–785, 2005.
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Alternate Leg Movement Amplifies Locomotor-Like Muscle Activity in Spinal Cord Injured Persons

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Kawashima, Noritaka, Daichi Nozaki, Masaki O. Abe, Masami Akai, and Kimitaka Nakazawa. Alternate leg movement amplifies locomotor-like muscle activity in spinal cord injured persons. *J Neurophysiol* 93: 777–785, 2005. First published September 22, 2004; doi:10.1152/jn.00817.2004. It is now well recognized that muscle activity can be induced even in the paralyzed lower limb muscles of persons with spinal cord injury (SCI) by imposing locomotion-like movements on both of their legs. Although the significant role of the afferent input related to hip joint movement and body load has been emphasized considerably in previous studies, the contribution of the "alternate" leg movement pattern has not been fully investigated. This study was designed to investigate to what extent the alternate leg movement influenced this "locomotor-like" muscle activity. The knee-locked leg swing movement was imposed on 10 complete SCI subjects using a gait training apparatus. The following three different experimental conditions were adopted: *1*) bilateral alternate leg movement, *2*) unilateral leg movement, and *3*) bilateral synchronous (in-phase) leg movement. In all experimental conditions, the passive leg movement induced EMG activity in the soleus and medial head of the gastrocnemius muscles in all SCI subjects and in the biceps femoris muscle in 8 of 10 SCI subjects. On the other hand, the EMG activity was not observed in the tibialis anterior and rectus femoris muscles. The EMG level of these activated muscles, as quantified by integrating the rectified EMG activity recorded from the right leg, was significantly larger for bilateral alternate leg movement than for unilateral and bilateral synchronous movements, although the right hip and ankle joint movements were identical in all experimental conditions. In addition, the difference in the pattern of the load applied to the leg among conditions was unable to explain the enhancement of EMG activity in the bilateral alternate leg movement condition. These results suggest that the sensory information generated by alternate leg movements plays a substantial role in amplifying the induced locomotor-like muscle activity in the lower limbs.

INTRODUCTION

It is now well recognized that the paralyzed lower limb muscles of a person with spinal cord injury (SCI) can be activated by body weight–supported stepping movement on a treadmill (Dietz et al. 1995, 2002; Dobkin et al. 1995; Ferris et al. 2004; Harkema et al. 1997) or by locomotion with the use of a gait orthosis (Kojima et al. 1999; Nakazawa et al. 2004). Since the stepping movement accompanies joint rotation, it is possible that such muscle activity might merely reflect the reflex responses induced by rhythmic muscle-tendon stretches (Dobkin et al. 1995; for review, see Harkema 2001). Nevertheless, this muscle activity is considered to come from the interaction of the central pattern generator (CPG) in the spinal cord (Dimitrijevic et al. 1998) with the sensory input rather than a mere reflex response (Dietz et al. 2002).

This interpretation is justified by several recent findings. Harkema et al. (1997) have shown that the magnitude of EMG activity induced in SCI persons is more closely related with the peak load applied to the leg than with muscle-tendon stretch. Similarly, Dietz et al. (2002) have shown, using a driven gait orthosis, that the ankle muscle activity observed in ordinary locomotion movement was not induced either when the ankle joint alone was moved or when the body weight was completely unloaded. The crucial role of the sensory information of load and hip position in generating and/or shaping the rhythmic output pattern from the CPG has been considerably emphasized by previous studies using reduced animal preparations (Duysens and Pearson 1980; Grillner 1985; Pearson 1995), and these findings also support the view that the muscle activity induced in SCI persons reflects the output from the locomotory CPG.

However, it remains unclear to what extent the induced muscle activity (locomotor-like muscle activity) is actually "locomotory," partly because almost all of the previous studies have not paid attention to a substantial feature of human bipedal locomotion, i.e., alternating leg movements. This is the main point that we focused on in this study. To investigate the significance of alternating leg movements to locomotor-like muscle activity, we compared the magnitude of the EMG activity induced in the complete SCI subjects using a gait-training apparatus in the following different conditions: *1*) ordinary bilateral alternating leg movement, *2*) unilateral leg movement, and *3*) bilateral synchronous (in-phase) leg movement. If the spinal CPG is actually involved in the neural mechanism of the locomotor-like muscle activity, the alternating leg movement pattern should contribute to the generation and/or coordination of the muscle activity.

Part of this study has been presented in abstract form (Kawashima et al. 2003).

METHODS

Participants

Ten male SCI persons (28.8 ± 6.0 yr) participated in this study. All of the subjects had an injury at the thoracic (T) level of the

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spinal cord somewhere between T_5 and T_{12}, complete motor paralysis in their lower limb muscles (American Spinal Injury Association Class: ASIA A or B; Maynard et al. 1997), and moderate degrees of spasticity. At least one-half a year had passed since they were injured. The physical characteristics of the subjects are summarized in Table 1. Each subject gave written informed consent to the experimental procedures, which were conducted in accord with the Helsinki Declaration of 1975 and approved by the ethics committee of the National Rehabilitation Center for Persons with Disabilities, Tokorozawa, Japan.

Passive leg movement apparatus

To impose locomotion-like movements on their legs, we used an apparatus (Fig. 1*A*) originally developed for physical exercise for persons with disabilities (Easy Stand Glider 6000, Altimate Medical). This apparatus enables the SCI persons to stand securely by immobilizing their trunk and pelvis using front and back pads and by preventing hyperextension of the knee joint using the knee pad. It also enables the subjects to swing their legs by moving the handle connected to the foot plate. In this study, the experimenter manually moved the handle back and forth (± 17.5 cm from default position) in a sinusoidal manner (Fig. 1*C*) by matching the movement frequency with the sound of a metronome (1 Hz). This handle movement could induce approximately ± 14 and $\pm 9°$ motion in the hip and ankle joints, respectively (these values of range of joint motion depend on the subject's lower limb length). This range of motion of each joint is similar to the data for the normal walking provided by Winter (1990). Although only reciprocal leg movement can be induced at the default setting, synchronous or unilateral leg movement can be induced by removing the bolts that connect bars to both sides.

Experimental protocol

Before the experiment, we checked that the standing posture was stable and that no hypotension was observed. First, bilateral alternate leg movement was imposed for 3 min so that the subjects could experience the standing posture and the imposed leg movement. Then, the experiments were performed under the following three conditions: *1*) bilateral alternate (anti-phase) leg movement; *2*) unilateral leg movement; and *3*) bilateral synchronous (in-phase) leg movement. In the unilateral leg movement, the right leg was moved while the position of the left leg was fixed to be vertical. In the bilateral synchronous leg movement, both legs were passively swung simultaneously in the same direction. Throughout the exercise period, subjects were asked to grasp the bar in front of them and to keep their upper limbs relaxed (Fig. 1*A*). The experimenters had conducted a sufficient number of practices before the testing session so that they could adjust the leg motion to the predetermined pattern (i.e., the range of motion and swing frequency) under all experimental conditions by monitoring the angle data from an electrogoniometer displayed on an oscilloscope. The duration of each session was 1 min, and an interval of ≥ 1 min was taken for rest between sessions. The order of conditions *1*), *2*), and *3*) was randomized.

