THE EFFECTS OF A NOVEL LOWER LIMB PROPRIOCEPTION TRAINING INTERVENTION ON SKILLED WALKING PERFORMANCE FOR INDIVIDUALS WITH A SPINAL CORD INJURY

by

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Abstract

Introduction: Proprioception gives us the ability to know the location of our limbs in space. It plays a critical role in movement control, including walking. After a spinal cord injury (SCI), individuals experience not only weakness or paralysis, but also proprioceptive deficits, which further compound difficulties with movement control. In this study, we tested the effects of a new robotic-based protocol to train proprioceptive sense in the lower limbs and assessed whether improvements in proprioceptive sense could also improve performance of a skilled walking task in people with SCI.

Methods: Skilled walking performance was assessed by participants' accuracy in matching their heel position during the swing phase of walking to a virtual target presented on a monitor. Proprioceptive sense was assessed by knee joint position sense with a validated protocol using the Lokomat robotic exoskeleton. Subjects then underwent proprioceptive training. The training protocol required subjects to detect whether their heel position was higher or lower compared to an initial position. After each trial, visual feedback about their accuracy was provided. The assessments of skilled walking and knee joint position sense were assessed post-training as well as 24-hours later.

Results and Conclusion: Our results showed that the training protocol was effective, with a significant improvement in knee joint position sense post-training that was also evident 24-hours later. A slight trend in improvement was also observed in skilled walking performance post-training. These findings indicate that it is possible to improve lower limb proprioceptive acuity following sensory training and that such improvements could further influence skilled walking performance.

Lay Abstract

After sustaining a spinal cord injury difficulty in movement is due to deficits in both the motor and sensory systems. In particular, the sensation of knowing where your legs are in space (proprioception) is essential for movement. This study is the first to test the idea whether we can enhance proprioception and if it leads to improved walking capabilities in people with a spinal cord injury. Findings from this study can help develop of new rehabilitation techniques for people with a neurological injury.

Preface

I was the lead investigator in conducting all aspects of this thesis project, including concept development, subject recruitment, data collection, data analysis, and thesis document preparation. Dr. Lara Boyd and Dr. Timothy Inglis contributed to study design. Dr. Tania Lam contributed to concept development and study design and supervised the data collection and analysis.

I presented preliminary data from this project at the 2016 Society for Neuroscience Annual Meeting (San Diego, USA).

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To my parents,

your love unconditional,
and dedication everlasting

Chapter 1: Introduction

1.1 Overview

The recovery of walking is considered a top priority among those with spinal cord injury (SCI). This goal is often limited by the damage to the descending motor pathways in SCI which impair the capability of muscles to receive motor commands sent out by the brain. This leads to varying degrees of paralysis (depending on injury severity), muscular atrophy and reduced movement control which collectively compromises walking function. In addition to motor deficits, impairments in touch and pain sensation are equally common following SCI.

The control of human movement is highly dependent on the integration of motor commands with various sensory feedback systems. Such integration occurs at multiple levels of the central nervous system to control precise voluntary movements. In particular, proprioception (sensory feedback of limb position and movement) plays a critical role in the motor control required for multi-joint, complex movements, such as walking. Thus, the loss of proprioceptive sensation after SCI impairs knowledge of limb location, further intensifying deficits in functional control of walking and other movements.

Most gait rehabilitation interventions for people with SCI have focused on strategies to improve voluntary control and strength in order to enhance community ambulation. The primary mode of rehabilitation today is intensive walking practice with the help of various devices, ranging from parallel bars to robotic exoskeletons. While these approaches can lead to meaningful improvements, their purpose is targeted towards strengthening motor output. The sensory system, particularly the proprioceptive system, is critical for movement control and can also be affected by a SCI. While there is some evidence pointing towards sensory plasticity of proprioception, minimal efforts have been made to integrate sensory training techniques into a clinical setting. Training to improve proprioceptive acuity has the potential to enhance movement control in populations with sensory deficits, such as SCI. Thus the aim of this thesis was to develop a technique to improve lower limb proprioceptive sensation and investigate if such an intervention could improve walking capacity in people with SCI.

1.2 About Spinal Cord Injury

1.2.1 Incidence and prevalence

Sustaining a SCI is a traumatic event that can leave individuals with lifelong paralysis, sensory deficits, and secondary health complications. There are estimated to be 85,000 people living with SCI in Canada and approximately 3500 new cases every year (Noonan et al. 2012). The SCI prevalence equates to about 52.5 out of every 1 million individuals in Canada, which is one of the highest in the world (Van den Berg et al 2010). Furthermore, there has been increasing incidence of SCI over recent years due to a rise in the number of the elderly, a population highly susceptible to fall-related injuries that could lead to SCI (DeVivo et al. 2012). Worldwide, there is a higher incidence of SCI in males (79%) with peak age of injury being less than 30 years of age (Singh et al. 2014; Pellatt 2008).

A SCI can result from either traumatic or non-traumatic causes. Traumatic SCI results from external factors such as motor vehicle accidents, violence, or falls and accounts for a little over half (51%) of the SCI community (Noonan et al. 2012; Cosar et al 2010; Farry and Baxter 2010). Non-traumatic SCI can occur from a variety of conditions including spondylosis, vascular diseases, syringomyelia, infections or tumors, and are typically seen in older individuals with equal distribution between both sexes (Pellatt 2008; Noonan et al. 2012; Farry and Baxter 2010).

Regardless of the underlying cause, damage to the spinal cord results in varying levels of impairment affecting both sensation and motor output.

1.2.2 Anatomy of the spinal cord

The spinal cord consists of 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal segments. The specific muscles and skin regions innervated by a given spinal segment are referred to as myotomes and dermatomes, respectively. Sensory input from the periphery enters the spinal cord through the dorsal root ganglion and into the dorsal horn grey matter. The dorsal horn houses cell bodies involved with sensory processing and is involved with relaying sensory information to higher brain centers. The intermediate zone houses interneurons and specialized nuclei. Lastly, the ventral horn is dedicated to cell bodies of lower motor neurons, which extend their axons through ventral nerve root filaments and continue as peripheral nerves towards their target muscles and glands.

Ascending and descending white matter columns/funiculi contain the axons carrying sensory and motor signals to and from the brainstem, cerebellum, and cerebrum. The descending motor pathways are categorized either as lateral motor or medial motor systems, based on their location within the spinal cord. These pathways mediate movement commands from higher brain centers to the effector muscles in the periphery. The lateral motor systems, namely the lateral corticospinal and the rubrospinal tracts, originate from the cerebral cortex and midbrain, respectively, and travel caudally via the lateral column to synapse with neurons of the lateral ventral horn. The lateral corticospinal tract is primarily responsible for controlling precise voluntary movements at individual joints (Blumenfeld 2010). Evidence of the rubrospinal tract function in humans is sparse (Blumenfeld 2010), but has been reported to be responsible for flexor tone in the upper limbs as seen through the decorticate posture (flexed arm and wrist) after cerebral damage (Blumenfeld 2010). While movement control directed by both lateral motor pathways arise from the CNS contralateral to the side of the effector, the medial motor tracts descend either ipsilaterally or bilaterally via the anteromedial columns of the spinal cord and synapses with interneurons or lower motor neurons in the most medial aspect of the ventral horn. The four medial tracts include anterior corticospinal, vestibulospinal, reticulospinal and tectospinal tracts. These pathways are responsible for controlling proximal muscles involved in postural control, balance, head stabilization, and repetitive gait movements (Blumenfeld 2010).

The ascending white matter columns, the posterior column-medial lemniscal (PCML) pathway and anterolateral pathways, all relay somatosensory input to the CNS. The PCML pathway carries information about proprioception, vibration sense, and fine touch. Neurons of the PCML enter the spinal cord through the dorsal horn and travel rostrally through the ipsilateral posterior column. At the medulla, the axons decussate and continue the relay of information to the thalamus via the contralateral medial lemniscus. PCML projections from the thalamus reach higher cortical regions such as the primary somatosensory cortex making conscious sensory perception possible. Such information flow is not limited to conscious perception, but also involves subconscious processes. (These systems will be discussed in later sections.) Sensory information pertaining to pain and temperature are transmitted via the anterolateral pathway. However, unlike the PCML, neurons of the anterolateral pathway decussate at the level of the spinal cord after entering through the dorsal horn. These neurons ascend contralaterally via the anterolateral white matter towards the thalamus and afterwards project to the sensory cortex. Considering the particular anatomy of these pathways, a SCI could result in different extents of proprioceptive, pain and/or crude touch deficits depending on the lesion site and level.

1.2.3 Neurological assessment of spinal cord injury

Lesions to the spinal cord that disrupt the longitudinal tracts cause an interruption or complete loss of communication between the brain and the body. Thus, in many SCI cases, both the sensory and motor systems are compromised. The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) is a widely used neurological assessment of SCI that determines both the severity and level of injury. (Kirshblum et al 2016). This exam relies on clinical measures of motor and sensory function in which key myotomes in the limbs and all dermatomal levels are assessed. Full body somatosensation is measured through light touch to assess the PCML pathway, and pinprick to assess the spinothalamic pathway. The level of preserved voluntary strength, which assesses the corticospinal pathway, is determined by manual muscle testing of key upper and lower limb muscle groups. Five key muscle groups in the arms and legs are tested, corresponding to specific spinal segments including C5-T1 for upper limb and L2–S1 for the lower limb. Motor function of the trunk muscles is not assessed and as such, level of injury in the thoracic region is determined by the sensory score. Together, the results of the sensory and motor testing are used to define the level as well as the severity (completeness) of the injury.

