The action of plantar pressure on flexion reflex pathways in the isolated human spinal cord

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Abstract

Objective: To investigate the conditioning effects of plantar pressure on flexion reflex excitability in patients with motor complete spinal cord injury (SCI).

Methods: In five motor complete SCI subjects, the non-nociceptive flexion reflex was evoked via electrical stimulation of the right sural nerve and was recorded from the ipsilateral tibialis anterior muscle. Pressure ranging from 25 to 80 kPa was applied to the metatarsal heads through an adjustable platform incorporated into a foot rest and a comparison of the reflex size made between control conditions and during pressure application.

Results: In all subjects, a significant depression of the long latency flexion reflex was observed when pressure was applied to the foot sole. The short latency flexion reflex appearing at latencies less than 100 ms was absent in all patients.

Conclusions: The results demonstrate that flexion reflex excitability in the isolated human spinal cord can be modulated by adequate activation of plantar mechanoreceptors.

Significance: Activation of plantar mechanoreceptors is a feature of normal standing and walking. Rehabilitation for standing and walking in SCI commonly uses body weight support based protocols. The strong inhibitory actions of plantar pressure on reflex pathways in the isolated human spinal cord suggest that sensory feedback from the foot sole may be an important factor in successful rehabilitation of standing and stepping in SCI patients.

Keywords: Flexion reflex; Load; Plantar; Rehabilitation; Spinal cord injury

1. Introduction

Integration of sensory signals from the foot sole has been implicated in the reflex regulation of locomotion (Aniss et al., 1992; Conway et al., 1995). Sensory afferents from the foot sole influence spinal interneuronal circuits which in turn delay or suppress the initiation of swing promoting stance, and contribute to the correct placement of the foot during stepping as documented in spinalized and decerebrated animals (Conway et al., 1995; Duysens, 1977; Duysens and Pearson, 1976; Bouyer and Rossignol, 2003). These studies signify that afferents from the foot sole interact with the neuronal circuits involved in stepping, while input from the foot sole has been associated with recovery of walking in spinalized animals (Côte and Gosseries, 2004). The latter may be related with the convergence of plantar cutaneous afferents onto common interneurones in the reflex pathways to α-motoneurones acting as a stabilizing mechanism for the foot during stance (Engberg, 1964; Kniffki et al., 1981), contributing to maintenance of human upright posture (Kavounoudias et al., 2001).

The flexion reflex in human spinal cord injury (SCI) displays a similar neural organization to that observed in L-DOPA-treated spinal animals where the interneuronal...
pathways that participate in the generation of the reflex are also considered to participate in pattern generation during fictive locomotion, like in real locomotion in normal animals (Jankowska et al., 1967; Lundberg, 1979). In human SCI, the ipsilateral flexion reflex is characterized by a synchronous long latency long lasting general excitation of flexor muscles at the hip, knee and ankle with concomitant inhibition of extensor muscle groups (Roby-Brami and Bussel, 1987). The contralateral limb a crossed reflex showing a reciprocal pattern of muscle actions can be observed (Roby-Brami and Bussel, 1987; Tax et al., 1995). Activation of flexor reflex afferent (FRA) pathways in SCI is also associated with presynaptic inhibition of the soleus H-reflex (Roby-Brami and Bussel, 1990, 1992). The close parallels seen in flexion reflex organization in L-animals (Jankowska et al., 1967; Lundberg, 1979). In human fictive locomotion, like in real locomotion in normal animals (Lundberg, 1979; Baldissera et al., 1981) create the opportunity to use the flexion reflex in SCI as a window into spinal pathways which may play a role in determining patterned motor activity.

Given the interest in body weight support based therapies for gait and standing training in SCI (Harkema et al., 1997; Dietz et al., 1998; Wirz et al., 2001; Field-Fote, 2001; Field-Fote et al., 2005) the question on how afferent feedback from the foot sole influences spinal reflex pathways has become pertinent. We have previously reported on the inhibitory action of plantar pressure on the excitability of the soleus H-reflex in SCI (Knikou and Conway, 2005), and we report here (for the same group of SCI subjects) on the effects of applying pressure to the foot sole on the magnitude of the non-nociceptive flexion reflex.

2. Methods

2.1. Subjects

The procedures were approved by the local Ethics Committee and were conducted in accordance with the 1965 Declaration of Helsinki. A written informed consent was obtained from five subjects aged 30–37 years with thoracic (T) lesions ranging from T5 to T12 as a result of trauma before testing (Table 1). All subjects had complete motor lesion with only one reporting preserved sensation below the level of the lesion (S5). None of the subjects was on anti-spasticity medication. Reflex recordings were performed with subjects seated (hip angle 120°, knee angle 160° and ankle angle 110°).

