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Limb compressive load does not inhibit post activation depression of soleus H-reflex in individuals with chronic spinal cord injury

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Abstract

Objective—We investigated the effect of various doses of limb compressive load on soleus H-reflex amplitude and post activation depression in individuals with/without chronic SCI. We hypothesized that SCI reorganization changes the typical reflex response to an external load.

Methods—Ten healthy adults and 10 individuals with SCI received three doses of compressive load to the top of their knee (10%, 25%, and 50% of the body weight, BW). Soleus H-reflexes were measured before (baseline) and during the loading phase.

Results—With persistent background muscle activity across all testing sessions, segment compressive load significantly decreased post activation depression in the control group, but did not change the post activation ratio in the SCI group. Normalized H2 amplitude significantly increased according to load (50% > 25% > 10%) in the control group whereas was minimally modulated to load in those with SCI.

Conclusions—Segment compressive load inhibits post activation depression in humans without SCI, but minimally modulates the reflex circuitry in people with chronic SCI. These findings suggest that spinal cord reorganization mitigates the typical response to load in people with chronic SCI.

Significance—Early limb load training may impact the reorganization of the spinal cord in humans with acute SCI.

Keywords

Compression; Homosynaptic depression; Spinal neural modulation

1. Introduction

Human paralyzed tissues have an enormous capacity to adapt to external mechanical stimuli. Early mechanical loading interventions via muscle contractions have successfully prevented the loss of bone, loss of muscle mass, and changes in spinal excitability in individuals with SCI (Shields et al., 2006, 2011; Shields and Dudley-Javoroski, 2006; Dudley-Javoroski and Shields, 2008a,b; Adams et al., 2011; Dudley-Javoroski et al., 2012). In healthy humans,

limb load is believed to trigger sensory inputs that control body dynamics during both static standing and walking via adaptations to spinal circuitry (Andersen and Sinkjaer, 1999; Petersen et al., 1999; Trimble et al., 2001; Faist et al., 2006; Phadke et al., 2006; Huang et al., 2009; Knikou et al., 2009a,b). In this study we explore the impact of passive segment compressive load on spinal circuitry in people with chronic and complete SCI.

When an H-reflex is immediately preceded by a single conditioning stimulus the subsequent test H-reflex is depressed and referred to as post activation depression (Crone and Nielsen, 1989; Hultborn et al., 1996; Kohn et al., 1997; Aymard et al., 2000). Individuals with SCI gradually lose some of the post activation depression as they progress from the acute to the chronic state supporting that the loss of sensory and motor input leads to a reorganization of the underlying spinal circuitry (Ashby et al., 1974; Calancie et al., 1993; Skinner et al., 1996; Hiersemenzel et al., 2000; Schindler-Ivens and Shields, 2000; Shields, 2002). The loss of post activation depression is associated with a velocity dependent increase in muscle stiffness in people with chronic SCI (Grey et al., 2008). Accordingly, we became interested in whether passive external mechanical stimuli can modulate the pathways associated with post activation depression.

In the absence of muscle contractions, segment compressive load significantly decreased post activation depression of the soleus H-reflex in healthy adults (Tseng and Shields, 2012). Importantly, the magnitude of the loss of post activation depression was scaled according to the dose of load delivered to the limb segment (50% body weight (BW) > 10% BW). These findings supported that compressive load “gates” afferent signaling associated with post activation depression in healthy humans, but raised the question as to what happens in people with SCI who already have a diminished capacity to depress the H-reflex. Clinically, an increment in muscle stiffness is often reported when individuals with SCI passively load their legs in weight bearing positions. Whether these clinical observations are supported by measureable changes in neurophysiology forms the underlying framework for this study. If compressive load causes a further loss of post activation depression in people with SCI, then it may explain these anecdotal clinical reports. Alternatively, if the reorganization of the spinal circuitry is saturated and no further loss of post activation depression is possible, then it suggests a different pathway underlying load induced stiffness in people with SCI.

