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Vibration Training after Chronic Spinal Cord Injury: Evidence for Persistent Segmental Plasticity

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Abstract

H-reflex paired-pulse depression is gradually lost within the first year post-SCI, a process believed to reflect reorganization of segmental interneurons after the loss of normal descending (cortical) inhibition. This reorganization co-varies in time with the development of involuntary spasms and spasticity. The purpose of this study is to determine whether long-term vibration training may initiate the return of H-reflex paired-pulse depression in individuals with chronic, complete SCI. Five men with SCI received twice-weekly vibration training (30 Hz, 0.6 g) to one lower limb while seated in a wheelchair. The contra-lateral limb served as a within-subject control. Paired-pulse H-reflexes were obtained before, during, and after a session of vibration. Untrained limb H-reflex depression values were comparable to chronic SCI values from previous reports. In contrast, the trained limbs of all 5 participants showed depression values that were within the range of previously-reported Acute SCI and Non-SCI H-reflex depression. The average difference between limbs was 34.98% ($p = 0.016$). This evidence for the return of H-reflex depression suggests that even for people with long-standing SCI, plasticity persists in segmental reflex pathways. The spinal networks involved with the clinical manifestation of spasticity may thus retain adaptive plasticity after long-term SCI. The results of this study indicate that vibration training may hold promise as an anti-spasticity rehabilitation intervention.

Keywords

H-reflex; post-activation depression; pre-synaptic inhibition; paralysis; spasticity

Introduction

Neural and musculoskeletal adaptations after spinal cord injury (SCI) lead to a range of secondary health conditions that limit post-SCI quality of life. Many rehabilitation interventions attempt to subsidize lost sources of stress, such as mechanical load or muscular

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contraction, as a way to prevent negative adaptations of paralyzed tissues. The optimal delivery method and dose of tissue stress is an area of extensive research.

Vibration in the frequency range of skeletal muscle contraction (30–60 Hz [10]) is a key source of mechanical stress in the non-paralyzed neuro-musculoskeletal system. The loss of this pervasive source of load may play an important role in the precipitous decline of bone integrity experienced by patients with SCI [1]. Studies that reintroduce vibration as an antiosteoporosis countermeasure are underway [8, 17]. Vibration is also being investigated as a method to reduce spasticity [2, 14], one of the most prevalent and bothersome secondary health conditions of SCI [6]. Our previous work has characterized the acute neurophysiologic response to vibratory load after SCI [5]. We observed a long-lasting (>1 minute) enhancement of H-reflex post-activation depression after acute vibration of a constrained limb segment. The time scale of this effect is far longer than would be required for normalization of pre-synaptic inhibition or primary afferent depolarization, two mechanisms believed to underlie H-reflex post-activation depression (<10 seconds [7]). This evidence for persistent effects of vibration on spinal reflex mechanisms prompted us to consider whether consecutive exposure to vibration, such as in a training protocol, could yield cumulative changes in H-reflex depression. This possibility could be of importance to individuals with SCI who experience spasticity, which has its roots in maladaptive reorganization of the paralyzed spinal circuitry.

H-reflex paired-pulse depression is gradually lost within the first year post-SCI [15], a process believed to reflect reorganization of segmental interneurons after the loss of normal descending (cortical) inhibition [3]. This reorganization is believed to reduce the efficacy of spinal pre-synaptic inhibition, which is observable as reduced post-activation depression of H-reflex amplitude during repetitive stimulation. Although there are many contributing causes of spasticity, this decreased ability to depress H-reflexes is a covariant of spasticity after chronic SCI [9]. Restoring H-reflex depression in individuals with SCI could indicate that neurophysiologic plasticity persists in the spinal circuitry that serves as the final common pathway for involuntary spasms.

The purpose of this study is to determine whether long-term unilateral vibration training alters H-reflex paired-pulse depression in individuals with chronic, complete SCI. We hypothesized that vibration training would restore H-reflex depression, which is typically lost after SCI.

