The intralimb coordination of the flexor reflex response is altered in chronic human spinal cord injury

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Abstract

The current study compared the intralimb coordination of flexor reflex responses in spinal intact and complete chronic spinal cord injured (SCI) individuals. Noxious electrocutaneous stimulation was applied at the apex of the medial arch of the foot (50 mA, 500 Hz, 1 ms pulse width, 20 ms) in 21 complete chronic SCI and 19 spinal intact volunteers and the flexor reflex response was quantified by measuring the isometric joint torques at the ankle, knee and hip. The results showed that SCI individuals had significantly smaller peak knee and hip joint flexion torques, often exhibited a net knee extension torque, and produced a much smaller hip joint flexion torque during the flexor reflex response in contrast to the spinal intact individuals. The latency of the reflex response, measured from the tibialis anterior electromyogram, was comparable in both test populations. These findings indicate that the intralimb coordination of the flexor reflex response of chronic complete SCI individuals is altered, possibly reflecting a functional reorganization of the flexion pathways of the spinal cord.

Keywords: Spinal cord injury; Flexor reflex; Joint torque; Plasticity

Changes in excitability of the flexor reflex have been observed in chronic human SCI. Indeed, it has been suggested that flexor spasms, which are common in individuals with chronic SCI [38], result from an enhanced excitability of the flexor reflex pathways [9,37, however, cf. 20]. Spastic reflexes, including the flexor reflex, can be measured using electromyograms (EMGs) of the muscle of the legs [39]. EMGs provide useful information about patterns of activity, but signal magnitude depends on electrode impedance, relative placement with respect to the muscle belly and distance from the muscle [5], which may change for atrophic muscles in SCI. In addition, flexor reflexes in individuals with chronic SCI commonly result in co-contraction, especially at the knee [9,35], which makes it difficult to identify the net output of the reflex response. Torque measurements provide an alternative technique for measuring flexor reflexes and may supply additional information regarding the pattern of the flexor reflex response. Specifically, these measurements can be used to quantify the magnitude of the response across subjects and.

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Therefore, allow for the evaluation of the behavioral response of the reflex without the need for normalization.

Previous studies using isometric joint torque measurements to examine the flexor reflex response of chronic complete SCI individuals suggest a strong ankle and hip response without a strong flexion torque at the knee [22,35], which is inconsistent with observations of spinal intact individuals [2,3]. In addition, local sign, defined as the dependence of the direction of the withdrawal of the limb on the location of a noxious skin stimulus is applied [17], is lost in chronic human SCI [36]. These studies suggest that the flexor reflex response becomes functionally reorganized in chronic SCI. This issue was examined further in the present study by comparing the intralimb coordination of the flexor reflex response of complete chronic SCI individuals and spinal intact individuals in terms of the isometric joint torques produced at the ankle, knee and hip.

Participants included 19 neurologically intact individuals and 21 individuals with clinically complete SCI (American Spinal Injury Association (ASIA) scale A) with injury level C5-T10. Five of the 21 SCI subjects were taking oral medications for management of spasticity. Informed consent was obtained from all participants in accord with the Helsinki Declaration of 1975 and approved by the Institutional Review Boards of Northwestern University and Marquette University.

The experimental apparatus used in this study has been described previously [22,35]. Briefly, each participant was seated in an adjustable chair of a Biodex Rehabilitation/Testing System 2 (Biodex Medical Systems, Inc., Shirley, NY, USA) with the ankle, knee and hip aligned in the sagittal plane and placed approximately at the mid-range of motion: ankle 100–135° (10–45° plantarflexion), knee 70–130° (110–50° flexion), hip 75–100° (105–80° flexion) and 0–10° abduction. Although there was a 60° range in knee angle, the mean knee position was not significantly different between the SCI (119°) and spinal intact (114°) populations (t test, p = 0.18). The medial and lateral aspects of the knee were braced with a plate fixture to prevent motion of the hip in the frontal plane. The foot was clamped to a fixation plate that was coupled to a six degrees-of-freedom load cell (Theta, ATI-Industrial Automation, Apex, NC) and mounted on a modified footplate. The load cell measurements were used to calculate the isometric joint torque response to the electrocutaneous stimulation as described previously [35]. The muscle activity of the tibialis anterior, medial gastrocnemius, rectus femoris, and medial hamstrings (semimembranosus/semitendinosus) was recorded using active, surface EMG electrodes (Model DE2.1, Delphys, Boston, MA, USA). The EMG signals were amplified (> 10,000; Bagnoli 4, Delsys), low-pass filtered (500 Hz) and sampled at 1000 Hz.

