Reciprocal Inhibition becomes Facilitation after Spinal Cord Injury: Clinical Application of a System Identification Approach*

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***Abstract*—Alteration in spinal inputs from descending pathways following spinal cord injury (SCI) affects different mechanisms including reciprocal Ia inhibition. However, whether there is a consistent pattern of change in reciprocal inhibition following SCI is uncertain. Typical attempts to evaluate reciprocal inhibition have been restricted to electrophysiological measurements, which may have limited translation to function. Our objective was to address the uncertainty regarding changes in reciprocal inhibition after SCI by quantitatively evaluating reciprocal inhibition of ankle extensors from ankle flexors using our novel, more functionally relevant system identification approach.**

To evaluate reciprocal inhibition using the system identification technique, a series of small-amplitude Pseudo-Random Binary Sequence (PRBS) perturbations were applied to the ankle when subjects contracted their dorsiflexors. Depression of reflex stiffness with tibialis anterior (TA) activation was evaluated as reciprocal inhibition. Our results showed that reflex stiffness decreased continuously as dorsiflexor torque increased in the healthy control subjects whereas it remained almost unchanged in the SCI subjects, indicating the absence of reciprocal inhibition in patients. This pattern was consistent with the results obtained from electrophysiological measures in a exploratory control experiment revealing depression of the control H-reflex but no change to the SCI H-reflex. These findings suggest that our system identification mechanical technique is a reliable and valid approach for evaluating reciprocal inhibition. Furthermore, our results demonstrate that reciprocal inhibition can diminish or change to reciprocal facilitation after SCI, which in turn can result in reflex hyperexcitability and unwanted activity of ankle extensors triggered by TA activity. This suggests that reciprocal facilitation may play a major role in pathophysiology of spasticity and impaired function.

Keywords—**reciprocal inhibition, spasticity, reflex, stiffness, system identification, ankle, spinal cord injury, facilitation.**

* This work was supported by grants from the NIH-R01 and the Craig. H. Neilsen Foundation.

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I. Introduction

Spasticity—a velocity-dependent exaggeration of stretch reflexes—is a common symptom that appears soon after spinal cord injury (SCI) in 65-78% of patients [1-3]. Spasticity usually causes pain and fatigue, disrupts daily activity, limits functional ability and results in poor quality of life [4, 5]. One of the mechanisms that may play a major role in spasticity and impaired function is reciprocal inhibition [6, 7]. Reciprocal Ia inhibition occurs via a disynaptic pathway fed by Ia afferents, linking the inhibition of the antagonist and the contraction of the agonist during flexion-extension movements [7].

Given that spinal pathways receive critical input from descending tracts, corticospinal lesions are likely to alter function of particular spinal pathways after SCI, including the pathway mediating reciprocal Ia inhibition. In healthy subjects, corticospinal input to ankle flexors such as tibialis anterior (TA) dominates that of extensors such as the soleus [8]. This dominant corticospinal input to ankle flexors yields supraspinal activation of Ia interneurons inhibiting soleus motoneurons [8]. Thus in spastic SCI, reciprocal Ia inhibition of ankle extensors is expected to decrease due to diminished descending input, which in turn results in hyperexcitability of reflexes associated with spasticity. However, conflicting results have been reported even for patients with the similar lesions. In one study, reciprocal Ia inhibition of the soleus H reflex was increased in patients with incomplete SCI compared to healthy subjects [9], while others have reported reduced reciprocal Ia inhibition in SCI subjects [9, 10]. While the standard electrophysiologic methods to probe the spinal circuitry presumed responsible for reciprocal inhibition are well established, they may have limited translation to how the system functions under volitional control., Whether there is a consistent pattern of change in reciprocal inhibition following SCI under functionally relevant conditions is still uncertain.

The primary objective of this study was to address the issue regarding changes in reciprocal inhibition after SCI by quantitatively assessing reciprocal inhibition of ankle extensors from ankle flexors using our novel, more functionally relevant system identification mechanical approach.

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II. Experimental Protocol

A. Subjects

Four spinal cord injury (SCI) subjects with incomplete motor function loss and ankle-joint spasticity were used to study biomechanical assessment of reciprocal inhibition. Two healthy subjects were used as control. All subjects gave informed consent according to the policies of the Institutional Review Board of Northwestern University.

B. Biomechanical assessment of reciprocal inhibition

Experimental Setup. A custom joint-stretching apparatus was used to apply a controlled-position perturbation to each subject's ankle. Subjects were seated and secured in an adjustable chair with the ankle strapped to the foot rest and the thigh and trunk strapped to the chair. The seat and footrest were adjusted to align the ankle axis of the rotation to be coincident with the center of the motor shaft (Fig. 1).