In preparation for this study, we developed a method to deliver compressive loads to a single limb segment to minimize supra spinal drive for healthy subjects (Tseng and Shields, 2012). Accordingly, the purpose of this study is to test if segment compressive load increases the loss of post activation potentiation in people with chronic SCI as compared to a group without SCI. A secondary aim is to determine if there is a relationship between the dose of compressive load and the magnitude of post activation potentiation in each group. We expect to confirm our previous findings that segment compressive load reduces post activation depression in healthy humans, however, we predict that post activation depression will not be modulated in the chronically reorganized spinal cord of those with chronic SCI.

2. Methods

2.1. Subjects

Ten healthy adults and 10 individuals with chronic spinal cord injury (SCI) participated in the study (Table 1). All able bodied subjects enrolled in the study had no known acute or ongoing orthopedic, neuromuscular, or neurological deficits or disorders. For the SCI group, inclusion criteria were (1) motor complete SCI classified according to the American Spinal Injury Association (ASIA) Impairment Scale, (2) able to passively achieve the neutral position at the paretic ankle with the knee flexed to 90° in a seated position, (3) clinical evidence of involvement of upper motor neuron lesions, measured by the presence of at least

mild to moderate resistance to stretch supporting the presence of hyper-reflexia. Exclusion criteria were (1) presence of pressure ulcers, (2) history of any other significant neurological, cardiac, vascular, pulmonary, orthopaedic, hematologic, infectious, immune, gastrointestinal, urogenital, integumentary, oncological, or endocrine diseases or disorders affecting neuromuscular function of the legs, (3) lesions involving lower motor neurons, (4) any medical conditions in which electrical stimulation is contraindicated such as pregnancy or the utilization of cardiac pacemaker or defibrillator. All subjects gave informed consent before participation and the study was approved by the University of Iowa Human Subjects Institutional Review Board.

2.2. Paradigm

The paradigm was comprised of a baseline session followed by three loading sessions (Fig. 1A). Each session was separated by 1 min. This paradigm was previously assessed for the reproducibility of soleus H-reflexes in healthy adults and was used to establish a dose (load)-response (H-reflex) relationship (Tseng and Shields, 2012). Briefly, the protocol always tested the soleus H-reflexes in a 1.25-min baseline session followed by three 2.5-min loading sessions in a random order. Each loading session consisted of one of three pre-determined compressive forces: 10%, 25%, and 50% of the individual's body weight (Fig. 1B). The order of the three loading sessions was random. Paired-pulse electrical stimulations (doublets) with inter-pulse intervals of 500 ms were delivered every 15 s to elicit H-reflexes across all four sessions (Fig. 1C). In the baseline session, there was no compressive load applied on the lower leg segment and five doublets were delivered to establish baseline H-reflexes. In each loading session, a pre-determined compressive force was applied over top of the right knee for 15 s (*load-on* phase; gray areas, Fig. 1B) followed by a 15-s rest period (*load-off* phase; White areas, Fig. 1B). The doublet was always delivered exactly in the middle of each phase in which the compressive force was continuously initiated or terminated for 7.5 s (dash lines, Fig. 1B). Thus, the loading session involved five 30-s cycles constituted by five 15-s *loading* phases and five 15-s *recovery* phases. As such, subjects experienced a constant compressive force intermittently applied on their right lower leg segments throughout the entire loading session. Hence, each subject underwent four testing sessions where 35 doublet activations were delivered in total: 5 doublets in a baseline session and 30 doublets during three loading sessions (5 doublets in each phase, two phases in each loading session, and three loading sessions). In addition, to manage the spasticity for each SCI individual throughout the entire experiment, we carefully controlled the total time duration for data collection, provided the special seating surface, and gave frequent breaks as needed between baseline and three loading sessions to allow pressure relief and prevent noxious stimuli known to trigger hypertonic contractions. Based on the modified Ashworth Scale, all subjects reported spasticity between levels 1 and 2. Thus, no relationship was developed between post activation depression and the modified Ashworth Scale.