Electrocutaneous stimulation (50 mA current intensity, 500 Hz frequency—10 pulses, 1 ms pulse width, 2 ms inter-pulse interval) was applied at the apex of the medial arch of the foot with a pair of skin electrodes (1 cm diameter; Blue Sensor, N-10-A, Medicotest Inc. Rolling Meadows, IL, USA) placed 1 cm apart. The electrodes were connected to a bipolar stimulator (Digitimer DS7A, Hertfordshire, England) that was controlled via a personal computer. These stimulation parameters were chosen because they produced a flexion withdrawal response in all subjects. The spinal intact population considered the stimulus noxious. Three to six repetitions of the stimuli were applied at 20 s intervals.

Sagittal plane isometric joint torques for the ankle, knee, and hip were calculated by multiplying the force and torque data measured with the load cell by a transformation matrix that accounted for the position of the load cell relative to the ankle axis of rotation, the ankle and knee angles, and the tibia and femur lengths [35]. The resulting joint torque calculations were then low-pass filtered (10 Hz cut-off frequency) with a fourth order Butterworth filter (butter function of MatLab, The Mathworks Inc., Natick, MA, USA) and the peak torque produced within 1 s of the stimulus was identified for each joint. The mean peak torque (of the three to six trials) was calculated for each joint, for each subject.

The latency of the flexor reflex was identified for both populations in order to ensure that comparisons of the joint torque measurements involved the same reflex response (e.g. [7,33]). Latency was calculated using the tibialis anterior EMG, which was band-stop filtered (55–65 Hz, fourth-order Butterworth filter) to remove line noise. The tibialis anterior EMG signal was then rectified and smoothed using a Butterworth low-pass filter (20 Hz, fourth order). The latency of the tibialis anterior EMG signal was determined relative to the onset of the stimulus pulse train. Tibialis anterior activity latency was detected in the 0.5 s period following the stimulus by determining the point at which the rate of change of its first derivative crossed a predefined threshold. The mean latency was calculated for each subject and the reflex latency for the SCI and spinal intact groups were compared using a Mann-Whitney test. This comparison was conducted to determine whether the reflex latencies of the two populations were similar. To determine whether the flexor reflex response of the SCI and spinal intact subjects differed significantly, the mean peak isometric joint torque responses at each of the three joints were calculated for each subject and analyzed collectively using a multivariate analysis of variance (MANOVA). If the result was significant, the MANOVA was followed by paired t tests to make pair-wise comparisons between the responses of the two groups of subjects at each joint. A t test was also used to compare the latency of the tibialis anterior activity between the two groups. The level of significance was set at α = 0.05 for all the statistical analyses.

Fig. 1 shows typical EMGs of the tibialis anterior, medial gastrocnemius, rectus femoris and medial hamstrings muscles during the flexor reflex response to an electrocutaneous (noxious) stimulus in an SCI individual. Note that the muscles on both sides of the joint (flexors and extensors) are often active at approximately the same time, suggesting co-contraction and highlighting the difficulty of quantifying the flexor reflex response in terms of muscle activity. The latency
Fig. 1. Representative EMGs of the tibialis anterior, medial gastrocnemius, rectus femoris, and medial hamstrings muscles during the flexor reflex response in an SCI individual. The arrow indicates the time at which the electrocutaneous stimulus was applied.

The mean latency of the tibialis anterior muscle was 94.1 ms (S.D. = 55.2 ms) for the spinal intact individuals and 97.6 ms (S.D. = 94.3 ms) for the SCI individuals. This small difference in latencies was not significant (Mann-Whitney test, $p = 0.51$).

The flexor reflex torque pattern exhibited by SCI subjects in response to the electrocutaneous stimulation was significantly different from that of the neurologically intact subjects (MANOVA, $p < 0.001$). Fig. 2 shows a single representative trial of the isometric joint torques at the ankle, knee, and hip of a spinal intact (left) and spinal cord injured (right) individual. Joint flexion torque (dorsiflexion at the ankle) is positive. The stimulus was applied at time = 0 s.
trial of the isometric joint torque responses observed at the ankle, knee and hip of the SCI and spinal intact subjects. Generally there was less knee flexion (or more extension) torque and a smaller hip torque in the SCI subjects. The group mean peak isometric flexion torque responses at the three joints are summarized in Fig. 3. The individuals with SCI exhibited significantly smaller joint torques at the knee and hip (t tests, \( p < 0.05 \)) but a similar joint torque at the ankle (t test, \( p = 0.16 \)) in comparison to the neurologically intact subjects. The mean knee torque for the SCI population was smaller than mean knee torque of the neurologically intact population (0.3 N m for SCI versus 8.6 N m for spinal intact). Moreover, 14 of the 21 SCI subjects exhibited an extension rather than flexion torque at the knee, a response observed in only 4 of the 19 spinal intact subjects. As a result, SCI subjects were significantly more likely to produce knee extension than the spinal intact population (chi-square test, \( p < 0.005 \)). The hip torque of the SCI subjects was twice as large as the ankle torque, whereas it was 4.7 times larger than the ankle torque for the spinal intact subjects.