Depending on the level of injury, individuals with SCI can be categorized as tetraplegic or paraplegic. Tetraplegia results from injury within the cervical region bringing about impairments in the arms, trunk, legs and pelvic organs (Maynard et al. 1997; Kirshblum et al. 2016). Injuries to the thoracic, lumbar or sacral segments result in paraplegia. Here, arm function is preserved, but depending on the level of injury, trunk, legs and pelvic organs may be involved (Maynard et al. 1997; Kirshblum et al. 2016). The ASIA Impairment Scale (AIS) is commonly used to grade the degree of impairment. In a complete injury (AIS A), there is no sparing of function below the injury, including no sacral sparing, as the entirety of the spinal cord at a given level has been lesioned. AIS B refers to sensory incomplete SCI with sensory, but no motor preservation below the level of injury. AIS C is a motor-incomplete classification, where more than half of key muscles below the injury level are incapable of moving the limb against gravity. AIS D is also classified as motor-incomplete, but at least half of the key muscles are able to move the limb against moderate resistance. With incomplete injuries, the preservation of neural tracts opens the possibility of functional recovery (Endo et al. 2011).

1.2.4 Rehabilitation and functional recovery

Sensorimotor impairments after SCI affect functional mobility, which in turn compromise, to varying degrees, activities of daily living. In particular, the inability to ambulate results in deleterious quality of life after SCI, necessitating reliance on mobility aids such as wheelchairs. This means that many people with SCI lead a sedentary lifestyle. As a consequence of this overall physical inactivity, secondary complications such as orthostatic hypotension, ventricular atrophy, dysrhythmias, vascular dysfunction, lipid disorders, muscular atrophy, bone loss, susceptibility to renal stone and immune dysfunctions are of major concerns after SCI (Scott et al. 2011). Such conditions can further limit community participation, thus leading to negative psychological and emotional health outcomes. As a result, individuals with SCI are also more prone to psychological morbidity involving abnormal levels of negative emotional and behavioral states (Craig et al. 2009). Depressive moods, abnormal levels of anxiety, post-traumatic stress disorder, low self-esteem, and a negative perceived quality of life are some of the psychological factors typically reported (Craig et al. 2009). Therefore, rehabilitation strategies that lead to improved community participation, including those that improve walking function, are a critical component of interventions directed towards improving the quality of life in people with SCI.

The primary outcome of SCI rehabilitation is to increase independence in order to facilitate community re-integration (DeVivo et al, 2012; Lim and Tow 2007; Tooth et al. 2003; Goodwin et al. 2010). It has been reported that walking is a high recovery priority among the SCI population, driving medical efforts towards improvements in ambulation of SCI patients (Ditunno et al. 2008). We have seen major developments in gait rehabilitation strategies over the years to further improve neuro-motor output of strength and voluntary control through interventions such as functional electrical stimulation, body weight supported treadmill training and more recently, exoskeletons (Field-Fote 2001, Lam et al. 2007, Lam et al. 2015). The training concepts underlying all of these strategies focus on eliciting and strengthening motor functionality (Lam et al.2007). However, the impact of sensory impairments in motor recovery seems to have been largely overlooked in rehabilitation research, despite the fact that sensory deficits are just as prevalent as motor impairment after SCI. Furthermore, the control of movements, especially complex, multi-joint movements such as walking, require motor and sensory integration. The following sections examine the significance of the sensory system, especially proprioception, in motor control and its implications in SCI populations.

1.3 Proprioception

Sensation is defined as a change in perception of the body state in response to stimuli (Carlson et al 2010). Classically, sensation has been divided into five main components: sight, sound, taste, touch and smell. But there is a sixth component that is just as crucial for daily function. Defined first by Sherrington (1907), proprioception is the ability to detect the spatial location and movement of the body and its limbs. The human body is supplied by a multitude of different receptors that give an accurate perceptual representation of the body's position within its environment. Proprioception is restricted to not only conscious perception of the body, but also mediates the subconscious feedback pathways necessary for various functions. Such subconscious processes include reflexive responses to maintain movement or balance, as well as visceral regulation through arterial, pulmonic and gastric distension (Proske and Gandevia 2012).

1.3.1 Proprioceptive receptors

There are numerous peripheral sensory receptors that collectively contribute to proprioceptive sense. During limb movement, there is a deformation in tissues - namely skin, muscles, tendons, fascia, joint capsules and ligaments - around joints which are innervated by mechano-sensitive receptors (Grigg 1994). Arguably, the primary source of proprioceptive input is from muscle spindles. These are intrafusal fibers embedded with extrafusal muscle fibers that run the full or partial length of the muscle fascicle (Proske et al. 2000). Each spindle is composed of nucleated bag and chain fibers with sensory afferents spiraled around them. Muscle stretch causes these spindle fibers to uniformly deform and consequently mechanically stimulate the afferent nerve fibers. Such sensory transmission from the muscle spindles are carried by primary Ia and secondary II afferent nerve fibers, each of which react differently to muscle stretch. Crowe and Matthews (1964) showed that muscle length corresponded to the amount of tonic discharge from both afferent fiber types. The secondary afferents tended to maintain a regular firing rate while the Ia fibers demonstrated an irregular firing pattern. During muscle stretch, the primary Ia afferent discharge is highly modulated by the speed of stretch while secondary afferent showed only gradual changes in impulse discharge. This data provided evidence that individual afferent fibers react differently to muscle stretch; the primary Ia afferents propagate information relevant to limb dynamics (movement and velocity) while the secondary afferents convey information about position (Crowe and Mathews 1964).

The role of such afferent feedback on conscious limb perception in humans has been examined with muscle tendon vibrations. Goodwin et al. (1972) artificially enhanced spindle discharge using biceps tendon vibration and examined changes in the perception of elbow angle using a matching limb task. Participants consistently reported a more extended arm as observed through the matching limb. This suggests that increased spindle discharge creates the conscious illusion of muscle lengthening. Moreover, the size of the illusion was directly related to the vibration frequency (Goodwin et al. 1972). During movement, such illusory effects were present only when the antagonist muscle was vibrated. This suggests that during movement, proprioceptive information about position sense predominates from spindle discharge as a result of antagonist lengthening more so than shortening of its counterpart agonist group (Inglis et al. 1990). In a more direct, but invasive experiment, McCloskey et al showed that even after anesthetizing a joint to remove any afferent information from other tissues such as cutaneous receptors, the joint position illusion was maintained when muscle tendons were surgically manipulated (McCloskey et al. 1983). Collectively these findings provide strong evidence of muscle spindle involvement in conscious proprioceptive sense.

In addition to muscle spindles, joint receptors have also been found to play a functional role in limb movement detection sense. Joint receptors are nerve endings found in the synovial junction between the bones that detect mechanical deformation within the capsule and the surrounding ligaments. Using lidocaine injection to remove cutaneous and muscle spindle input, Gandevia et al. (1983) were able to cause an overall increase in movement detection threshold in the distal middle finger. However, when dextran was additionally injected into the joint as a means to increase joint receptor sensitivity via swelling, an improvement in movement detection threshold was seen (Gandevia et al. 1983). While this may be evidence for joint receptors contributing to proprioceptive sense, discharge characteristics of such receptors differ from those of muscle spindles. Ferrell (1980) showed that the discharge rate of joint receptors remained relatively low in the middle of a joint's range of motion. As the joint was brought to its end range in either full flexion or full extension, joint receptor impulse rates drastically increased. However, such afferent firing rates were indistinguishable from flexion versus extension. Thus, afferent information from joint receptors are explained as ambiguous and directionally independent, which may be indicative of their role as movement range limiters (Ferrell and Smith 1988, Ferrell 1980). Nonetheless, these data support joint receptors as contributors to proprioception.

Cutaneous sensory input also contributes to proprioception. Edin et al. (1995) investigated the role of such receptors by providing an anesthetic ring block to the skin and deeper tissues of the second proximal interphalangeal joint. While keeping the finger steady to prevent muscle spindle and joint receptor input, the skin on the anesthetized portion of the finger was manipulated in a way to mimic skin displacement during actual movement at the metacarpophalangeal joint. All participants were asked to demonstrate the perceived joint position with the opposite hand. The results showed that participants perceived a change in finger position based on how the experimenter manipulated the skin. For example, if the skin was tensed on the dorsal surface and slacked on the ventral surface, the position was perceived as flexed as indicated by the response by the non-experimental finger. Thus, it was concluded that skin stretch manipulation creates an illusion of finger joint position that correspond to the pattern of skin stretch, demonstrating the contribution of cutaneous input to proprioception.

Although there are multiple afferent inputs that contribute to proprioception, Proske and Gandevia (2012) argue for the primary role from muscle spindles. The main evidence for this is from observations in individuals with total hip joint replacements involving removal of capsular and ligamentous components. In these individuals, the ability to detect the magnitude of passive hip abduction was evaluated on a motor apparatus. When compared to the normal hip, the operated hip demonstrated no differences in the capability to differentiate the magnitude of passive abduction. Furthermore, the same apparatus was used to record the accuracy of active hip abduction to various target positions. The ability to accurately abduct to a target was similar between the hip joints among post-operative patients. The lack of deficits in both joint and movement detection senses suggest that proprioceptive sense in the hip joint after the removal of capsular and ligamentous tissues is intact (Grigg et al 1973). Such findings support the possibility that joint receptors and skin deformity might not play a major role in signaling proprioception. Nevertheless, even though greater deficits are seen when muscle spindles information is removed, input, even if limited, from skin and joint receptors still provide proprioceptive inputs in creating the most sensitive movement and position sense system (Proske and Gandevia 2012; Gandevia and McCloskey 1976).

1.3.2 Role of proprioception in motor control

Proprioception plays a critical role in controlling movements. This is best exemplified by the dense anatomical projections from the sensory to motor regions of the brain. Afferent fibers from the PCML pathway reach the thalamus and thereafter project to the primary sensory cortex located in the parietal brain region, which mediates the conscious perception of sensation. Additionally, sensory area 2, 2 praeinsularis, 3a, and rostral area 5 give rise to nerve fibers that transmit the sensory information in the form of association fibers to the motor cortex, creating cortico-cortical input connections (Grant et al. 1975; Sakamoto et al. 1987; Waters et al. 1982; Yumiya and Ghez 1984). Furthermore, there is evidence suggesting some dorsal tracts bypass the sensory cortex completely through the ventralis posterolateralis pars oralis of the thalamus to directly synapse with the motor cortex (Asanuma et al. 1979; Horne and Tracey 1979; Lemon and Van Der Burg 1979; Asanuma et al. 1979). This indicates that some sensory information does not reach conscious perception but is directly dedicated to motor system integration.

