Operant conditioning to increase ankle control or decrease reflex excitability improves reflex modulation and walking function in chronic spinal cord injury

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Manella KJ, Roach KE, Field-Fote EC. Operant conditioning to increase ankle control or decrease reflex excitability improves reflex modulation and walking function in chronic spinal cord injury. J Neurophysiol 109: 2666–2679, 2013. First published March 6, 2013; doi:10.1152/jn.01039.2011.—Ankle clonus is common after spinal cord injury (SCI) and is attributed to loss of supraspinally mediated inhibition of soleus stretch reflexes and maladaptive reorganization of spinal reflex pathways. The maladaptive reorganization underlying ankle clonus is associated with other abnormalities, such as coactivation and reciprocal facilitation of tibialis anterior (TA) and soleus (SOL), which contribute to impaired walking ability in individuals with motor-incomplete SCI. Operant conditioning can increase muscle activation and decrease stretch reflexes in individuals with SCI. We compared two operant conditioning-based interventions in individuals with ankle clonus and impaired walking ability due to SCI. Training included either voluntary TA activation (TA↑) to enhance supraspinal drive or SOL H-reflex suppression (SOL↓) to modulate reflex pathways at the spinal cord level. We measured clonus duration, plantar flexor reflex threshold angle, timed toe tapping, dorsiflexion (DF) active range of motion, lower extremity motor scores (LEMS), walking foot clearance, speed and distance, SOL H-reflex amplitude modulation as an index of reciprocal inhibition, presynaptic inhibition, low-frequency depression, and SOL-to-TA clonus coactivation ratio. TA↑ decreased plantar flexor reflex threshold angle (−4.33°) and DF active range-of-motion angle (−4.32°) and increased LEMS of DF (+0.8 points), total LEMS of the training leg (+2.2 points), and nontraining leg (+0.8 points), and increased walking foot clearance (+4.8 mm) and distance (+12.09 m). SOL↓ decreased SOL-to-TA coactivation ratio (−0.21), increased nontraining leg LEMS (+1.8 points), walking speed (+0.02 m/s), and distance (+6.25 m). In sum, we found increased voluntary control associated with TA↑ outcomes and decreased reflex excitability associated with SOL↓ outcomes.

ankle clonus; soleus stretch reflex; reciprocal inhibition; presynaptic inhibition; antagonist coactivation

IN PERSONS WITH SPINAL CORD INJURY (SCI) (see Glossary for complete list of abbreviations), walking function is impaired by reduced ability to produce voluntary muscle contraction and by hyperactive spinal reflex activity (hyperreflexia). In those with motor-incomplete SCI, the impaired voluntary muscle contraction arises primarily from corticospinal tract disruption, but reduced corticomotor excitability, maladaptive cortical changes (Beekhuizen and Field-Fote 2005, Thomas and Gorassini 2005), and limited motor unit rate modulation (Zijdewind and Thomas 2003) also contribute to this impairment. During normal human walking, control of the tibialis anterior (TA) muscle is strongly related to corticospinal input (Capaday et al. 1999; Schubert et al. 1997). Evidence demonstrates that TA corticospinal excitability is enhanced with dorsiflexion (DF) imagery during imagined walking in nondisabled individuals (Bakker et al. 2008), functional electrical stimulation after chronic central nervous system lesions (Thompson et al. 2009), and locomotor training in persons with chronic motor-incomplete SCI (Thomas and Gorassini 2005).

Beyond the impairment of voluntary control, SCI also results in loss of modulation of involuntary reflex circuits. Clonus is a common manifestation of stretch reflex hyperexcitability (Decq 2003). Clonus manifests as involuntary 5-7 Hz joint oscillations (Wallace et al. 2005) and commonly occurs at the ankle in individuals with motor-incomplete SCI and other forms of central nervous system pathology. Clonic soleus (SOL) activity due to inadequate modulation of the SOL stretch reflex may impede walking progression (Yang et al. 1991), compromise independent walking (Beres-Jones et al. 2003), and restrict quality of life in individuals with motor-incomplete SCI.

Reflex pathophysiology contributes to ankle clonus after SCI (Katz and Rymer 1989). Disrupted supraspinal input and maladaptive reorganization of spinal reflex pathways give rise to impaired modulation of peripheral sensory feedback (Field-Fote 2004; Hultborn 2003) and aberrant reflex responses (Gracies 2005); exaggerated SOL stretch reflexes emerge (Davis et al. 1995; Dietz 1997) and contribute to clonus in plantar flexors (PF). After SCI, impaired SOL disynaptic reciprocal Ia inhibition (RI) manifests as SOL coactivation during TA contractions (Boorman et al. 1996), SOL reciprocal facilitation after TA activation (a reversal of the normal response) (Crone and Nielsen 1994; Crone et al. 2003; Morita et al. 2001), and antagonist response to SOL or TA tendon tapping (Xia and Rymer 2005). In individuals with motor-incomplete SCI, decreased SOL presynaptic inhibition (PI) contributes to SOL stretch reflex hyperexcitability (Dietz 2001; Faist et al. 1994).

Increased SOL motoneuron excitability, reduced postactivation depression of repeated stretch activations, and antagonist coactivation may promote clonus. Elevated SOL H-reflex-to-M-wave ratio (H/M), found in individuals with clonus (Koelman et al. 1993), has been associated with increased PF reflex threshold angle (RTA) (the angle at clonus onset) (Manella 2011) and number of clonic oscillations (Katz and Rymer 2005). In individuals with motor-incomplete SCI, decreased SOL presynaptic inhibition (PI) contributes to SOL stretch reflex hyperexcitability (Dietz 2001; Faist et al. 1994).
ticity and electromyography (EMG) SOL-to-TA cocontraction ratio (Levin and Hui-Chan 1994), suggesting a relationship between the amount of voluntary TA control and SOL hyperexcitability. After motor-incomplete SCI, coactivation of SOL and TA (SOL/TA coactivation) during clonus has been reported (Manella 2011). Therefore a myriad of factors, including SOL reflex hyperexcitability, diminished SOL LFD, decreased voluntary DF activation, and SOL/TA coactivation appear to influence clonic activity.

Control of both voluntary movement and reflex activity is known to be modifiable with operant conditioning training, wherein reward is contingent upon performance of a targeted motor task. Operant conditioning training induces neuroplasticity in supraspinal and spinal reflex pathways. Such training increases voluntary EMG responses (Brucker and Bulaeva 1996; Seymour and Bassler 1977; Stein et al. 1990) and firing rates of spared motor units (Stein et al. 1990) after motor-incomplete SCI and decreases stretch reflex excitability in individuals with and without spasticity (Evatt et al. 1989; Segal 1997; Wolf and Segal 1996). Successful SOL H-reflex suppression in animals (Wolpaw and Herchenroder 1990; Wolpaw and Chen 2001, 2006) and humans (Thompson et al. 2006, 2009, 2013) provides clear evidence of activity-dependent plasticity in spinal circuitry induced by operant conditioning training.

Based on the foregoing evidence that both impaired voluntary DF control and PF hyperexcitability contribute to functional deficits and spasticity in persons with spastic hypertonia, we designed two operant conditioning-based interventions intended to improve ankle motor control in individuals with motor-incomplete SCI. The interventions were as follows: 1) TA EMG activation (TA↑) to enhance supraspinal drive to spinal circuits; and 2) SOL H-reflex suppression during voluntary DF (SOL↓) to modulate reflex pathways at the spinal cord level. TA↑ was intended to improve ability to voluntarily drive corticospinal activation of spared TA motoneurons and activate inhibitory interneurons (Iles and Pisini 1992) comprising SOL RI and PI pathways. We hypothesized TA↑ would be associated with increased DF active range of motion (ROM) and DF strength, foot clearance in swing phase, and walking speed and distance. SOL↓ was intended to suppress SOL H-reflex amplitude responses during DF. We hypothesized SOL↓ would be associated with enhanced SOL H-reflex LFD, decreased SOL/TA coactivation, decreased clonus duration, decreased PF RTA, and increased toe tapping ability. We compared TA↑ and SOL↓ interventions and assessed 15 outcomes: 1) two measures of ankle clonus (clonus duration, PF RTA); 2) two measures of ankle motor control (toe tap test, DF active ROM); 3) four measures of lower extremity strength (DF strength, PF strength, (training and nontraining leg)]; 4) three walking-related measures (foot clearance, speed, and distance); and 5) four neurophysiological measures (SOL H-reflex RI, PI, and LFD, and SOL/TA coactivation). Secondarily, we also explored relationships among changes in outcome measures to determine if neurophysiological mechanisms are associated with changes in training, clinical, or walking measures.