Methods

Subjects

Five men with chronic, complete SCI participated in the study (Table 1). The study methodology was approved by the University of Iowa Human Subjects Institutional Review Board. All subjects provided written informed consent before participating in the study. Participants were recruited from an ongoing study of vibration training as an anti-osteoporosis measure after SCI [8]. In brief, these participants received twice-weekly vibration training (30 Hz, 0.6 g) to one lower limb while seated in a wheelchair. The contra-

lateral limb served as a within-subject control. Subjects recruited for the present study had received an average of 47 vibration sessions over an average of 29 weeks.

Experimental Paradigm

At the end of the vibration training protocol, participants underwent a single session of H-reflex testing in the trained and the untrained limb. Subjects sat in a custom wheelchair with the foot on a vibrating platform (Figure 1) [11]. Straps over the top of the knee and at the foot secured the lower limb to the vibrating surface. A servo-control system (Ling Dynamic Systems Ltd, Royston, Herts, UK), applied vertical oscillations to the lower leg. Vertical peak-to-peak displacement of the lower leg segment at 0.6 *g* was 0.33 mm.

At the outset of the study, maximal soleus M-waves (MaxM) were obtained, followed by H-reflexes at a target amplitude (15–25% MaxM). The experiment consisted of three phases: Before, During, and After vibration. In each phase, paired-pulse stimuli (doublets) were given to elicit an unconditioned H-reflex (H1) and a conditioned H-reflex (H2). We expected that H2 amplitude would be lower, demonstrating post-activation depression. During the vibration phase, participants received doublet stimulation during vibration of the lower limb for 2 minutes. 5 minutes after the end of the vibration phase, we repeated all doublet stimuli in the After phase.

Electrophysiologic Measurements

Bipolar Ag-AgCl surface electromyographic (EMG) electrodes recorded soleus H-reflexes and M waves. The skin over the soleus muscle was abraded and cleaned with alcohol swabs. A recording electrode was placed 2 cm lateral to midline of the calf and 2 cm distal to the lowest palpable extent of the gastrocnemius. A reference electrode was placed on the anterior aspect of the right tibia. EMG signals were on-site preamplified with a gain of 35, then further amplified by 1,000 to 10,000 (Therapeutics Unlimited, Iowa City, IA). A constant-current electrical stimulator (Digitimer Ltd, Welwyn Garden City, Herts, UK) delivered square waves with a pulse width of 1000 μ s (400V). The stimulator was triggered by a digital pulse from a data acquisition board (USB-6259, National Instruments Corp., Austin, TX) controlled by LabVIEW software (National Instruments, Austin, TX). The stimulating electrode (1 cm diameter) was secured over the tibial nerve in the popliteal fossa, with a dispersive electrode (10 $\times$ 10 cm) over top of the femoral condyles.

To obtain maximal M-waves, the stimulator output was increased until M-wave amplitude no longer continued to increase. The output was then adjusted to 120% of this value and three maximal M-waves were obtained. The stimulator output was then adjusted to elicit a stable H-reflex equivalent to ~50% of the maximal H-reflex response on the ascending limb of the H-reflex recruitment curve. These H-reflexes corresponded to 15 – 25% MaxM. During doublet testing, the stimulator delivered paired stimuli with an inter-pulse interval of 500 ms every 15 seconds. We obtained a minimum of 10 doublets Before vibration, 5 doublets During vibration, and 10 doublets After vibration.

Data Analysis

Data were analyzed with custom Matlab software (MathWorks, Natick, MA). Raw EMG was zero offset, and then paired H-reflexes were manually identified as H1 and H2. H-reflex peak-to-peak amplitude was computed and expressed as a percentage of H-reflex amplitude in the baseline condition (HB). This provided an index of the stability of H-reflex recruitment throughout the experiment. To quantify post-activation depression of H2, we calculated the depression ratio: $100 * (HB - H2) / HB$. Our previous work [5] indicated that during vibration in participants with SCI, H1 is unstable and is occasionally absent. This limits its suitability in calculations of H2 depression. Using HB in the calculation of H2 depression provided a more meaningful estimate of H2 behavior in both the vibration and non-vibration experimental phases. A depression ratio of 0 indicated that no post-activation depression occurred, while a ratio of 100 indicated that depression of H2 was complete (equal to the HB amplitude).