TABLE 1. *Characteristics of the SCI subjects*

Subject	Age, yr	Weight, kg	Lesion Level	Grade of ASIA	Duration of Paraplegia, mo
S1	19	53	T_5	B	24
S2	30	74	T_8	A	12
S3	24	75	T_{12}	A	24
S4	32	68	T_{12}	A	32
S5	22	70	T_{10}	A	11
S6	39	67	T_{12}	A	13
S7	35	55	T_6	A	46
S8	27	75	T_{12}	A	22
S9	30	72	T_{11}	B	23
S10	30	60	T_8	A	17

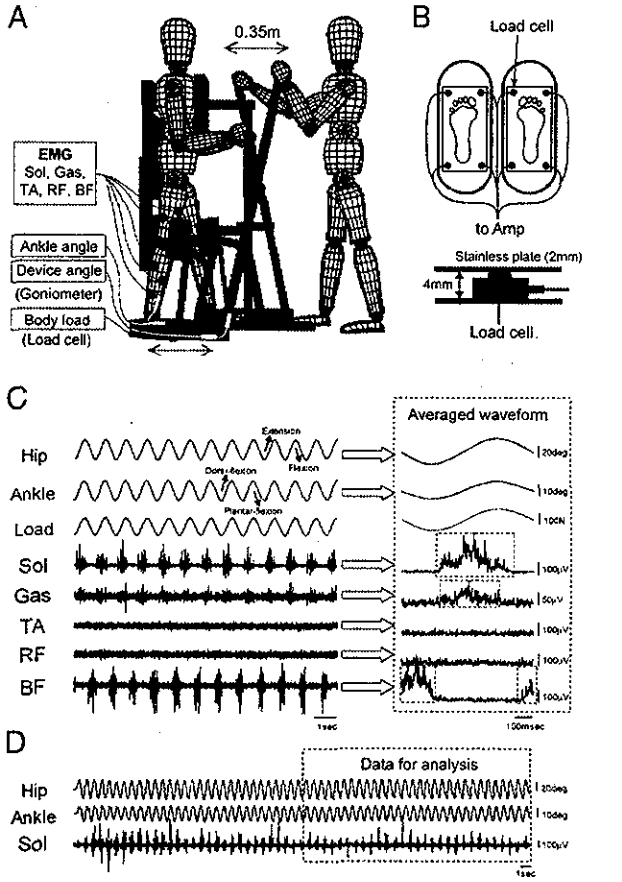

FIG. 1. *A*: overview of the experimental setup. During the experiment, the spinal cord injury (SCI) subject stood securely on a special device (Easy Stand Glider 6000, Altimate Medical). The subject's legs were moved passively by moving the lever back-and-forth in a sinusoidal manner in pace with the tempo of a metronome (1 Hz). *B*: load applied to the foot soles of each leg was measured by 4 load cells placed under the stainless foot plate. *C*: typical example of hip and ankle joint motion and induced EMG activity of an SCI subject (level of lesion, T_{12}) during passive leg movement (Sol; soleus, Gas; medial head of gastrocnemius, TA; tibialis anterior, RF; rectus femoris, BF; biceps femoris). To quantify level of muscle activity, the averaged EMG signal was calculated (*right*). *D*: adaptation-like phenomenon in EMG activity in the Sol. It took ~30 s for the EMG activity to reach steady state. Therefore data from the 1st 30 s were disregarded in the calculation of the averaged EMG signals (*C*).

Data recording

The surface EMG signal was recorded from the soleus (Sol), the medial head of the gastrocnemius (Gas), the tibialis anterior (TA), the rectus femoris (RF), and the long head of the biceps femoris (BF) muscles of both legs with the use of a bipolar electrode. Care was taken to exclude any artifact in the EMG signal (e.g., the skin was washed with a scrub gel and rubbed with sandpaper to reduce the resistance of the skin). The EMG signal was amplified (Bagnoli-8 EMG System, DELSYS) with band-pass filtering between 20 and 450 Hz. Ankle joint motion was recorded with an electrogoniometer (Goniometer System, Biometrics), whose two sensor heads were placed on the lateral part of the shank and foot of the subject (Fig. 1*A*). Hip joint motion was estimated from the data recorded by using another goniometer attached to the lateral aspect of the apparatus (Fig. 1*A*).

In six subjects, the VICON 370 system (Oxford Metrics) was used to analyze the lower limb motion more accurately. Eight markers were attached to the right and left sides of the subject on the skin overlying the following landmarks: the acrominon (SHO), greater trochanter (GTR), lateral malleolus (AKL), and the top of the great toe (TOE). We defined the hip and ankle joint angles as the angles formed by the SHO, GTR, and AKL and by the GTR, AKL, and TOE, respectively. Furthermore, in these subjects, the actual load applied to each foot sole was measured using four load cells (LMA-A-1KN, Kyowa, Tokyo, Japan) placed under the four corners of the stainless foot plate (Fig. 1*B*). During the experiment, all data were continuously monitored by Power Lab software (Chart version 4, AD instruments) and were digitized at 1 kHz for later analysis.

Data analysis

The digitized EMG signal was full-wave rectified after the DC component was subtracted. It was then averaged over the last 30 locomotion cycles (Fig. 1*C*). The data of the first 30 cycles were discarded, because the EMG activity often showed gradual decay, and it took ~30 s (i.e., 30 cycles) to become stationary (Fig. 1*D*). The locomotor-like EMG activity was quantified using the integrated value of the averaged EMG signal and the duration over which the muscle was active (Fig. 1*C*). We regarded the muscle to be active when its averaged EMG signal consistently exceeded the level of resting EMG activity (mean value + 3 × *SD*). Furthermore, to examine the phase-dependent changes in the EMG activity, the averaged EMG signal was divided into 10 bins, and the mean amplitude in each bin was calculated. The ranges of hip and ankle movements were calculated from the data obtained by electrogoniometers, and those were compared with the VICON data. The load applied on each foot sole was quantified by calculating the summation of the data from four load cells.

Statistics

Values are given as means ± SE. Two-way ANOVA was used to test the difference in the EMG magnitude, duration, and hip and ankle joint range of motion among the three conditions. Tukey's post hoc test was applied to identify differences among the conditions. Significance was accepted at $P < 0.05$.

RESULTS

Pattern of the locomotor-like EMG activity

Figure 2*A* shows the averaged waveform of the joint angle (estimated by electrogoniometers) and the EMG activity obtained from an SCI subject during alternate leg movement. In this subject, EMG bursts modulated with the locomotion cycle were observed in Sol, Gas, and BF. A similar muscle activation pattern was observed in other subjects. Figure 2*B* indicates the number of subjects whose muscle activity was judged to be significant in each of 10 leg movement phases. For all subjects, the EMG activity was observed in Sol and Gas during the backward leg swing phase corresponding to the stance phase in normal locomotion. Similarly, the EMG activity was observed