**Glossary**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AIS</td>
<td>ASIA Impairment Scale</td>
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<tr>
<td>ASIA</td>
<td>American Spinal Injury Association</td>
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<tr>
<td>CPN</td>
<td>Common peroneal nerve</td>
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**METHODS**

**Research Participants**

Of 16 volunteers recruited from The Miami Project to Cure Paralysis research subject registry, 12 signed written consent and were enrolled in the study (Fig. 1). Participants were 16–75 yr old, with stable motor-incomplete SCI (>1 yr), lesion level of T12 or above, and ability to walk 6 m with devices or assistance as needed. All participants exhibited an American Spinal Injury Association (ASIA) Impairment Scale D (AIS D) category of SCI (ASIA 2002; Marino et al. 2003), and in at least one lower extremity had a palpable TA contraction, a SOL H-reflex response, and ankle clonus elicited by manual PF stretch. Participants were without other conditions impairing walking function, or cognitive deficits that would impede adherence to the study protocol. Participants were stratified according to toe tap score (toe taps in 10 s) into one of two categories, indicating extent of voluntary ankle control: low control (<15 taps) and high control (>15 taps) (Fig. 1), with each training session lasting ~2 h, including setup time. Following stratification, participants were randomly assigned to the TA↑ group (n = 6, mean age = 44.2 yr, 6 men) or the SOL↓ group (n = 6, mean age = 45.2 yr, 4 men) (Table 1). We trained the ankle with most severe clonus as assessed by clonus duration after manual PF stretch. Training was conducted three times weekly for 5 wk for a total of 15 sessions (3 baseline and 12 training sessions) (Fig. 1). Testing was performed the week before and the week after training. All 12 participants completed the study (mean age = 44.6 yr, 10 men).

The study was conducted in accordance with the standards of the Declaration of Helsinki and was approved by the University of Miami Human Subjects Research Office.

**Clinical Measures of Ankle Clonus, Motor Control, and Walking**

Ankle clonus. The Ankle Clonus Drop Test (Manella 2011) provides reliable ankle clonus measures that correlate with the Spinal Cord Assessment Tool for Spastic reflexes clonus score (Benz et al. 2005) and SOL H/M (Manella 2011). Briefly, with the individual sitting, the foot was placed on a 10-cm high platform, the leg was lifted to a height of 10 cm above the platform and released; impact of the forefoot with the platform edge provided a SOL stretch to elicit clonus (Fig. 2). Kinematic ankle angles and SOL and TA EMG activity were recorded for three trials. Clonus duration was measured from first PF deflection after platform impact to last PF deflection of at least 1° greater than the rest angle. The PF RTA (Manella 2011)
was identified kinematically as first PF deflection after platform impact. Mean clonus duration and PF RTA were calculated. 

Ankle motor control. Timed toe tapping (Knights and Moule 1967) was performed seated with the forefoot positioned on a pressure-sensitive foot switch embedded in a platform. DF activated the foot switch that triggered data acquisition (Spike 2 version 7, Cambridge Electronic Design, Cambridge, UK). With the heel maintaining platform contact, the participant performed voluntary concentric and eccentric DF contractions as quickly as possible for 10 s for four trials with 60-s rest periods between trials. Mean number of taps achieved in the best three of four trials was calculated. 

Voluntary DF active ROM was recorded using an eight-camera Peak Motus 8.5 motion analysis system (Vicon, Centennial, CO). Reflective markers were placed laterally on the fifth metatarsal head, malleolus, heel, and knee. In sitting, hip and knee were flexed to 90° and 30°, respectively, with the lower leg supported allowing unrestricted ankle motion. Three trials of maximal voluntary DF and 5 s of relaxation were performed; mean maximum DF angle was calculated.

Bilateral lower extremity strength was assessed using ASIA lower extremity motor scores (LEMS) (ASIA 2002; Marino et al. 2003). With the subject supine, hip flexors, knee extensors, DF, great toe extensor, and PF were graded from 0 (no palpable contraction) to 5 (maximal resistance against gravity); LEMS for DF, PF, training leg, and nontraining leg were recorded.

Walking function. Foot clearance and walking speed were analyzed using an eight-camera Peak Motus 8.5 motion analysis system (Vicon); data were sampled at 60 Hz, smoothed (zero-lag Butterworth filter), and low-pass filtered (6 Hz). Twenty-one reflective markers were placed bilaterally at lateral fifth metatarsal head, malleolus, heel, and knee, and greater trochanter, anterior superior iliac spine, posterior wrist, lateral elbow, and shoulder; and at C7, T10, and the sacrum. Participants, wearing a safety harness, walked with assistance and/or devices as needed at their fastest comfortable speed over a 6-m walkway for three trials. Foot clearance, defined as maximal vertical excursion of the fifth metatarsal marker, was quantified for three swing phases for each trial. Walking speed was calculated for the central 4 m of each trial. Mean foot clearance and speed were computed. Distance traversed during a 2-min period was determined by participants walking, with assistance and/or devices as needed, at fastest comfortable speed around an 80-ft. (24.39 m) track.

Neurophysiological Tests

SOL H-reflexes (peak-to-peak amplitude, mV) in response to RI, PI, and LFD conditioning stimuli were recorded using surface electrodes (interelectrode distance, 36 mm) positioned as described by Rainoldi et al. (2004). SOL electrodes were placed at midline, 10 cm proximal to the calcaneus. Instrumentation included a constant-current stimulator (Digitimer DS7A, Digitimer, Hertfordshire, UK), AC amplifier (Grass PS511, Grass Technologies, West Warwick, RI), and analog-to-digital converter (CED 1401, Cambridge Electronic Design). Interstimulus intervals (ISIs) were controlled with an electrical

Fig. 1. Methodological design of study. RI, reciprocal inhibition; PI, presynaptic inhibition; LFD, low-frequency depression; SOL/TA, soleus/tibialis anterior; PF, plantar flexor; DF, dorsiflexion; ROM, range of motion; LE, lower extremity; MVC, maximum voluntary contraction.
Table 1. Analysis of differences in participant baseline characteristics and preintervention outcome measures between TA and SOL groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>TA†</th>
<th>SOL†</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Age, yr</td>
<td>44.2±12.0</td>
<td>45.2±12.8</td>
<td>1.00</td>
</tr>
<tr>
<td>Postinjury, yr</td>
<td>10.8±10.0</td>
<td>10.8±08.8</td>
<td>1.00</td>
</tr>
<tr>
<td>Sex</td>
<td>6 men</td>
<td>4 men, 2 women</td>
<td>0.12 ($^a$)</td>
</tr>
<tr>
<td>Injury level</td>
<td>C7 (median)</td>
<td>C5 (median)</td>
<td>0.39 ($^a$)</td>
</tr>
<tr>
<td>AIS</td>
<td>D (all)</td>
<td>D (all)</td>
<td>N/A</td>
</tr>
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Clinical measures

- **Clonus duration, s**: 11.3±14.5 vs. 12.4±10.2, 0.75
- **PF RTA**: 83.7±5.5 vs. 85.2±7.2, 0.75
- **Toe Tap Test Score**: 13.5±10.9 vs. 11.5±6.3, 0.75
- **DF active ROM**: 96.9±13.7 vs. 112.4±11.8, 0.05*
- **DF LEMS**: 3.5±1.1 vs. 3.8±0.8, 0.55
- **PF LEMS**: 2.5±0.8 vs. 2.5±0.6, 0.78
- **Training leg LEMS**: 17.3±3.4 vs. 16.2±3.2, 0.42
- **Nontraining leg LEMS**: 22.5±2.0 vs. 19.2±2.8, 0.04*

Walking measures

- **Foot clearance, mm**: 5.0±2.0 vs. 5.1±1.6, 0.87
- **Speed, m/s**: 0.29±0.26 vs. 0.14±0.08, 0.15†
- **Distance, m**: 44.9±49.3 vs. 21.3±17.2, 0.52†

Neurophysiological measures

- **RI SOL H-reflex, %**: 98.9±4.5 vs. 99.6±1.1, 0.87
- **PI SOL H-reflex, %**: 7.8±5.8 vs. 4.2±1.6, 0.20
- **LFD SOL H-reflex, %**: 91.9±16.5 vs. 95.0±10.0, 0.75
- **SOL/TA coactivation ratio**: 0.49±0.23 vs. 0.52±0.39, 0.63

Values are means ± SD, Mann-Whitney U-test for all analyses, except $^a$test for nominal data. TA, tibialis anterior; TA†, TA EMG activation; SOL, soleus; SOL†, SOL H-reflex suppression; C, cervical; AIS, American Spinal Injury Association Impairment Scale (ASIA, 2002); PF, plantar flexor; RTA, reflex threshold angle; DF, dorsiflexion; ROM, range of motion; LEMS, lower extremity motor score; RI, reciprocal inhibition as a %control reflex; PI, presynaptic inhibition as a %M-wave maximum amplitude; LFD, low-frequency depression as a %control reflex. *Significant difference (P ≤0.05). †Large, but not significant, difference.

