

Comparison of Single Bout Effects of Bicycle Training Versus Locomotor Training on Paired Reflex Depression of the Soleus H-Reflex After Motor Incomplete Spinal Cord Injury

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ABSTRACT. Phadke CP, Flynn SM, Thompson FJ, Behrman AL, Trimble MH, Kukulka CG. Comparison of single bout effects of bicycle training versus locomotor training on paired reflex depression of the soleus H-reflex after motor incomplete spinal cord injury. *Arch Phys Med Rehabil* 2009; 90:1218-28.

Objective: To examine paired reflex depression changes post 20-minute bout each of 2 training environments: stationary bicycle ergometer training (bicycle training) and treadmill with body weight support and manual assistance (locomotor training).

Design: Pretest-posttest repeated-measures.

Setting: Locomotor laboratory.

Participants: Motor incomplete SCI (n=12; mean, 44±16y); noninjured subjects (n=11; mean, 30.8±8.3y).

Intervention: All subjects received each type of training on 2 separate days.

Main Outcome Measure: Paired reflex depression at different interstimulus intervals (10s, 1s, 500ms, 200ms, and 100ms) was measured before and after both types of training.

Results: (1) Depression was significantly less post-SCI compared with noninjured subjects at all interstimulus intervals and (2) post-SCI at 100-millisecond interstimulus interval: reflex depression significantly increased postbicycle training in all SCI subjects and in the chronic and spastic subgroups ($P<.05$).

Conclusions: Phase-dependent regulation of reflex excitability, essential to normal locomotion, coordinated by pre- and postsynaptic inhibitory processes (convergent action of descending and segmental inputs onto spinal circuits) is impaired post-SCI. Paired reflex depression provides a quantitative assay of inhibitory processes contributing to phase-dependent changes in reflex excitability. Because bicycle training normalized reflex depression, we propose that bicycling may have a potential role in walking rehabilitation, and future studies should examine the

long-term effects on subclinical measures of reflex activity and its relationship to functional outcomes.

Key Words: Bicycling; H-reflex; Rehabilitation; Spinal cord injuries.

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AFTER SCI, SEGMENTAL REFLEX excitability is initially reduced during spinal shock and then becomes progressively enhanced.¹⁻⁴ The loss of descending control and enhanced synaptic effectiveness of peripheral afferents results in a reduced ability to modulate the stretch reflex⁵ and H-reflex⁶⁻⁸ during gait. This loss of modulation can result in unwanted interference contractions of lower-limb muscles during locomotor phases that require rapid lengthening of muscles.^{9,10} One of the ways in which the impaired spinal modulation manifests post-SCI is a change in the transmission of successive volleys from Ia afferents to motoneurons.^{4,11-16} In noninjured subjects, 2 successive stimuli result in the second H-reflex being smaller in amplitude compared with the first, which is termed paired reflex depression.¹⁷ This depression is an indirect measure of the probability of neurotransmitter release at the Ia afferent synapse.¹⁸ The degree of depression of the second reflex amplitude is dependent on the interstimulus interval: the shorter the interval, the greater the depression.¹⁹⁻²² This depression is also termed homosynaptic depression, postactivation depression,^{18,23-25} or paired reflex depression.²⁶

Post-SCI, however, paired reflex depression in both the H-reflex and stretch reflex pathways is significantly impaired (lower).^{25,27} Accordingly, when a series of volleys of electrical stimulation are carried via Ia afferents, the depression of H-reflex that is normally seen is impaired or lost after SCI.² The firing of muscle spindles in response to stretch of soleus muscle (eg, swing phase of walking) post-SCI has a much higher probability of producing reflex muscle activity in the soleus muscle when it is normally inactive.^{5,28} Results from others^{7,29} and from our own previous work^{8,30} have shown that H-reflex modulation during serial lengthening of the soleus muscle (as occurs in stance and swing phases of walking) post-SCI is impaired and reflex amplitudes are significantly greater com-

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List of Abbreviations

AIS	American Spinal Injury Association Impairment Scale
BWS	body weight support
EMG	electromyography
GABA	gamma-aminobutyric acid
MAS	Modified Ashworth Scale
SCI	spinal cord injury
5-HT	5-hydroxytryptamine

Table 1: Demographic Information for Subjects With Incomplete SCI

Subject	Age (y)	Duration of Injury (mo)	Level of Injury	Sex	ASIA Grade	Ashworth Scale (Ankle)				Motor Score	Medication	Dose	Assistive Device
						Sitting		Supine					
						R	L	R	L				
1	50	4	C7	M	D	1	1	1	1	83	Clonipen	4×/wk	Cane
2	48	26	C5	M	D	NA	NA	NA	NA	87	None	NA	W
3	76	35	C3-4	M	D	0	0	0	0	NA	Zanaflex	2×/d	None
4	48	5	C6-7	M	D	1	0	0	0	87	Gabapentin	1000mg; 4×/d	PW
5	42	88	C5-6	M	D	1	1	1	1	88	None	NA	None
6	55	3	C5-6	M	D	NA	3	NA	3	73	Baclofen	5mg; 2×/d	W+R-AFO
7	23	84	C5-6-7	M	D	NA	NA	NA	NA	NA	NA	NA	B/L LC
8	44	33	C6	M	D	2	2	3	3	64	NA	NA	PW
9	51	21	C5-6	F	D	2	2	0	2	70	None	NA	None
10	50	6	C8, T1	F	D	0	1	1	2	87	None	NA	None
11	22	12	C5	M	D	3	3	3	3	87	N/A	NA	None
12	22	19	C5-6	F	C	3	2	3	2	47	None	NA	PW+B/L AFO

NOTE. MAS scores of 2 indicates a slight increase in muscle tone in less than half the range of ankle dorsiflexion. Scores of 2 or higher indicate greater increase in muscle tone and through the complete range of motion and scores less than 2 indicate lower tone. Abbreviations: AFO, ankle foot orthosis; ASIA, American Spinal Injury Association; B/L, bilateral; C, cervical; L, left; LC, loftstrand crutches; NA, not available; PW, platform walker; R, right; SCI, spinal cord injury; T, thoracic; W, walker.

pared with noninjured subjects. Thus, one of the problems during walking post-SCI appears to be an impaired modulation of reflex activity during task-specific lengthening of lower extremity muscles. Hence, a task-specific therapeutic strategy consisting of alternating stretch-shortening cycles may improve H-reflex modulation during muscle lengthening. Walking on a treadmill with body weight support and manual trainers (locomotor training) and training on a stationary assisted bicycle ergometer (bicycle training) both feature rhythmic shortening and lengthening of lower-extremity muscles.