Studies in animals have shown the critical role of sensorimotor integration in the performance of coordinated and fine-tuned movements. Prud'Homme and Kalaska (1994) recorded proprioceptive afferent discharge characteristics in the primary somatosensory cortex as a monkey moved the arm in 8 different directions. Neurons demonstrated a direction-dependent discharge pattern during movement analogous to the observation of Georgopoulos et al. (1982) on cortical motor neuron excitability, where greater impulses were seen when the limb was moved in the preferred direction of the neuron. This is indicative of a conscious perception of the direction of limb movement. Moreover, these neuronal activities were heightened during active versus passive movements, providing evidence of sensory involvement in motor performance. In primates, transection of the dorsal column from the thalamus to the motor cortex led to only minor motor deficits that resolved completely over the span of 2 weeks (Asanuma and Arissian 1984). Similarly, when association fiber tracts between the sensory and motor cortices were removed, little to no motor deficit was seen (Asanuma and Arissian 1984). On the other hand, ablation to both these sensorimotor pathways resulted in devastating movement disruptions, including the inability to coordinate limb movements, loss of finger dexterity, and also deficits in spatial orientation. Moreover, localized damage to specific thalamic structures brings about various kinesthetic disorders such as ataxia, dysmetria, paralysis and orientation deficits that resolve only if the association fibers from the sensory cortex are still intact (Bornschlegl and Asanuma 1987). From these results, it can be seen that both the direct (from the thalamus) and indirect (from the sensory cortex) dorsal column connection to the motor system plays a vital role in precision movement control and if one pathway is lost, the other takes over as a compensatory mechanism (Asanuma and Arissian 1984; Bornschlegl and Asanuma 1987).

Results from animal studies have also shown that learning novel motor tasks is dependent on sensorimotor integration. Ipsilateral ablation of association fibers between the sensory and motor cortex led to prolongation of training required to learn a motor skill in the lesioned limb compared to the intact limb (Sakamato et al. 1989). Cats were tasked to pull out a food pellet from a beaker in a fashion that promoted the use of a new motor skill set in the forepaw. The limb ipsilateral to the lesion acquired the skill at a significantly faster rate than the contralateral affected limb. After learning, the remaining sensory pathways were ablated and this led to a drastic reduction in forepaw motor control. Intriguingly, the learned food pellet skill persisted despite the deficit in movement control. Similarly, Pavlides et al. (1993) observed that following a complete elimination of sensory pathways, learning to catch a falling food pellet was severely impaired in monkeys. However, if the skill was taught prior to the lesion, preservation of the motor skill was observed. These studies suggest that when sensorimotor pathways are ablated, previously mastered skills remain unaffected, although the ability to learn new skills is impaired (Pavlides et al. 1993; Sakamoto et al 1989).

In humans, the role of sensorimotor integration on motor control could be most readily observed in studies of people following various neurological disorders, such as Parkinson’s disease (PD), large fiber neuropathy, or stroke. In these conditions, individuals may have loss of some or all proprioceptive sense either centrally or peripherally. For example, individuals with

PD may have difficulty with functional tasks, such as eating with a spoon. It is possible for them to complete the task, but they can experience a high degree of difficulty smoothly moving the spoon to their mouth unless they visually track their arm movement (Proske and Gandevia 2012). As the disease progresses, people with PD increasingly rely on external stimuli such as vision and sound to initiate and control movements (Poizner at al. 2000; Konczak et al. 2009; Arias and Cudeiro 2008). This is primarily due to the deprivation of critical proprioceptive information. In addition, individuals with PD have higher movement detection thresholds when compared to age-matched controls (Konczak et al. 2007). Mano et al. (1979) investigated the underlying changes in muscle spindles in people with PD using microneurography. Recordings from a single afferent of the median nerve demonstrated that the dynamic and static responses of the muscle spindle afferents to stretch in PD do not differ from those seen in able-bodied individuals. As such, the data suggests an intact peripheral muscle spindle system in PD patients, implying that deficits in proprioceptive sense in PD involve impairments in some aspect of central proprioceptive processing (Mano et al. 1979). To address this speculation, Rossini et al. (1989) recorded evoked potentials through electrodes on the scalp while stimulating the median nerve of PD patients. When compared to age-matched controls, these patients showed similar impulses arriving to the primary somatosensory cortex. However, frontal somatosensory evoked potentials were either significantly reduced or absent when compared to controls. Such evoked potentials are used to reflect modulatory control of motor cortical outputs from the supplementary motor cortex in response to sensory inputs (Rossini et al. 1989; Abbruzzese and Berardelli 2003). With a reduction of described cortical characteristics, these results support the notion that central processing abnormalities in sensorimotor integration among PD patients contribute to motor deficits.

People with stroke similarly experience a central lesion to the nervous system, impairing central processing of proprioceptive sense, thus resulting in motor performance and learning deficits (Vidoni and Boyd 2009; Fisher et al. 2000). Vidoni and Boyd (2009) investigated the ability to learn an upper limb tracking task in individuals with chronic stroke. The capability to learn such a task was found to be strongly associated to the amount of spared central proprioceptive processing as assessed through limb position matching. Interestingly, motor function, as measured by the Fugl-Meyer scale, demonstrated no such correlation to motor learning. This study supports the notion that the level of proprioception impairment, more so than the degree of motor paralysis, predicts motor learning capacity in individuals with stroke (Vidoni and Boyd 2009). To further elaborate this concept, Dukelow et al. (2012) examined the relationship between proprioceptive deficit and a visually guided upper limb motor task. Proprioception was assessed using the KINARM robotic exoskeleton. The affected arm was passively moved to a target location in the horizontal plane. Proprioceptive sense was quantified by the size of the matching errors when participants were instructed to use the unaffected arm in order to mirror the position of the affected arm while vision was blocked. Participants were also tested in a visually guided reaching task, which required them to make accurate reaching movements to various targets in space. The results showed that the proprioceptive scores were independent of performance of this motor task. However, proprioceptive scores did strongly relate to a functional independence measure used in the stroke population to assess the ability to perform daily motor activities such as dressing and grooming (Dukelow et al. 2012; Mostafavi et al. 2015). The disparity in these results may indicate that complex whole movements performed in real-world settings reflect functional motor control better than restricted highly controlled reaching tasks within a laboratory setting. Nevertheless, the results of these studies are consistent with the influential role of proprioception in motor control and learning.

While individuals with stroke or PD may have sensory deficits due to impairments in central processing, it is also possible that sensory deficits arise as a result of peripheral damage. The most extreme example of such peripheral full body deafferentation is the specific and complete loss in proprioception due to large-fiber sensory neuropathy (Cole 2009). Although rare, large-fiber sensory neuropathy can be caused by various factors such as, but not limited to, nutrient deficiency, toxin exposure, viral infections and alcoholism (Misra et al. 2008). Cole (2007) reports these patients having a feeling of disembodiment as if floating in midair and unable to move. There are several published reports of an individual, subject IW, who regained walking function only with strong cognitive efforts and high reliance on visual feedback after deafferentation. The subject reported constantly having to focus on the performance of movement in the presence of vision. Yousif et al. (2014) reported IW having decreased static position sense, but preserved active proprioception. This allowed IW to adapt to reaching perturbations only when visual feedback was presented (Yousif et al. 2014). However, in the absence of vision, the subject was unaware of the location of his limbs in space and lost all control of movement (Yousif et al. 2014). Studies of motor coordination in people with deafferentation reveal the critical contribution of proprioception in mediating the inter-joint coordination required for complex multi-joint movements. Sainburg et al. (1993) examined the multi-joint movement patterns in deafferented individuals, who were asked to perform a gesture similar to that of slicing bread requiring coordination between the shoulder, elbow and the wrist. Able-bodied participants were able to maintain a consistent and straight wrist trajectory even in the absence of vision. Conversely, deafferented patients experienced difficulty maintaining a straight wrist path, where curved, nonplanar and temporally abnormal cycles were observed. This indicates that the loss of proprioception disrupts inter-joint coordination where a failure to control interaction among limb segments during movement causes unwanted end point trajectories.

1.3.3 Proprioceptive feedback in the control of walking

Unlike goal-directed movements, walking is considered automatic, with little requirement for conscious effort. However, like goal-directed movements, proprioception is critical for the proper coordination of the repetitive movements of the legs. The neural control of walking involves an interaction between central interneuronal circuits and peripheral sensory feedback. A network of interneurons known as a central pattern generator (CPG) are housed within the lumbosacral spinal cord and are responsible for producing the basic rhythmic locomotor pattern (Grillner and Wallen 1985). Even when isolated from cortical inputs, the lumbosacral spinal cord is capable of generating limb trajectories for gait (Sherrington 1907). Graham-Brown (1911) proposed a half center model to explain such behavior, where the spinal locomotor circuitry consists of extensor and flexor generating centers. Excitatory interneurons responsible for flexor motor neuron activation inhibit excitatory interneuron connected to the extensor motor neurons and vice versa to ensure a repetitive pattern of alternating muscle activation that help a limb transition from swing to stance phase.

While the CPG may suggest a self-sufficient locomotor system, proprioceptive input plays a critical role in shaping locomotor outputs. Hiebert and Pearson (1999) showed that removal of afferent input through lack of ground support significantly reduces extensor muscle activity in decerebrated cats during walking. However, such reduction in activity could be restored by selectively loading the ankle plantarflexor muscles to improve sensory cues.

Furthermore, artificial stimulation of proprioceptive afferents has shown to prolong the stance phase during gait in cats (Whelan et al. 1995). Such data has suggested that sensory inputs adequately represent body weight support which are responsible for triggering the phasic patterns seen through CPG. Hiebert et al. (1996) further demonstrated that stretch of the hip flexor muscles at the end of stance is a critical signal for inhibition of extension in the CPG. Together with unloading of the limb at the end of stance, this underlying mechanism regulates the timing of the stance to swing phase transition. Collectively, these studies illustrate the important role of proprioceptive feedback in regulating the production and timing of normal gait patterns.