Fundamental differences exist between the intralimb coordination of the flexor reflex response of the chronic complete SCI individuals and the spinal intact individuals in this study. Hip torques dominated the response of the spinal intact subjects to a much larger extent than that of the chronic SCI subjects. Particularly striking was the finding that individuals with SCI were more likely to exhibit an extension rather than flexion torque at the knee joint, confirming previous anecdotal observations [22,35]. Interestingly, the ankle joint torque did not differ significantly between the two groups, a finding that contrasts with EMG studies showing enhanced [9,38] or reduced [20] tibialis anterior muscle activity during the flexor reflex response in individuals with chronic SCI.

The results of this study may be explained in several ways. One explanation takes into consideration the contribution that force generating properties of the muscles (i.e. atrophy) may have in altering the flexor reflex response. Given that the lower leg muscles of SCI individuals have a reduced contractile capacity due to atrophy (e.g. see [15] for review), the finding that the ankle joint torques of the two test populations was similar leads to the interpretation that the neural response of the SCI individuals was larger. In addition, atrophy may not occur uniformly in the muscles throughout the leg. Hidler et al. [19] found that SCI individuals can produce a similar ankle plantar flexion (extension) torque magnitude as spinal intact individuals in response to tibial nerve stimulation, possibly related to a prevalent spastic activation of the ankle plantarflexors. For the flexor reflex, the ankle dorsiflexors have a lower threshold than more proximal muscles [9], which might be an indicator of more spastic activity in these muscles, thereby resulting in lower atrophy of the ankle dorsiflexors. This type of differential atrophy could account for the relative difference in hip and ankle torques observed in the current study.

Reorganization of the flexion pathways within the spinal cord circuitry is another possible explanation for the altered pattern of joint torques observed in this study. The smaller knee flexion observed in the flexor reflex response of the SCI individuals is consistent with kinematic studies showing that chronic SCI individuals have reduced knee flexion during the swing phase of assisted treadmill [11] or unassisted over-ground [23] walking in comparison to spinal intact individuals, although see [1]. The commonality in findings provides support for the hypothesis that the same spinal pathways may be engaged in the flexor reflex response and swing phase of locomotion [7,28,31] and leads to the speculation that a substantial portion of pathologic gait in chronic SCI may be due to functional modifications of the flexion pathways. This idea is supported by the fact that chronic SCI individuals also exhibit the Babinski sign [14,24,34]. While fundamental changes in the flexor reflex in the relaxed individual may be indicative of changes in reflex pathways during functional movements, these effects would need to be tested directly.

A change in the functional organization of the flexion reflex pathways may be attributed to the loss of descending drive onto the spinal cord. A number of inhibitory supraspinal inputs influence the pathways of the flexion reflex, including the corticospinal [27,29], rubrospinal [21], vestibulospinal [6] and medullary reticulospinal [40] tracts. Other spinal reflex circuits modified as a result of the injury may also influence, through interneuronal connections, the functional organization of the flexion pathways. The fact that individuals with pyramidal tract lesions alone have been found to exhibit the Babinski sign illustrates how the absence of a single descending input to the spinal cord circuitry can lead to a change in the pattern of a reflex response to a stimulus [14,25,26,41].

The long-term loss of descending input to the spinal cord may also result in neuroplastic changes within the flexion reflex circuitry. The absence of local sign in chronic SCI [36] is one example of reorganization of the flexion reflex pathways. Another indication that neuroplasticity can occur in the spinal pathways in chronic SCI comes from studies showing that locomotor training can modify the walking patterns of individuals with SCI even those who are classified as
clinically-complete [8,10,16,18,30]. Incorporating the flexor reflex to assist the swing phase of locomotion during training further improves kinematics during locomotion [11,12,32], even though fundamental changes in the flexor reflex have not been quantified.

In sum, this study demonstrated differences in the intralimb coordination of the flexor reflex response of chronic SCI individuals in comparison to that of spinal intact individuals. The SCI individuals exhibited a smaller knee flexion, and often knee extension torque and a lower relative hip joint flexion torque. The flexor reflex response pattern may be due to nonuniform muscle atrophy, an absence of descending influences on the spinal cord or neuroplastic changes within the flexion pathways of the spinal cord circuitry.

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References