A peripheral nerve stimulator (Grass S88, Grass Technologies). A peripheral nerve stimulator (MimiStim MS-IVA, Life-Tech, Stafford, TX) was used to locate the posterior tibial nerve (PTN) in the popliteal fossa, common peroneal nerve (CPN) distal to the fibular head, and femoral nerve (FN) in the femoral triangle. Cathodes were placed at the nerve site where the largest muscle contraction was evoked with lowest stimulus intensity; anodes were placed on the patella medially for PTN, laterally for CPN, and superiorly for FN stimulation. Stimulus intensity (mA) was maintained between 10 and 30% M-wave maximum amplitude (Mmax) (Crone et al. 1990).

**RI test.** For testing RI of the SOL H-reflex (Crone et al. 1987), TA electrodes were placed on the muscle belly, lateral to tibial crest and at midpoint between tibial tuberosity and intermalleolar line. Twenty interleaved test (PTN) and conditioned (CPN-PTN, 2 ms ISI) reflexes were evoked at 0.10 Hz. RI testing was repeated using CPN-PTN conditioning stimuli at 3-ms ISI. The conditioned reflex amplitude was normalized to the test amplitude and expressed as percentage (%) of control reflex: for each ISI interval, the mean %RI was calculated, and smallest mean %RI was selected.

**PI test.** PI of the SOL H-reflex was assessed using heteronymous SOL H-reflex facilitation (Faist et al. 1994). Electrodes were placed on quadriceps of the training leg at midline on the muscle belly, 15 cm proximal to the patella. A 0.5-ms PTN test pulse was administered prior to a 0.1-ms FN conditioning pulse. FN stimulus intensity was four times motor threshold. The ISI at onset of SOL H-reflex facilitation was identified and increased by 0.4 ms. Twenty interleaved test and conditioned reflexes were evoked at 0.10 Hz. The difference between test and conditioned reflex amplitudes was expressed as a percentage of Mmax. Values ranged from 2 to 18%, consistent with Faist et al. (1994). The largest %PI was selected for analysis.

**LFD test.** SOL H-reflexes were evoked using paired-pulse PTN stimuli with ISI of 1 s. Ten trials with 10-s rests between trials were recorded. The amplitude of the conditioned (second) response was expressed as percentage of the control (first) reflex amplitude (%LFD); mean %LFD was calculated (Field-Fote et al. 2006).

**Coactivation during clonus.** SOL and TA EMG activity were recorded during the ankle clonus test (described above). The coactivation ratio of SOL and TA EMG bursts (±2 SD mean resting EMG) during a 2-s window of clonus was calculated using customized software (MATLAB, The MathWorks, Natick, MA) (Manella 2011). Mean SOL/TA coactivation ratio for three trials was calculated.

**Training Procedures.**

Surface recording electrodes were placed after standard skin preparation. For both interventions, the participant was seated with ~100° hip flexion, 70° knee flexion, and 120° ankle PF; the training foot was positioned on a foot switch embedded in a platform. A shoe was worn if foot-switch activation was achieved with it on; if not, then a sock and shower slipper were used. An auditory signal cued the participant to perform DF at 0.10 Hz for 30 repetitions; 10 bouts of 30 repetitions were performed with 60-s rest intervals between each bout. During baseline testing, no visual or auditory feedback was provided. During training EMG biofeedback and a visual tally of the number of repetitions that met or exceeded target during each bout were displayed (methods for determining target TA† and SOL† EMG are described below in the respective sections). Immediate verbal reward of “good job” or similar accolade was given and faded to summary feedback upon 80% success rate (number of repetitions exceeding target/total repetitions) (Fig. 1).

**TA†.** TA electrodes were placed as described previously. EMG signals were amplified (×2k) (Grass amplifier, Grass Technologies), notch filtered (60 Hz), band-pass filtered (10–1,000 Hz), sampled at 1 kHz, full-wave rectified, and smoothed (RMS, 8-ms moving average filter). The foot switch was activated by DF, and triggered a transistor-transistor logic input to an analog-to-digital converter (CED 1401, Cambridge Electronic Design). For each participant, at session start, three 3-s TA maximal voluntary contractions (MVCs) were performed with 60-s rest intervals. Mean MVC peak amplitude was computed, and %MVC amplitude target for the session was identified. TA EMG biofeedback using customized software (Spoke 2, version 7, Cambridge Electronic Design) was displayed on a split screen (Fig. 3A). On the right, the %MVC amplitude target was displayed (horizontal line), and a vertical bar moved up or down reflecting increasing or decreasing TA EMG activity. Instructions were to dorsiflex the foot and move the TA EMG bar above the target line; when the target was exceeded, the screen flashed green. On the left side of the screen, reward, EMG, and foot-switch activations were displayed; a gold icon appeared when TA EMG activity exceeded target. For training *session 1*, the mean %MVC amplitude of the prior baseline session was used as the training target. For training *sessions 2–12*, each %MVC amplitude target was based on prior session performance; for session success rates of at least 50%, the target was increased 10% for the next session.

**SOL†.** Foot-switch activation, EMG recording, and signal amplification equipment and parameters were as described above for TA†. During training, SOL H-reflexes during brief voluntary DF contractions were recorded as described by Crane et al. (1987), Crone and Nielson (1989), Morin and Pierrot-Deseilligny (1977), and Pierrot-Deseilligny and Burke (2005). Electrodes were placed as described earlier for PTN stimulation and SOL H-reflex recording, and the foot was positioned on the platform over the embedded foot switch. The foot switch was connected to a stimulator (Grass S88, Grass Technologies) that provided a 50-ms delay between foot-switch activation and SOL H-reflex stimulation. This delay reflected the time course of coactivation.
depression of SOL H-reflex by voluntary DF, which increases greatly from 50 to 100 ms following movement onset in nondisabled individuals (Crone et al. 1987). For each participant, at session start, SOL H-reflex and M-wave recruitment curves at rest and during voluntary DF were obtained by incrementally increasing the stimulus intensity by 2 mA; H-reflex maximum amplitudes and Mmax were recorded. PTN stimulus intensity was maintained at 20% of Mmax during DF by 2 mA; H-reflex maximum amplitudes and Mmax were recorded. DF were obtained by incrementally increasing the stimulus intensity

**Data Analysis**

Nonparametric statistical tests were conducted using SPSS Statistics 18 software (SPSS, Chicago, IL) because the assumption of normal distribution required for use of parametric test was not met due to small sample size. Mann-Whitney U or χ² statistics were used to compare demographic and preintervention clinical characteristics for each intervention group. Spearman correlation coefficients were used to determine preintervention relationships between outcome measures.