1.3.4 Role of proprioception in skilled walking

Although walking consists of highly stereotyped movement patterns, a hallmark of locomotion is the ability to modulate the pattern to navigate everyday environments. External challenges such as obstacles or uneven surfaces require a person to adjust and modify gait kinematics accordingly to ensure safe navigation (Winter 1992). Winter (1992) reported that various joints require different degrees of change to meet similar vertical adjustments of foot trajectory. For example, change of 2˚ at the ankle joint can account for a change of 0.45 cm of vertical foot displacement, while movement of as little as 0.9˚ of hip abduction can account for a similar displacement. With such variability in sensitivity, it was suggested that to achieve minimal toe clearance during swing phase, adjustments along multiple joints across both limbs serve as a requirement for safe locomotion (Winter 1992). This analysis among others (Grasso et al 1998; Grasso et al. 2000), make clear that walking is a precision task driven by regulation of end-point trajectories that are reliant on coordination across multiple joints.

Such end-point based control of gait has been reasoned to be part of complex neural coding that is reliant on the integration of proprioceptive inputs (Lam and Dietz 2009; Lam et al.

2006; Nielsen and Sinkjaer 2002; Pearson 2000; Erni and Dietz 2001). Dorsal spinocerebellar pathway (DSCT) have been recognized as a crucial mediator of inter-limb coordination by consolidating the necessary information of limb position. Sensory neurons that carry lower limb proprioceptive information travel in the posterior fasciculus (PCML pathway). However, some of these neurons synapse with the nucleus dorsalis of Clark and continue to ascend via the DSCT in the dorsolateral funiculus. This pathway carries proprioceptive information from the lower extremity to the cerebellum, and so, unlike the sensory input of PCML, does not reach conscious perception. Extracellular recordings of the axons of the DSCT during passive hindlimb movements of anesthetized cats showed that neurons encode for both paw position and direction of movement simultaneously (Bosco and Poppele 1997). Moreover, neurons showed specificity of discharge, where particular limb positions resulted in higher impulse rates for some neurons than others. This suggests dedicated neuronal clusters responsible for particular limb positions in space. Interestingly, such direction-dependent activity patterns were more strongly correlated to the end point position, as opposed to specific joint angles or muscle lengths. This data provides evidence of the DSCT's role in processing inter-joint information suggesting the cerebellum's role in consolidating and coding sensory signals. (Bosco and Poppele 1997).

Information flow to the cerebellum is critical for multi-joint whole limb movements, such as reaching or locomotor gait adjustments to cross obstacles. Fuentes and Bastian (2007) in a review article explain the role of cerebellum as a predictor of self-generated movements. The cerebellum utilizes a predictive forward model to allow for efficient movement control where early online corrections are driven by the constant comparison between predicted and desired movement trajectories (Fuentes and Bastian 2007). Such sensorimotor mechanisms have been studied at both physiological and behavioral levels. In a review of the mechanisms of locomotor control in the cerebellum, Yanagihara (2010) discussed the mossy fiber input of proprioceptive information from the DSCT to Purkinje neurons in the cerebellum, which in turn modulate the efferent output to multiple joints to regulate the complex movements of locomotion (Yanagihara 2010). Furthermore, Vinueza Veloz et al. (2014) showed that mice with impaired Purkinje cell output exhibit severe impairments in locomotor control, as demonstrated through inconsistent walking patterns, dysfunctional inter-joint coordination and the use of maladaptive obstacle crossing strategies.

Obstacle crossing is widely used to study the contribution of sensorimotor integration to a skilled walking task. In quadrupeds, such as cats, observation of the characteristic interaction between the forelimb and hindlimb provides valuable insight into the sensorimotor integration required for obstacle crossing (Drew and Marigold 2015). During obstacle crossing, cats cross first with the forelimbs, followed afterwards by the hindlimb. However, unlike the forelimb, the hindlimb does not benefit from direct visual feedback control of obstacle crossing. Thus, it was theorized that there must be some form of working memory interaction between the limbs in order to ensure successful hindlimb obstacle crossing. To investigate this, McVea and Pearson (2007b) stopped the cat after the forelimb but before the hindlimb had crossed an obstacle. Surprisingly, it was observed that information pertaining to the obstacle size and spatial location was transferred to the hindlimb even after a delay of 10 minutes, a period that significantly exceeded previously held assertions of working memory (McVea and Pearson 2006). Furthermore, even in the absence of vision, cutaneous information provided in the forelimb was enough to elicit similar locomotor modifications in the hindlimb (McVea and Pearson 2007a). It was suggested that this prolongation of working memory to transfer spatial information to other parts of the body is possible due to the integration of proprioceptive among other sensory information such as visual or cutaneous feedback (McVea and Pearson 2007b). It has been postulated that the posterior parietal cortex (PPC) is responsible for the mechanism used in the clearance of obstacles (Marigold et al. 2011; McVea and Pearson 2007a). Andujar et al. (2009) recorded various cells from the PPC as cats crossed obstacle targets. It was observed that in the presence of an obstacle, 84% of neurons display modulated activity from basic locomotor rhythmic patterns during or prio the obstacle step. The general theme to consider from these studies is that sensory input which signal environmental context pertaining to perturbations, such as obstacle information, plays an essential role in shaping the basic pattern of locomotion.

In humans, insight into the role of proprioception during precise obstacle crossing tasks has been further elaborated by studies involving SCI participants (van Hedel et al. 2005). Participants were tasked to cross an oncoming obstacle with minimal toe clearance while input from the lower visual field was blocked during treadmill walking. Acoustic feedback was provided to inform the participant how accurately they were able to cross the obstacle at the desired target height. When compared to able-bodied controls, SCI participants were slower to learn the task and exhibited poorer overall performance. Further, the SCI participants with greater somatosensory impairment demonstrated the highest variability and worst performance. It was suggested that in the absence of vision, acoustic information provides the needed feedback to integrate lower limb proprioception in order to fine tune inter-limb coordination required for effective obstacle crossing. Since individuals with SCI have variable impairments in tactile and proprioceptive inputs, it is expected that such integration is difficult and leads to deficits in accurate locomotor adjustments.

1.4 Plasticity In The Sensory System

Neural plasticity refers to the ability of the nervous system to reorganize itself systematically to adapt to environmental or circumstantial changes. This notion challenges the previously held consensus that most neural changes, especially cortical, occur during childhood development and that the adult brain is rather static. It is now well known that the nervous system constantly changes not only in response to learning, but also after injury and far into adult life (Pascual-Leone 2005). This section outlines the evidence for plasticity within the sensory system and examines research on how to foster such changes.

1.4.1 Evidence of sensory plasticity

There is compelling evidence in support for spontaneous changes within the somatosensory cortex as a result of skill learning. Moreover, these skills can be regained in other brain regions if the cortex is damaged. Xerri et al (1998) showed that when a monkey was taught a small object retrieval task, changes in somatosensory brain region 3b, which represents cutaneous input of digits important for skill acquisition, occurred. It was then observed that destruction of area 3b through micro-lesion deteriorated the learned motor skill. However, over several weeks, the monkeys showed recovery of these skills, and this occurred in parallel to a re-mapping of the cortical cutaneous representation to a different part of the somatosensory cortex including areas 1 and 3a (Xerri 1998). Similarly, Merzenich et al. (1984) observed that by providing digit amputation, monkeys show an increased topological representation of adjacent digits instead of cortical atrophy of the lost body part. These findings were primarily due to the plastic changes of the somatosensory cortex when the cortical representation of adjacent non-amputated digits took over non-functioning amputated territories (Merzenich et al. 1984).

1.4.2 Sensory plasticity after spinal cord injury

Sensory plasticity in humans has mostly been demonstrated through cases of amputation and various neurological conditions such as SCI. Changes are evident within the sensory homunculus, a topological sensory representation of various body parts in the cerebral cortex. Anatomically the homunculus is systematically organized where lower limb, arm, hand and face representations are found in a mediolateral fashion respectively. Ramachandran and Hirstein (1998) reported that individuals with hand amputations perceived hand sensory stimulus when touched either on the face or the amputation stump, and interpreted these observations as evidence for plastic changes occurring within the sensory homunculus. With cortical reorganization, adjacent functioning homunculus regions, including the face and the stump, invade territories of the now deafferented body representation of the amputated hand. Since functioning areas expanded into novel regions, sensory stimulation of the face and stump will lead to the perception of the hand being touched.

Sensory reorganization has also been shown following SCI. Henderson et al. (2011) used functional magnetic resonance imaging (fMRI) to investigate sensory reorganization in people with complete SCI at the thoracic level. Somatosensation of the little finger was elicited by a plastic brush and changes were tracked based on fMRI activity. The results showed that there was a medial shift of the adjacent hand areas as they took over the representation of the lower limb. Interestingly, the degree of cortical reorganization was independent of injury level, but was strongly correlated to the time since injury when images were taken. This indicates that not only is sensory plasticity prevalent among SCI individuals, but chronicity serves as an important factor on the degree of reorganization. Moreover, Wrigley et al. (2009) reported similar fMRI findings of the little finger and correlated the degree of reorganization to the level of neuropathic pain experienced by individuals with SCI. Pain levels were assessed using the International Association for the Study of Pain SCI Pain Taxonomy. It was determined that higher pain scores correlated with larger medial displacement of the little finger into the lower limb territory. This indicates that higher levels of somatosensory pain may be a result of greater cortical reorganization following SCI (Wrigley et al. 2009). The mechanism of such reorganization has been thought to be due to either sprouting of new neurons in the cortex, or unmasking of dormant connections elicited through injury. Recent findings by Kambi et al (2014) indicate that plastic changes might be driven by the brainstem instead of previously mentioned cortical mechanisms. In monkeys with dorsal column lesion, it was found that given enough recovery time, somatosensory cortical expansion of the chin area into the adjacent affected hand region occurred. Even when neural activity of the chin somatosensory cortical area was blocked with lidocaine, evidence of the cortical reorganization was still detected. However, when lidocaine was infused to the cuneate nucleus in the brainstem, all traces of cortical reorganization were abolished. These findings thus indicate that the manifestation of somatosensory cortical expansion of the chin area occurred due to plasticity in brainstem nuclei rather than the cortex. Kambi et al (2014) suggested that a major reason for this might be the fact that the topological representation of the homunculus was more confined within the brainstem versus the cortex and axonal sprouting of just short distances within the cuneate nucleus could lead to more widespread plastic changes seen cortically upstream. Moreover, Green et al. (1998) has shown that in SCI, motor sparing is possible for muscles below the lesion area due to somatosensory reorganization accommodating for the motor loss. Normally cortical somatic areas have well-organized motor outflows that function during motor performances. As such, it was explained that reorganization of the somatosensory cortex serves as motor reinforcements in the event injury compromises muscle function.