2.2. TA flexion reflex elicitation and recording procedures

The flexion reflex was evoked by two Ag-AgCl pre-gelled electrodes (Ambu Inc., Ølstykke, Denmark) placed over the course of the sural nerve at the lateral submalleolar region of the right ankle. The reflex was evoked by a 30 ms duration train of 1 ms pulses delivered at 300 Hz every 10 s (Knikou and Conway, 2005), and was recorded via disposable pre-gelled electrodes (A-10-N, Ambu Inc., Denmark) from the ipsilateral tibialis anterior (TA) muscle. In individual subjects, the stimulus intensity was set between 1.2 and 2 times the intensity required to evoke an EMG response in the TA muscle, and remained fixed during the course of each experiment. At these intensities and stimulation intervals, the reflex is stable and does not habituate (Knikou and Conway, 2005).

All EMG signals were amplified (Digitimer Neurolog, Hertfordshire, UK) and band-pass filtered (10 Hz–1 kHz) before being sampled at 2 kHz (1401 + laboratory interface running Spike 2 software; Cambridge Electronics Design Ltd., Hertfordshire, UK). The digitized EMG signals were rectified and the size of the flexion reflex was quantified by measuring the area beneath the EMG recording from the time of reflex onset to the point where the EMG returned to baseline. Separate averages of the size of the control and conditioned flexion reflexes were obtained from 20 individual reflexes. The estimate of the size of the control reflex was performed before and after each application of applied pressure. All EMG recordings were made during periods free from any background EMG activity or during periods of spasms or clonus (see Fig. 1).

2.3. Mechanical plantar loading

Plantar mechanical loading was applied through a flat rectangular platform (15 cm²) incorporated into the right footrest. The platform was positioned at the heads of the metatarsal bones and could be manually raised or lowered in order to alter the pressure applied to the metatarsals. Calibrated strain gauges were incorporated into the platform design allowing the magnitude of the applied plantar

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Injury level</th>
<th>Time post-injury (years)</th>
<th>Ashworth score</th>
<th>ASIA scale</th>
<th>Medication</th>
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<td>T7</td>
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<td>T5</td>
<td>8</td>
<td>0</td>
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</table>

* Lesion completeness was classified according to the ASIA (Maynard et al., 1997) impairment scale with ASIA-A representing sensory and motor complete spinal cord lesion and ASIA-B representing sensory incomplete and motor complete lesion. The spasticity at the ankle was scored based on the Ashworth scale (Ashworth, 1964).
pressure to be monitored and recorded. Velcro straps attached to the foot-plate secured the position of the foot. At the start of each experiment, the platform was positioned to be flush with the surface of the footrest. This was the position used during the collection of control data. Subsequently, small adjustments to the platform height altered the pressure applied to the skin in contact with the platform. After adjusting the platform height, the pressure applied to the foot sole was allowed to stabilize before reflex testing. The applied pressure ranged from 25 to 80 kPa.

2.4. Data analysis

The conditioned flexion reflex was expressed as a percentage of the mean control flexion reflex. Depending on the number of the applied loads, a paired t-test or a one-way analysis of variance (ANOVA) was applied to the data of each subject. Then the average sizes of the conditioned reflex from each subject were grouped according to the range of the applied loads and one-way ANOVA along with post hoc Bonferroni tests was employed to test for significant differences across subjects and load trials using $P < 0.05$ as the criterion of significant difference. Results are presented as mean values and standard deviation (SD).

3. Results

The TA flexion reflex had a latency that ranged from 140 to 170 ms, and this was regarded as the long latency flexion reflex. Short latency flexion reflexes occurring at latencies less than 100 ms were not present, either under control conditions or during mechanical reflex conditioning. For all subjects, flexion reflexes were recorded following plantar pressure that ranged from 25 to 30 kPa. In three of these subjects (S2, S4, S5), a second trial corresponding to an applied pressure within the range of 50–60 kPa was completed and in a single case (S5) a third data set was obtained with an applied pressure of 80 kPa.

In Fig. 2A, the effects of plantar mechanical loading on the average long latency flexion reflex (solid line is the control reflex) recorded from subject 5 are shown following applied plantar pressures of 50–60 kPa (dotted line) and 80 kPa (dashed line). The conditioning stimuli can be seen to reduce the amplitude of the long latency flexion reflex. A significant depression in the size of the long latency flexion reflex was observed in all subjects and trials ($P < 0.05$). At 25–30 and 50–60 kPa of plantar pressure, the conditioned flexion reflex reached overall amplitude of 40.5 ± 6% and 47 ± 5% of the control flexion reflex, respectively. No significant difference in the magnitude of the conditioned flexion reflexes was encountered at these different applied pressures ($P = 0.272$). However, in subject 5, the depression in the flexion reflex at 80 kPa was significantly greater compared to reflexes seen during lower applied pressures (25–30 and 50–60 kPa). At 80 kPa the conditioned flexion reflex amplitude was 32 ± 3% of the control reflex.