Training dosage was compared between TA↑ and SOL↓ groups using Mann-Whitney U-test. For each group, the magnitude of change in the training measure was examined with one-tailed Wilcoxon signed ranks test. For the SOL↓ group, only SOL H-reflexes that were elicited with stimulus intensities between 10 and 30% Mmax were included in data analysis, to ensure equivalence of stimuli across trials. Effect size was assessed with standardized response mean (SRM) (Liang et al. 1990), wherein mean pre-post intervention change is divided by standard deviation of the change. SRM interpretation, based on Cohen’s criteria, was 0.20, 0.50, and 0.80 for small, moderate, and large effects, respectively (Liang et al. 1990). For TA↑, mean %MVC amplitude was compared between three baseline sessions and the final three training sessions. For SOL↓, stability of SOL Mmax across sessions was assessed using repeated-measures ANOVA; SOL Mmax values were obtained from the recruitment curve for each session and were found to be stable (P = 0.24). Mean SOL H-reflex amplitude during DF (HDF) was calculated for the last three training sessions (conditioned SOL HDF) and was normalized to the mean SOL HDF for three baseline sessions and expressed as percentage (%) of baseline (Thompson et al. 2009). In four participants, the mean SOL HDF value for baseline session 3 was identified as an outlier (>2 SD of mean of baseline sessions 1 and 2) and was removed from analysis.

Change was determined by subtracting the pretest from the posttest measure. One-tailed Mann-Whitney U-tests were used to compare magnitude of change between TA↑ and SOL↓ groups for each outcome measure. Within each group, some outcome measures exhibited change that appeared to be clinically relevant; therefore, for each group separately, we analyzed change in outcome measures using one-tailed Wilcoxon signed-ranks tests, calculated SRM (Liang et al. 1990) for each outcome, and explored relationships among outcome changes with one-tailed Spearman correlation coefficients.
TA EMG and SOL H-reflex Training Improves Function in SCI

RESULTS

Preintervention Characteristics

The TA↑ and SOL↓ groups were similar in preintervention demographic, clinical, and neurophysiological measures. However, for clinical measures, the TA↑ group had greater DF active ROM (96.9° vs. 112.4°, P = 0.04) and nontraining leg strength (22.5 vs. 19.2 LEMS, P = 0.04) (Table 1). Stratification of participants by toe tap score resulted in equal distribution of participants between the two groups based on level of ankle motor control; each group had four individuals with low control (<15 taps) and two with high control (≥15 taps). Appendix A illustrates the preintervention correlations between neurophysiological measures and clinical and walking measures (see Table A1), and between walking and clinical measures (see Table A2).

Change in Training Measures and Effect Size (SRM)

Training dosage (repetitions) was similar between TA↑ and SOL↓ groups (3,100 vs. 2,740, P = 0.21). For TA↑, TA %MVC amplitude increased between baseline (43 ± 17%) and final training sessions (91 ± 18%, P = 0.01) (Table 2) and a large training effect was observed (SRM = 5.19). For SOL↓, the conditioned SOL %HDF resulted in a decrease from baseline that approached statistical significance (−16.17 ± 26.22%, P = 0.09) (Table 2), and a moderate training effect was observed (SRM = −0.62). SOL Hreflex reflex responses during training sessions 2 and 11 for an example participant are illustrated in Fig. 4.

Change in Clinical Measures and Effect Size (SRM)

Change in PF RTA was the only clinical measure for which there was a between-groups difference that approached statistical significance (Table 2). This angle decreased toward more DF for TA↑ (−4.33°) and did not change significantly for SOL↓ (−3.15°) (Table 2). Within-group analysis of data from the TA↑ group identified five clinical measures that achieved statistical significance and had a large effect size. These outcomes were as follows: decreased PF RTA (−4.33°) and DF active ROM angle (−4.32°), and increased DF LEMS (+0.8 points), walking foot clearance (+4.8 mm), and walking distance (+12.09 m) (Table 2). In addition, an increase in LEMS for training leg (+2.2 points) and nontraining leg (+0.8 points) approached statistical significance and demonstrated a large effect size (Table 2). Within-group analysis of data from the SOL↓ group identified one clinical measure, increased walking distance (+6.25 m), achieved statistical significance, and had a large effect size (Table 2). In addition, two clinical measures approached statistical significance: increased nontraining leg LEMS (+1.8 points), which demon-

Fig. 3. Feedback displays and change in performance measures. A: TA↑ training display: left, TA EMG feedback and reward; right, TA %MVC amplitude target and response. B: SOL↓ training display: left, SOL H-reflex stimulus, M-wave, and H-reflex during DF (HDF)-reflex; right, SOL HDF-reflex amplitude target and response. C: TA↑ graph of change in mean TA %MVC amplitude. *P = 0.02. D: SOL↓ graph of change in conditioned SOL HDF reflex (%baseline). †P = 0.09. Week 1 = baseline; week 5 = last week of training. Wilcoxon signed ranks one-tailed tests.

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stratified a large effect size and increased walking speed (+0.02 m/s), which demonstrated a moderate effect size (Table 2). A power analysis of the training and clinical outcomes that approached statistical significance revealed that our study was considerably underpowered to detect change in the following measures: SOL %HDF (31%), SOL and TA nontraining LEMS (33%), TA nontraining LEMS (20%), SOL walking speed (14%), and between-groups difference for PF RTA (34%).

### Change in Neurophysiological Measures and Effect Size (SRM)

The only neurophysiological measure in which we observed a significant change was SOL/TA coactivation ratio, which decreased (−0.21) for the SOL↓ group and exhibited a moderate effect size (Table 2).

### Relationship Among Training, Clinical, and Neurophysiological Outcomes

**TA↑.** We had hypothesized TA↑, which was intended to activate SOL RI and PI pathways, would be associated with increased DF active ROM and strength, walking foot clearance, speed, and distance. We did not find a significant change in SOL RI, PI, or walking speed. However, increased walking distance was moderately correlated with increased DF (r = 0.66, P = 0.08) and training leg strength (r = 0.62, P = 0.10) (Fig. 5). Appendix B illustrates, for the TA training group, correlations between changes in neurophysiological measures and clinical, walking, and training measures (see Table B1), and between changes in walking, clinical, and training measures (see Table B2).

**SOL↓.** We had hypothesized SOL↓ would be associated with increased SOL H-reflex LFD and decreased SOL/TA coactivation that would be related to decreased clonus duration, decreased PF RTA, and enhanced toe tap count. We did not find significant change in SOL LFD, clonus duration, PF RTA, or toe tap count. However, decreased SOL/TA coactivation (−0.21, P = 0.02) was moderately correlated with increased walking speed and distance (both r = −0.60, P = 0.10) (Fig. 6). Appendix C illustrates, for the SOL training group, correlations between changes in neurophysiological measures and clinical, walking, and training measures (see Table C1), and between changes in walking, clinical, and training measures (see Table C2).

## DISCUSSION

We investigated whether operant conditioning to either increase voluntary TA activation or decrease SOL H-reflexes improved ankle clonus, motor control, or walking function in individuals with AIS D SCI. We also explored relationships among change in training, clinical, and neurophysiological outcomes. Our hypotheses that TA↑ would increase DF active ROM and strength, walking foot clearance, and walking distance were supported; however, improvement in walking speed was not attained. In addition, an unexpected outcome of decreased PF RTA was observed. For SOL↓, our hypothesis of decreased SOL/TA coactivation was supported; however, decreased clonus duration and PF RTA and increased toe tap count were not observed. Unexpectedly, SOL↓ was associated with increased walking distance. Only one measure, PF RTA, differed substantially between the two groups. Our findings provide evidence that both TA↑ and SOL↓ were associated with significant improvement in distance walked during a 2-min period. Each training protocol may have modulated clinical and neurological variables in unique ways.

