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Discharge rates and discharge variability of muscle spindle afferents in human chronic spinal cord injury

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HIGHLIGHTS

- For the first time, microneurographic recordings of muscle spindle afferents have been obtained from the paralyzed leg muscles of patients with spinal cord injury.
- Compared to intact individuals, there were no differences in either the ongoing firing rates or discharge variability of spontaneously active muscle spindle endings, nor were there overt differences in the responses to manually-applied passive stretch.
- These results argue against any increase in static (and possibly dynamic) stretch sensitivity of muscle spindle endings as a contributing factor to spasticity.

ABSTRACT

Objectives: To test the hypothesis that the firing rates and discharge variability of human muscle spindles are not affected by spinal cord injury.
Methods: Tungsten microelectrodes were inserted into muscle fascicles of the peroneal nerve in six individuals with complete paralysis of the lower limbs following spinal cord injury: 12 afferents were spontaneously active at rest and 7 were recruited during passive muscle stretch. For comparison, recordings were made from 17 spontaneously active and 9 stretch-recruited afferents in 12 intact subjects.
Results: Firing rates for the spontaneously active muscle spindles were not significantly different between the spinal (9.8 ± 1.6 Hz) and intact (10.2 ± 1.3 Hz) subjects; the same was true for the stretch-recruited afferents – static firing rates, measured over the final 1 s of a ramp-and-hold stretch, were not different between the spinal and intact groups (13.1 ± 3.1% vs 10.0 ± 2.5 Hz). There were also no differences in discharge variability between the spinal and intact subjects, either for the spontaneously active spindles (8.1 ± 2.0% vs 5.7 ± 0.9%) or for the stretch-activated spindles, calculated over the final 1 s of static stretch (19.7 ± 5.6% vs 17.0 ± 1.9%). In addition, the responses to stretch imposed manually by the experimenter provided no evidence for an increase in the dynamic response to stretch in the patients.
Conclusions: The static stretch sensitivity of human muscle spindles is not affected by chronic spinal cord injury, suggesting that there is no difference in static (and possibly dynamic) fusimotor drive to paralyzed muscles in chronic spinal cord injury.
Significance: This study provides no evidence for an increase in fusimotor drive as a mechanism for the spasticity associated with chronic spinal injury, though further studies using controlled stretch would be required before it can be concluded that dynamic fusimotor drive is "normal" in these patients.

1. Introduction

A complete lesion of the spinal cord causes a complete paralysis of muscles supplied by spinal nerves originating below the level of the lesion, expressed immediately following the injury as a flaccid paralysis. This period of spinal shock, characterized by absent tendon reflexes, lasts 1–3 days (Ditunno et al., 2004). Over several weeks, however, spastic paralysis develops: patients exhibit exaggerated myotatic reflexes and may also generate rhythmic oscillatory movements (clonus) to muscle stretch, symptoms that can affect quality of life (Adams and Hicks, 2005). What causes this increase in stretch sensitivity is unknown. While it has been argued that clonus is due to recurrent muscle stretch reflexes brought about by spindle activation during the relaxation phase of the contraction (Hagbarth et al., 1975; Rossi et al., 1990), recent work suggests that it is more a reflection of the output of a central

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(spinal) pattern generator (Beres-Jones et al., 2003). As to the hyperreflexia of spasticity, changes in both the stretch sensitivity of muscle spindles and central synaptic excitability have been hypothesized to contribute (Little and Halar, 1985), as has reduced descending inhibition of spinal circuitry (Ditunno et al., 2004).

Muscle spindles are exquisitely sensitive length receptors located in skeletal muscles, unique in the somatosensory system in having their own motor innervation. Gamma (fusimotor) motoneurones innervate the intrafusal muscle fibres, the shortening of which causes stretch-induced excitation of the primary (Ia afferents) and secondary (II afferents) endings of the spindle: an increase in dynamic fusimotor drive increases the dynamic stretch gain of Ia afferents (Hulliger et al., 1977) and II afferents (Cussons et al., 1977), while an increase in static fusimotor drive increases their background firing but decreases their sensitivity to dynamic changes in muscle length (Hulliger et al., 1977; Cussons et al., 1977; Matthews, 1981). If dynamic fusimotor drive was to increase in spinal cord injury, and a greater spindle response generated for a given mechanical stimulus, then tendon jerks would be exaggerated. Conversely, an increase in static fusimotor drive may, through autogenetic facilitation of the alpha motoneurone pool, be expected to increase excitability of the pool and potentially contribute to spasticity. However, it is not known whether the spasticity associated with chronic spinal cord injury is due to an increased sensitivity of the muscle spindles to stretch, brought about by an increase in fusimotor drive to the relaxed muscles, or exclusively to disturbances in excitability of the spinal motoneurones. It is known that spinal excitability is altered following spinal cord injury, with a reduction in spinal inhibitory mechanisms being prominent (Nielsen et al., 2007); indeed, it is by increasing inhibitory action within the spinal cord that Baclofen – a $GABA_B$ agonist – is generally effective in controlling spasticity in spinal cord injury (Adams and Hicks, 2005). Moreover, functional reorganization of spinal circuitry occurs, such that reciprocal inhibition of antagonistic muscles during muscle stretch is transformed into a reciprocal facilitation that occurs at monosynaptic latencies (Xia and Rymer, 2005). The gain and sensitivity of the soleus H-reflex has been shown to be increased in human spinal cord injury, which argues in favour of increases in spinal excitability (Little and Halar, 1985). Nevertheless, in the absence of data, one cannot exclude the possibility that muscle spindle stretch sensitivity may, through segmental circuitry, be increased when the spinal cord is deprived of supraspinal excitatory and inhibitory drives.