2.3. Instrumentation

Bipolar Ag–AgCl surface electrodes (8 mm in diameter, with a fixed inter-electrode distance of 20 mm) were used to record H-reflexes and M-waves from the soleus muscle of the right leg. Electromyographic (EMG) signals were on-site preamplified with a gain of 35. The EMG signals were then further amplified by a GCS 67 differential amplifier (Therapeutics Unlimited, Iowa City, IA) with a gain range from 1000 to 10,000. The differential amplifier had an input impedance of 15 M Ω at 100 Hz, a frequency response of 15–1000 Hz, a common mode rejection ratio of 87 dB at 60 Hz, and a bandwidth of 20–4000 Hz.

A constant-current electrical stimulator (DS7A, Digitimer Ltd, Welwyn Garden City, Herts, UK) with a constant current range from 50 μ A to 1 A and a total output capacity of 400 V was used to deliver square waves with a pulse width of 1000 μ s. The stimulator was

triggered by a digital pulse from a data acquisition board (USB-6259, National Instruments Corp., Austin, TX) controlled by custom LabVIEW software (National Instruments, Austin, TX). Through custom LabVIEW programming, the stimulator delivered paired-pulse electrical stimulation (doublets) with inter-pulse intervals of 500 ms every 15 s. Stimulation was administered via a single surface probe (cathode, 1 cm in diameter) secured over the tibial nerve in the right popliteal fossa. The anode was positioned through a dispersive electrode (10 × 10 cm) placed over top of the femoral condyles.

2.4. Servo-controlled segment loading

The custom designed servo-controlled system utilized an air compressor (Super Silent 20A, Silentaire Tech, Houston, TX), an electronic pressure regulator (550× Miniature E/P Transducer, Control Air Inc, Amherst, NH), a pneumatic cylinder (Clippard USA Corp, Cincinnati, OH), a load cell (1210, Interface, Scottsdale, AZ), and custom-built integrated circuit to control the system under software control. The design allows precise control of the duration and amplitude of a compressive load over the lower leg for a pre-determined number of cycles. The compression control system generated the compressive loads in <500 ms. In addition, the compression control system employed a unique safety mechanism in which the pressure was continuously monitored by a pressure switch (Solon Manufacturing Co, Chardon, OH) and was allowed to shut off instantaneously when necessary. The pneumatic cylinder was positioned directly over the knee in a seated position and programmed to deliver the compressive load.

2.5. Data collection

Subjects sat on a custom designed chair with the hip and knee flexed at 120° and the ankle in the neutral position (Fig. 2). The testing leg was secured by a Velcro strap around the foot to maintain a fixed position on the platform attached to the compressor system. Subjects were instructed to relax and sit quietly throughout the entire experiment. Subjects were also instructed to engage in light reading to maintain a similar level of consciousness between the SCI and control groups. The skin over the soleus muscle was abraded with sandpaper and cleaned with alcohol swabs. The recording EMG electrode was placed 2 cm lateral to midline of the posterior calf and 2 cm distal to the lowest end of the palpable border of the gastrocnemius muscle. A reference electrode was placed on the anterior aspect of the tibia of the right leg.

For soleus H-reflex measures, the tibial nerve was electrically activated via a stimulating electrode positioned in the popliteal fossa. The location for the stimulating electrode was determined by the conditions whereby H-reflexes were elicited without M-waves at very low stimulation intensities and M-waves appeared as increasing stimulation intensity. The maximal M wave (M-max) was first defined as the peak-to-peak value at the time when the M wave amplitude failed to increase with increasing stimulation current. To ensure the tibial nerve was activated supra maximally, the stimulation intensity was then adjusted to a value >120% of the last current intensity, and at least three pulses were delivered. To compare the H-reflex depression elicited by doublets across sessions and groups, the stimulation intensity was adjusted to the level that elicited a stable soleus H-response equivalent to ~50% of the maximal H-reflex response. The H-reflexes corresponded to 15–25% of the M-max. All data were recorded at 4000 Hz using custom LabVIEW software and time-synchronized with the compressor system.