## Change in Training Measures

**TA↑** was associated with an increase in TA contraction strength (%MVC amplitude) of ~48% (Fig. 5), a finding consistent with prior reports of increased voluntary EMG

**Table 2. Analysis of change in training and outcome measures within each group (Wilcoxon signed rank one-tailed test) and between groups (Mann-Whitney U-test)**

<table>
<thead>
<tr>
<th>Training measures</th>
<th>Mean ± SD</th>
<th>P value</th>
<th>SRM</th>
<th>SOL↓ Group</th>
<th>Mean ± SD</th>
<th>P value</th>
<th>SRM</th>
<th>Between-Groups</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA %MVC amplitude</td>
<td>48.19 ± 9.29</td>
<td>0.01*</td>
<td>5.19</td>
<td></td>
<td>−16.17 ± 26.22</td>
<td>0.09†</td>
<td>−0.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conditioned SOL H_reflex, %baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonus duration, s</td>
<td>−7.38 ± 12.63</td>
<td>0.22</td>
<td>−0.58</td>
<td></td>
<td>−2.39 ± 4.69</td>
<td>0.11</td>
<td>−0.51</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>PF RTA, °</td>
<td>−4.33 ± 2.23</td>
<td>0.02*</td>
<td>−1.86</td>
<td></td>
<td>3.15 ± 11.53</td>
<td>0.22</td>
<td>0.27</td>
<td>0.06†</td>
<td></td>
</tr>
<tr>
<td>Toe tap test score</td>
<td>2.3 ± 5.13</td>
<td>0.16</td>
<td>0.43</td>
<td></td>
<td>1.3 ± 2.0</td>
<td>0.22</td>
<td>0.43</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>DF active ROM angle, °</td>
<td>−4.32 ± 4.53</td>
<td>0.05*</td>
<td>−0.95</td>
<td></td>
<td>−4.20 ± 9.24</td>
<td>0.22</td>
<td>−0.45</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>DF strength (LEMS)</td>
<td>0.8 ± 0.4</td>
<td>0.03*</td>
<td>2.08</td>
<td></td>
<td>0.5 ± 0.8</td>
<td>1.00</td>
<td>0.63</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>PF strength (LEMS)</td>
<td>0.3 ± 0.8</td>
<td>0.19</td>
<td>0.41</td>
<td></td>
<td>0.5 ± 0.8</td>
<td>1.00</td>
<td>0.63</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>Training leg strength (LEMS)</td>
<td>2.2 ± 1.9</td>
<td>0.06†</td>
<td>1.16</td>
<td></td>
<td>1.3 ± 2.0</td>
<td>0.13</td>
<td>0.65</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>Nontraining leg strength (LEMS)</td>
<td>0.8 ± 0.8</td>
<td>0.06†</td>
<td>1.11</td>
<td></td>
<td>1.8 ± 2.1</td>
<td>0.06†</td>
<td>0.86</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>Foot clearance, mm</td>
<td>4.8 ± 5.3</td>
<td>0.05*</td>
<td>0.91</td>
<td></td>
<td>1.6 ± 6.0</td>
<td>0.42</td>
<td>0.27</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>Speed, m/s</td>
<td>0.04 ± 0.07</td>
<td>0.11</td>
<td>0.54</td>
<td></td>
<td>0.02 ± 0.04</td>
<td>0.08†</td>
<td>0.69</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Distance, m</td>
<td>12.09 ± 9.03</td>
<td>0.02*</td>
<td>1.34</td>
<td></td>
<td>6.25 ± 2.96</td>
<td>0.02*</td>
<td>2.11</td>
<td>0.17</td>
<td></td>
</tr>
</tbody>
</table>

SRM, standardized response mean; MVC, maximum voluntary contraction; H_reflex, H-reflex during DF. *P < 0.05, achieved statistical significance. †P > 0.05 but ≤ 0.10, approached statistical significance. SRM interpretation of effect size = 0.20, 0.50, and 0.80 for small, moderate, and large effects, respectively.

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responses after such training (Brucker and Bulaeva 1996; Seymour and Bassler 1977). SOL$\downarrow$ was associated with a decrease in SOL H-reflex excitability (conditioned SOL $%\text{HDF}$) of about 16% that approached statistical significance (Fig. 6). Thompson et al. (2013) reported a 31% reduction after down-conditioning of SOL H-reflex in standing for nine individuals with SCI. Our mean training dosage was $\sim$3,000 repetitions (300 repetitions per session) for TA$\uparrow$ and SOL$\downarrow$ and was less than the dosage of 5,400–6,750 repetitions used in other studies (Birkenmeier et al. 2010; Thompson et al. 2009, 2013). Our results are similar to Thompson et al. (2009) who used 225 repetitions per session and reported a significant

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**Fig. 4.** Example of effect of SOL$\downarrow$ training on SOL H$_{\text{DP}}$-reflex amplitude responses in one participant. A: training session 2. B: training session 11. Black line, SOL H$_{\text{DP}}$-reflex responses; gray line, M-wave responses evoked at 10–30% M-wave maximum amplitude stimulus intensity. Baseline bout, 30 repetitions without feedback; training bouts, 30 repetitions with feedback with 1-min rests between bouts.

**Fig. 5.** Effects of TA$\uparrow$ training. Change in outcome measures and change in score correlations are shown. Solid single-headed arrow, $P \leq 0.05$, change achieved significance; dashed single-headed arrow, $0.05 < P \leq 0.10$, change approached statistical significance; dashed double-headed arrow, moderate correlation, $0.5 \leq r < 0.75$, $0.05 < P \leq 0.10$; Spearman correlation coefficients, one-tailed test. LEMS, lower extremity motor scores.
decrease in the conditioned SOL H-reflex within sessions 7–12 that continued to decrease through session 24, change the investigators attributed to early-phase task-dependent adaptation. Thompson et al. (2009) also identified a significant change in the control SOL H-reflex within sessions 19–24 that was attributed to a long-term change in spinal cord plasticity. In our participants with SCI, we observed a decrease in conditioned SOL H-reflex that approached significance after 12 sessions; an additional 6 sessions (total of 5,400 repetitions) may have improved the effectiveness of SOL↓ training. Further study is needed to assess the most effective dosage-response parameters.

Effects of TA↑ and SOL↓ on Clinical Measures of Ankle Motor Control

Change in PF RTA was the only outcome that differed substantially between the two groups. TA↑ exhibited a decreased angle (i.e., toward more DF, indicating a more lengthened PF position at which stretch of the SOL evoked a reflex contraction), signifying decreased responsiveness to muscle stretch and, therefore, decreased spasticity (Ness and Field-Fote 2009). TA↑ was effective in enhancing TA activation, as exhibited by increased DF active ROM and strength. In addition, increased DF strength was associated with increased walking distance (Fig. 5). Functional magnetic resonance imaging studies suggest that voluntary ankle DF is a useful measure of motor control of walking that depends, in part, upon increased TA activation (Dobkin et al. 2004).

In nondisabled individuals, PI of SOL motoneurons increases 60–80 ms after onset of voluntary TA EMG activation, and the extent of inhibition is proportional to TA contraction strength (Meunier and Morin 1989). Our findings for TA↑ of increased DF active ROM and strength are congruent with a supraspinally mediated enhancement of SOL PI. Therefore, our findings of no change in PI are in conflict with a mechanism of enhanced SOL PI. A possible explanation is that SOL PI was tested at rest, which may not reflect modulation of the PI pathway during active DF.

TA↑ was associated with an increase in both training leg and nontraining leg strength that approached statistical significance (Fig. 5), while SOL↓ was associated with an increase in nontraining leg strength that approached statistical significance (Fig. 6). The finding of increased strength in the nontraining leg for both groups was unexpected. For TA↑, increased DF strength and training leg strength were correlated with increased walking distance (Fig. 5). We surmise that TA↑ improved the ability to isolate and activate DF in the weaker training leg, which likely contributed to the ability to walk farther distances. Participants were not restricted from walking outside of training sessions and reported the ability to walk farther distances during their daily activities, which likely provided an opportunity for reconditioning of the nontraining leg. Our finding of increased nontraining leg strength is also congruent with studies of contralateral effects of strength training, wherein increased motoneuron output, increased strength, and decreased H-reflex gain in the untrained contralateral homonymous muscle have been reported (Carroll et al. 2006; Dragert and Zehr 2012; Hortobagyi 2005). Wolf et al. (1995) reported a contralateral effect after down-training of biceps brachii stretch reflexes in human subjects, wherein contralateral responses were reduced to 80% of baseline. The authors suggested that both intraspinal mechanisms and bilateral descending systems may contribute to this contralateral training effect.

Effects of TA↑ and SOL↓ on Walking Function

Both TA↑ and SOL↓ were associated with increased walking distances (Table 2) that exceeded the minimally important difference of 4 m reported for the 2-min walk test in individuals with motor-incomplete SCI (Field-Fote and Roach 2011). The cumulative effects of TA↑ (decreased PF RTA and increased DF active ROM, DF and leg strength, foot clearance, and walking distance) (Fig. 5) are consistent with a mechanism of increased corticospinal activation. Upon initiation of voluntary DF, the corticospinal tract activates TA motoneurons in parallel with activation of interneurons mediating PI and RI of SOL motoneurons (Iles and Pini 1992). Our findings are consistent with studies of locomotor training effects in chronic motor-incomplete SCI that report increased voluntary activation of TA and slope of transcranial magnetic stimulation-elicted TA motor-evoked potential recruitment curves, findings that provide evidence of a training-induced increase in corticospinal excitability (Thomas and Gorassini 2005).