It is known that muscle spindles show an increased number of intrafusal fibres in human spinal cord injury (Stilwill and Sahgal, 1977), but the functional significance of this is not known. However, we have learnt, from studies in spinalised cats, that muscle spindle primary endings possess an increased dynamic sensitivity to muscle stretch (Alnaes et al., 1965). It has been argued that this is due to an increase in background firing of dynamic fusimotor neurones but not static fusimotor neurones (Alnaes et al., 1965); indeed, direct recordings from gamma motoneurones in the spinal cat show that some 40% of fusimotor neurones exhibit a spontaneous discharge (Hunt and Paintal, 1958). However, another study in the cat showed that spindle responses to muscle stretch were depressed immediately after spinal transection and remained depressed from control levels 2 months after the transection, despite the hypertonia and hyper-reflexia (Bailey et al., 1980); another study showed no significant changes in fusimotor outflow in the chronic spinal cat (Lieberman et al., 1979), so there remains uncertainty.

The spontaneous discharge of muscle spindle afferents is dependent on the resting length of the muscle, and can be increased – and additional spindle afferents recruited – by applying pressure to the tendon or muscle belly or by rotating the joint in the direction that increases muscle stretch (Vallbo, 1974; Burke et al., 1988). The purpose of the present study was to test the hypothesis that firing rates and discharge variability are not increased in patients with chronic spinal cord injury. To this end the spontaneous and stretch-evoked discharges of individual muscle spindle afferents were recorded via tungsten microelectrodes inserted percutaneously into muscle fascicles of the common peroneal nerve and compared with the firing properties of spindle afferents recorded from intact subjects.

2. Methods

Experiments were performed on 6 patients with chronic spinal cord injury (22–45 years), who had sustained a motor-complete injury 3 months to 5 years previously. None of the patients had a history of peripheral nerve abnormality or co-existent disease process known to affect peripheral nerve function. All patients exhibited spasticity. Patients were recruited from the SCI unit of Prince of Wales Hospital and gave informed consent to the procedures, which were approved by the Human Research Ethics Committees of the University of New South Wales and the South Eastern Sydney Area Health Service Human Research Ethics Committee (Eastern Section). Able-bodied (intact) subjects were recruited from the University population. The studies were performed in accordance with the Declaration of Helsinki.

The participants were seated in a semi-reclined posture in a comfortable chair with the legs supported in the extended position and the ankles held at ~25° plantar flexion on a footplate. The common peroneal nerve at the fibular head was located by external stimulation (0.2 ms pulses, 1 Hz, 3–10 mA; Stimulus Isolator; ADInstruments, Sydney, Australia). In some experiments in the spinal patients longer pulse durations (1 ms) and currents up to 32 mA were required, via a high current Stimulus Isolator (DS3, Digitimer, Welwyn Garden City, Herts, UK), owing to the greatly elevated stimulation thresholds of human motor axons following spinal cord injury (Lin et al., 2007). Intraneural recordings were made from muscle fascicles of the common peroneal nerve via tungsten microelectrodes (FHC, Bowdoinham, ME, USA) inserted percutaneously at the level of the fibular head. Muscle fascicles were identified as supplying either the peronei muscles, extensor digitorum longus, extensor hallucis longus or tibialis anterior muscles according to the muscle twitches produced by intraneural stimulation. Neural activity was amplified (gain 20,000, bandpass 0.3–5.0 kHz) using an isolated amplifier (ISO-80, World Precision Instruments, USA) and stored on computer (10 kHz sampling) using a computer-based data acquisition and analysis system (PowerLab 16SP hardware and LabChart 7 software; ADInstruments, Sydney, Australia). Surface EMG over the pretibial flexors was recorded with Ag/AgCl electrodes located over tibialis anterior on the same side as the spindle recording (10 Hz–1 kHz bandpass, 2 kHz sampling; BioAmplifier; ADInstruments, Sydney, Australia).

Intraneural recording confirmed that the microelectrode tip was located within a muscle fascicle: there were no afferent responses to light stroking of the skin but afferent activity could be evoked by passive stretch or palpation of the muscle belly, or percussion over the tendon. Muscle spindles were identified as such if they presented a tonic discharge, the mean frequency of which could be increased by stretching the receptor-bearing muscle and decreased by unloading the muscle. These spontaneously active spindles were further subdivided into presumed primary, secondary and unclassified endings. Primary endings showed a characteristic silent period following release of the stretch (passive shortening), and typically expressed a high dynamic sensitivity to passive stretch. Secondary endings typically decelerated their discharge, without ceasing completely, when the stretched muscle was returned to its resting length. Because of the motor paralysis,