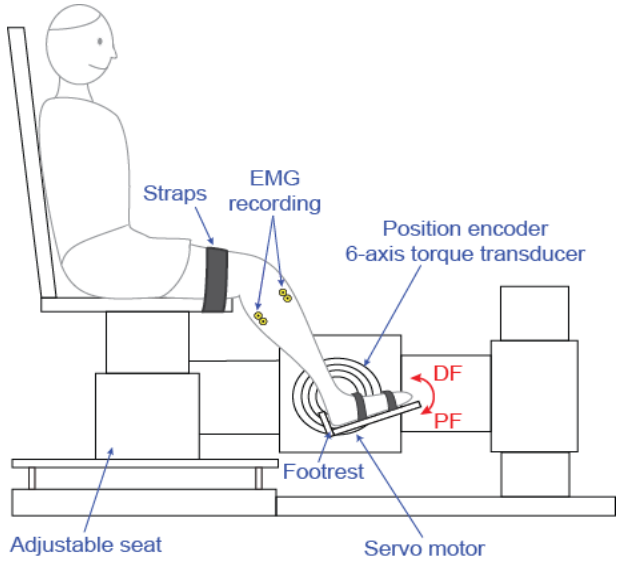

Fig.1: Experimental Setup

Joint position was recorded by a rotary encoder, while a six-axis torque transducer recorded joint torque about the center of ankle rotation. Electromyograms (EMGs) placed at the tibialis anterior (TA) and gastrocnemius (GS) were recorded using bipolar surface electrodes. These signals were sampled at 1 kHz by a 16 bit A/D converter, and low-pass filtered at 230 Hz on-line to prevent aliasing.

Isometric Maximum Voluntary Contraction. Muscle strength at the ankle joint was quantified by measuring isometric maximum voluntary contraction (MVC). MVCs were determined by having subjects contract their muscles maximally toward the dorsiflexion and plantarflexion directions while the subject's ankle is held at the neutral position (i.e., ankle flexed at 90°). The reaction torque and EMG was sampled for 5 s while the MVC was maintained.

Experimental Procedure. To characterize reflex stiffness and separate it from intrinsic mechanical properties, the servomotor applied a series of pseudorandom binary sequences with an amplitude of 0.03 rad and a switching-rate of 150ms to perturb the ankle at neutral position (NP), defined as 90° while the knee was held at 30° flexion. To characterize the reciprocal inhibitory effects of TA activation on GS reflex stiffness, subjects were asked to maintain several different tonic dorsiflexor contractions between 0-40% MVC.

The ankle considered more spastic— as determined by the Modified Ashworth Scale (MAS) [12-14]— was used for evaluation.

C. Electrophysiological assessment of reciprocal inhibition

As a control experiment, we compared our mechanical method to reciprocal inhibition tested in a single subject from each group using two electrophysiological methods evaluating depression of the SOL H-reflex (1) by conditioning stimulation of the common peroneal nerve (CPN) and (2) by tonic voluntary contraction of the antagonist TA. A constant-current stimulator applied single-pulses over the tibial nerve to stimulate the GS and SOL muscles, and over the CPN to activate the TA while the subject was at rest. Once the optimal site of stimulation had been located (in the popliteal fossa for GS and SOL; distal to the head of the fibula for TA), the intensity of stimulation was progressively increased in 5-mA increments until the peak-to-peak amplitude (Mmax) of the resulting M-wave failed to increase with further increases in stimulator intensity. While seated with knee and ankle joint positions fixed to ~90º, the SOL H-reflex was evoked at rest by constant current electrical stimulation of the tibial nerve at an intensity that yields a test reflex of magnitude 20-40% Mmax. The SOL M-wave was monitored on-line to ensure consistent stimulation throughout.

To assess depression of the SOL H-reflex by conditioning stimulation of the CPN, the CPN was stimulated at a level of 1.2x the TA motor threshold. Ten test H-reflexes and ten conditioned H-reflexes were collected at each of the conditioning-test intervals of 2 to 4 ms in a random block design, with each reflex elicited no frequently than every 5s.

To assess depression of the SOL H-reflex by tonic voluntary contraction of the TA, subjects used visual feedback of real-time TA EMG activity on a computer monitor to match four target contraction levels corresponding to 5–50% of the maximal voluntary contraction for their TA. At each contraction level, ten SOL H-reflexes were collected in a random block design, with each reflex elicited no frequently than every 5s. Ten test H-reflexs were collected with the TA at rest.

III. Analytical Methods

A. Reciprocal Inhibition: System Identification Technique

Reflex and intrinsic contributions to the ankle stiffness dynamics were separated using a parallel-cascade identification technique [15, 16].