1.4.3 Training dependent sensory plasticity

Sensory reorganization is dynamically maintained and use-dependent. If the cortical area is chronically disengaged (e.g. through lack of tactile stimulation or use), reduction in sensory representation can be seen (Xerri et al. 1996). For instance, Xerri et al. (1996) showed a 50% degradation of the forepaw representation in somatosensory cortex after a period of restricted tactile feedback in adult rats. Such evidence has led to the idea of training based plasticity in order to induce neural recovery following SCI (Xerri 2012). Xerri (2012) has suggested that constant environmental engagement leads to continuous refining of the neural system. As a result, the employment of rehabilitation strategies has the potential to improve SCI recovery (Xerri 2012).

It is well known now that plastic changes can be facilitated through training and rehabilitation interventions. While this is commonly used to drive motor changes, there is some emerging evidence in support of the possibility of changes in proprioception through training. Proprioception, until recently, has been considered static or innate in which the system remains unaltered unless damaged. Using a hand-held manipulandum controlled by a robot, Ostry et al. (2010) trained the upper limb in a reaching task where movements were perturbed either to the right or left by a force-field. Once participants adjusted their reaching movements to the presence of the force field, upper limb proprioception thresholds were evaluated by means of a forced choice protocol to test the subjects' perceived left-right boundary and compared to before task learning. It was reported that there was a shift in subjects' left-right perceptual boundary in the direction opposite the force field, and such changes persisted up to 24 hours after training.

Similarly, a study by Wong et al. (2011) employed a motor task that required the participant grasp a robotic arm and guide a cursor to a randomly displayed visual target. Proprioceptive acuity was measured using a passive forced choice methodology where participants were asked whether the perceived hand location was either right or left to a previously known location. It was demonstrated that improvements in distinguishing hand position was seen as a result of motor learning, but that was only persistent when assessed within the workspace of the training. Thus, changes in sensory function may occur in parallel with changes in motor function when learning a new task.

Not only can motor learning alter proprioception, but training proprioceptive sense may also provide benefits for motor performance. Ju et al. (2013) investigated the effects of passive training intervention on knee proprioceptive acuity. This training required a motorized apparatus and provided repetitions of passive high velocity (90˚/s) joint angle changes to the knee joint. It was determined that those who were given multiple rapid passive movements of the knee showed enhancements in proprioception as measured by the error in active repositioning of previously known joint angles (Ju et al. 2013). Wong et al. (2012) examined the ability to improve upper limb proprioceptive sensation and its effects on motor performance. In the absence of vision, training of the upper limb was done passively, as a robot moved the arm in a circular pattern for a number of trials. When asked to actively retrace the shape, it was determined that those who received feedback about their upper limb during the passive movement training were better able to do so accurately. Additionally, upper limb proprioceptive scores significantly improved post training. Such data suggests that given meaningful feedback, passive limb movements can enhance proprioceptive acuity which further leads to improvements in motor performance of similar caliber (Wong et al. 2012). In a similar paradigm, Darainy et al. (2013) had individuals partake in a perceptual learning task. These are tasks that require certain sensory aspects to effectively learn a motor task. Individuals performed a perceptual learning task where the arm was passively moved in a fan shaped trajectory. Subjects were required to indicate whether the robot moved the limb right or left after which feedback on judgment accuracy was provided. Darainy et al. (2013) showed that such training caused improvements in the rate and extent of learning a subsequent reaching task. Since accurate reaching is strongly dependent on sensory integration, it can be explained that sensory improvements through perceptual learning enhances motor performance. Additionally, Lee et al. (2015) found that training lower limb proprioception on balance boards shows positive effects on balance capabilities in stroke patients (Lee et al. 2015). Moreover, when motor imagery training of focusing on hip, knee and ankle joint position senses was employed in conjunction with proprioception training, greater balance improvements were seen (Lee et al. 2015). Collectively, these results support the malleability and plastic nature of the proprioceptive sense as a result of different training interventions.

1.5 Summary and Rationale

Proprioception is critical in the control of all movements. During walking, the requirement for the precise, multi-joint coordination relies on online monitoring of proprioceptive input to adjust for ongoing changes in walking conditions. Moreover, proprioception is malleable and acuity can be modified by training or experience.

In SCI, there is damage to neural structures impairing motor output as well as sensation, including proprioception. As a result, the motor control of walking becomes extremely difficult causing dramatic impact on activities of daily living and functional independence. Current rehabilitation interventions have been built on a foundation of treatment based on motor recovery. Although the recovery of motor output is important, little effort has been made to integrate sensory training into contemporary clinical practice. Since impairments in sensory function can impact motor output, it is imperative that some form of proprioceptive training be implemented after SCI, especially considering the critical role of proprioception on functional ambulation. Thus the overall objective of this thesis was to develop and test a novel intervention to improve lower limb proprioceptive sense and to investigate whether such improvements could translate to improvements in skilled walking in people with chronic SCI.

1.5.1 Specific hypothesis

Hypothesis 1: Feedback based proprioceptive training of end-point (foot) position will improve proprioceptive acuity, as measured by a) knee joint position sense and b) end-point position sense.

Hypothesis 2: Feedback based proprioceptive training of end-point position will improve skilled walking performance.

Hypothesis 3: Improvements in knee joint position sense, end-point position sense and skilled walking performance will persist for up to 24 hours after proprioception training.

Chapter 2: Methods

2.1 Subjects

Individuals with SCI and able-bodied (AB) participants were recruited for this study. The inclusion criteria for participants with SCI were: 1) SCI at least 9 months ago; 2) motor-incomplete or sensory-incomplete spinal cord injury (AIS B, C or D as determined by the ISNCSCI); and 3) able to modulate foot height for at least 40 steps with or without an aid while walking over a treadmill (for those individuals able to perform a skilled walking task). The exclusion criteria were: 1) AIS A classification (complete injury paralysis with no sensory or motor preservation); 2) presence of any musculoskeletal injury or other neurological or cardiovascular condition; 3) severe spasticity which interferes with proprioception training or walking assessments; 4) demonstrated cognitive impairments with a score of 25 or less on the Montreal Cognitive Assessment (MOCA); and 5) weight greater than 136 kg or height taller than 1.85 m. Inclusion and exclusion criteria for the AB subjects were the same, except for history of SCI. All study procedures were approved by the UBC Clinical Research Ethics Board and all subjects gave their written, informed consent prior to participation

2.2 Protocol

2.2.1 Experimental procedures

The study was completed in 3 sessions. During the first session, manual muscle testing was performed as outlined by the ISNCSCI for the SCI individuals (Appendix A). The muscle testing assessed hip flexor, knee extensor, ankle plantarflexor, ankle dorsiflexor and great toe extensor muscles bilaterally and scored on a scale out of 5. The sensory component of the ISNCSCI assessment measured the light touch and pinprick scores of each dermatome. The sensory scores were used to determine the sensory weaker leg and that limb was used for the remainder of the assessments and training. In the AB subjects, the non-dominant leg was identified, as per the Edinburgh footedness questionnaire (Appendix B). All SCI participants also completed the MOCA to screen for any attention or memory deficits (Appendix C).

Participants then performed a skilled walking test to record Pre-training motor performance, followed by an assessment of knee joint position sense (JPS) and heel end-point discrimination (EPD) tasks to record Pre-training proprioception scores. This was followed by the lower limb proprioceptive acuity training consisting of 6 blocks of training distributed over a 2-day period. Immediately after training, the skilled walking, knee JPS and heel EPD tests were repeated. These measures were also assessed on the third day to evaluate 24-hr retention. Unfortunately, not all subjects were able to complete the 24-hr retention testing. Details of the skilled walking, lower limb proprioception testing, and training protocols are provided in the following sections. AB subjects did not perform the skilled walking task. Please refer to Figure 1 for procedure outline.

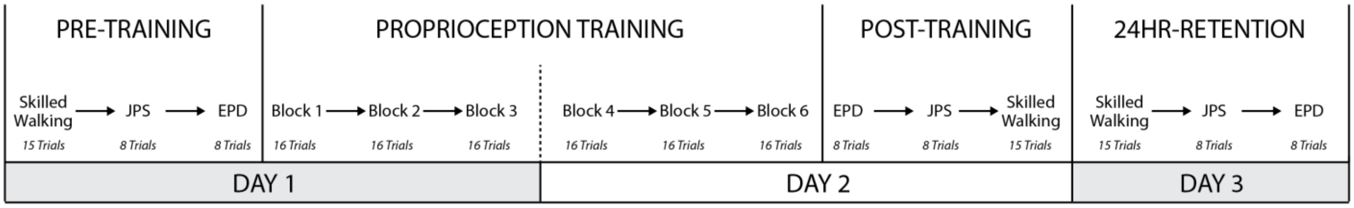

Figure 1 Experimental protocol.