Statistical Analysis

For each subject we computed the mean of the baseline H-reflex (HB) and the mean of H1 and of H2 at each experimental condition (Before, During, and After). To verify the consistency of H-reflex recruitment across the experiment, we used a repeated-measures 1-way ANOVA to contrast HB with each mean H1 value. Significance was set at $p < 0.05$.

For each subject we computed the mean depression ratio for each limb (trained, untrained) in each of the three experimental conditions (Before, During, and After). We analyzed these data via a two-way (condition $\times$ limb) repeated measures ANOVA with post-hoc (Tukey) tests as indicated ($\alpha = 0.05$). Because depression ratio did not differ Before and After vibration (results shown below), we pooled these conditions and compared to During vibration with a non-parametric test (Mann-Whitney Rank Sum).

Results

Baseline H-reflexes (HB) were elicited at 24.73% (7.32) and 25.26% (6.10) of MaxM for the trained and untrained limbs, respectively ($p = 0.949$). HB did not differ from H1 in Before ($p = 0.801$) or from H1 in After ($p = 0.194$) but as expected, H1 diminished when vibration was applied ($p = 0.012$). This validates the use of HB rather than H1 for calculation of depression ratio.

Figure 2 depicts all H1 and H2 values normalized to the baseline H-reflex (HB). A significant main effect of Condition indicated that both H1 and H2 were lower During vibration as compared to Before or After vibration (both $p < 0.002$). No differences existed between trained and untrained limbs ($p > 0.05$).

Figure 3A depicts the H2 depression ratio for the three experimental conditions. A significant main effect of Condition indicated that depression ratio was higher During vibration than Before or After (both $p < 0.006$). No differences existed between trained and untrained limbs ($p > 0.05$).

Because no difference in depression ratio existed between the Before and After conditions, we pooled these data by obtaining the mean for both conditions for each subject (Figure 3B). For the pooled Before/After data, 4 of 5 participants showed a between-limb difference in depression ratio in the hypothesized direction (Trained > Untrained), the average difference between limbs was 29.19%, but the limbs did not differ significantly ($p = 0.095$). During vibration, all 5 participants showed a between-limb difference in depression ratio in the hypothesized direction, the average difference between limbs was 34.98%, and the limbs differed significantly ($p = 0.016$). Multiple linear regression revealed no significant relationships between demographic covariates and the between-limb difference in depression ratio. ($P = 0.876, 0.823$ and 0.616 for # sessions, age, and SCI years, respectively, for the pooled Before/After data. $P = 0.903, 0.601, 0.674$ for # sessions, age, and SCI years, respectively, for During vibration data.)

Discussion

The purpose of this study was to determine whether long-term vibration training alters H-reflex paired-pulse depression in individuals with chronic, complete SCI. We hypothesized that vibration training would restore H-reflex depression, which is typically lost after SCI. All five participants demonstrated evidence of enhanced H-reflex depression in the trained limb (Figure 3B). Our previous work provides context for the magnitude of depression observed in these participants. Schindler-Ivens and Shields [15] demonstrated that conditioned H-reflex amplitude (analogous to H2 in the present study) was ~30% of H1 for participants with acute SCI and for non-SCI individuals. Conditioned H-reflexes in participants with chronic SCI (> 2 years) were ~60%, indicating a loss of H-reflex depression with the passage of time post-SCI. In the present cohort of individuals with chronic SCI (> 3 years), H2 amplitude was 28.9% of H1 for the trained limb and 58.1% of H1 for the untrained limb (pooled Before and After data). Thus for the present cohort, 1) untrained limbs demonstrated H2 depression similar to chronic SCI, and; 2) trained limbs demonstrated H2 depression similar to acute SCI.