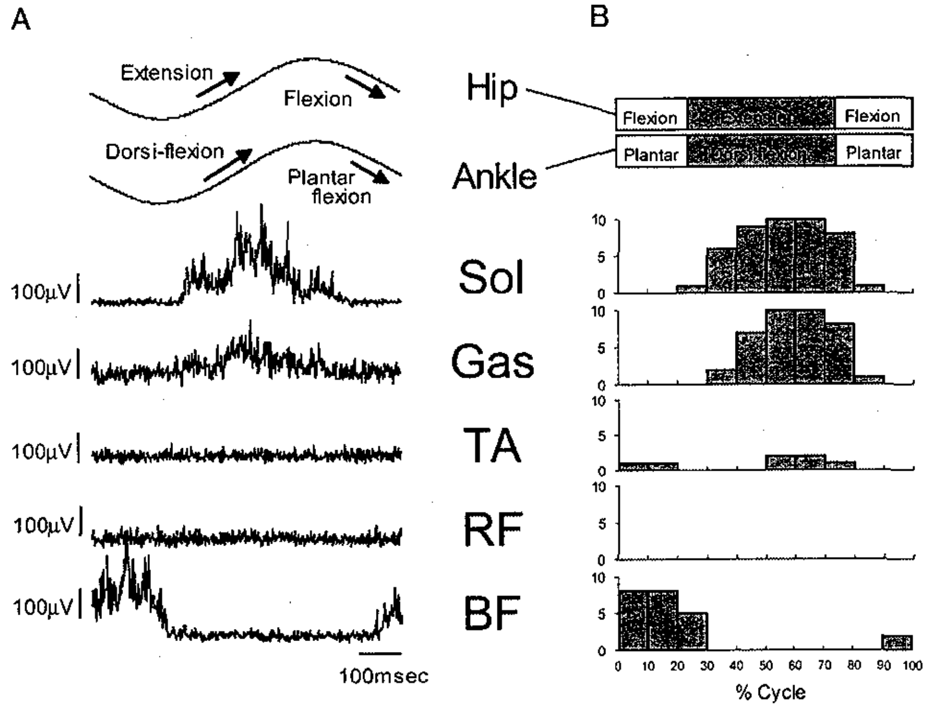

FIG. 2. *A*: ensemble averaged waveform of hip and ankle joint motion and induced EMG activity in each lower limb muscle obtained from an SCI patient. *B*: probability of the occurrence of EMG activity in the lower limb muscles during passive leg movement. Data show number of subjects who showed EMG activity in each leg movement cycle (total number of subjects is 10). Muscle activity was determined to be active when its averaged EMG signal consistently exceeded the level of resting EMG activity (mean value + 3 × SD).

in BF for 8 of 10 subjects during the hip-flexion phase corresponding to the swing phase in normal locomotion. Namely, the active phase of these muscles mainly corresponded with the phase during which they were mechanically stretched. The EMG activity of the TA was observed for two subjects, and no EMG activity was induced in the RF. In the RESULTS and DISCUSSION sections, we will focus only on these activated muscles (Sol, Gas, and BF).

Typical averaged waveforms of the EMG activity for three experimental conditions obtained from two subjects are shown in Fig. 3 (*A* and *D*, bilateral alternate; *B* and *E*, unilateral; *C* and *F*, bilateral synchronous leg movements). As clearly shown in these waveforms, the amount of EMG activity varied from condition to condition. In the unilateral leg movement (Fig. 3, *B* and *E*), no EMG activity was observed in the nonmoving left leg. The magnitude of the EMG activity was smaller for the unilateral leg movement condition (Fig. 3, *B* and *E*) than for the ordinary bilateral alternate leg movement condition (Fig. 3, *A* and *D*). In the bilateral synchronous leg movement condition, the EMG activity was present for both legs (Fig. 3, *C* and *F*); however, its magnitude was smaller than that for the bilateral alternate leg movement condition (Fig. 3, *A* and *C*).

Leg motions and load to foot sole

Figure 4*A* shows a typical example of the hip and ankle joint angle movements obtained using the VICON system. In the right (experimental) leg, both the hip and ankle joint angles moved in a similar manner among three conditions. On the other hand, the left leg movement was completely out of phase between the alternate and synchronous leg movement conditions, and no obvious hip and ankle motion was observed during the unilateral leg movement condition. There was no significant difference in the range of motion of each joint among three conditions for the right leg and between the alternate and synchronous leg movement conditions for the left leg (Fig. 4*B*). In the unilateral leg movement condition, the left leg movement was kept at almost zero (Fig. 4*B*). It should be noted that the data in Fig. 4*B* contain the data measured with electrogoniometers, because the joint angle movement estimated using electrogoniometers was not different from that measured directly using the VICON system.

Figure 5*A* shows a typical example of the load applied to the foot sole in the three conditions. The load was modulated almost sinusoidally with the leg movement cycle. The load was maximal and minimal, respectively, when the hip joint was maximally extended and flexed. Although the load averaged over time was not different from condition to condition (Fig. 5*B*), there was a statistically significant ($P < 0.05$) difference in the peak-to-peak load among the three experimental conditions (Fig. 5*C*). In comparison with the alternate leg movement condition, the load applied to the right leg was 85.5 ± 3.8% in the unilateral leg movement condition and 64.3 ± 12.5% in the synchronous leg movement condition. On the other hand, the peak-to-peak load applied to the left leg was 22.5 ± 4.4% in the unilateral leg movement condition and 69.9 ± 11.9% in the synchronous leg movement condition compared with the alternate leg movement condition.

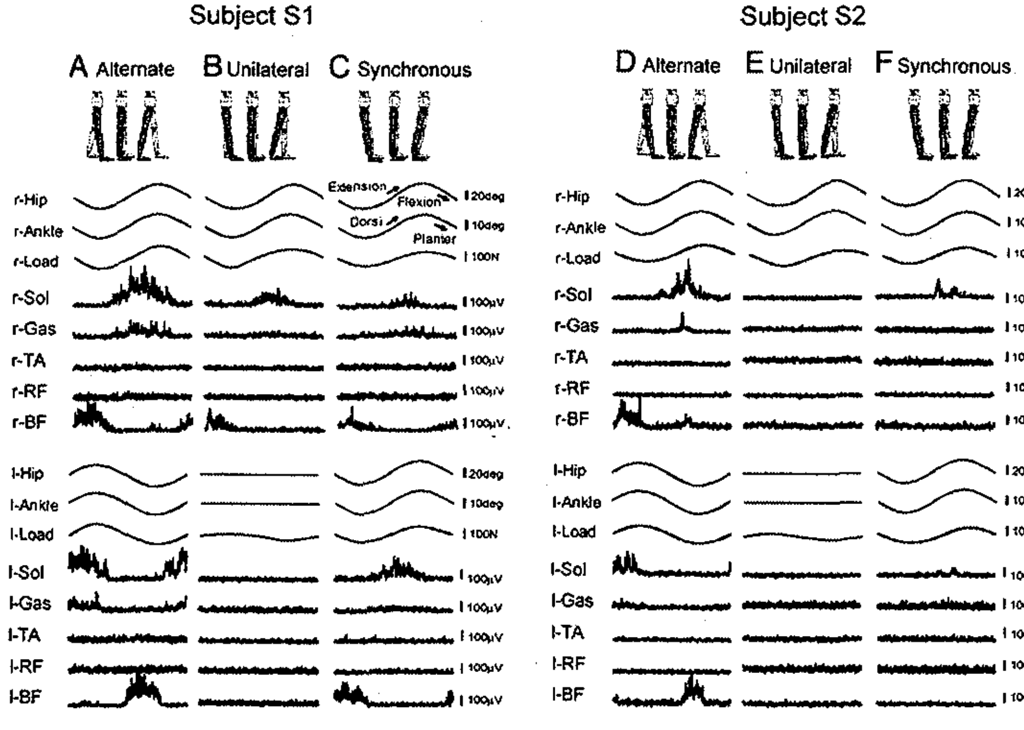

FIG. 3. Averaged waveforms of hip and ankle joint motion, load on the leg, and induced EMG activities of limb muscles recorded from subjects S1 and S2 (*top*, right leg; *bottom*, left leg). *A* and *D*: alternate leg movement condition. *B* and *E*: unilateral leg movement condition. *C* and *F*: synchronous leg movement condition.