2.6. Data analysis

All analyses were conducted using Custom Matlab software (MathWorks, Natick, MA). Offline, raw EMG signals were first zero offset prior to any advanced processing. In each doublet, paired H-reflexes 500-ms apart were first identified and were categorized as the test

H-reflex (H1) and conditioned H-reflex (H2) to investigate the neural mechanism of post-activation depression (Fig. 1C). The peak-to-peak amplitude of each H-reflex was then computed and expressed as a percentage of M-max across all available trials for each testing session. In addition, to monitor changes in neural excitability at the peripheral site across all testing sessions, background soleus muscle activity was quantified by calculating the root-mean square (RMS) over a 50-ms window prior to each stimulus. The RMS values were then expressed as a percentage of the maximal M-wave. To quantify post-activation depression of soleus H-reflexes, we first calculated the depression ratio by dividing the amplitude difference between the test H1 reflex and the conditioned H2 reflex divided by the test H1 reflex amplitude, and then expressed as the percent of H1 amplitude

$$\left[\text{ratio} = \frac{(H1 - H2)}{H1} \times 100 \right]$$
 A depression ratio of 0 indicated that no post-activation depression occurred; whereas a ratio of 100 indicated that the greatest depression occurred such that the decrement of H2 was equal to the H1 amplitude. To quantify the modulation of the soleus H-reflex corresponding to cyclical compressive loads, H-reflex amplitudes and depression ratios were computed independently during each *Load-on* phase and *Load-off* phase within each loading cycle. Thus, we could determine whether the modulation of soleus motor neuron excitability coincides with the presence of load stimuli cyclically.

The test H1 reflex, conditioned H2 reflexes, and the depression ratios obtained during the three loading sessions were normalized to baseline values and expressed as three ratios. The normalized H1 ratio = H1/(baseline mean H1); The normalized H2 ratio = H2/(baseline mean H2); The Overall normalized ratio = (depression ratio)/(baseline mean ratio). This allowed us to normalize across the various load levels within each group and compare the dose (load)-response (H-reflex) relationship between the SCI and control groups. A ratio equal to 1.0 indicates no effect of segment loading on reflexes no depression ratio. A ratio >1.0 indicates enhancements of reflexes and depression ratio during the load session as compared to the baseline session; whereas a ratio <1.0 indicates a reduction of reflexes and depression ratio during the load session as compared to the baseline session. All variables were first averaged across all available trials from each subject and then were averaged over all subjects to create group means for each session.

2.7. Statistical analysis

Statistical comparisons were made using SAS/STAT software (SAS, Cary, NC, USA). We used a two-way (group × time) mixed model ANOVA with repeated measures on one factor (time) to test for the effect of segment compressive load (baseline, 10%, 25%, and 50% BW *load-on* phases) and group (SCI vs Control). When the ANOVA was significant, post hoc analyses were performed using Tukey's honest significant difference test. The level for statistical significance was set at $P < 0.05$.

3. Results

An example of the individual H-reflexes elicited by doublet stimuli across the baseline session, the *load-on* phase, and *load-off* phase during the 50% BW loading session are depicted in Fig. 3 from a typical subject with chronic SCI and a healthy control. Stable M-waves were observed throughout the entire test supporting that stimulation conditions remained constant. Also noteworthy is that the test H1 amplitudes were consistent across all testing sessions for both SCI and control subjects (the first H-reflex shown in each overlaying trace; Fig. 3B–D, respectively). It is clear that the conditioned H2 amplitude for the control subject was less suppressed (Gray zone, left panel in Fig. 3C) during the *load-on* phase (50% BW load) as compared to the baseline or *load-off* phase; whereas the

conditioned H2 amplitude for the SCI subject showed no changes across different sessions (Gray zone, right panel in Fig. 3C).