2.2.2.1 Target matching task

The walking task was conducted on a treadmill (Woodway, Wisconsin, USA) at each participant’s self-selected comfortable speed. The goal of the skilled walking task was to match peak foot trajectory height in the swing phase to the height of a virtual target displayed on a monitor. An infrared-emitting diode (Optotrak, NDI, Waterloo, ON) affixed to the lateral aspect of the heel below the lateral malleolus of the sensory weaker limb was used to provide visual feedback of the participant’s foot position relative to the target height. The monitor projected a sagittal plane view of the participant’s foot and target position. The target was displayed as a yellow bar with a circle representing the target height. At the time of heel strike, the virtual target appeared on the monitor (real-time streaming at 100 Hz) and participants were instructed to match the height of their foot during the subsequent swing phase to the target. Visual feedback was provided via a green dot, which appeared for 500 ms at the end of the swing phase, representing the actual position in relation to the target height. Errors were measured as the vertical distance between the foot’s position and the target (Figure 2). Therefore, a lower score is indicative of better performance. The target was presented every second step. Participants completed 15 target-matching trials prior to and after passive proprioceptive training to track changes in motor performance.

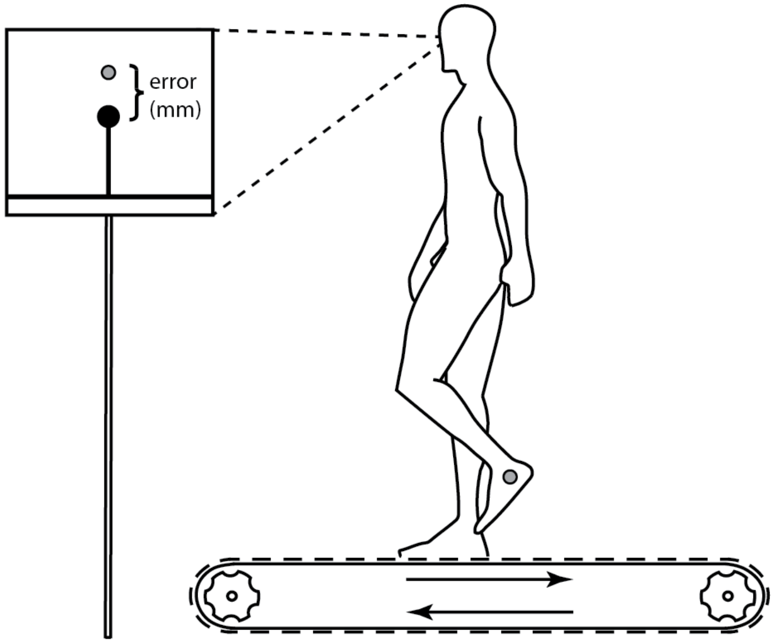

Figure 2 Skilled walking task. Participants performed a skilled walking task on a treadmill requiring them to match vertical foot height during swing with a virtual target displayed on a monitor in front of them. The vertical foot position in relation to the target height (error) was provided as visual feedback and to measure motor performance.

2.2.2.2 Determining obstacle height

Due to the heterogeneity of the degree of motor impairment among people with motor-incomplete SCI, we scaled the target height to each person's walking ability. Participants were asked to walk 'normally' on the treadmill for 1 minute. They were then asked to 'walk while stepping as high as possible' for another minute. Normal heel height (*Norm*) and maximum heel height (*Max*) during swing phase were calculated from these trials. Target height for each participant was then determined by the following equation:

$$\frac{Max - Norm}{4} + Norm$$

2.2.3 Knee proprioceptive sense assessment

Static knee JPS was measured using custom-written software of the Lokomat robotic exoskeleton (Hocoma AG, Volketswil, Switzerland) (Domingo and Lam 2014). Participants were strapped to the exoskeleton by leg cuffs around the mid-thigh and lower leg while being stabilized by a waist belt and harness connected to a counter-weight body weight support system. The ankle was additionally supported in a neutral position by a passive foot lifter. Participants were raised so that their sensory weaker leg was suspended in the air to ensure that the leg could move freely; the other leg was supported by a raised platform placed on the treadmill belt. Vision of both legs was blocked by a drape. Participants were instructed to remain passive during proprioceptive testing. This was confirmed visually by the experimenter during the test by real time streaming of surface electromyography data (Delsys, Massachusetts, USA) of tibialis anterior, medial gastrocnemius, rectus femoris, and biceps femoris muscles.

The test protocol consisted of 8 trials and the target position was always 25˚ of knee flexion. First, the Lokomat positioned the knee joint to the target position and participants were asked to memorize the position. Five seconds later, the Lokomat displaced the leg by either 5˚, 10˚, or 15˚ in either flexion or extension to a secondary position, moving at a speed of 7˚/s. Participants were instructed to then moved their leg back to the memorized target position by using a joystick that moved the Lokomat at 3 or 6°/s, depending on how far they pushed the joystick handle (Domingo and Lam 2014) (Figure 3). Ten trials (5 flexion and 5 extension trials) were presented in random order. A lower score indicated better position sense (scoring details provided below in Data Analysis). Domingo and Lam (2014) have previously shown the high test retest reliability of this robotic based joint position sense assessment within able bodied and SCI individuals (ICC at the knee joint = 0.656 for AB and 0.882 for SCI).

To account for any thixotropic effects of muscle on proprioception (Proske and Gandevia 2012), the muscle was passively flexed and extended to relieve any cross bridges in the myocytes. This was done once prior to the start of the assessment or in cases where the participant experienced spasm or clonus during the test session.

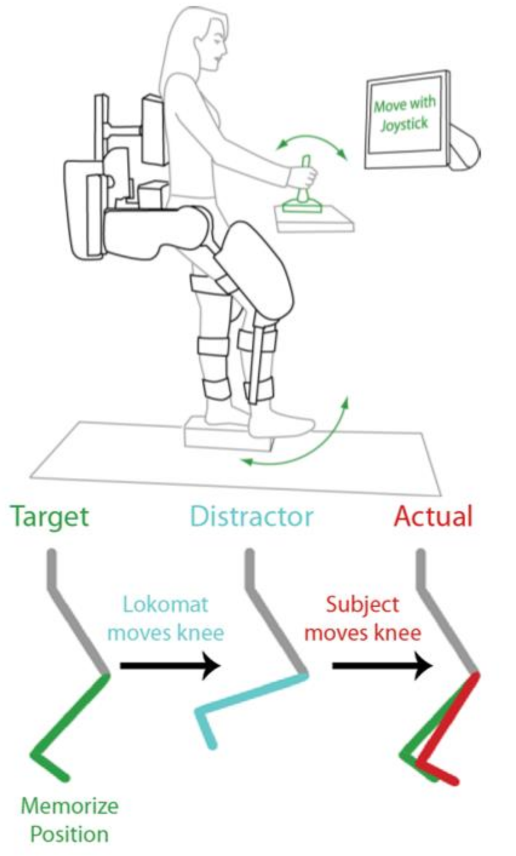

Figure 3 Knee JPS assessment. Participants were asked to memorize a target knee position. The exoskeleton then moved the leg to a distractor position and using a joystick, participants were asked to match the knee angle to the memorized target position.

2.2.4 Heel end-point discrimination assessment

Heel EPD assessment was also done within the Lokomat where participants were suspended and harnessed similar to JPS assessment. The Lokomat started at a position where the limb angle (defined as the angle between midline and a straight line drawn between the hip joint center and heel position) was 5˚ and the knee flexed at 47˚. This initial position mimicked the typical position of the lower limb at approximately mid-swing phase, when the foot crosses the target. Participants were asked to focus on their heel position in space and memorize it. The Lokomat then moved the limb away from the start position to a neutral position (5˚ of knee flexion and 5˚ of hip flexion) at 15˚/s and held that position for 5 seconds. The robotic leg then moved to a new position that was either higher or lower relative to the memorized position (mimicking target crossing positions of various heights). The participants were then asked to report whether they felt their heel position was higher, lower, or in the same position as the memorized position. Responses of 8 trials of various heel displacements were recorded (calculations and distribution of heights are explained in the Proprioception Training section) (Figure 4).

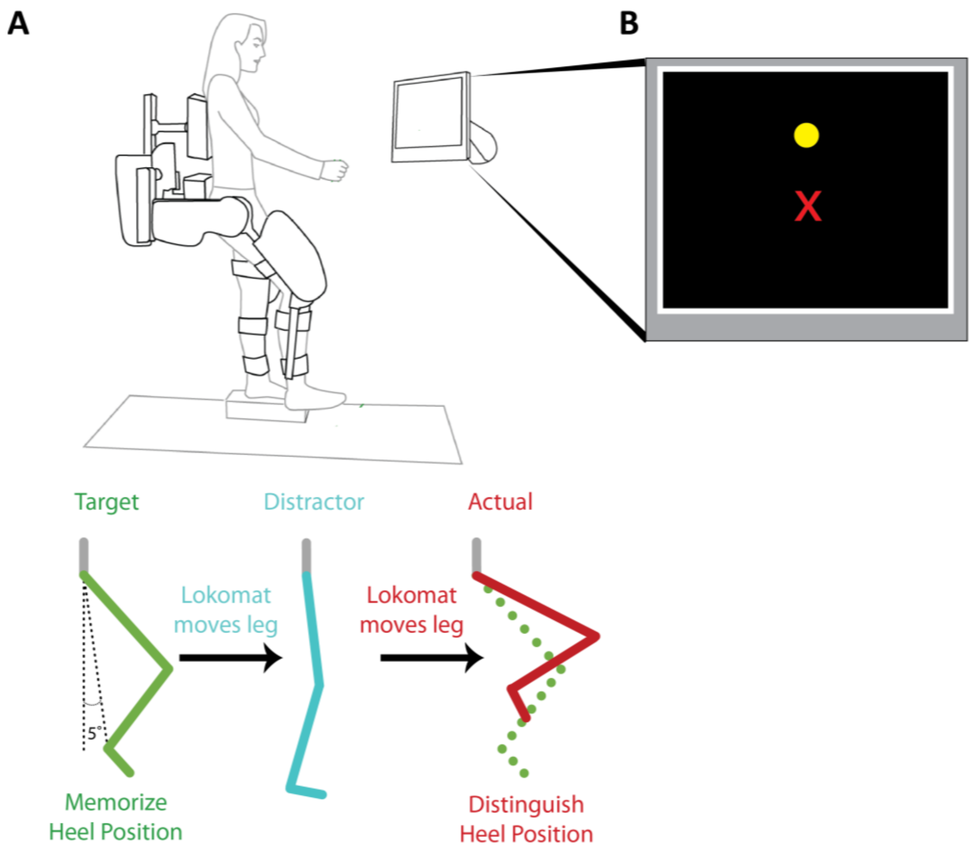

Figure 4 A) EPD assessment and training protocol. Participants were asked to memorize a target heel position. The leg was then moved to a distractor neutral position. The heel position then moved to a position that was higher or lower than the memorized position. B) Visual feedback that was provided to participants after each trail during training. The red X denotes the memorized heel position while the yellow dot represents the final heel position

2.2.5 Proprioception training

Here we aimed to train lower limb proprioceptive sense by providing feedback during a forced choice task. Participants practiced the heel EPD task (described above), but with the addition of visual feedback after every response. Visual feedback was provided on a monitor, with a red X representing the memorized position and a yellow dot representing the new position (Figure 4).