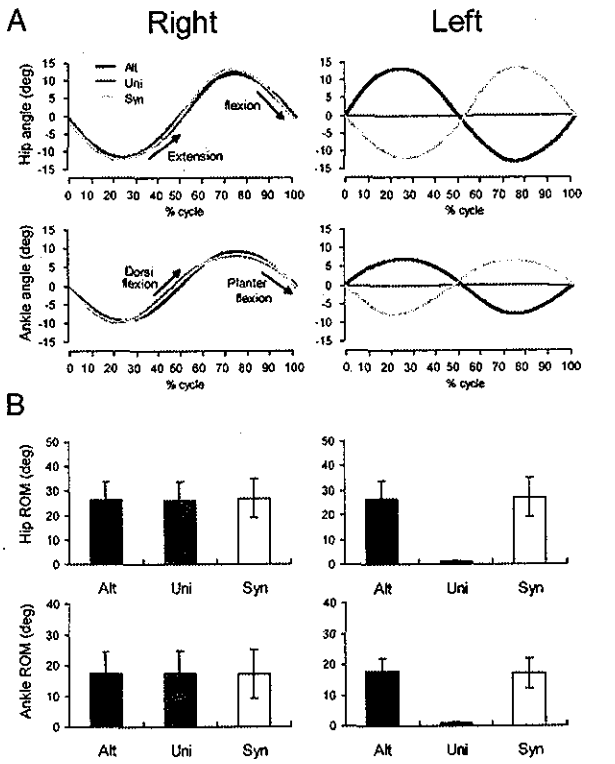

FIG. 4. Kinematical characteristics of imposed leg movement. *A*: changes of hip (*top*) and ankle (*bottom*) joint angular motions in 1 cycle of leg movement recorded from 1 subject using the VICON system. *B*: mean value of range of motion (ROM) of the hip (*top*) and ankle (*bottom*) joint (n = 10). Alt, Uni, and Syn indicate the alternate, unilateral, and synchronous leg movement conditions, respectively. Error bars indicate SE.

Difference in the induced EMG activity among experimental conditions

Figure 6 summarizes the integrated EMG activity of the Sol, Gas, and BF in three experimental conditions. The integrated EMG activity induced by bilateral alternate leg movement was significantly larger (P < 0.05) than that induced during the other conditions. The values of the percentage increase in EMG magnitude induced by alternate leg movement compared with that induced by unilateral leg movement were 291 ± 70, 163 ± 16, and 278 ± 71% for Sol, Gas, and BF, respectively.

Figure 7 shows the mean EMG amplitude in each 10% bin of the locomotion cycle (*top*) and in the period during which the muscle was evaluated to be active (*bottom*). The amplitude of the Sol EMG activity in the bilateral alternate movement was significantly larger (P < 0.05) than that in the unilateral movement from the 30 to 60% cycles, and significantly larger than that in the synchronous movement from the 30 to 70% cycles (Fig. 7*A*). The duration of the EMG activity of the Sol muscle during alternate leg movement was significantly longer (P < 0.05) than that during the other conditions (Fig. 7*A*). Such an amplifying effect of alternate leg movement on the EMG activity was also observed for the Gas and BF muscles (Fig. 7, *B* and *C*).

DISCUSSION

These results show that the locomotor-like EMG activity was significantly larger for alternate leg movement than for unilateral and bilateral synchronous movements. In the DISCUSSION section, the neuronal mechanism underlying these results, mainly in the context of what is known about the spinal locomotor system that was revealed in previous animal and human studies, will be addressed.

Muscle activity induced by passive leg movement

We used the gait-training apparatus (Fig. 1*A*) to impose the locomotory movement. However, the leg movement achieved by this apparatus is different from the ordinary stepping movement in the following two ways. First, the knee joint is locked in an extended position throughout the entire locomotion cycle. Second, the sole always touches the foot plate even during the forward leg swing phase. That is, the sensory information from the foot sole exists even in the swing phase, and there is no clear instant that corresponds to "heel contact." Despite these differences in the movement pattern, the EMG activity was observed in the paralyzed lower limb muscles during the passive leg movement, as was shown during the body weight–supported stepping movement on a treadmill in previous reports (Dietz et al. 1995, 2002; Dobkin et al. 1995; Ferris et al. 2004; Harkema et al. 1997; Ivanenko et al. 2003). This is because several factors that are important to this phenomenon, i.e., hip joint motion (Andersson and Grillner 1983; Grillner and Rossignol 1978) and load information (Dietz and Duysens 2000; Duysens and Pearson 1980), were well preserved, even in our experimental setting. In fact, as for the first difference regarding the knee joint motion, Dietz et al. (2002) have shown

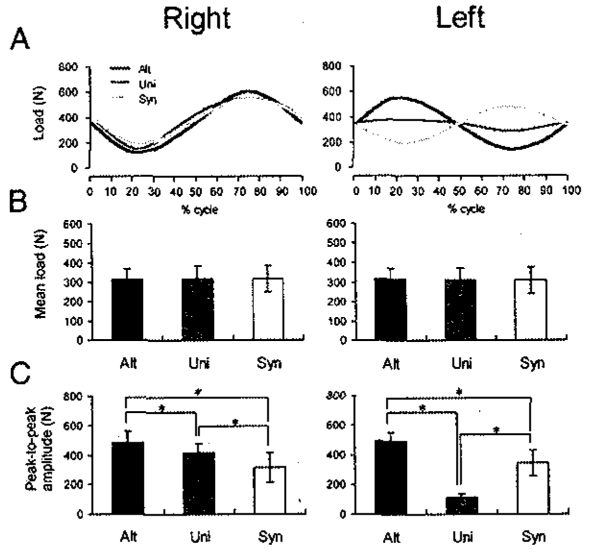

FIG. 5. Characteristics of load change during passive leg movement. *A*: changes of load applied to the foot sole of each leg in 1 cycle of leg movement. *B*: mean value of load averaged over 1 cycle (n = 6). *C*: mean value of peak-to-peak amplitude of load (n = 6). Alt, Uni, and Syn indicate the alternate, unilateral, and synchronous leg movement conditions, respectively. Error bars indicate SE. *Significant difference (P < 0.05).

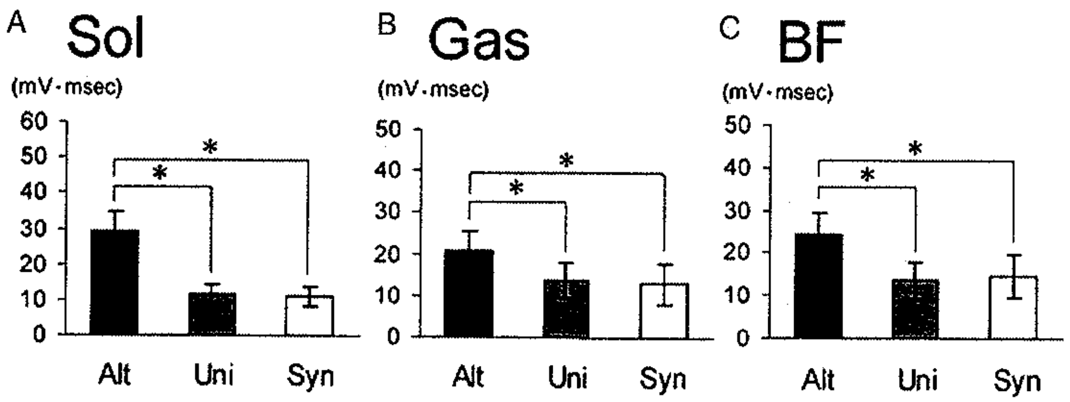

FIG. 6. Effect of leg movement pattern on muscle activity. Mean values of integrated rectified EMG induced by 3 types of leg movement. *A*: soleus (Sol). *B*: gastrocnemius (Gas). *C*: biceps femoris. Induced activity level of all 3 muscles was significantly larger ($P < 0.05$) during the alternate leg movement (Alt) than the unilateral (Uni) and synchronous (Syn) leg movement conditions. Error bars indicate SE. *Significant difference ($P < 0.05$).

that the knee-locked stepping movement (hip walking) does not affect the induced muscle activity. The only difference between normal and hip walking was that RF activity was almost absent in hip walking (see Fig. 4 in their study), a finding that agrees with our result (Figs. 3 and 5). The second difference regarding foot contact might influence the load information associated with the ordinary locomotion cycle; however, as shown in Fig. 5, we ensured that the load applied to the leg was periodically changed with the leg motion cycle in our experimental setting. The load was maximal when the hip joint was nearly maximally extended (Fig. 5), and this loading pattern resembled that observed when a stepping movement was imposed on a treadmill (Ferris et al., 2004). It is therefore likely that a considerable portion of the afferent neural inputs during normal walking could be preserved in our experimental setting.