Similar trends were also observed in group averages of H-reflex amplitudes across different sessions (Fig. 4A). The average test H1 amplitudes were similar across all sessions for both SCI and control groups, which ranged from 23.5% to 28.4% of M-max for the SCI group and 15.9–19.9% of M-max for the control group. By comparing across sessions, there were no significant effects of group and time (both P values = 0.1) or group $\times$ time interaction effect ($P = 0.74$) on the test H1 amplitudes (black bars, Fig. 4A). Interestingly, there was a borderline significance of group $\times$ time interaction effect ($P = 0.08$) on the conditioned H2 amplitude (white bars, Fig. 4A), suggesting different dose (load)-response (H-reflex) relationships between the SCI and control groups. There was a trend demonstrating the conditioned H2 amplitudes systematically increased with increasing loads in the control group (white bars, left panel in Fig. 4A); whereas the conditioned H2 amplitudes were less responsive to varying loads in the SCI group (white bars, right panel in Fig. 4A).

Fig. 4B illustrates the relationships of soleus H-reflex amplitudes and levels of compressive load for both SCI and control groups. Notice that H1 and H2 obtained during three loading sessions were divided by their baseline mean values and expressed as ratios of the baseline means. Group averages of the normalized tested H1 amplitudes did not change across different loads and were indifferent between groups ($P = 0.39$ and 0.13 , respectively; black bars, Fig. 4B). Interestingly, there is a clear trend demonstrating that an increment of the compressive load systematically facilitates the conditioned H2 amplitude in healthy adults. In contrast, the conditioned H2 amplitude in the SCI group appears to be less responsive to increasing load. Statistically, there were significant effects of load ($P = 0.02$) and group load interaction ($P = 0.0007$) on the normalized conditioned H2 amplitude (white bars, Fig. 4B). For the control group, the average conditioned H2 amplitude during the 50% BW *load-on* phase was significantly greater than the baseline session, 10% and 25% BW *load-on* phases (post hoc, $P = 0.0005$, $P = 0.0003$ and $P = 0.027$, respectively); whereas for the SCI group, the average conditioned H2 amplitudes during 10%, 25%, and 50% BW *load-on* phase were indifferent from the baseline session (post hoc, all P s = 1.0).

The depression ratio also showed significant effects of load and group $\times$ load interaction ($P = 0.0006$ and 0.0496 , respectively; Fig. 5A). A clear pattern reveals a negative relationship between depression ratios and compressive loads for the control group. That is, the depression ratio systematically decreases with increments of load, and it decreases to a greater extent at the 50% of BW load. However, this negative relationship is less pronounced in the SCI group. For the control group, the depression ratios during the 25% and 50% BW *load-on* phases were significantly smaller than the baseline session (post hoc, $P = 0.02$ and $P = 0.001$, respectively); whereas for the SCI group, the depression ratios during all loading sessions were indifferent from the baseline session (post hoc, all P s = 1.0). Similar trends were also observed in group averages of normalized depression ratios across different sessions (Fig. 5B). For the control group, normalized depression ratios during the 25% and 50% BW loading sessions were significantly smaller than the baseline (post hoc, $P = 0.0495$ and $P = 0.002$ respectively; white bars, Fig. 5B). In contrast, the normalized depression ratios during three loading sessions were indifferent from the baseline session (post hoc, all P s = 1.0). Post-hoc analysis also indicated that load influenced the excitability such that the depression ratio and normalized depression ratio was significantly smaller at 50% of BW load as compared to 10% of BW load (post hoc, $P = 0.015$ and $P = 0.02$).

The analysis of average background muscle activity confirmed that altered descending neural drive did not influence the post-activation depression between the healthy and SCI groups. The level of background muscle activity was consistently low throughout the entire

experiment (Fig. 4C). Specifically, the average RMS values were always $<0.5\%$ of the M-max for all groups. Statistically, background muscle activity was not different across sessions ($P = 0.34$ and $P = 0.8$ for test H1 and conditioned H2 measures, respectively).

Taken together, these findings support that isolated limb segment load modulates post-activation depression in healthy humans, but does not modulate the post activation depression in humans with chronic spinal cord injury.