Intrinsic stiffness dynamics were estimated by determining the Impulse Response Function (IRF) between position and torque (Fig. 2). A second-order model was fit to the IRF, and the intrinsic stiffness gain was calculated and tracked as a function of TA activation.

Reflex stiffness dynamics were modeled as a differentiator, in series with a delay, a static nonlinear element (half-wave rectifier in velocity) and then a third-order dynamic linear element. Reflex stiffness dynamics were estimated by determining the impulse response function between velocity and the reflex-torque, using Hammerstein identification methods. The reflex stiffness *gain* (G_R) was calculated and tracked as a function of TA contraction. This analysis was performed separately for each of the evaluated TA voluntary contraction levels, yielding reflex stiffness vs. dorsiflexor torque.

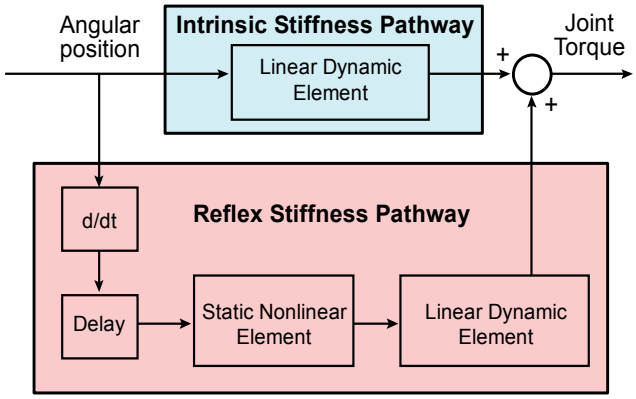

Fig. 2: Parallel-cascade system identification model.

B. *Reciprocal Inhibition: Electrophysiological Method*

Reciprocal inhibition was quantified as the mean size of the conditioned SOL H-reflex expressed as a percentage of the mean size of the unconditioned SOL H-reflex at each interstimulus interval, or TA contraction level tested. For each subject, the interstimulus interval condition that yielded maximum inhibition as well as the slope of the relationship between TA contraction and inhibition were calculated. For each reflex recorded, M-wave amplitude was used to screen H-reflexes for analysis across conditions. Responses were eliminated from analysis if the M-wave amplitude exceeds ±2% of the mean for that session. By keeping the M-wave amplitude stable, the number of group-Ia afferent fibers recruited by the stimulus was well-controlled [17].

IV. Results

Pilot data conducted in four SCI and two healthy subjects using our reflex stiffness approach demonstrates the ability our novel system identification method to assess reciprocal inhibition. Figure 3 shows modulation of G_R of the ankle joint vs. voluntary contraction level of ankle flexor muscles for a typical SCI and a typical control subject. G_R decreased continuously as dorsiflexor torque increased in the healthy control subjects whereas it remained almost unchanged in the SCI patients, indicating the absence of reciprocal inhibition in SCI patients. These findings were consistent among the SCI subjects. This revealed similar results obtained using the standard electrophysiological approach (see Fig. 4).

When conditioning the soleus H-reflex with stimulation of the CPN innervating the TA, there was a 35% depression of the control H-reflex (Fig 4., left, blue) but no change to the SCI H-reflex (right, blue). This absence of inhibition following SCI was also observed using a "natural reciprocal inhibition" approach [17, 18] where increasing levels of TA contraction progressively decreased the SOL H-reflex magnitude of a healthy control subject (Fig 4., left, red) but had no influence on reflex magnitude in the SCI subject.

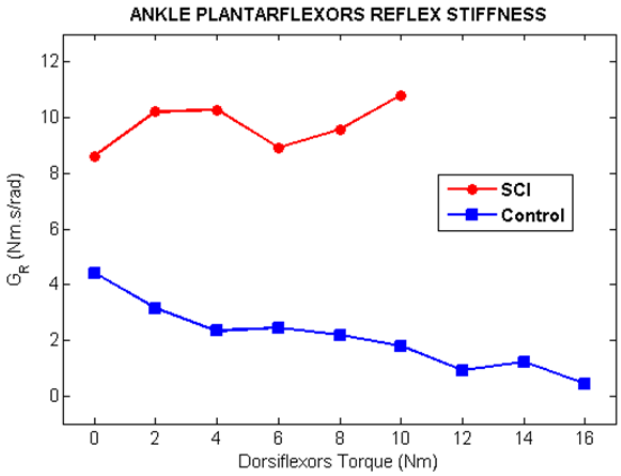

Fig. 3: Reflex stiffness (G_R) versus voluntary contraction level of ankle dorsiflexors

V. Discussion

In this study, we evaluated, for the first time, the reciprocal inhibitory effect of ankle dorsiflexors' activation on the reflex response of ankle extensors using system identification technique. The findings were consistent with our results obtained using standard electrophysiological approaches, indicating the validity of our approach for assessing reciprocal inhibition. Our system identification mechanical approach has advantages over standard electrophysiological approaches because it measures mechanical properties of a functioning reflex response rather than one elicited artificially by nerve stimulation.