In all subjects, coordinated EMG bursts can be induced by imposing passive leg movement in the lower limb muscle. As shown in Figs. 2 and 7, the phase in which the muscle activity was observed coincided with the phase in which it was mechanically stretched. That is, Sol and Gas were active while the leg swung toward the backward, and BF was active while the leg swung toward the forward. It is therefore possible that the muscle activity was associated with the stretch reflex response. However, these results show that the muscle activity was observed even in the muscle's shortening phase (Figs. 2 and 7). Concerning this point, Dietz et al. (1998) have also observed that the leg muscle activity is equally distributed during shortening and it seems therefore likely that the locomotor-like muscle activity results from the complex interaction of the afferent inputs and the spinal neural circuits rather than simple stretch reflex.

Contribution of alternate leg movement

One of the most substantial features of human bipedal locomotion is alternating leg movement. Therefore investigating how such an alternate leg movement pattern affects the amount of locomotor-like EMG activity would give us important information, especially regarding the problem of whether the activity is actually "locomotory" or not. A relevant approach has been partly taken by Ferris et al. (2004). They found that muscle activity could be induced for complete SCI patients even in the nonmoving leg when the stepping movement was imposed only on the other leg. Their results have provided evidence that the human spinal cord has a mechanism to efficiently realize alternating leg movement. However, we did not observe any muscle activity in the nonmoving left leg (Fig. 3). This result was similar to the results of the study by Dietz et al. (2002), who ascribed the contradiction with the work of Ferris et al. (2004) to the difference in the speed of stepping and the amount of the load (Dietz and Harkema 2004). Likewise, one of the possible reasons for the contradiction between the results of Ferris et al. (2004) and our results is the difference in the load pattern on the nonmoving leg. In this study, the load was tonically applied and the amount of modulation was small (Fig. 5), while in their study, a load pattern resembling normal stepping was applied.

On the basis of the absence of muscle activity in the nonstepping leg, Dietz et al. (2002) referred the possibility that the interlimb coordination observed in normal subjects requires the supraspinal systems. Concerning this point, a recent study revealed that the interlimb coordination includes the activity of the supplemental motor cortex area (Debaere et al. 2001). However, our data have provided strong evidence that the spinal cord has an ability to coordinate the movement of both legs. Figure 8 shows the relationships between Sol EMG activity and ankle ROM (*left*), hip ROM (*center*), and the peak-to-peak load (*right*) on the right foot sole. The EMG level was significantly larger for locomotion-like alternate leg movement than for unilateral and bilateral synchronous movements, although the hip and ankle joint movements were kept identical in all experimental conditions. This result also indicates that the stretch reflex alone is insufficient to explain the modulation of the EMG activity. If the EMG activity were merely a response to the rhythmic muscle-tendon stretches, the level of muscle activity should have been independent of the contralateral leg movement.

One remaining concern is the difference among the three conditions in the load applied to the right leg (Fig. 8, *right*), because the load-related afferent inputs, such as proprioceptive inputs from the extensor muscle and the sole of the foot, are known to influence the magnitude of the EMG activity

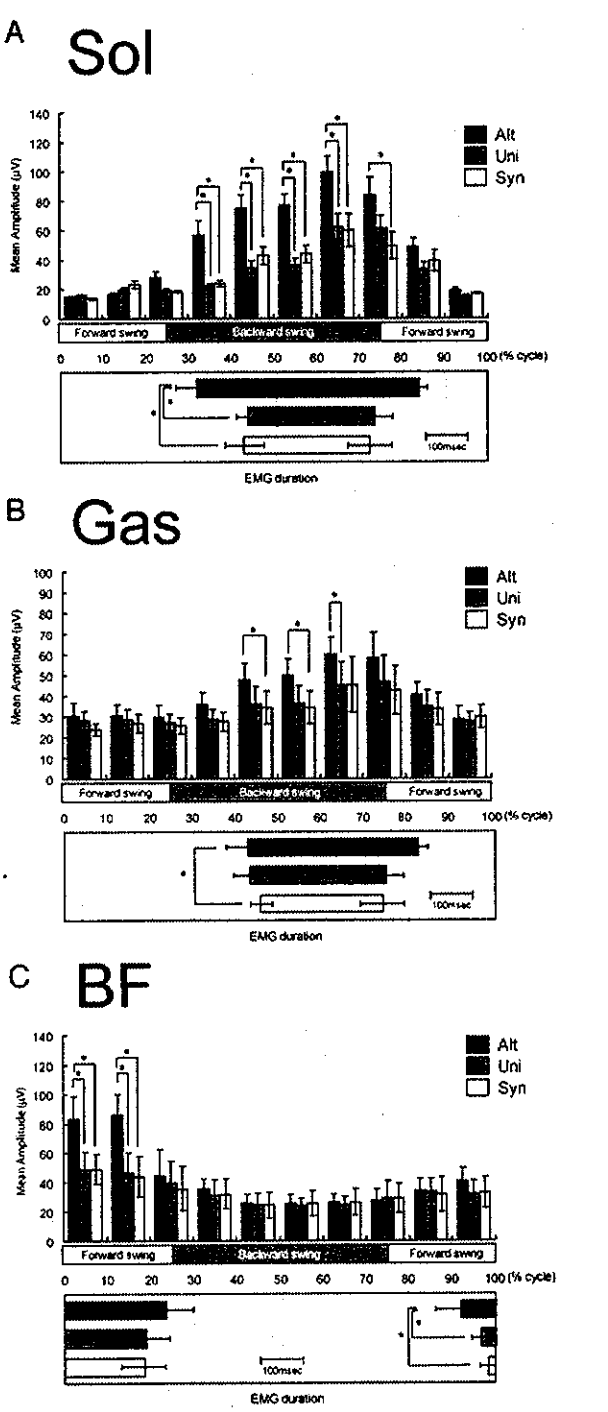

FIG. 7. Comparison of mean EMG amplitude in each 10% cycle bin (*top*) and duration of EMG activity (*bottom*) among the 3 experimental conditions. *A*: soleus (Sol). *B*: gastrocnemius (Gas). *C*: biceps femoris (BF). Alt, Uni, and Syn indicate the alternate, unilateral, and synchronous leg movement conditions, respectively. Error bars indicate SE. *Significant difference ($P < 0.05$).

(Harkema et al. 1997; Kojima et al. 1999). Therefore the larger EMG activity in the alternate leg movement condition could simply result from the load on the right leg having larger peak-to-peak amplitude. However, this is unlikely because the distribution of the Sol EMG activity with respect to the peak-to-peak amplitude of the load is distinctly different from other two conditions (Fig. 8, *right*). Therefore it is difficult to explain such a drastic enhancement of Sol EMG activity based only on the difference in load. In addition, although the peak-to-peak load was larger in the unilateral condition than in the synchronous condition, the Sol activity was almost similar between these two conditions (Fig. 8, *A* and *C*, *right*) and even smaller for the unilateral condition in subject S2 (Fig. 8*B*, *right*), suggesting that the Sol activity does not depend only on the load modulation.