4. Discussion

In this study, we investigated the effects of limb segment compressive load on spinal neuronal excitability in individuals with chronic SCI and contrasted these findings with healthy adults. In the control group, we found that increasing segment compressive load results in less suppression of conditioned H2 response. However, the results from the SCI subjects showed that: (1) segment compressive load has no effect on the modulation of the test H1 or conditioned H2 response, (2) the dose-response for the effect of load on post activation depression is reduced, and (3) the loss of post activation depression as a result of chronic paralysis negates further modulation with segment compressive load. These findings suggest that the pathways reorganized from the acute to the chronic state that lead to the loss of post activation depression, also have a diminished capacity to respond to acute episodes of external stimuli like load. These findings have implications to individuals with acute and chronic SCI as we explore new strategies to reorganize tissues after SCI.

The findings from healthy adults in the current study are consistent with our previous work, showing that segment compressive load significantly decreases post activation depression of the soleus H-reflex (Tseng and Shields, 2012). Specifically, an increase in the conditioned H2 amplitude was observed during loading while the tested H1 amplitude remained constant, resulting in a reduction of post activation depression ratio. Furthermore, the magnitude of the loss of post activation depression is scaled according to level of load, with the greatest reduction of post activation depression during the 50% of BW compressive load and the least reduction during the 10% of BW compressive load. Importantly, findings from our studies in healthy adults suggest that load diminished the capacity to gate afferent input via pre-synaptic inhibitory pathways (Tseng and Shields, 2012). Load-induced H-reflex modulation is likely attributed to sensory afferents at multiple sites. Previous research supports that low-threshold cutaneous afferents and joint receptors are likely activated during loading and therefore alter the excitability of spinal neuronal circuits. (Wood and Ferrell, 1984, 1985; Iles, 1996; Knikou and Conway, 2001; Hiraoka, 2003; Nakazawa et al., 2004; Knikou, 2007; Sayenko et al., 2007, 2009; Conway and Knikou, 2008). Thus, segment compressive load, via cutaneous afferents and/or joint mechanoreceptor inputs, decreased the capacity to depress a monosynaptic pathway to a conditioning stimulus and resulted in a reduction of post activation depression (Tseng and Shields, 2012).

The novel findings of this study are that in the absence of supra spinal descending drive in individuals with complete paralysis, we demonstrated that segment load has a weak influence on post activation depression, likely a result of the re-organized spinal circuits. Contrary to findings in healthy adults, the conditioned H2 amplitudes in those with SCI did not increase as a result of applying a compressive load. Furthermore, there was a trend for the test H1 amplitude to decrease as the compressive load increased in the individuals with chronic complete SCI whereas the healthy adults showed no changes in test H1 amplitudes across all levels of loads. As a result of load-induced inhibition of both H1 and H2 responses, post activation depression decreases at the higher dose of compressive load in individuals with chronic SCI, but clearly to a lesser extent than healthy adults. This finding supports our hypothesis that the individuals with SCI will show diminished modulation of

post activation potentiation after SCI. It is known that individuals with chronic complete SCI show impaired post activation depression, defined as a loss of monosynaptic inhibition to a conditioning stimulation (Skinner et al., 1996; Schindler-Ivens and Shields, 2000; Grey et al., 2008). Indeed, the current study observed smaller depression ratios in the SCI group during the baseline session (i.e. unloaded condition) as compared to healthy adults. The possible mechanism is that following SCI the spinal motor neurons become more excitatory than pre injury level as a result of a compromised capacity to gate sensory afferent input at the pre-synaptic Ia terminals (Schindler-Ivens and Shields, 2000; Grey et al., 2008; Shields et al., 2011). It is plausible that for the SCI subjects, the conditioned H2 amplitude is already increased to its plateau value during the unloaded condition and, therefore, cannot be modulated by loading. Accordingly, an increment of limb load is unlikely to produce any further facilitator effect on this inhibitory pathway, demonstrating an increment of conditioned H2 amplitude according to the level of load. Thus, it is not surprising that we observed a diminished modulation of the H-reflex to load in individuals with chronic SCI.