Locomotor training that induces task-specific patterns of sensory and motor activity may enhance the recovery of walking by optimizing the activity-dependent neuroplasticity of the nervous system.^{31,32} Neuronal circuits may reorganize by strengthening existing and previously inactive connections.³²⁻³⁴ It is hypothesized that such reorganization could improve the sequencing of spinal inhibitory mechanisms such as reciprocal inhibition^{9,35} and presynaptic inhibition^{6,7,36} and increase the modulation of reflex excitability during walking (eg, lengthening of the soleus muscle).

Although research indicates that recovery of walking can be obtained with task-specific training such as locomotor training on a treadmill, thus providing load-bearing and sensorimotor practice of walking,^{33,37} others have suggested that the coordinated coupling of the legs, the alternative phasing of the flexors and extensors of the limbs, and cyclical feedback from peripheral afferents are important task-relevant components of locomotion.^{38,39} Therefore, a task such as pedaling a bicycle ergometer may induce neuroplastic changes that are beneficial to improving modulatory neural processes (reciprocal inhibition, presynaptic inhibition).

The nature of the relationship between paired reflex depression and neurologic injury is not clearly understood.⁴⁰ The purpose of this experiment was to compare, in noninjured and subjects with motor incomplete SCI, paired reflex depression before and after a single bout of training on a bicycle ergometer and locomotor training on a treadmill (with partial BWS and trainer assistance). On the basis of previous research,^{25,27} we hypothesized that reflex depression post-SCI will be significantly lower than recorded in noninjured subjects. In noninjured subjects, we hypothesized that reflex depression would not change after both forms of training. Stationary bicycling

and walking on a treadmill involve repetitive stretching and shortening of the soleus muscle; hence, we hypothesized that paired reflex depression would increase after both forms of training in subjects with incomplete SCI.

METHODS

Subjects

Data were obtained from 12 subjects with incomplete SCI (mean age, 44±16y) (table 1) and 11 noninjured subjects (mean age, 30.8±8.3y). Inclusion criteria for the subjects with incomplete SCI were: (1) adults more than 18 years old, (2) a diagnosis of first-time SCI including etiology from trauma, vascular, or orthopedic pathology at cervical or thoracic levels, (3) a range of 3 months to 3 years post-SCI, AIS class C or D, (5) a medically stable condition, (6) no other degenerative spinal disorders, (7) the ability to walk independently a minimum of ~18 meters continuously with or without an assistive device, (8) the ability to walk at least ~90 meters total per day, and (9) the ability to give informed consent. The above criteria, specifically AIS class C or D and ability to walk a minimum of 60 feet continuously, were set to ensure that SCI subjects would be able to participate in the complete protocol and minimize subject dropout. In addition, we wanted to recruit subjects who could actively participate in both the training protocols rather than training passively. Able-bodied subjects served as noninjured controls and had no history of neurologic or orthopedic problems that could impair walking function. All subjects signed written consent as approved by the institutional review board at the University of Florida.

Initial Testing

The initial subject evaluation (1wk before testing) began with a clinical evaluation of the subjects with incomplete SCI to identify levels of impairment and initial levels of function by the AIS and bilateral upper- and lower-extremity motor and sensory scores.⁴¹ Bilateral ankle plantar flexor spasticity was evaluated by the modified Ashworth scale.⁴²

Experimental Protocol

Each subject returned 1 week later to undergo their initial experiment. All persons with incomplete SCI first walked with

their customary assistive device on a level walkway (.63m long digitized mat with embedded microswitches) at their self-selected walking speed. Three consecutive trials of walking were recorded and comfortable walking velocity determined by GAIT MAT II^a software. This test was repeated immediately posttraining.

The soleus H-reflex was evoked, for the purpose of consistency, on the more involved side of persons with incomplete SCI (determined by AIS lower-limb motor score) and on the dominant side of noninjured control subjects. Similar testing conditions were maintained for all tests. The skin was shaved and cleaned for application of electrodes. A bipolar (2cm interelectrode distance) Ag-AgCl surface EMG electrode^b was placed longitudinally over the soleus muscle approximating the fiber orientation of the muscle (just medial to the Achilles' tendon). The electrodes are embedded in an epoxy mount with preamplifier circuitry. The preamplifier and second stage amplifier provided a total amplification of 1000× with a frequency band pass of 20Hz to 4kHz. We fixed the electrode to the skin with adhesive collars and foam tape wrapped around the electrode and the subject's leg to minimize movement artifact. The tibial nerve was stimulated to evoke H-reflexes; 1-millisecond current pulses were delivered via a constant-current stimulator^c with a 2cm half-sphere silver cathode placed in the popliteal fossa and a circular 10cm-diameter silver dispersive pad (anode) positioned just superior to the patella. The half-sphere shape of the cathode helped in ensuring good contact with the skin; the cathode was held in place with a custom-fabricated Velcro strap. Data were acquired at a sampling rate of 10kHz per channel and stored digitally by Data-Pac III software^d on a personal computer.

H-Reflex Testing in Semireclined Position

Subjects were positioned semireclined, and soleus H-reflex recruitment curves were derived. Subsequently, paired H-reflexes were then evoked with stimulus intensities that produced M-wave amplitude of $10 \pm 3\%$ Mmax. Stimulation intensity was adjusted throughout the experiment to maintain stimulation levels that evoked an M wave amplitude $10 \pm 3\%$ Mmax. Interstimulus intervals used were 10 seconds, 1 second, 500 milliseconds, 200 milliseconds, and 100 milliseconds.⁴³ A period of approximately 30 seconds was allowed to lapse between testing at 2 consecutive interstimulus intervals in order to prevent a carryover effect. This testing procedure was repeated immediately after both types of training.