Therefore our results strongly suggest that the afferent input from the contralateral leg plays a substantial role in amplifying the induced locomotor-like muscle activity in the lower limb. In particular, the contralateral leg movement has to be out of phase so that the muscle activity of the ipsilateral leg is well amplified. That is, the alternate leg movement should be added to the recipes for generating locomotor-like muscle activity that have been previously suggested, such as hip joint motion and the load applied to the lower limbs (Pearson 1995).

Interlimb coordination generated within the spinal cord

Previous animal studies, using a variety of preparations, indicate that basic neuronal circuits that generate the locomotive motor output exist in the lumbar level of the spinal cord (Forssberg et al. 1980; Pearson and Rossignol 1991; for a review, see Duysens and Van de Crommert 1998). Such neuronal circuits can operate in the absence of any afferent input (Grillner 1985), whereas the significance of the interaction of such a spinal neuronal circuit with the afferent input has also been pointed out (Duysens and Pearson 1980; Pearson 1995). Recent human studies have shown that the afferent signal from one limb affects the muscle activity of the contralateral limb in locomotory movement in a functional way (Pang and Yang 2001; Ting et al. 2000). However, since these studies were conducted in infants (Pang and Yang 2001) or in healthy subjects (Ting et al. 2000), the supraspinal system's contribution remains unclear. Although the supraspinal system such as the supplementary motor area might contribute to the interlimb coordination (Debaere et al. 2001), these results indicate that some mechanism coordinating the alternate leg movement might exist within the human spinal cord itself. The precise mechanism(s) are unknown at this stage, but it is possible that the neuronal circuits associated with our results have a common origin in the crossed flexor/extensor reflex (Duysens and Loeb 1980; Duysens et al. 1991). Further research is needed to clarify this point.

In summary, this study was designed to investigate to what extent the alternate leg movement influences the locomotor-like EMG activity in the lower limbs of SCI subjects. These results indicated that the alternate leg movements play a substantial role in amplifying the induced muscle activity, and not only suggest the existence of neuronal circuits enabling interlimb coordination within the spinal cord, but might reinforce the interpretation that the muscle activity induced by passive stepping movement is actually locomotory.

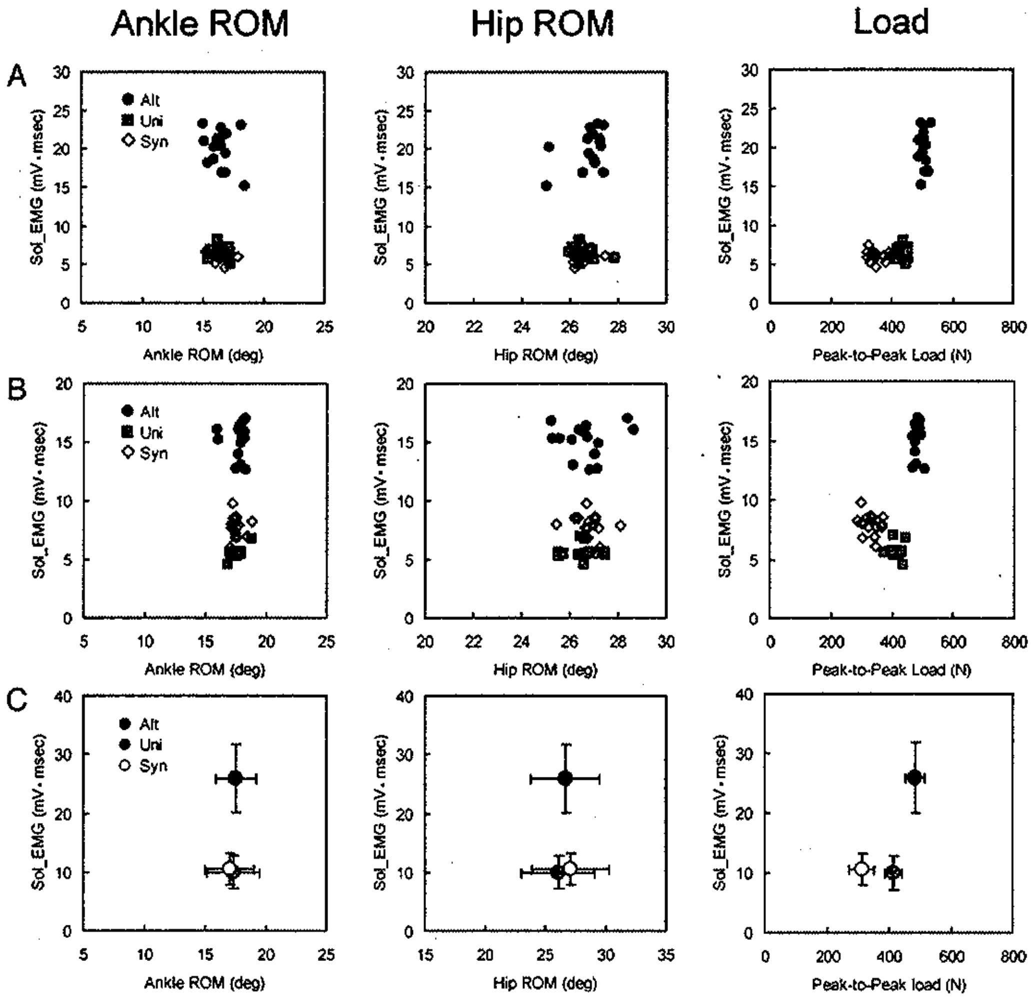

FIG. 8. Relationships between the right soleus EMG magnitude and ROM of the hip joint, ROM of the ankle joint, and peak-to-peak amplitude of load applied to the right leg. *A*: subject S1. *B*: subject S2. *C*: mean data ($n = 6$). In *A* and *B*, each point corresponds to the value obtained in each cycle. Alt, Uni, and Syn indicate the alternate, unilateral, and synchronous leg movement conditions, respectively. In *C*, error bars indicate SE.

REFERENCES

Andersson O and Grillner S. Peripheral control of the cat's step cycle. II. Entrainment of the central pattern generators for locomotion by sinusoidal hip movements during "fictive locomotion." *Acta Physiol Scand* 118: 229–239, 1983.

Debaere F, Swinnen SP, Beatse E, Sunaert S, Van Hecke P, and Duysens J. Brain areas involved in interlimb coordination: a distributed network. *Neuroimage* 14: 947–958, 2001.

Dietz V, Colombo G, Jensen L, and Baumgartner L. Locomotor capacity of spinal cord in paraplegic patients. *Ann Neurol* 37: 574–582, 1995.

Dietz V and Duysens J. Significance of load receptor input during locomotion. *Gait Posture* 11: 102–110, 2000.

Dietz V and Harkema SJ. Locomotor activity in spinal cord-injured persons. *J Appl Physiol* 96: 1954–1960, 2004.

Dietz V, Muller R, and Colombo G. Locomotor activity in spinal man: significance of afferent input from joint and load receptors. *Brain* 125: 2626–2634, 2002.

Dietz V, Wirz M, Colombo G, and Curt A. Locomotor capacity and recovery of spinal cord function in paraplegic patients: a clinical and electrophysiological evaluation. *Electroencepharogr Clin Neurophysiol* 109: 140–153, 1998.

Dimitrijevic MR, Gerasimenko Y, and Pinter MM. Evidence for a spinal central pattern generator in humans. *Ann NY Acad Sci* 860: 360–376, 1998.

Dobkin BH, Harkema S, Requejo P, and Edgerton R. Modulation of locomotor-like EMG activity in subjects with complete and incomplete spinal cord injury. *J Neuro Rehab* 9: 183–190, 1995.