An impaired dose-response relationship between levels of loads and H-reflex responses may be attributed to the type of spinal reorganization that occurs several months following SCI (Schindler-Ivens and Shields, 2000; Shields, 2002; Frigon and Rossignol, 2006; Frigon et al., 2011; Shields et al., 2011). As a result of spinal reorganization, pre synaptic inhibition at Ia afferent terminals via homosynaptic depression is altered and are less responsive to the modulation of load (Thompson et al., 1992; Calancie et al., 1993; Skinner et al., 1996; Schindler-Ivens and Shields, 2000). Importantly, a recent study suggested that the loss of post activation depression after SCI is associated with the level of spasticity (Grey et al., 2008). It is also possible that a loss of supra spinal drive may contribute to the impaired dose response of H-reflex to load (Capaday et al., 1999; Frigon and Rossignol, 2006). It is known that supra spinal descending commands also modulate the excitatory state of the soleus alpha motor neurons via interneuronal pathways (Aymard et al., 2000; Bretzner and Drew, 2005). The H-reflex is not only dependent on the characteristics of sensory inputs but also on the state of the spinal inter-neuronal circuits (Knikou, 2007). Although we verified a persistent low level of background EMG in this study, we do not know the status of the inter-neuronal networks in response to small changes in background EMG across the entire experimental session. However, randomly introducing the loads precluded any systematic influence of any subtle fluctuations in spinal excitability due to inter-neuronal firing. Findings from the SCI group supported that the suppression of post activation depression was minimally influenced by descending drive, therefore, was attributed to the modulation of afferent inputs (i.e. loading).

Although not statistically significant, we observed a trend in the chronic SCI group that was consistent with the control group. Specifically, the post activation depression decreased, at least descriptively, to a greater extent at the higher dose of compressive load. This finding raises the question as to whether repetitive use of mechanical load may regulate the loss of post activation depression over time and serve as a method to trigger a new organization that is more consistent with the healthy populations. A recent animal preparation verified that repeated activation of afferent pathways, particularly via Group I and II afferent inputs may be a critical modulator to normalize post activation depression following SCI (Ollivier-Lanvin et al., 2010). A novel component of this study is that segment load alters gating capacity of the pathway contributing to post activation depression. Perhaps routinely loading paralyzed legs with a precise dose of load based on an individual's body weight will offer an alternative mode of afferent input to attempt to normalize post activation depression after SCI. Clinically, a decreased ability to depress the alpha motor neuron pool via pre synaptic inhibition is thought to be one mechanism associated with spasticity in people with SCI (Schindler-Ivens and Shields, 2000; Grey et al., 2008). Impaired post activation depression does not occur immediately post injury (i.e. acute SCI), but evolves and persists over time,

coincident with ensuing spasticity through spinal circuit reorganization (Schindler-Ivens and Shields, 2000; Shields et al., 2011). The current study demonstrated that this load-induced reduction of post activation depression is mitigated in people with chronic SCI because they have already lost the capacity to depress the H-reflex to a conditioning stimulus. The most important clinical implication of our findings is that limb load, in the ranges used in this study, do not further impair the post activation depression or enhance spasticity in people with chronic SCI, contrary to the observations often reported by clinicians. The clinical observation is that increased muscle stiffness is detected when individuals with chronic SCI are passively moved into an upright position with their limbs loaded. Further study is needed to determine if post activation depression can be sustained longitudinally after SCI by timely doses of limb compressive loads. Future studies are underway to examine the longitudinal effects of compressive loading on spinal circuitry excitability in people with CNS injury.

5. Conclusion

In the absence of descending drive, limb segment load has a minimal influence on post activation depression of the soleus H-reflex in individuals with chronic SCI, a finding that is not consistent in those without SCI. Our findings support that impaired load-induced spinal modulation is associated with the loss of post activation depression in individuals with chronic SCI. Future studies will determine if individuals with acute SCI, who have not lost post activation depression, can sustain their capacity to depress a conditioned H-reflex, by using daily limb loading therapeutic inputs.

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HIGHLIGHTS

- Segment compressive load minimally modulates the soleus H-reflex response in individuals with chronic SCI.
- Diminished spinal reflex modulation to compressive load is associated with a loss of post activation depression in a reorganized spinal cord.
- Findings raise a question as to whether compressive load can influence spinal neuronal reorganization from the acute to the chronic state after SCI.