The paired-reflex methodology has been reported to have strong test-retest reliability using a mean of 4 paired pulses.⁴⁴ Accordingly, at each interstimulus interval, 4 paired reflexes were evoked with a minimum 30-second interval between 2 consecutive paired reflexes. To counter an order effect, subjects were randomly assigned to undergo locomotor training or bicycle training first, and the 2 training days were separated by at least 1 day. We did not control for the order effect of the presentation of the interstimulus intervals. Surface EMG data were also collected from bilateral tibialis anterior, soleus, quadriceps, and hamstrings during both training conditions. Surface EMG data were continuously recorded for 1 minute each in the 2nd, 10th, and 18th minute of both types of training.

Overground Walking H-Reflex Testing

Subjects walked at a self-selected pace, and H-reflexes were evoked according to a standardized procedure.^{7,45} Electrode placement for the soleus muscle, the cathode, and the anode was the same as described earlier. The step cycle was divided into 2 components, midstance and midswing, and the stimuli

were presented randomly during a continuous gait cycle (eg, every fourth step at midstance) to acquire 15 responses per phase component. The phase of walking when the ipsilateral leg completely bore the body weight (ipsilateral ankle and hip in neutral position) was considered the midstance phase. Similarly, the phase when the contralateral leg completely bore the body weight (contralateral ankle and hip in neutral position) was considered the midswing phase. Because most subjects post-SCI in this study walked slowly, it was not difficult to accurately stimulate in the midstance and the midswing phases. Approximately 50 milliseconds on either side of the exact midpoint was considered as midpoint of the stance or swing phases. The same experimenter evoked H-reflexes in all the subjects and in all the conditions. The electrical stimulation was manually delivered by visually determining midstance and midswing phases (confirmed by foot-switch recording). It is preferable to trigger electrical stimulation through foot switches, but in order to use this method, consistent foot contact pattern is necessary. In our subjects, we found that the footfall pattern was very inconsistent, and step-to-step variations were common. Thus, it was difficult to precisely trigger stimulation at midstance phase. Hence, we chose the manual method, which controlled for the interstep variability and allowed the experimenter to visually detect the midstance or midswing phase of walking. The consistency of stimuli current was determined by maintaining a minimum test M-wave of $10 \pm 3\%$ of maximal M-wave. H-reflexes of the same effective stimulus strength, reflected by consistent M-wave amplitude, were included, normalized to Mmax, and compared before and after training. Peak-to-peak reflex amplitudes of the H and M responses for each walking phase were pooled and averaged.

Locomotor Training Over Treadmill

For locomotor training, subjects walked with 40% BWS with a special harness^e with 1 thoracic band, 1 pelvic band, and 2 thigh straps on a Biodex rehabilitation treadmill.^f Manual assistance while walking was provided by gait facilitators (2 people trained to facilitate the subject's gait by assisting foot placement and knee extension and 1 trainer to assist with pelvic movement and trunk alignment). Gait velocity was increased toward normal values (1.2m/s) to the velocity at which the subject's gait kinematics (knee, hip, and ankle motions) visually appeared to be most efficient. Subjects trained for 5 to 10 minutes at a time with the goal of a total training duration of 20 minutes.

Bicycle Training

A tandem bicycle ergometer^g setup was used in which the subject rode on the first bicycle while a laboratory assistant rode the second to provide assistance in maintaining a consistent cadence. All subjects had their feet strapped to the pedals. The pedal was very small, and only the forefoot (metatarsal heads and toes) was supported on the pedal; this design encouraged soleus activity during bicycling. A harness was used to help the subject maintain a comfortable sitting position and to provide a safety mechanism to prevent falls; however, no BWS was provided. Subjects' feet were secured over the pedals with Velcro straps. The height of the bike seat was adjusted such that the knee position ($5-10^\circ$ of flexion when the foot was in the lowest position while pedaling) was similar for all the subjects. Subjects pedaled at a frequency ($\approx 54-56$ rpm)⁴⁶ that approximately matched phasic soleus EMG bursts seen during overground walking at normal speed of 1.2m/s.⁴⁷ Subjects trained for 5 to 10 minutes at a time, with the goal of 20 minutes' total training duration. After training, paired reflex depression was immediately retested.

Data Analysis

In all the pairs of H-reflexes, the second H-reflex was normalized to the amplitude of the first H-reflex (tested at the respective interstimulus intervals). Thus, the reflex depression data are presented as a percentage of the control (first) H-reflex. So a lower value of paired reflex depression indicates greater depression and a higher value indicates lesser depression. Typically, in noninjured subjects, paired reflex depression values are low because noninjured subjects produce greater depression of the second H-reflex compared with the first. To facilitate interpretation of the data, from this point on, paired reflex depression will be referred to as "depression." H-reflex amplitude (mean of 4 trials) at each interstimulus interval was compared within the same condition pre- and posttraining by nonparametric tests (Wilcoxon signed-rank and Mann-Whitney *U* test) and between controls and incomplete SCI by parametric statistics (independent samples *t* test). Statistical significance was set at *P* less than .05. We were specifically interested in exploring the differences between pre- and posttraining at 100-millisecond interstimulus interval. The human muscle spindle afferents usually fire at the rate of approximately 8 to 15Hz.⁴⁸ Thus, the 100-millisecond interval approximated normal firing rates of muscle spindles. Subsequently, we performed post hoc tests (pre- vs posttraining) in subgroups on the basis of spasticity and chronicity at 100-millisecond interstimulus interval (Wilcoxon signed-rank test). To adjust for increased type I error, we divided the *P* value by the number of post hoc tests (*P*/2). After the Bonferroni adjustment, the new *P* value was *P* equal to .025. For the ease of data interpretation, actual *P* values are shown for all tests.

RESULTS

H-reflex depression was compared between noninjured subjects and subjects with incomplete SCI at each interval by

independent-samples Mann-Whitney *U* tests. Within the training conditions, paired Wilcoxon signed-rank tests were performed comparing H-reflex paired reflex depression pre- versus posttraining at each interstimulus interval in subjects with incomplete SCI and noninjured controls.