Duysens J and Loeb GE. Modulation of ipsi- and contralateral reflex responses in unrestrained walking cats. *J Neurophysiol* 44: 1024–1037, 1980.

Duysens J and Pearson KG. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res* 187: 321–323, 1980.

Duysens J, Tax AA, van der Doelen B, Trippel M, and Dietz V. Selective activation of human soleus or gastrocnemius in reflex responses during walking and running. *Exp Brain Res* 87: 193–204, 1991.

Duysens J and Van de Crommert HWAA. Neural control of locomotion: The central pattern generator from cats to humans. *Gait Posture* 7: 131–141, 1998.

Ferris DP, Gordon KE, Beres-Jones JA, and Harkema SJ. Muscle activation during unilateral stepping occurs in the nonstepping limb of humans with clinically complete spinal cord injury. *Spinal Cord* 42: 14–23, 2004.

Forssberg H, Grillner S, and Halbertsma J. The locomotion of the low spinal cat. I. Coordination within a hindlimb. *Acta Physiol Scand* 108: 269–281, 1980.

Grillner S. Neurobiological bases on rhythmic motor acts in vertebrates. *Science* 228: 143–149, 1985.

Grillner S and Rossignol S. On the initiation of the swing phase of locomotion in chronic spinal cats. *Brain Res* 146: 269–277, 1978.

Harkema SJ. Neural plasticity after human spinal cord injury: application of locomotor training to the rehabilitation of walking. *Neuroscientist* 7: 455–468, 2001.

Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, and Edgerton VR. Human lumbosacral spinal cord interprets loading during stepping. *J Neurophysiol* 77: 797–811, 1997.

Ivanenko YP, Grasso R, Zago M, Molinari M, Scivoletto G, Castellano V, Macellari V, and Lacquaniti F. Temporal components of the motor patterns expressed by the human spinal cord reflect foot kinematics. *J Neurophysiol* 90: 3555–3565, 2003.

Kawashima N, Abe M, Nozaki D, Nakazawa K, and Akai M. Alternate leg movements contribute to amplify locomotor-like muscle activity in spinal cord injured patients. Washington, DC: Society for Neuroscience, 2003.

Kojima N, Nakazawa K, and Yano H. Effects of limb loading on the lower-limb electromyographic activity during orthotic locomotion in a paraplegic patient. *Neurosci Lett* 274: 211–213, 1999.

Maynard FM Jr, Bracken MB, Creasey G, Ditunno JF Jr, Donovan WH, Ducker TB, Garber SL, Marino RJ, Stover SL, Tator CH, Waters RL, Wilberger JE, and Young W. International standards for neurological and functional classification of spinal cord injury. *Spinal Cord* 35: 266–274, 1997.

Nakazawa K, Kakihana W, Kawashima N, Akai M, and Yano H. Induction of locomotor-like EMG activity in paraplegic persons by orthotic gait training. *Exp Brain Res* 157: 117–123, 2004.

Pang MY and Yang JF. Interlimb co-ordination in human infant stepping. *J Physiol* 533: 617–622, 2001.

Pearson KG. Proprioceptive regulation of locomotion. *Curr Opin Neurobiol* 5: 786–791, 1995.

Pearson KG and Rossignol S. Fictive motor patterns in chronic spinal cats. *J Neurophysiol* 66: 1874–1887, 1991.

Ting LH, Kautz SA, Brown DA, and Zajac FE. Contralateral movement and extensor force generation alter flexion phase muscle coordination in pedaling. *J Neurophysiol* 83: 3351–3365, 2000.

Van de Crommert HWAA, Mulder T, and Duysens J. Neural control of locomotion: sensory control of the central pattern generator and its relation to treadmill training. *Gait Posture* 7: 131–141, 1998.

Winter DA. *Biomechanics and Motor Control of Human Movement,* 2nd ed. Toronto, Canada: John Wiley, 1990.

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Muscle oxygenation of the paralyzed lower limb in spinal cord injured persons

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ABSTRACT

Purpose: Even in the paralyzed lower limb muscle, electromyographic (EMG) activity can be induced by imposing passive leg movement under standing posture in persons with spinal cord injury (SCI). The purpose of the present study was to ascertain whether or not the oxygenation level of the paralyzed lower limb muscle co-varied with the muscle EMG activities during imposed passive leg movement.
Methods: Six motor-complete SCI subjects and four neurologically normal controls were placed on a gait training apparatus that enabled the SCI subjects to stand and move their legs passively. After a 1-min resting stage, consecutive passive alternate leg movements were performed at different frequencies (0.8, 1, 1.2, and 1 Hz, for 3 min at each stage). In order to obtain post-exercise data, subjects were kept in a standing posture for 5-min after passive movement ceased. The EMG activity and concentration changes in the oxygenated (oxy-) and deoxygenated hemoglobin (deoxy-Hb) by using near infrared spectroscopy (NIRS) were continuously measured from the gastrocnemius muscle.
Results: In all SCI subjects, muscle EMG activity was observed during passive leg movement. The oxy-Hb level gradually increased while the deoxy-Hb decreased, and these changes were independent of the total Hb changes. In the recovery stage, the total Hb level was found to exceed the pre-exercise level. In contrast to the SCI patients, the normal subjects showed neither EMG activity nor changes in oxy- or deoxy-Hb.
Conclusion: The present results demonstrate that passive leg movement can induce not only muscular activity but also alteration of muscle oxygenation level in the paralyzed lower leg. Particularly, induced muscular activity seems to correlate with increased perfusion of the muscle.

Key Words:
Spinal cord injury; paralyzed muscle; oxygenation level; near infrared spectroscopy; reflexive muscle contraction; passive movement.

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INTRODUCTION

Previous studies have indicated that spinal cord injury (SCI) leads to extreme muscle atrophy (Lotta et al. 1991, Castro et al. 1999), fiber type transformation towards fast-fatigable fibers (Grimby et al. 1976, Martin et al. 1992), and lower bone mineral density (Frey-Rindova et al. 2000, Szollar et al. 1998). This musculoskeletal degeneration can be attributed largely to the dramatic reduction of muscular activity and mechanical stress in the paralyzed limbs, which is due primarily to the motor paralysis following SCI. Furthermore, long-term immobilization of the paralyzed limb may bring about vascular effects such as reduction in vessel diameter (Boot et al. 2002, Olive et al. 2002), and changes in muscle blood flow (Nash et al. 1995) and vascular compliance (Hopman et al. 1994, Olive et al. 2002). Because chronic inactivity and hypo-circulation of the paralyzed area are especially crucial factors in cardiovascular-related complications such as pressure sores and deep venous thrombosis (Boudaoud et al. 1997), enhancement of the metabolism and circulation in the paralyzed area is particularly important in preventing these problems.

It is now well recognized that, even in the paralyzed muscles of SCI patients, locomotor-like muscle activity can be induced by imposing stepping movement on a treadmill (Dobkin et al. 1995, Dietz et al. 1995, 2002). Induced muscle activity is believed to have the potential to prevent degeneration of the musculoskeletal system in SCI patients. From the perspective of muscle metabolism, an important issue is whether the muscular activity induced by imposed passive leg movement is accompanied by alterations in the oxygenation level and/or circulation in the paralyzed area. The present study was designed to address this question by simultaneously recording the electromyographic (EMG) activity and the muscle oxygenation using near infrared spectroscopy (NIRS). NIRS, a non-invasive and reliable technique for measuring oxygenation and hemodynamics in tissue, is based on the principle that the near-infrared light absorption properties of hemoglobin (Hb) and myoglobin (Mb) depend on their O2 saturations. Recently, NIRS has been applied in clinical fields to measure metabolic and circulatory patterns in a variety of diseases, and is recognized to be a useful method for identifying impairment of muscle metabolism (for a review, see Boushel 2001).