To standardize the training to each individual's baseline proprioceptive sense, participants were given heel EPD trials that were based on the vertical change in heel height corresponding to the Pre-training knee JPS. The heel EPD trials were categorized as Easy, Medium, or Hard that were higher (H) or lower (L) than the memorized position (Figure 5). H Easy trials were test trials that moved the heel to a position that was higher by a distance corresponding to the average Pre-training knee JPS plus 0.5 SD. Test trials that moved the heel to a position corresponding to the average Pre-training knee JPS were denoted by as H Med and those that corresponded to the average Pre-training knee JPS minus 0.5 SD were defined as H Hard. Similarly, there were corresponding training positions that moved the heel to a lower position (L Easy, L Med, and L Hard). More training trials at the Hard trials were provided and relatively fewer at the Easy trials. To achieve this, a bell curve for 16 trials per block was determined where 4 trials each of H Hard and L Hard, 3 trials each of H Med and L Med, and 1 trial each of H Easy and L Easy were given to participants. Training took place over 2 separate days, each with 3 training blocks (total of 96 trials) (Figure 5).

Table 1 shows the calculated average and range of hip and knee angle joints during proprioception training and heel EPD. The majority of angle changes to reach the vertical height displacement was through the knee joint while minimal displacement of the hip joint occurred.

Table 1 Heel EPD and proprioception training average hip and knee angle changes

	EASY				**MED**				**HARD**			
	Higher		**Lower**		**Higher**		**Lower**		**Higher**		**Lower**	
	Hip	**Knee**	**Hip**	**Knee**	**Hip**	**Knee**	**Hip**	**Knee**	**Hip**	**Knee**	**Hip**	**Knee**
Mean	3.4	6.0	3.4	6.0	2.6	4.6	2.6	4.6	1.8	3.2	1.8	3.2
SD	2.6	4.7	2.5	4.7	2.0	3.6	1.9	3.6	1.4	2.5	1.4	2.5
Min	0.7	1.3	0.7	1.3	0.6	1.0	0.6	1.0	0.4	0.7	0.4	0.7
Max	11.3	20.8	11.2	20.8	8.6	15.9	8.6	15.9	6.0	11.0	5.9	11.0

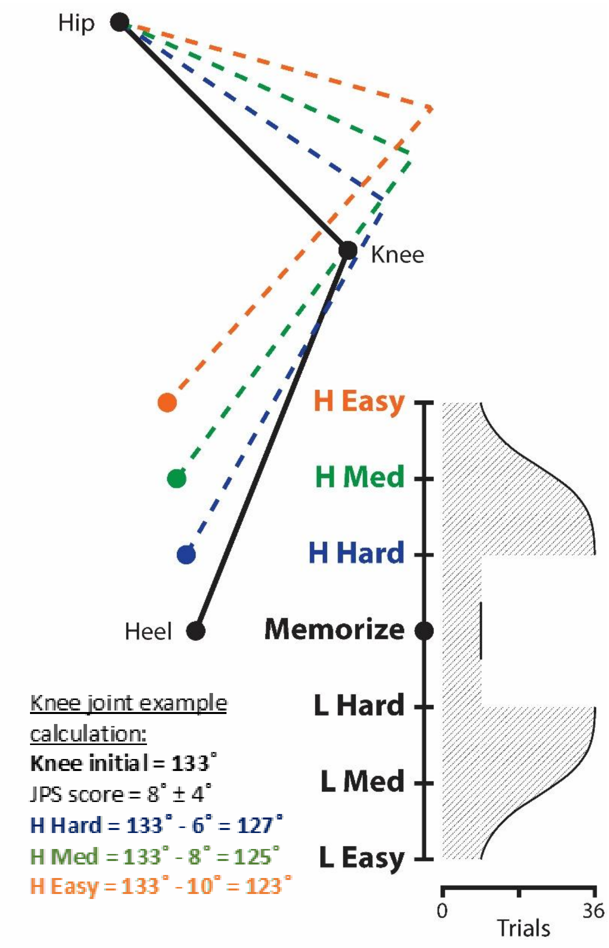

Figure 5 Proprioception training protocol calculation. Target heel positions were determined by using participant's knee JPS average score assessed at Pre-training. Training was therefore based on a range of vertical heel height displacements corresponding to the average knee joint angle error. Number of trials were given based on a normal distribution (right) where H Hard and L Hard trials are presented and trained more often. For the purposes of simplicity, only the higher trial positions and sample calculations are shown.

2.3 Data Analysis

During training, correct and incorrect responses were coded as 1 or 0, respectively. An average response score (ARS) was calculated for difficulty level (Easy, Med, Hard) and specific trial direction (Higher or Lower). Response score variability was also determined by calculating the coefficient of variation of the response scores (CoVRS) according to difficulty level and specific trial direction.

Knee JPS error was determined as the absolute error in degrees away from the target knee joint position. The average knee JPS score across 8 trials was calculated for each subject during Pre-training, Post-training, and 24Hr-retention.

Heel EPD scores were coded as 1 (for correct responses) or 0 (for incorrect responses). The average heel EPD score across 8 trials was then calculated for each subject during Pre-training, Post-training, and 24Hr-retention.

Skilled walking performance was determined as the average error, in mm, of the last 10 target-matching steps during Pre-training, Post-training, and 24Hr-retention. Variability in skilled walking was also calculated by CoV across the last 10 target-matching steps during Pre-training, Post-training, and 24Hr-retention tests. We also calculated the average error of the first 5 steps during Pre-training, Post-training, and 24Hr-retention to determine whether there were any carry over effects from prior exposure to the skilled walking assessment.

2.4 Statistical Analysis

All statistical tests were analyzed at an alpha of 0.05 using SPSS software (SPSS Inc, Armonk, New York). Data were checked for normality using the Shapiro-Wilk test and were log-transformed, if necessary (specified below), prior to the following statistical analysis.

To determine if there were any differences in the ARS among the different target positions used during training, we used a 2 x 3 ANOVA to compare the within subject variable of trial direction (Higher and Lower) with the between subject variables of trial difficulty (Easy, Med, Hard). Pairwise post-hoc comparisons were performed using the Bonferroni correction for multiple comparisons. The same analysis was conducted for the CoVRS.

Spearman's rank correlation coefficient was calculated to describe the relationship between Pre-training Knee JPS and Post-training Knee JPS. To determine if knee JPS changed after proprioception training, we utilized a 2 x 2 ANOVA after $\log_{10}$ transforming the JPS values, where the within-subjects variable was time (Pre-training and Post-training) while the between-subjects variable was group (SCI and AB). Because not all subjects were able to complete the 24-hr retention testing, we performed a secondary 3 (Pre-training, Post-training, 24Hr-retention) x 2 (SCI, AB) ANOVA with repeated measures for on the subset of data where retention data were available (n = 10 SCI; n = 5 AB), with Pre-training knee JPS as a covariate. Pairwise post-hoc comparisons were performed using the Bonferroni correction for multiple comparisons. The same analysis was conducted for Heel EPD.

To assess if there were any improvements in skilled walking performance (SCI group only) from Pre-training to Post-training, we utilized a paired student's t-test. We also performed a repeated measures ANOVA on skilled walking performance to compare Pre-training, Post-training, and 24Hr-retention only for those individuals who completed retention testing (n = 4). Pairwise post-hoc comparisons were performed using the Bonferroni correction for multiple comparisons. The same analysis was conducted for the CoV of the skilled walking performance. Similar analysis was done for the data from the first 5 steps to determine whether there was any carry over effect from previous skilled walking assessment.

Chapter 3: Results

3.1 Subject Characteristics

13 SCI (mean age of 50 ± 13) and 10 AB (mean age 27 ± 4.4) participants participated in this study. Seven SCI participants were classified as ASIA D, 5 as ASIA C and 1 as ASIA B. All participants were within the normal cognitive functional range as determined by the MOCA test. Full SCI and AB participant characteristics are outlined in Tables 2 and 3, respectively.