Likewise, Chang and coauthors [5] observed depression ratios in neurologically-intact subjects that were commensurate with depression ratios observed in the trained limbs of the present cohort. Depression ratio in that study's non-SCI subjects was 72%, compared to 71% in the trained limbs of the current participants (Figure 3B). In contrast, depression ratio for the untrained limbs was only 42%. Thus when viewed in the context of our previous reports, constrained-limb vibration training initiates a return of H-reflex depression in trained limbs during application of a vibratory stimulus. A strong trend existed for normalization of H-reflex depression before and after application of the vibratory stimulus as well. Four of five participants showed a between-limb difference in depression ratio without vibration (Figure 3B, $p = 0.095$), suggesting that adaptations to vibration training may be observable beyond the vibration intervention itself. Normalization of H-reflex depression during the resting state could be of particular importance for rehabilitation interventions.

The constrained limb vibration model used in the present study provides us with an opportunity to carefully dose vibration as a physiologic stimulus. We have investigated the

effect of various levels of gravitational acceleration [4] and of overlaying various limb compressive loads during vibration [16]. It is more difficult to draw mechanistic conclusions from whole-body vibration (WBV) studies, in which vibration and limb compressive load are modified by influences from vestibular activation, visuomotor systems, and additional sources of afferent input (e.g. joint compression). Nonetheless, most WBV studies support that vibration of the entire body may trigger adaptations in H-reflexes and clinical measures of spasticity (see [13] for review). Sayenko and coauthors observed short-term reductions of H-reflex amplitude during WBV, although the effect was blunted in participants with SCI compared to neurologically-intact subjects [14]. Ness and Field-Fote observed long-lasting (> 8 days) reductions in clinical measures of spasticity between WBV sessions in a 12-week intervention [12]. The present study suggests that the spinal networks regulating the clinical manifestation of spasticity may likewise retain adaptive plasticity after long-term SCI. The restoration of H-reflex depression in this cohort's trained limbs supports that vibration training merits further study as an anti-spasticity rehabilitation intervention.

Conclusion

Long-term (~29 weeks) exposure to isolated limb segment vibration initiated a return of H-reflex post-activation depression in participants with chronic, complete SCI. This finding suggests that even for people with long-standing SCI, plasticity persists in the neural circuitry regulating the monosynaptic reflex arc. Future studies are needed to determine the extent to which vibration-induced plasticity may affect the clinical manifestation of spasticity.

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Highlights

- H-reflex depression is lost after SCI due to maladaptive neural reorganization.
- Vibration training initiated normalization of H-reflex depression in trained limbs.
- Vibration-induced plasticity may be harnessed by rehabilitation interventions.

Figure 1.
Schematic representation of the constrained-limb vibration system.

Figure 2. Mean (SE) H1 and H2 normalized to HB Before (leftmost bars), During (grey region) and After vibration (rightmost bars) for the trained and untrained limbs. * = significantly different from Before and After, $p < 0.002$.

Figure 3.

A) Mean (SE) Depression ratio ($100 \times (\text{HB}-\text{H2})/\text{HB}$) for the Before, During and After conditions for the trained and untrained limbs. * = significantly different from Before and After, both $p < 0.006$. B) Mean (SE) depression ratio for the pooled Before/After condition versus During vibration. The dotted line indicates the depression ratio we previously published for non-SCI control subjects [5]. * = significantly different from the untrained limb ($p = 0.016$). Before/After condition; 4 of 5 subjects showed a training effect ($p = 0.095$).

Table 1

Subject Demographics

Subject	Gender	Age	Years post-SCI	SCI level	Vibration Sessions
1	M	19	3.3	T8	65
2	M	27	7.6	T9	64
3	M	49	5.3	T4	48
4	M	31	5.6	T10	35
5	M	35	13.3	T9	25