For SOL↓, decreased SOL/TA coactivation was associated with increased walking distance and increased walking speed that approached statistical significance (Fig. 6). However, the increase in speed did not exceed the minimally important difference of 0.05 m/s reported for individuals with SCI (Musselman 2007). The SOL↓ effects are consistent with improved SOL reflex modulation during walking and concur with the findings of Thompson et al. (2013). Both excitatory and inhibitory Ib interneuron pathways to ankle extensors are easily activated by the corticospinal tract during voluntary movement (Jankowska 1992) and appear to regulate stance-to-swing phase transition during locomotion (Pearson et al. 1992). The cumulative effects of SOL↓ may be attributable to a Ib neuroplastic effect of SOL↓ that may have contributed to improved walking function (Fig. 6).

Effects of TA↑ and SOL↓ on Neurophysiological Measures

The only substantial neurophysiological effect, exhibited by SOL↓, was decreased SOL/TA coactivation from 52% to 31%...
Table A1. Preintervention relationships between neurophysiological measures and clinical and walking measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Clonus Duration</th>
<th>PF RTA</th>
<th>Toe Tap Test</th>
<th>DF Active ROM</th>
<th>DF Strength</th>
<th>PF Strength</th>
<th>Training Leg Strength</th>
<th>Nontraining Leg Strength</th>
<th>Foot Clearance</th>
<th>Distance</th>
<th>Speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>0.355</td>
<td>2.280</td>
<td>0.028</td>
<td>0.077</td>
<td>0.085</td>
<td>0.486</td>
<td>0.169</td>
<td>0.139</td>
<td>0.042</td>
<td>0.217</td>
<td>0.105</td>
</tr>
<tr>
<td>P value</td>
<td>0.457</td>
<td>0.189</td>
<td>0.465</td>
<td>0.406</td>
<td>0.396</td>
<td>0.054</td>
<td>0.299</td>
<td>0.333</td>
<td>0.448</td>
<td>0.249</td>
<td>0.373</td>
</tr>
<tr>
<td>PI, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>-0.287</td>
<td>0.014</td>
<td>0.392</td>
<td>-0.294</td>
<td>0.074</td>
<td>0.247</td>
<td>0.261</td>
<td>0.275</td>
<td>-0.294</td>
<td>0.448</td>
<td>0.573</td>
</tr>
<tr>
<td>P value</td>
<td>0.183</td>
<td>0.483</td>
<td>0.104</td>
<td>0.177</td>
<td>0.410</td>
<td>0.219</td>
<td>0.206</td>
<td>0.193</td>
<td>0.177</td>
<td>0.072</td>
<td>0.026</td>
</tr>
<tr>
<td>LFD, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>0.350</td>
<td>-0.343</td>
<td>-0.018</td>
<td>-0.049</td>
<td>-0.052</td>
<td>-0.020</td>
<td>-0.141</td>
<td>-0.018</td>
<td>0.140</td>
<td>0.161</td>
<td>0.077</td>
</tr>
<tr>
<td>P value</td>
<td>0.133</td>
<td>0.138</td>
<td>0.478</td>
<td>0.440</td>
<td>0.436</td>
<td>0.475</td>
<td>0.331</td>
<td>0.478</td>
<td>0.332</td>
<td>0.309</td>
<td>0.406</td>
</tr>
<tr>
<td>SOL/TA coactivation ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>0.112</td>
<td>0.133</td>
<td>0.042</td>
<td>0.524</td>
<td>-0.333</td>
<td>0.056</td>
<td>-0.533</td>
<td>-0.543</td>
<td>-0.364</td>
<td>-0.140</td>
<td>-0.091</td>
</tr>
<tr>
<td>P value</td>
<td>0.365</td>
<td>0.340</td>
<td>0.448</td>
<td>0.040</td>
<td>0.145</td>
<td>0.432</td>
<td>0.037</td>
<td>0.034</td>
<td>0.123</td>
<td>0.332</td>
<td>0.389</td>
</tr>
</tbody>
</table>

that was associated with the ability to walk faster and farther (Fig. 6). These findings may suggest that reduced SOL/TA coactivation during clonus was associated with improved SOL• walking outcomes.

Prior studies have described adverse antagonist coactivation and impaired SOL RI and PI after SCI (Boorman et al. 1996; Crone and Nielsen, 1994; Crone et al. 2003; Dietz 2001; Faist et al. 1994; Morita et al. 2001; Xia and Rymer 2005). We observed decreased SOL/TA coactivation after SOL• training; however, no significant changes in SOL RI or PI were identified. In individuals with PF hyperexcitability, Crone et al. (2003) reported reciprocal facilitation of PF after CPN stimulation (as opposed to RI) and proposed that activation of disynaptic Ib pathways may contribute to adverse antagonist cocontraction. Our finding of a predominant pattern of SOL/TA coactivation during clonus is consistent with Xia and Rymer (2005), who reported altered agonist and antagonist activation after SCI as a consequence of reciprocal facilitation of TA during SOL tendon taps, as well as response latencies that are consistent with oligosynaptic short-latency pathways. Citing animal studies, these investigators proposed Ib afferent excitation as a possible source of reciprocal facilitation after SCI (Xia and Rymer 2005).

Recently it has been postulated that increased facilitation or suppressed inhibition of the antagonist muscle following perturbation of the agonist involves Ib force-sensitive pathways (Lewis et al. 2010). Yanagawa et al. (1991) observed that weak TA contractions increased Ib inhibition of SOL H-reflexes and concluded that Ib inhibition, which arrived prior to spinal-level TA-induced inhibitory effects on SOL Ia reflex, was cortico-spinally activated. We surmise that decreased coactivation of SOL and TA during clonus following SOL• (which employed weak TA contractions) may be attributable to enhanced Ib inhibitory mechanisms.

Conclusion and Functional Implications

Two operant conditioning training programs, one to increase voluntary DF motor control and the other to decrease PF stretch reflex excitability, were both associated with improved walking function in individuals with chronic motor-incomplete SCI.

TA• decreased PF spasticity, increased ankle motor control and was associated with increased walking foot clearance and walking distance. Step initiation is mediated by supraspinal input to spinal interneurons that activate stepping (Armstrong 1986), and the corticospinal tract is more closely linked with TA and leg flexor spinal motor circuits (Capaday et al. 1999; Schubert et al. 1997). Intensive, repetitive TA EMG activation during TA• may have unmasked dormant corticospinal pathways that preferentially increased recruitment of TA and leg flexor motoneurons, step initiation, and walking function.

SOL• was associated with decreased SOL/TA coactivation during clonus and increased walking distance. Antagonist coactivation modulation has been attributed to Ib input to spinal interneurons (Feldman 1993; Morita et al. 2006; Yanagawa et al. 1991). It is possible that intensive training to inhibit SOL H-reflexes during weak voluntary TA contractions enhanced corticospinal activation of SOL Ib interneurons, and the combined effects of decreased SOL/TA coactivation and increased SOL stretch reflex inhibition improved ankle motor control and walking function.