We observed that reciprocal inhibition reduced substantially or diminished in three SCI subjects consistent with [6, 10]. In one SCI patient, we found that reflex stiffness increased as TA activation increased indicating replacement of reciprocal inhibition by reciprocal facilitation. This is in agreement with an early facilitation replacing the early inhibition was seen in half of SCI patients reported by Crone *et al*. [6]. Reciprocal Ia inhibition occurs via a disynaptic pathway fed by Ia afferents, linking the inhibition of the antagonist and the contraction of the agonist during flexion-extension movements [7]. The reduced reciprocal inhibition or a change to facilitation, could be caused by altered spinal inputs from injured descending pathways after SCI [6, 7]. This could in turn result in hyperexcitability of stretch reflexes and contribute to spasticity. Furthermore, this facilitation may have produced unwanted stretch reflex activity and co-contraction of ankle extensors, triggered by contraction of ankle dorsiflexors, which can contribute to impaired gait and overall lower limb function [7].

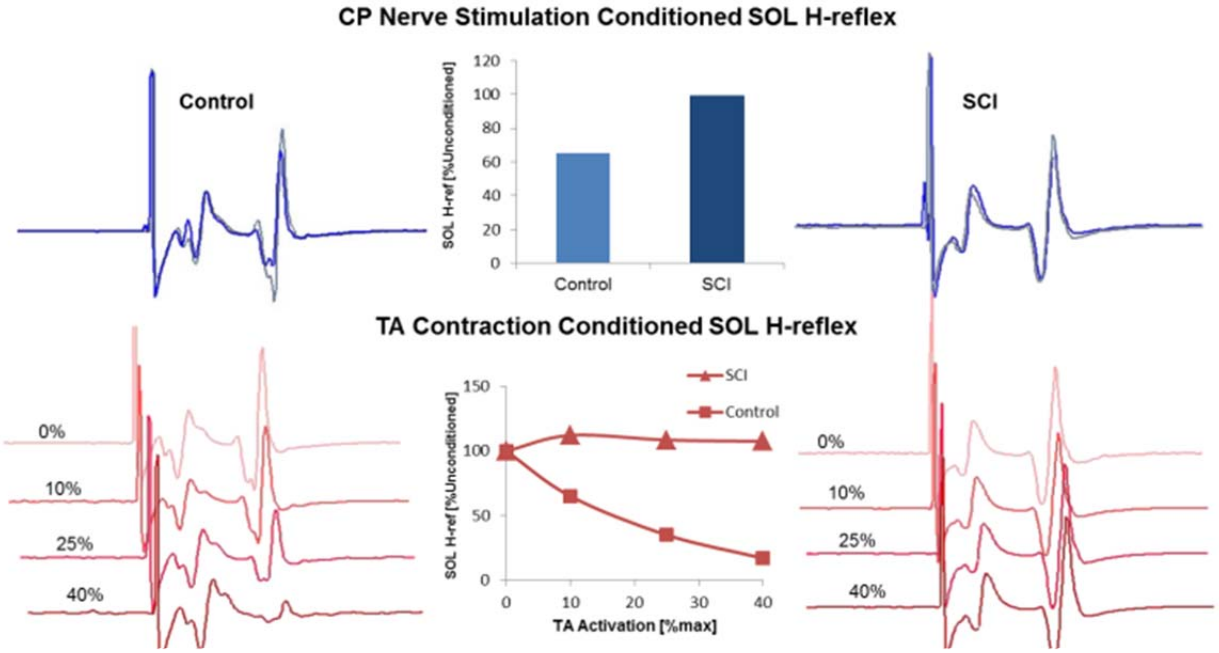

Fig. 4: Reciprocal Inhibition of the SOL H-reflex by CP nerve stimulation (blue) and active contraction of the TA (red) for a single example subject tested from each SCI and control group.

VI. Conclusion

Our results demonstrate that reciprocal inhibition is diminished, or even reversed to facilitation in SCI patients. The reduced reciprocal inhibition, or reciprocal facilitation, can play a significant role in pathophysiology of spasticity and impaired function. Thus, evaluation of reciprocal inhibition and tracking its behavior after SCI has both scientific and clinical significance. Our results demonstrate that our biomechanical system identification technique is reliable and is advantageous to standard electrophysiological measurements because it is more functionally relevant.

Acknowledgment

This work was supported by grants from the NIH-R01 and the Craig. H. Neilsen Foundation.

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