Paired Reflex Depression in Noninjured Subjects

Noninjured control subjects revealed a decrease in the amplitude of the second response relative to the first (paired reflex depression) (fig 1). The greatest depression was observed at an interval of 100 milliseconds (after both types of training), where the second H-reflex amplitude was approximately 46% of the amplitude of the first H-reflex (fig 2).

At an interstimulus interval of 100 milliseconds, depression postlocomotor training ($.49 \pm .33$) was significantly greater than depression pretraining ($.60 \pm .27$; $P = .011$). Although paired reflex depression pre- and postbicycle training at a 100-millisecond interval was not significantly different, there was a trend toward greater depression postbicycle training (pretraining $.46 \pm .25$ and posttraining $.37 \pm .24$; $P = .11$). There were no significant differences in pre- versus posttraining in the amount of reflex depression for the rest of the interstimulus intervals (10s, 1s, 500ms, and 200ms) in both types of training (fig 3).

Paired Reflex Depression: Incomplete SCI vs Noninjured

Significantly less depression was seen in subjects with incomplete SCI (when compared with noninjured subjects) at all interstimulus intervals ($P = .000$, $P = .000$, and $P = .001$, respectively for comparisons at 1s, 500ms, 200ms intervals) except intervals of 100 milliseconds, where although the difference was not statistically significant, there appeared to be a trend for lesser depression post-SCI (58% in the subjects with incomplete SCI compared with 46% in noninjured subjects; $P = .21$) (see fig 2).

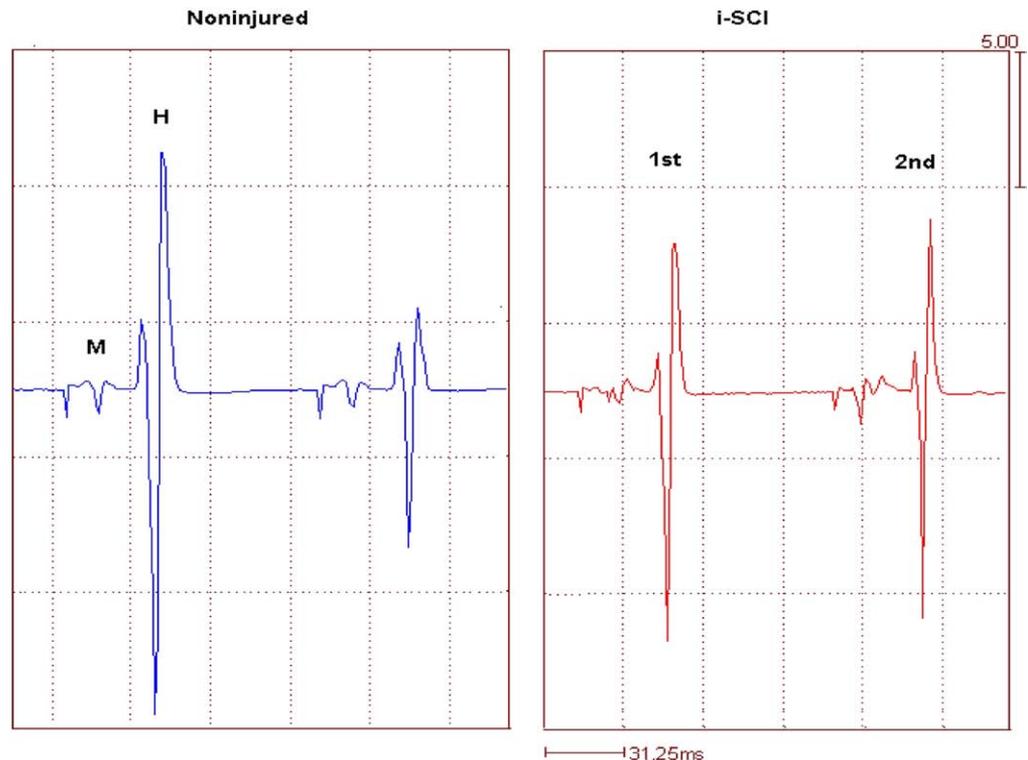


Fig 1. Raw H and M waves in a single noninjured and SCI subject. Abbreviations: 1st, first H-reflex; H, H wave; i-SCI, incomplete SCI; M, M wave; 2nd, second H-reflex.

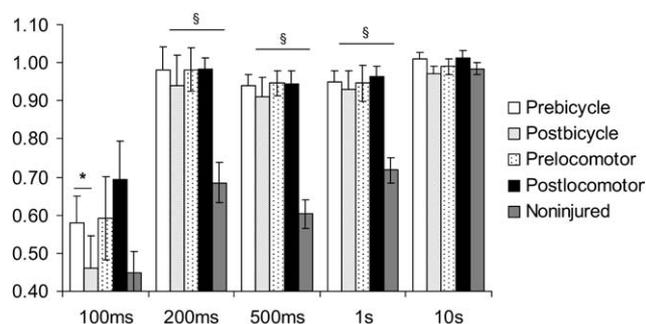


Fig 2. Comparison paired reflex depression between subjects with incomplete SCI pre- and posttraining and comparison between pooled SCI pretraining and noninjured subjects. *Statistically significant differences pre- vs postbicycle training at 100ms interval; §Statistically significant difference between noninjured and SCI at interstimulus interval of 200ms, 500ms, and 1s; vertical bars represent SE; SCI (n=24; data were pooled from prebicycle training and prelocomotor training) and noninjured (n=24; data pooled for all subjects prebicycle training and prelocomotor training).

Paired Reflex Depression: Influence of Training Type in Subjects With Incomplete SCI

No detectable change was observed in depression between pre- and postlocomotor training at any interstimulus interval ($P > .05$); however, depression postbicycle training was greater than prebicycle training at all interstimulus intervals, but reached statistical significance for only the 100-millisecond interval ($P = .011$) (see fig 2). On average, the depression significantly increased from 58% pre- to 46% postbicycle training for the 100-millisecond interval, thus approaching the amount of depression seen in noninjured subjects (see fig 2). The EMG data from the tibialis anterior and soleus muscles did not show a consistent pattern of change during the course of 20 minutes of either type of training.