Our study was considerably underpowered to detect change in SOL %HDF, TA training LEMS, TA and SOL nontraining

Table A2. Preintervention relationships between walking and clinical measures

| Measure                        | Clonus Duration | PF RTA | Toe Tap Test | DF Active ROM | DF Strength | PF Strength | Training Leg Strength | Nontraining Leg Strength | Foot Clearance | Distance | Speed |
|--------------------------------|-----------------|--------|--------------|---------------|-------------|-------------|-----------------------|---------------------------|                |          |       |
| Foot clearance                 | -0.259          | -0.580 | -0.409       | -0.154        | -0.026      | -0.187      | 0.014                 | 0.079                      |                |          |       |
| Spearman correlation coefficient | 0.208           | 0.024  | 0.093        | 0.317         | 0.468       | 0.280       | 0.483                 | 0.404                      |                |          |       |
| P value                        |                 |        |              |               |             |             |                       |                            |                |          |       |
| Speed                          | -0.538          | -0.091 | 0.166        | -0.594        | 0.100       | 0.614       | 0.476                 | 0.718                      |                |          |       |
| Spearman correlation coefficient | 0.035           | 0.389  | 0.303        | 0.021         | 0.379       | 0.017       | 0.059                 | 0.004                      |                |          |       |
| P value                        |                 |        |              |               |             |             |                       |                            |                |          |       |
| Distance                       | -0.294          | 0.021  | 0.374        | -0.524        | 0.344       | 0.702       | 0.646                 | 0.711                      |                |          |       |
| Spearman correlation coefficient | 0.177           | 0.474  | 0.116        | 0.040         | 0.137       | 0.005       | 0.012                 | 0.005                      |                |          |       |
### Table B1. Relationship between changes in neurophysiological, clinical, walking, and training measures for TA↑ group

<table>
<thead>
<tr>
<th>Measure</th>
<th>↓ Clonus Duration</th>
<th>↓ PF RTA</th>
<th>↑ Toe Tap Test</th>
<th>↓ DF Active ROM</th>
<th>↑ DF Strength</th>
<th>↑ PF Strength</th>
<th>↑ Training Leg Strength</th>
<th>↑ Nontraining Leg Strength</th>
<th>↑ Foot Clearance</th>
<th>↑ Distance</th>
<th>↑ Speed</th>
<th>↑ %MVC Amplitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>^RI, % Spearman correlation coefficient</td>
<td>-0.086</td>
<td>0.657</td>
<td>0.609</td>
<td>0.429</td>
<td>-0.393</td>
<td>-0.525</td>
<td>-0.883</td>
<td>-0.278</td>
<td>0.714</td>
<td>-0.429</td>
<td>-0.257</td>
<td>-0.486</td>
</tr>
<tr>
<td>P value</td>
<td>0.436</td>
<td>0.078</td>
<td>0.100</td>
<td>0.198</td>
<td>0.221</td>
<td>0.143</td>
<td>0.010</td>
<td>0.297</td>
<td>0.055</td>
<td>0.198</td>
<td>0.311</td>
<td>0.164</td>
</tr>
<tr>
<td>^PI, % Spearman correlation coefficient</td>
<td>-0.086</td>
<td>-0.829</td>
<td>-0.551</td>
<td>-0.771</td>
<td>-0.393</td>
<td>-0.216</td>
<td>0.265</td>
<td>0.802</td>
<td>-0.371</td>
<td>-0.486</td>
<td>0.429</td>
<td>0.657</td>
</tr>
<tr>
<td>P value</td>
<td>0.436</td>
<td>0.021</td>
<td>0.129</td>
<td>0.036</td>
<td>0.221</td>
<td>0.341</td>
<td>0.306</td>
<td>0.027</td>
<td>0.234</td>
<td>0.164</td>
<td>0.078</td>
<td></td>
</tr>
<tr>
<td>↓LFD, % Spearman correlation coefficient</td>
<td>-0.600</td>
<td>-0.086</td>
<td>0.145</td>
<td>-0.714</td>
<td>-0.655</td>
<td>-0.463</td>
<td>-0.618</td>
<td>0.309</td>
<td>-0.200</td>
<td>-0.714</td>
<td>0.600</td>
<td>-0.086</td>
</tr>
<tr>
<td>P value</td>
<td>0.104</td>
<td>0.436</td>
<td>0.392</td>
<td>0.055</td>
<td>0.079</td>
<td>0.178</td>
<td>0.096</td>
<td>0.276</td>
<td>0.352</td>
<td>0.055</td>
<td>0.104</td>
<td>0.436</td>
</tr>
<tr>
<td>↓SOL/TA coactivation ratio Spearman correlation coefficient</td>
<td>-0.029</td>
<td>0.257</td>
<td>0.348</td>
<td>0.143</td>
<td>0.655</td>
<td>0.309</td>
<td>0.265</td>
<td>-0.772</td>
<td>-0.314</td>
<td>0.771</td>
<td>-0.200</td>
<td>-0.771</td>
</tr>
<tr>
<td>P value</td>
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<td>0.311</td>
<td>0.250</td>
<td>0.394</td>
<td>0.079</td>
<td>0.276</td>
<td>0.306</td>
<td>0.036</td>
<td>0.272</td>
<td>0.036</td>
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</tbody>
</table>

Arrows indicate direction of change.

### Table B2. Relationship between changes in walking, clinical, and training measures for TA↑ group

<table>
<thead>
<tr>
<th>Measure</th>
<th>↓ Clonus Duration</th>
<th>↓ PF RTA</th>
<th>↑ Toe Tap Test</th>
<th>↓ DF Active ROM Angle</th>
<th>↑ DF Strength</th>
<th>↑ PF Strength</th>
<th>↑ Training Leg Strength</th>
<th>↑ Nontraining Leg Strength</th>
<th>↑ Foot Clearance</th>
<th>↑ Distance</th>
<th>↑ Speed</th>
<th>↑ %MVC Amplitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Foot Clearance</td>
<td>0.257</td>
<td>0.314</td>
<td>0.058</td>
<td>0.714</td>
<td>-0.131</td>
<td>-0.432</td>
<td>-0.441</td>
<td>-0.093</td>
<td>0.029</td>
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<td></td>
<td>0.029</td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>0.311</td>
<td>0.272</td>
<td>0.457</td>
<td>0.055</td>
<td>0.402</td>
<td>0.196</td>
<td>0.190</td>
<td>0.431</td>
<td>0.479</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.143</td>
<td>-0.486</td>
<td>0.290</td>
<td>-0.543</td>
<td>-0.655</td>
<td>-0.926</td>
<td>-0.265</td>
<td>0.463</td>
<td>-0.200</td>
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</tr>
<tr>
<td>P value</td>
<td>0.394</td>
<td>0.164</td>
<td>0.289</td>
<td>0.133</td>
<td>0.079</td>
<td>0.004</td>
<td>0.306</td>
<td>0.178</td>
<td>0.352</td>
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</tr>
<tr>
<td>↑ Distance</td>
<td>0.314</td>
<td>0.143</td>
<td>0.147</td>
<td>0.275</td>
<td>0.655</td>
<td>0.617</td>
<td>0.618</td>
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<tr>
<td>Spearman correlation coefficient</td>
<td>0.272</td>
<td>0.394</td>
<td>0.371</td>
<td>0.311</td>
<td>0.079</td>
<td>0.096</td>
<td>0.096</td>
<td>0.178</td>
<td>0.272</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.143</td>
<td>-0.486</td>
<td>-0.754</td>
<td>-0.086</td>
<td>-0.131</td>
<td>-0.185</td>
<td>0.353</td>
<td>0.679</td>
<td>1.000</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>↑ %MVC amplitude</td>
<td>0.394</td>
<td>0.164</td>
<td>0.042</td>
<td>0.436</td>
<td>0.402</td>
<td>0.363</td>
<td>0.246</td>
<td>0.069</td>
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</tbody>
</table>

Arrows indicate direction of change.
Table C1. Relationship between changes in neurophysiological, clinical, walking, and training measures for SOL↓ group