The purpose of the present study was to ascertain whether or not the oxygenation level of the paralyzed lower limb muscle changed with muscle EMG activity during imposed passive leg movements. If muscle oxygenation and circulation can be facilitated by imposing passive movement, it may have significant ramifications for rehabilitation in cases of SCI, and especially in the prevention of secondary impairment following SCI. In the present study, we hypothesized that the muscle oxygenation level should change with the appearance of the EMG activities in the paralyzed lower limb muscle.

METHODS

Participants

Six male SCI persons (26.4 ± 4.4 years) and four neurologically normal subjects (25.3 ± 2.4 years) participated in the present study. All SCI patients had traumatic spinal cord injuries at the thoracic level (between Th4 and Th12) and had complete paralysis of their lower limb muscles (American Spinal Injury Association (ASIA) Class A or B; Maynard et al. 1997) with moderate spasticity. Their post-injury time was greater than six months. The physical characteristics of the subjects are summarized in Table 1. The subjects gave their written informed consent for the experimental procedures, which were conducted in accord with the Helsinki Declaration of 1975 and approved by the ethics committee of the National Rehabilitation Center for the Disabled, Tokorozawa, Japan.

Table 1 Characteristics of the SCI subjects

Group	*Subject*	*Age (years)*	*weight (kg)*	*Lesion level*	*Grade of ASIA*	*Duration of paraplegia (months)*
SCI	S1	24	75	Th12	A	26
	S2	21	60	Th12	B	25
	S3	30	74	Th8	A	14
	S4	19	53	Th5	B	26
	S5	39	67	Th12	A	15
	S6	32	68	Th12	A	34
	Mean	27.5	66.2			23.3
	SD	7.56	8.42			7.58
Normal	Mean	26.4	64.2			
	SD	4.54	5.43			

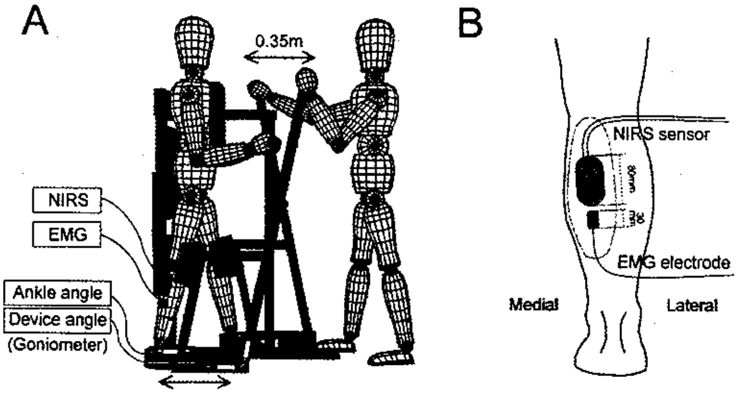

Figure 1 A: experimental set-up. This apparatus enables SCI patients to stand securely by immobilizing their trunk and pelvis using front and back pads, and by preventing hyperextension of the knee joint using a kneepad. It also enables them to swing their legs by moving a handle connected to a foot plate. In this study, the experimenter manually moved the handle back and forth in a sinusoidal manner by matching the movement frequency with the sound of a metronome. B: Location of the EMG electrode and the NIRS sensor. Because it was impossible to place both the NIRS sensor and the EMG electrode at the same place, they were placed proximally and distally on the medial side of the muscle.

Experimental procedure

Passive leg movement: In order to impose locomotion-like movement on the legs, we used an apparatus (Fig. 1A) developed for the physical exercise of persons with disabilities (Easy Stand Glider 6000, Altimate Medical, Inc., Morton, MN, USA). This apparatus enables SCI subjects to stand securely by immobilizing their trunk and pelvis using front and back pads and by preventing hyperextension of the knee joint using a kneepad. It also enables them to swing their legs by moving a handle connected to a foot plate. In the present study, the experimenter manually moved the handle back and forth in a sinusoidal manner.

Protocol: Subjects were asked to abstain from alcohol and caffeine for at least 12 hours prior to the experiment. The subjects were placed in the device and held in standing posture. We verified that the standing posture was stable and that there was no hypotension. We had initially planned to measure post-exercise data for 10 minutes, but some subjects showed orthostatic hypotension over 8 or 9 minutes after the cessation of the exercise in the preliminary experiment. We therefore set the duration of post-exercise measurement at 5 minutes. After a 1 min resting stage, consecutive passive movements were performed for 3 minutes at each of the following frequencies: 0.8, 1, 1.2 and 1 Hz. This protocol was used to examine whether EMG activity and muscle oxygenation are dependent on the frequency of passive movement. The 1 Hz movement was repeated to examine time dependent changes of muscle activity and oxygenation. During the movement, the hip joint range of motion was set at 40 degrees. The experimenter manipulated the lever, keeping pace with the rhythm of a metronome. The experimenter had conducted a sufficient number of practices before the resting session so that they could adjust the leg motion to the predetermined pattern (i.e., the range of motion and swing frequency) by monitoring the angle data from an electrogoniometer displayed on an oscilloscope. Since our aim was to estimate the muscle oxygenation due to EMG activity in the paralyzed muscle, the subjects were asked to relax their upper limbs.

Near-infrared spectroscopy: During passive leg movement, the oxygenation levels of the medial head of the gastrocnemius (MG) muscle were continuously measured by a NIRO-300 (Hamamatsu Photonics, Inc., Hamamatsu, Shizuoka, Japan) with dual-channel near-infrared laser diodes. The NIRS signal has been assumed to reflect the combined absorption of the oxygenation level of Hb and Mb. Though it is impossible to distinguish between Hb and Mb because of identical spectral characteristics, contribution from myoglobin to the overall signal is quite small. Changes in oxygenated- (oxy-) and deoxygenated hemoglobin (deoxy-Hb) were calculated by measuring light attenuation at 775, 813, 850 and 913 nm wavelengths, and were then analyzed with an algorithm incorporating the modified Beer-Lambert law. The NIRS probe was placed on the upper portion of the bellies of the MG muscle, and a calibration procedure was carried out in order to ascertain if the range of measurement was within the optimal range. Prior to the beginning of the passive leg movement, subjects were kept in standing posture on the apparatus until the total Hb value reached a constant level; that is, until the pooling of venous blood was completed. At that time, the concentrations of each Hb value were set at zero. Changes in the Hb values were calculated relative to the resting level, and are represented in μm.

Electromyography: The surface EMG signal was recorded from the MG muscle using bipolar electrodes. Because it is impossible to place both the NIRS sensor and the EMG electrode at the same place, they were placed proximally and distally on the medial side of the muscle (Fig. 1B). The electrode (DE-2.3, DelSys, Inc., Boston, MA, USA) was placed at least 2 cm proximal to the endpoint of the MG muscle. This electrode has parallel-bars (1cm long and 1mm wide) spaced 1 cm apart, and is designed with a built-in filter from 20-450 Hz. The common mode rejection ratio at 60 Hz is >80 dB. SCI patients tend to have larger impedance in their paralyzed legs, and special care was thus taken to eliminate any artifacts of the EMG recording. The electrodes were attached using double-sided adhesive tape after careful preparation of the skin. The EMG signal was amplified (Bagnoli-8 EMG System, DelSys, Inc., Boston, MA, USA).

Electrogoniometer: In order to ascertain the similarity of the leg motion throughout the