Paired Reflex Depression in Subjects With Spasticity Versus No Spasticity

To compare the depression patterns between spastic and nonspastic subjects, we divided the subjects with incomplete SCI based on scores on the MAS.⁴² We grouped all subjects with an MAS score of 2 or higher into the spastic group (n=5) and the rest of the subjects into the nonspastic group (MAS < 2, n=5; MAS data not available in 2 subjects) (see table 1).

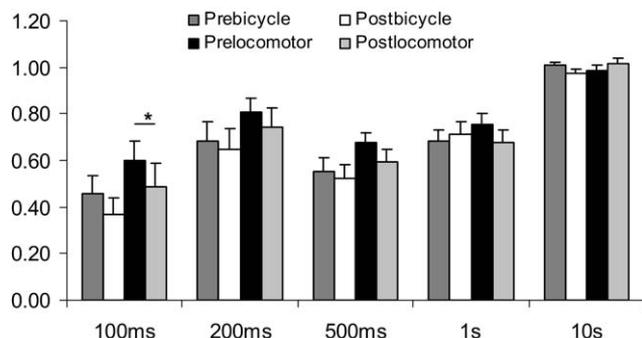


Fig 3. Effect of bicycle and locomotor training on paired reflex depression in noninjured subjects. *Statistically significant difference between prebicycle training and postbicycle training; SE bars shown.

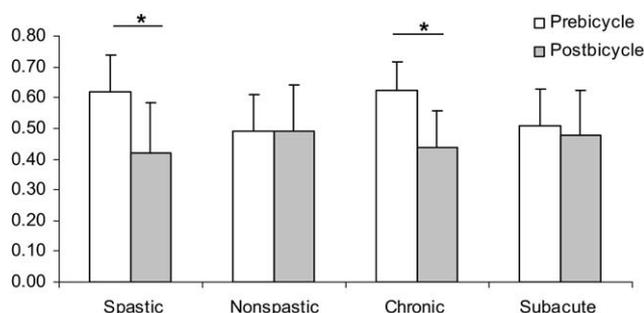


Fig 4. Effect of bicycle training in spastic and nonspastic; and chronic and subacute groups post-SCI at 100ms interstimulus interval. *Statistically significant difference ($P < .025$); SE bars shown; spastic and nonspastic groups each had n=5; chronic group n=7; subacute group n=5.

Pretraining depression values for both types of training were pooled together, and at a 100-millisecond interval, we used a Mann-Whitney *U* test to compare depression in the spastic (n=10) and nonspastic groups (n=10). The spastic group showed less mean depression (73%) compared with the nonspastic group (49%; $P = .04$). Subsequently, we used a Wilcoxon signed-rank test to compare the depression postbicycle training and postlocomotor training at 100-millisecond intervals in both the spastic and nonspastic groups. Subjects with spasticity showed a statistically significant approximately 19% increase in depression postbicycle training (42%; n=5) compared with prebicycle training (62%; n=5) at 100-millisecond interval ($P = .020$) (fig 4). In addition, the spastic group also showed a significant increase in overground gait speed from .61 to .74m/s (Wilcoxon signed-rank test; $P = .021$). Interestingly, 3 out of 5 subjects in the nonspastic group were receiving antispasticity medications (see table 1). The groups based on spasticity, however, did not show any significant differences pre- versus postlocomotor training at all interstimulus intervals. The nonspastic group did not show any change in walking speed after any type of training.

Paired Reflex Depression in Subjects With Subacute Versus Chronic Incomplete SCI

To evaluate the influence of injury duration on the level of depression, we subdivided the subjects into 2 groups: subacute (n=5; duration ≤ 12 mo) and chronic (n=7; duration > 12 mo). We used the Wilcoxon signed-rank test to compare the effect of bicycle training and locomotor training in these 2 groups. We found a statistically significant increase in depression postbicycle training at 100-millisecond interstimulus interval in the chronic group ($P = .009$) (see fig 4). In addition, the chronic group also increased their overground gait speed from .59 to .69m/s (Wilcoxon signed-rank test; $P = .036$). The subacute group did not show any change in walking speed after any type of training.

Correlation: H-Reflex Amplitudes (Stance and Swing) Versus Percentage of H-Reflex Depression

For the purpose of correlation, depression was calculated by the following formula:

$$\text{(First H-reflex - second H-reflex) / First H-reflex}$$

Spearman's bivariate correlation coefficient was calculated, and the correlation was moderately strong between stance H-reflex amplitudes and reflex depression ($\rho = -.47$; $P = .09$)

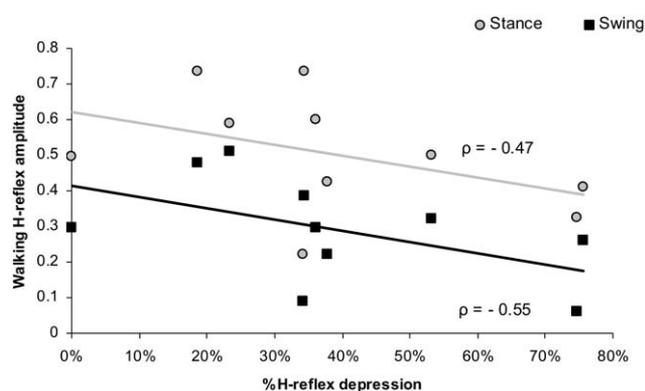


Fig 5. Correlation between walking H-reflexes (stance and swing) and percentage of paired H-reflex depression.

and between swing H-reflex amplitudes and reflex depression ($\rho = -.55$; $P = .05$) (fig 5).

Overground Gait Speed

The gait speeds tested before and after training in both conditions are listed in table 2. The mean posttraining gait speed was significantly greater compared with mean pretraining speed in both training conditions ($P = .008$ bicycle training and $.002$ locomotor training).