<table>
<thead>
<tr>
<th>Measure</th>
<th>↑ Clonus Duration</th>
<th>↑ PF RTA</th>
<th>↑ Toe Tap Test</th>
<th>↑ DF Active ROM Angle</th>
<th>↑ DF Strength</th>
<th>↑ PF Strength</th>
<th>↑ Training Leg Strength</th>
<th>↑ Nontraining Leg Strength</th>
<th>↑ Foot Clearance</th>
<th>↑ Distance</th>
<th>↑ Speed</th>
<th>↓ H_{DF} %Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIL % Spearman correlation coefficient</td>
<td>-0.314</td>
<td>-0.714</td>
<td>0.290</td>
<td>-0.086</td>
<td>-0.169</td>
<td>0.372</td>
<td>0.232</td>
<td>0.464</td>
<td>-0.754</td>
<td>-0.200</td>
<td>-0.143</td>
<td>-0.029</td>
</tr>
<tr>
<td>P value</td>
<td>0.272</td>
<td>0.055</td>
<td>0.289</td>
<td>0.436</td>
<td>0.354</td>
<td>0.234</td>
<td>0.329</td>
<td>0.177</td>
<td>0.042</td>
<td>0.352</td>
<td>0.394</td>
<td>0.479</td>
</tr>
<tr>
<td>PI % Spearman correlation coefficient</td>
<td>0.086</td>
<td>-0.314</td>
<td>0.754</td>
<td>-0.143</td>
<td>0.304</td>
<td>-0.270</td>
<td>0.609</td>
<td>0.174</td>
<td>-0.116</td>
<td>0.029</td>
<td>-0.143</td>
<td>-0.143</td>
</tr>
<tr>
<td>P value</td>
<td>0.436</td>
<td>0.272</td>
<td>0.042</td>
<td>0.279</td>
<td>0.302</td>
<td>0.100</td>
<td>0.371</td>
<td>0.413</td>
<td>0.479</td>
<td>0.394</td>
<td>0.394</td>
<td>0.394</td>
</tr>
<tr>
<td>LFD % Spearman correlation coefficient</td>
<td>0.667</td>
<td>0.203</td>
<td>-0.132</td>
<td>0.551</td>
<td>0.017</td>
<td>-0.051</td>
<td>0.206</td>
<td>0.162</td>
<td>-0.309</td>
<td>-0.232</td>
<td>-0.232</td>
<td>0.551</td>
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<tr>
<td>P value</td>
<td>0.074</td>
<td>0.350</td>
<td>0.401</td>
<td>0.487</td>
<td>0.461</td>
<td>0.348</td>
<td>0.380</td>
<td>0.276</td>
<td>0.329</td>
<td>0.329</td>
<td>0.129</td>
<td>0.129</td>
</tr>
<tr>
<td>SOL/TA coactivation ratio</td>
<td>0.371</td>
<td>-0.143</td>
<td>-0.029</td>
<td>0.714</td>
<td>-0.845</td>
<td>0.778</td>
<td>-0.580</td>
<td>0.464</td>
<td>-0.377</td>
<td>-0.600</td>
<td>-0.600</td>
<td>0.371</td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>0.234</td>
<td>0.394</td>
<td>0.478</td>
<td>0.055</td>
<td>0.017</td>
<td>0.034</td>
<td>0.114</td>
<td>0.177</td>
<td>0.231</td>
<td>0.104</td>
<td>0.104</td>
<td>0.234</td>
</tr>
</tbody>
</table>

Arrows indicate direction of change.

Table C2. Relationship between changes in walking, clinical, and training measures for SOL↓ group

<table>
<thead>
<tr>
<th>Measure</th>
<th>↑ Clonus Duration</th>
<th>↑ PF RTA</th>
<th>↑ Toe Tap Test</th>
<th>↑ DF Active ROM Angle</th>
<th>↑ DF Strength</th>
<th>↑ PF Strength</th>
<th>↑ Training Leg Strength</th>
<th>↑ Nontraining Leg Strength</th>
<th>↑ Foot Clearance</th>
<th>↑ Distance</th>
<th>↑ Speed</th>
<th>↓ H_{DF} %Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot clearance Spearman correlation coefficient</td>
<td>0.116</td>
<td>0.638</td>
<td>-0.059</td>
<td>-0.058</td>
<td>-0.017</td>
<td>-0.189</td>
<td>-0.471</td>
<td>-0.426</td>
<td>-0.928</td>
<td>0.004</td>
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<tr>
<td>P value</td>
<td>0.413</td>
<td>0.087</td>
<td>0.456</td>
<td>0.457</td>
<td>0.487</td>
<td>0.360</td>
<td>0.173</td>
<td>0.200</td>
<td>0.044</td>
<td>0.475</td>
<td>0.449</td>
<td>0.100</td>
</tr>
<tr>
<td>Distance Spearman correlation coefficient</td>
<td>-0.771</td>
<td>-0.257</td>
<td>-0.319</td>
<td>-0.886</td>
<td>0.778</td>
<td>-0.372</td>
<td>0.638</td>
<td>-0.116</td>
<td>0.257</td>
<td>0.311</td>
<td>0.311</td>
<td>0.086</td>
</tr>
<tr>
<td>P value</td>
<td>0.036</td>
<td>0.311</td>
<td>0.269</td>
<td>0.009</td>
<td>0.034</td>
<td>0.234</td>
<td>0.087</td>
<td>0.413</td>
<td>0.311</td>
<td>0.436</td>
<td>0.436</td>
<td>0.436</td>
</tr>
<tr>
<td>Speed Spearman correlation coefficient</td>
<td>-0.771</td>
<td>-0.429</td>
<td>0.029</td>
<td>-0.543</td>
<td>0.372</td>
<td>0.788</td>
<td>0.290</td>
<td>-0.812</td>
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<td>0.025</td>
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<tr>
<td>P value</td>
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<td>0.478</td>
<td>0.133</td>
<td>0.234</td>
<td>0.034</td>
<td>0.289</td>
<td>0.025</td>
<td>0.436</td>
<td>0.025</td>
<td>0.025</td>
<td>0.025</td>
</tr>
<tr>
<td>H_{DF} %baseline Spearman correlation coefficient</td>
<td>-0.029</td>
<td>-0.543</td>
<td>-0.058</td>
<td>-0.200</td>
<td>-0.034</td>
<td>0.068</td>
<td>0.377</td>
<td>0.232</td>
<td>1.000</td>
<td>0.329</td>
<td>0.329</td>
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</tr>
<tr>
<td>P value</td>
<td>0.479</td>
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<td>0.457</td>
<td>0.352</td>
<td>0.475</td>
<td>0.449</td>
<td>0.231</td>
<td>0.323</td>
<td>0.329</td>
<td>0.329</td>
<td>0.329</td>
<td>0.329</td>
</tr>
</tbody>
</table>

Arrows indicate direction of change.
LEMS, and SOL walking speed. However, change in these
measures did approach statistical significance, and since the
minimal clinically important difference for most of these mea-
sures is not known, it is possible that the changes observed may
be clinically relevant. The minimal clinically important differ-
ence for walking speed is 0.05 m/s; the mean change of 0.04
m/s in the TA↑ approached this value. There were subjects in
both groups who met the criteria for clinically meaningful
improvement in walking speed. We included these outcomes in
our discussion and interpretation of results to elucidate clini-
cally relevant relationships among change in training and
clinical measures.

Limitations

Our two-group pretest posttest randomized design allowed us
to compare two different interventions. Our study design
lacked a no-treatment control group, which limits interpreta-
tion of whether either training approach was more beneficial
than no intervention (Portney and Watkins 2000). However,
given the chronicity of SCI in our participants, little change in
motor function and reflex activity would be expected in the
absence of an intervention. We did not monitor or control for
background SOL EMG during SOL↓ training; therefore, the
effects of SOL EMG activity on modulation of the SOL
H-reflex are not known, which may have limited our ability to
fully assess the extent of inhibition. Additionally, the neuro-
physiological tests for SOL RI, PI, and LFDT were performed at
rest. Performing these tests during active DF may have better
elucidated modulation of these pathways during movement.
Our conclusions are restricted to outcomes observed in a small
sample of individuals with AIS D SCI. Further research is
warranted to corroborate effects of TA↑ and SOL↓ in AIS D
SCI and generalizability to individuals with other similar upper
motorneuron pathology and functional limitations.

Appendix A

See Tables A1 and A2 for preintervention correlations between
outcome measures.

Appendix B

See Tables B1 and B2 for correlations between change in outcome
measures for the TA training group.

Appendix C

See Tables C1 and C2 for correlations between change in outcome
measures for the SOL training group.

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contributions of Drs. Christine K. Thomas and T. George Hornby to manu-
script development, and the time and effort volunteered by our research
participants with SCI.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: K.J.M., K.E.R., and E.C.F.-F. conception and design of
research; K.J.M. performed experiments; K.J.M., K.E.R., and E.C.F.-F. analyzed
data; K.J.M., K.E.R., and E.C.F.-F. interpreted results of experi-
ments; K.J.M. prepared figures; K.J.M. drafted manuscript; K.J.M., K.E.R.,
and E.C.F.-F. edited and revised manuscript; K.J.M., K.E.R., and E.C.F.-F.
approved final version of manuscript.

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inhibition during voluntary dorsiflexion of the foot. J Physiol 416: 255–272,
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