4. Discussion

Pressure applied to the foot sole induced a significant depression of the long latency flexion reflex in all SCI sub-
jects examined. Pressure to the foot sole is anticipated to lead to deformation of the skin and sub-cutaneous tissue including tendon and muscle in a manner similar to that seen when the foot is bearing weight during standing or stepping resulting in the activation of load sensitive mechanoreceptors. The modulation pattern agrees well with the notion that flexion reflexes will be suppressed during limb loading. However, it should be noted that loading of the foot sole also generates a depression of the soleus H-reflex in this SCI patient group (Knikou and Conway, 2001).

In spinalized and decerebrated cats, electrical stimulation of the tibial or plantar nerves of the foot delays or suppresses the initiation of swing, inhibits the long latency flexion reflex, and promotes stance (Duyens and Pearson, 1976; Duysens, 1977; Conway et al., 1995). In a similar manner, sural nerve stimulation during 1-DOPA induced fictive locomotion terminates flexor activity and induces extensor activity when delivered during the extension phase (Schomburg et al., 1998). It is thus apparent that sensory feedback from the foot sole interacts with spinal interneuronal circuits that participate in the neural control of locomotion.

The flexion reflex depression we observed here might be related to reflex mechanisms which operate in animals and humans to further assist postural stability during standing or stepping (Duysens et al., 2000; Van Wezel et al., 1997), and to the sensory processing associated with the adaptive regulation of locomotor patterns (Bouyer and Rossignol, 2003). While it is tempting to speculate that the flexion reflex depression during foot sole loading is related to the adaptive regulation of spinal reflexes during walking, the result cannot be discussed in isolation from the observation that plantar mechanical loading also induces soleus H-reflex depression in motor complete SCI subjects (Knikou and Conway, 2001). The presence of concomitant depression in flexion and soleus H-reflex pathways during plantar loading suggests that a simple adaptive mechanism that integrates load related sensory feedback from the foot sole is not demonstrated in this group of motor complete SCI patients. One interpretation of these findings is that both the gain of the stretch and flexion reflexes in SCI patients is decreased during the application of plantar pressure.

Current rehabilitation strategies for gait training often employ body weight support and external manual assistance for repetitive presentation of kinematic and kinetic sensory cues in a rhythmic pattern. During this form of rehabilitation the decrease in reflex gain seen with plantar loading (stance) may assist in depressing flexor activation in stance but would not positively contribute to the promotion of extensor activity. In this line, similar effects (facilitatory) on the soleus H-reflex and TA flexion reflex have been observed following electrical and not mechanical stimulation of the foot sole (Knikou, 2007). The soleus H-reflex and TA flexion reflex facilitation following excitation of plantar cutaneous afferents (Knikou, 2007), and their depression after plantar mechanical loading (Knikou and Conway, 2001) might be related not only to the degree of contribution of different excited afferents under these conditions but also to lack of upright posture and thus body-leg loading. A differential control of extensor and flexor reflex pathways might be accomplished when limb peak loading is present in standing SCI subjects after repetitive step training (Harkema et al., 1997) features that were absent in our current experiments. It is thus likely that alternative reflex pathways to flexors and extensors may be driven by body loading sensory feedback.

At this point we should consider the possible neuronal mechanisms mediating the depression of the long latency flexion reflex in SCI. In the spinal-intact man, cutaneous afferent input modulates transmission in presynaptic inhibitory pathways of forearm flexor group I afferents (Nakashima et al., 1990). Studies addressing similar effects in human SCI have shown that sural nerve stimulation exciting non-nociceptive afferents leads to facilitation of the ipsilateral soleus H-reflex and decrement of heteronymous Ia facilitation exerted from quadriceps to soleus z-motorneurons, suggesting that FRA volleys induce presynaptic inhibition of Ia afferent terminals (Roby-Brami and Bussel, 1990). Further, in normal subjects, afferents of the foot sole modulate the amount of postsynaptic inhibition by affecting actions of Ib and Ia inhibitory interneurones (Pierrot-Deseilligny et al., 1981; Rossi and Mazzocchio, 1988).

However, given that spinal inhibitory control mechanisms are impaired after a SCI in humans (Calancie et al., 1993; Morita et al., 2006), it is likely that the concomitant depression of the soleus H-reflex and TA flexion reflex by plantar pressure might be the result of pathological integration of these mechanisms.

In conclusion, the demonstration that plantar cutaneous mechanoreceptors depress the flexion reflex suggests that the isolated human spinal cord can integrate sensory signals from the foot sole through interneuronal circuits that are likely involved in human gait. Our findings suggest that spinal processing of load related sensory feedback from the human foot sole might assist in counteracting increases in muscle tone due to hyper-reflexia in flexor and extensor motor pools. It remains, however, to be tested that normalization of muscle tone or sensorimotor recovery after step training in SCI patients is mediated through these pathways.

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References