Fig. 1.

Illustrations of study paradigm (A), cyclically compressive loads (B), and electrical stimulation protocols (C). The study consisted of one baseline session followed by three loading sessions in a random order. The middle panels illustrate the amplitudes and timing of the compressive load applied to the subject's leg across all testing sessions. The bottom traces depict soleus muscle activity and H-reflexes elicited by doublets over time. Arrows indicate the timing when electrical stimuli were delivered to the tibial nerve. H1: test reflex; H2: conditioned reflex, BW: body weight.

Fig. 2.

Lateral view of the experimental setup. An air cylinder connected to a force transducer was placed on the top of the right knee joint and aligned perpendicularly to the longitudinal axis of the lower leg to deliver a cyclically compressive load (gray panel); the force transducer then recorded the net force acting on the lower leg.

Fig. 3.

M-waves and H-reflexes from a typical healthy control and an individual with chronic spinal cord injury across a baseline session, and *load-on* and *load-off* phases of the 50% body-weight load session. Top panels show time series data of paired-pulse electrical stimulation (doublet) in which voltage signals were plotted 10 ms before and 50 ms after each electrical stimulus was delivered. The maximal M-wave (M-max) was overlaid on the bottom right in each top panel. Dashed vertical lines indicate the time when each electrical stimulus was delivered for each doublet. Ten traces of M-waves (M) and H-reflexes (H1: test reflex and H2: conditioned reflex) repeatedly elicited by doublets were overlaid across baseline (A), *load-on* (B), and *load-off* (C) phases.

Fig. 4. Group averages of H-reflexes (A), normalized H-reflexes (B), and background soleus muscle activity across different sessions (C). Gray areas indicate the testing conditions in which three levels of compressive loads were applied (*load-on* phases). Error bars, ± 1 SEM. Asterisks indicate significant post hoc differences between conditions. H1: test reflex; H2: conditioned reflex; RMS: root-mean-square. BW: body weight.

Fig. 5.

Group averages of depression ratios (A) and normalized depression ratios (B) across various levels of compressive loads. Depression ratios obtained during three loading sessions were divided by their baseline mean values and expressed as ratios of the baseline means. Gray areas indicate the loading conditions. H1: test reflex; H2: conditioned reflex; BW: body weight. Error bars, ± 1 SEM. Asterisks indicate significantly post hoc differences between conditions.

Table 1

Subject characteristics.

Subject	Age (yrs)	Sex	Weight (kg)	Height (cm)	NLI	ASIA	Duration of injury (yrs)
<i>SCI group (N = 10)</i>							
S1	50	M	52	178	T1	A	25
S2	64	F	66	175	C8/T1	B	9
S3	17	M	61	178	T6/T7	A	1
S4	33	M	79	196	T7	A	5
S5	47	M	102	178	T4	A	3
S6	26	M	68	191	T8/T9	A	5
S7	42	M	73	183	C6	A	25
S8	30	M	52	163	T7	A	9
S9	47	F	64	160	T4	B	4
S10	46	F	86	178	T7/T8	B	24
Mean ± SD	40.2 ± 13.7	3F, 7M	70.3 ± 15.5	178.0 ± 10.9	–	–	11.0 ± 9.7
<i>Control group (N = 10)</i>							
Mean ± SD	24.3 ± 2.5	7F, 2M	67.6 ± 16.5	169.2 ± 10.0	–	–	–

SCI: spinal cord injury; NLI: neurological level of injury; The NLI is defined as most caudal segment with normal motor and sensory function for classification of spinal cord injury. ASIA: American spinal injury association. The severity of injury is quantified based on ASIA Impairment Scale: A = complete; no motor or sensory function is preserved in the sacral segments S4–S5; B = incomplete; sensory but not motor function is preserved below the neurological level and includes the sacral segments S4–S5; C = incomplete; motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade <3; D = incomplete; motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more. E = normal; motor and sensory function are normal. M: male; F: female; SD: standard deviation.