Patterns of Electromyography Activity Postspinal Cord Injury: Bicycle Versus Locomotor Training

Although the EMG did not show a consistent pattern of change during the course of 20 minutes of either type of training, there were key differences in EMG activity between the 2 training conditions. Surface EMG data were collected during training in 10 subjects with SCI. Three subjects showed no EMG activity and 4 subjects low muscle activity in either the left or right tibialis anterior in the bicycle training condition; however, these same subjects showed good rhythmic firing of bilateral tibialis anterior muscles in the locomotor training environment. In general, the EMG activity in the lower limbs was lower in the bicycle training condition compared with the locomotor training condition (fig 6). During bicycle training, soleus EMG activity was either low/absent (tibialis anterior 5 of 10 subjects; soleus, quadriceps, and hamstrings muscles in 3 of 10 subjects) or comparable to EMG activity in the locomotor training condition. Although some muscles showed lower activation compared with locomotor training, in general, the bicycle training condition was not passive and required active participation from the subjects. The median motor score of the SCI subjects was 85 (range, 47–88; score out of 100), and thus most subjects were able to actively participate in both types of training.

Overground H-Reflexes

Mean H-reflex amplitude was almost identical pre- and posttraining in both swing and stance phase in both types of training (not significantly different; $P > .05$) (fig 7).

DISCUSSION

The major findings of this study are: (1) Subjects with incomplete SCI had significantly less depression than noninjured subjects at all interstimulus intervals (except 100ms). (2) Noninjured subjects showed a significant increase in depression postlocomotor training (at 500ms and 100ms interstimulus

interval) and a robust trend toward an increase in depression postbicycle training (at 100ms interstimulus interval). (3) Subjects with incomplete SCI displayed significantly greater depression postbicycle training ($\approx 21\%$ greater) at the 100-millisecond interstimulus interval. (4) The spastic incomplete SCI group had a significant increase in depression postbicycle training ($\approx 32\%$), in contrast with the nonspastic group, which did not show any significant difference before versus after for either type of training. (5) The chronic group showed a significant increase in depression postbicycle training at 100-millisecond interstimulus interval. (6) In SCI subjects, overground walking speed was significantly different before versus after for either type of training. (7) H-reflexes tested over ground were not significantly different before versus after types of training. (8) There was a moderate negative correlation between reflex depression and walking H-reflexes.

As reported in earlier studies, we found that depression was significantly lower post-SCI compared with noninjured controls.^{25,27,49,50} The fact that the average level of depression in noninjured subjects increased 18.3% and 19.5% postlocomotor training and postbicycle training, respectively, suggests that both types of training can induce a robust neurologic effect. Although we did not anticipate a change in reflex depression posttraining in noninjured subjects, this result demonstrates the inherent neuroplastic capacity of the uninjured spinal cord in response to repetitive sensory input. Reflex depression has been previously reported to be modulated after a short duration bicycle training task.⁴⁶ Meunier et al⁴⁶ also reported that noninjured subjects who were used to regularly exercising the locomotor muscles (such as in treadmill walking) showed larger reflex modulation posttraining compared with sedentary subjects.⁴⁶ It has been suggested that modulation of reflex depression may be related to the task-specific pattern of sensory feedback.⁴⁶

An unexpected finding of this study was that although a single bout of both types of training resulted in a significant increase in overground walking speed, only bicycle training—but not locomotor training group—showed increased depression in subjects with incomplete SCI. Comparison of the EMG activity during the 2 training conditions revealed that EMG activity was greater in the locomotor training condition. In a recent study, Stein et al⁵¹ reported that when the soleus muscle is voluntarily activated, the phenomenon of paired reflex depression was diminished or lost. They argued on the basis of their results that paired reflex depression may not have any functional significance or relevance to an active task that re-

Table 2: Overground Walking Speed (m/s)

Subject	Bicycle Training		Locomotor Training	
	Pre	Post	Pre	Post
1	0.71	0.73	0.50	0.98
2	0.23	0.24	0.21	0.26
3	0.60	0.71	0.69	0.69
4	0.57	0.52	0.50	0.93
5	1.00	0.99	0.99	1.48
6	0.21	0.30	0.19	0.36
7	0.23	0.28	0.21	0.27
8	1.43	1.83	1.27	1.84
9	0.83	0.87	0.76	1.24
10	0.16	0.26	0.18	0.24
11	1.12	1.23	0.88	1.59
12	0.06	0.07	0.11	0.12
Mean	0.60	0.67	0.54	0.83

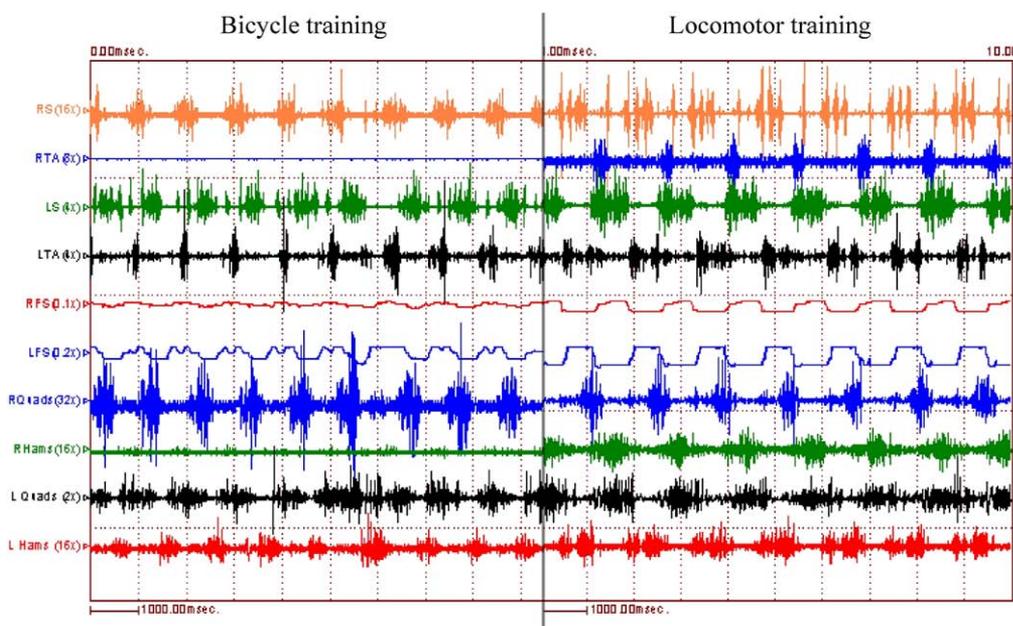


Fig 6. Surface EMG activity from a representative subject with SCI collected during a 10s interval during bicycle and locomotor training. Abbreviations: FS, foot switch; Hams, hamstrings; L, left; Quads, quadriceps; R, right; S, soleus; TA, tibialis anterior.

quires active firing of muscles. It is likely that the greater muscle activation during the locomotor training condition, compared with the bicycle training condition (see fig 5), may have resulted in a loss of sensitivity to changes in reflex depression. We did not record ankle movement velocity and ankle angles, which may have produced specific effects we have not accounted for during the 2 types of training. Thus, it appears that paired reflex depression may not be a sensitive measure to detect changes postlocomotor training.

Our previous work shows an increase in depression of H-reflex amplitude in the locomotor training environment post-SCI^{8,30}; thus, it is possible that changes in presynaptic inhibition may have led to improvement in walking speed postlocomotor training. Training principles for locomotor training have been established and continue to be refined⁵²; a primary target of these training protocols is to provide optimal sensory cues for activating the central pattern generators. In light of the rehabilitation potential of training locomotor activity with bicycle and treadmill, it will be important to

continue considering the similarities and differences of these 2 training environments. Bicycling does not typically require as much loading as locomotor training; hence, we anticipated greater H-reflex depression posttraining on the treadmill. On the other hand, cycling is a relatively rhythmical, constant, repetitive task, alternating between flexion and extension without the added element of postural control. With a more structured, controlled task such as cycling (with trainer assistance to maintain cadence; feet strapped to pedals), the afferent input may be more consistent, providing a better opportunity for reorganization around this afferent information. In contrast, walking is a complex task that requires postural control (even with 40% BWS), relative control over hip/knee/ankle movements (even with trainers assisting), and some consideration for foot placement. Accordingly, this level of supraspinal attention and control with stepping may have reduced the consistency of alternating flexion/extension input to the nervous system. In addition, a recent report shows that the soleus H-reflex amplitude is directly proportional to the level of postural threat during walking on a treadmill.⁵³ The bicycle training environment was clearly less of a postural threat compared with walking in the locomotor training environment.

Animal studies have provided the rationale for the use of bicycle training; 2 separate studies reported that passive exercise can normalize H-reflex depression in a rat SCI model.^{54,55} Subsequently, Kiser et al⁵⁶ reported normalization of frequency dependent H-reflex depression after a passive cycling regime in a human SCI single case study; this increase in depression was also correlated with a decrease in spasticity. Recently, Motl et al⁵⁷ reported a decrease in both spasticity and H-reflex amplitude after 20 minutes of cycling exercise in people with multiple sclerosis. In the current study, we found that spastic subjects had a greater loss of depression and responded to bicycle training better than the nonspastic subjects (see fig 4). Thus, it appears from our results that bicycle training could potentially be used as a modality to decrease spasticity.

Our subject population was heterogeneous in their chronicity, which ranged from 3 to 88 months (see table 1). We analyzed H-reflex depression in groups on the basis of chronicity of SCI (subacute and chronic). Thompson et al¹² re-

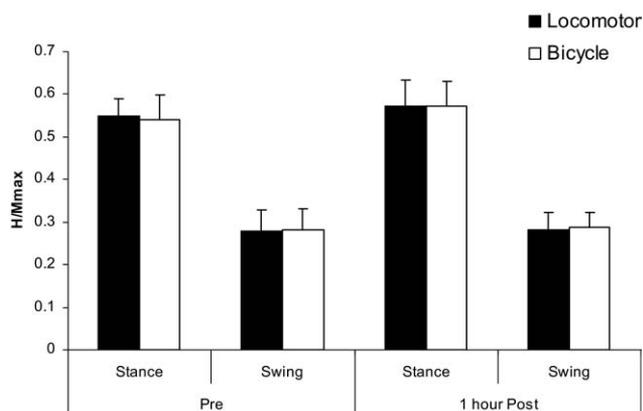


Fig 7. Overground walking H-reflexes pre- vs posttraining. NOTE: H/Mmax on the y-axis represents mean H-reflex normalized to maximum M wave; vertical SE bars shown.

ported that acute SCI injured rats show almost normal patterns of H-reflex rate depression (another measure of homosynaptic depression) and that as they progress to the chronic stage, they lose the rate depression. Schindler-Ivens and Shields² confirmed in human subjects that rate depression is relatively unaffected in acute SCI, but as the subjects progress to the chronic SCI, they successively begin to lose rate depression. Although not statistically different in the current study, within the pretraining groups, there was a trend for the subacute subgroup to have greater depression compared with the chronic subgroup (subacute $.51 \pm .26$; chronic $.62 \pm .24$). Consistent with earlier studies reporting a training effect of increased rate depression,^{43,54,55} bicycle training in this study resulted in greater depression in subjects with chronic SCI.

In a spinal cord-injured nervous system, reflex modulation is impaired in both static state (such as in the semireclined position in the current study) and dynamic states (stance and swing phases of walking). The impaired ability to modulate reflexes in a task-specific manner is reflected in the findings of increased reflex amplitudes during walking post-SCI.^{7,8,30} Similarly, paired reflex depression is impaired post-SCI and the second H-reflex (percentage of the first) is not significantly depressed (see fig 2). Thus, the inability to modulate reflexes tested in 2 different ways (paired reflex depression paradigm and phase specific H-reflex modulation in walking) and 2 different postures suggests the possibility of shared common neural elements. We found a moderate negative correlation between walking H-reflexes (dynamic state) and reflex depression tested in semireclined position (static state) in the current study. Thus, in SCI subjects with greater than normal amplitudes of walking reflexes (dynamic position), a similar loss of depression is also seen in the semireclined static position. This correlation between reflex depression and walking reflexes suggests that the increased depression seen postbicycle training may also be related to a concomitant decrease in H-reflex amplitudes in walking; however, the design of our current study did not allow us to test walking H-reflexes immediately posttraining. In the current study, the H-reflexes tested during walking did not change posttraining (locomotor and bicycle). It has been previously reported that a single bout of bicycle training⁵⁸ and locomotor training³⁰ increases soleus H-reflex amplitude depression. In the current study, we did not test overground H-reflexes immediately after training (reflex depression was tested immediately posttraining). It is conceivable that any potential neurophysiologic changes in walking H-reflex modulation may not have persisted at approximately 1 hour posttraining.

Training effects such as improvements in synaptic efficacy and increase in H-reflex paired reflex depression^{46,59} and smaller peak amplitude⁵⁸ have been reported in noninjured human subjects after a single bout of bicycle training. The above studies, however, used a skilled bicycling task that involved variable resistance, whereas we used a simple bicycling task with consistent cadence and no resistance. In the current study, although we did not observe significant difference in depression pre- versus postbicycle training in noninjured subjects, there was a robust trend toward an increase in depression postbicycle training. It is likely that this study was somewhat underpowered for statistical significance. The effect of bicycle training is not global but is targeted in the spinal segments (motor and sensory) that are actively participating in the task of bicycling.⁶⁰ In addition, bicycling has been reported to induce phase-specific modulation of transmission in the corticospinal pathways (increases during early downstroke) and the presynaptic inhibition (depressed soleus H-reflex during late downstroke and upstroke).^{9,61-63}

The current study and others^{56,59} report an activity-dependent increase in paired reflex depression posttraining. It will be important to examine the paired reflex depression in a dynamic task such as bicycling. Serially examining reflex depression during the course of several weeks of bicycle training in subjects with incomplete SCI may provide us with an opportunity to examine the functional correlation between reflex depression and walking recovery. Although walking speed increased significantly postbicycle training and postlocomotor training, the change postlocomotor training (.29m/s) was clinically more significant compared with the increase postbicycle training (.07m/s). Thus, it is clear that the magnitude of change is greater postlocomotor training. It is unlikely that bicycle training by itself will produce changes in walking speed of the magnitude such as that seen postlocomotor training. However, the finding that bicycle training significantly increased reflex depression suggests that bicycling may have a role as an adjunct, complementary, and interactive effect with other walking retraining strategies, including locomotor training.

Possible Mechanisms

Impaired reflex depression in subjects with incomplete SCI as compared with noninjured control subjects is in agreement with earlier studies.^{13,25,27} The underlying mechanism for paired reflex depression is believed to be presynaptic in nature^{4,12,18,20,23,64-67} and likely regulated by the probability of neurotransmitter release in the Ia afferent nerve endings in the spinal cord.^{18,27} It is believed that this presynaptic effect is likely controlled by activation of GABA-ergic interneurons^{68,69} through controlled release of synaptic transmitter.⁷⁰

Treatment of spasticity with baclofen (a GABA-B agonist that presumably produces a tonic presynaptic inhibition; antispastic) decreases muscle tone and/or increases voluntary motor control⁷¹ and has been reported to improve modulation of the stretch reflex during walking.⁷² In the current study, 4 subjects were receiving antispastic medication and 5 subjects were not. All SCI subjects receiving spasticity medication showed greater depression compared with the subjects receiving no spasticity medication (antispastic medication .29; no medication .69). In the medication group, the level of depression increased postbicycle training but not postlocomotor training. It is therefore possible that the impaired depression observed in the subjects with SCI in the current study may have been due to disruption of the normal GABAergic regulation of presynaptic processes. However, the reverse may not be true, and H-reflex has not been shown to be predictive of outcomes post-SCI.

Synaptic efficiency is modulated by various neurotransmitters (eg, serotonin or 5-HT). It follows, then, that the damage to the descending tracts from the brain stem that carry a steady supply of neurotransmitter may cause an impaired depression post-SCI. Paired reflex recordings performed in lampreys have revealed that activity in spinal cord interneurons is either depressed or potentiated based on physiologic frequencies of stimulation (interstimulus interval range of 200ms to 50ms, respectively). Interestingly, the presence of neuromodulators such as substance P and 5-HT catalyzes the depression of paired-reflex amplitudes.⁷³ Post-SCI, the 5-HT receptors caudal to injury level become hypersensitive to 5-HT, most likely because of meager amounts of endogenous 5-HT below the lesion.⁷⁴ On the basis of animal studies, it is possible that in the current study, bicycle training (compared with training on the treadmill) may have induced a greater release of 5-HT in the lumbar spinal cord, resulting in an increase in paired reflex depression.^{75,76} Along with an increase in spinal excit-

ability, concomitant reemergence of persistent inward currents is seen after chronic SCI.^{77,78} The lower level of depression post-SCI and the increase after bicycle training may be related to alteration in the modulation of the persistent inward currents^{78,79}; future studies need to explore this relationship.

CONCLUSIONS

On the basis of the results of bicycle training in the current study, 2 important questions arise: first, could the increase in depression after a single bout of bicycling be due to the consistency of movement kinematics, lack of weight bearing on the legs, or the lesser demands placed on posture? Second, is there a direct correlation between level of depression and functional outcome measures?⁴⁰ At the 100-millisecond interval, single-session bicycle training normalized (increased depression) to a level commensurate with noninjured subjects. In order to understand its potential role in walking rehabilitation, future studies need to examine the long-term effects of bicycle training on subclinical measures of reflex activity. Soleus H-reflex amplitude has been correlated to locomotor function in the rat SCI model⁸⁰; similar relationships between H-reflex and functional outcomes need to be tested in human subjects with SCI.

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Suppliers

- a. EQ, Inc, PO Box 16, Chalfont, PA 18914-0016.
- b. Therapeutics Unlimited, Iowa City, IA (company out of business).
- c. Grass Technologies, 600 E Greenwich Ave, West Warwick, RI 02893.
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