Table 2 SCI participant characteristics

Code	Age	Sex	Height (cm)	Weight (kg)	AIS Classification	Light Touch AIS (/112)	Light Touch L1-S3 AIS (/16)	Injury Level	Years post injury	Cause of injury	MOCA score (/30)
S01	61	F	155	64	D	102	16	L2-S1	49	Surgery	27
S02	35	M	175	60	C	71	8	C5-C6	14	Fall	27
S03	58	M	178	88	D	55	8	C3-C5	41	Motor vehicle accident	31
S04	30	M	165	70	C	57	4	T9, C7	7	Transverse myelitis	26
S05	50	M	188	86	D	76	8	C3-C7	7	Fall	26
S06	65	M	175	80	D	76	8	C4-C5	5	Surgery	29
S07	48	F	165	64	D	59	8	C4	4	Tumor	31
S08	50	M	170	85	D	82	9	C3-C6	3	Tumor	30
S09	40	M	183	84	D	86	7	C7	14	Motor vehicle accident	31
S10	43	M	173	68	B	66	8	C7	10	Work injury	30
S11	34	M	172	81	C	65	7	T5-T6	15	Trauma	28
S12	68	M	188	75	C	43	8	C3-C4	4	Trauma	28
S13	63	M	180	78	C	72	2	T12-L1	10	Motor vehicle accident	30

Table 3 AB participant characteristics

Code	Age	Sex	Height (cm)	Weight (kg)
A01	50	F	N/A	N/A
A02	24	M	170	62
A03	34	M	189	93
A04	29	M	173	85
A05	23	F	173	75
A06	30	M	172	68
A07	30	F	160	52
A08	21	M	168	50
A09	29	M	180	80
A10	23	F	157	50

3.2 Training Trials

ARS during the training trials did not significantly differ across difficulty level ($F_{2,63}$ = 0.720, p=0.491), but there was a main effect of trial height ($F_{2,63}$ = 6.446, p = 0.014). During training, ARS were better for higher targets (M = 0.774, SD = 0.220) versus lower targets (M = 0.681, SD = 0.263). There was no interaction effect ($F_{2,63}$ = 0.980, p=0.381) (Figure 6). Over the course of training, a pattern towards increasing ARS was observed for Med trials, but such a pattern was not as apparent in the Easy and Hard trials (Figure 7).

CoVRS during training did not vary across trial difficulty ($F_{2,63}$ = 0.210, p=0.811) but there was a main effect of trial height ($F_{2,63}$ = 7.734, p = 0.007). CoVRS during training was lower for higher targets (M = 0.516, SD = 0.435) versus lower targets (M = 0.761, SD = 0.721). There were no significant interaction effects ($F_{2,63}$ = 1.402, p=0.254) (Figure 6).

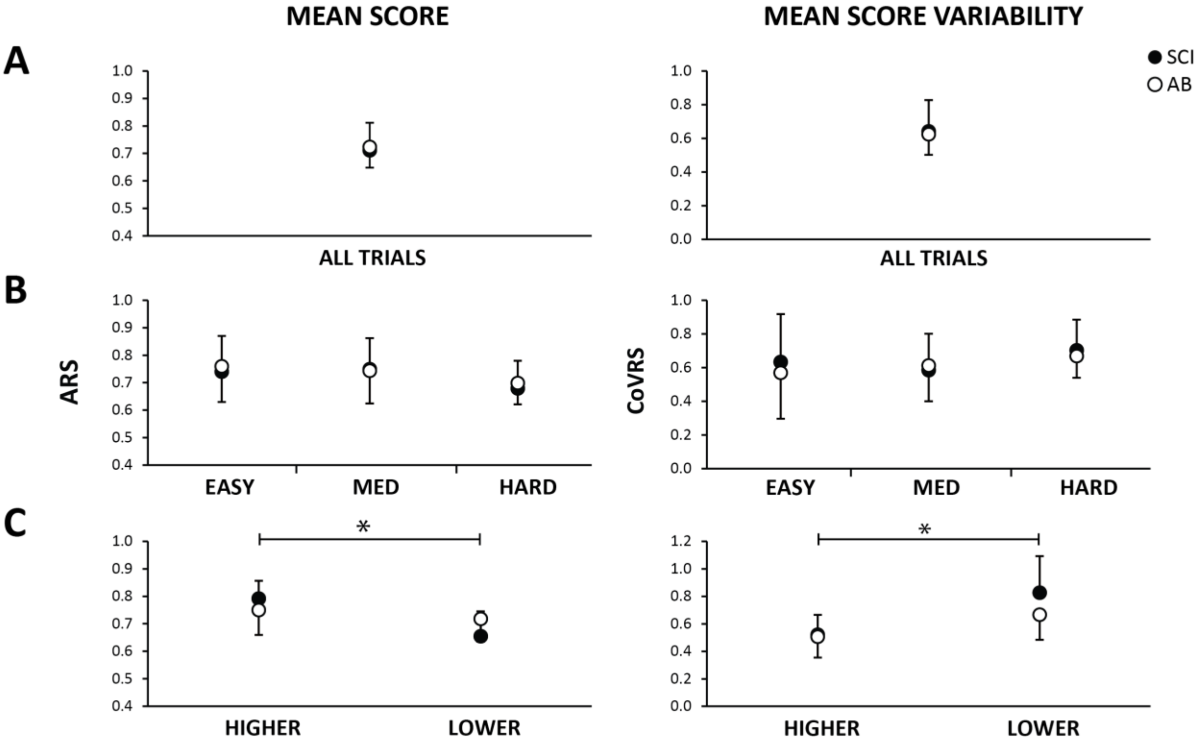

Figure 6 Mean ARS and its variability during training. Mean ARS (left panel) and CoVRS (right panel) for SCI and AB participants in terms of all trials (A), trials divided by difficulty level (B) and trials divided into specific heights (C). Error bars represent the 95% confidence interval. Significant differences are indicated by asterisk.

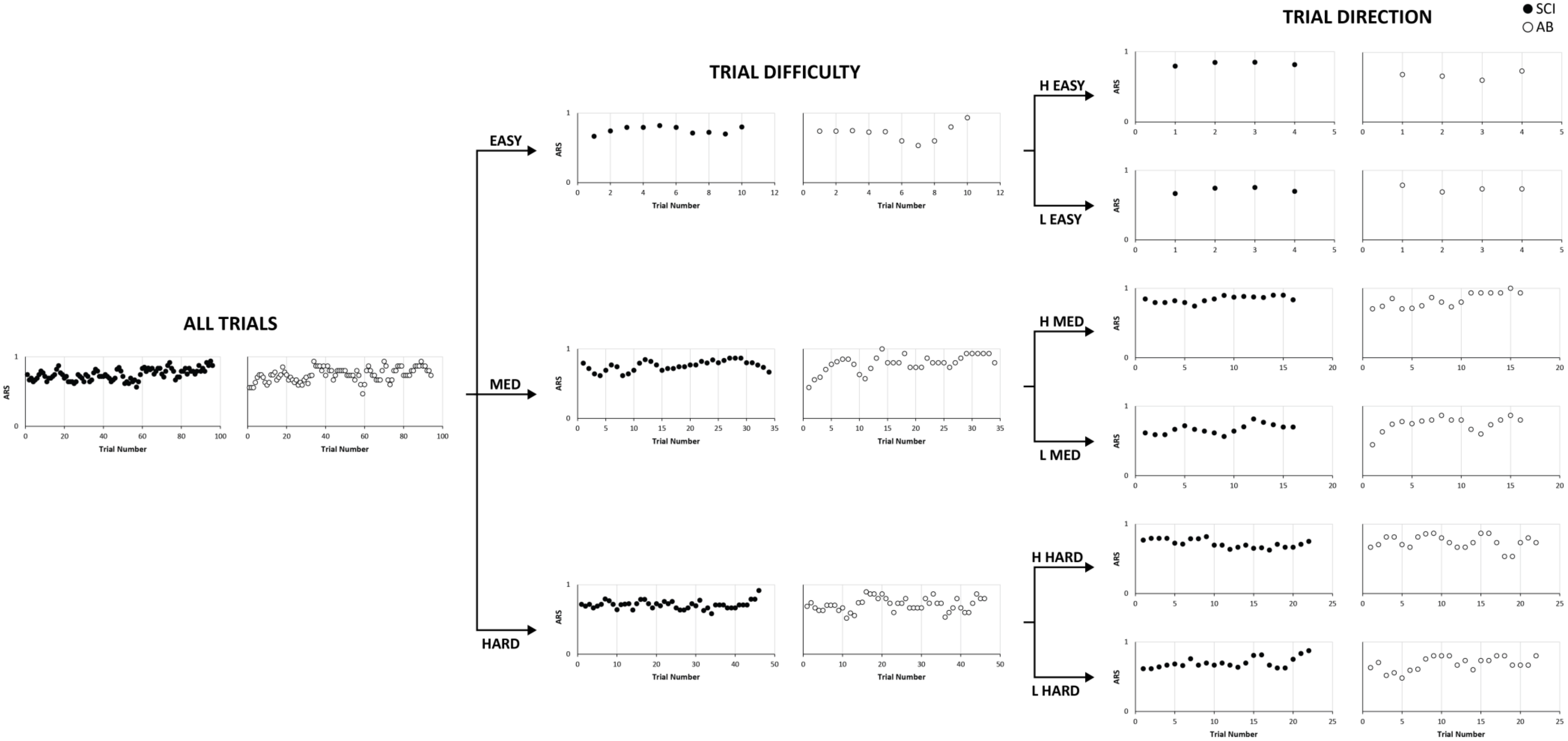

Figure 7 Average response scores (ARS) across all subjects over the course of the training trials. For ease of visualization, ARS were filtered with a 3-point moving average. Data are presented for SCI and AB participants as overall ARS across all training trials (left panel), trials divided by difficulty level (middle panel), and trials divided into specific heights (right panel).

3.3 Joint Position Sense

Spearman's correlation indicated a significant relationship (Spearman's rho = 0.694, $p < 0.001$) between Pre-training Knee JPS and Post-training knee JPS (Figure 8). There was a significant main effect of time between Pre- and Post-training in knee JPS ($F_{1,21} = 5.10$, $p=0.035$). Mean knee JPS error at Pre-training was 4.70° (SD = 3.52°) and that at Post-training was 3.67° (SD = 2.13°). There was a significant main effect of group ($F_{1,21} = 4.72$, $=0.041$) nor were there any significant interaction effects ($F_{1,21} = 0.28$, $p = 0.605$) (Figure 9).

In the subset of subjects who completed the 24Hr-retention assessment, there was no significant effect of time on knee JPS ($F_{1,13} = 0.50$, $p=0.615$). There was no significant main effect of group ($F_{1,14} = 2.35$, $p=0.149$) nor were there any significant interaction effects ($F_{1,14} = 1.69$, $p = 0.205$) (Figure 9). Please refer to Appendix D for raw proprioception assessment values for each participant.

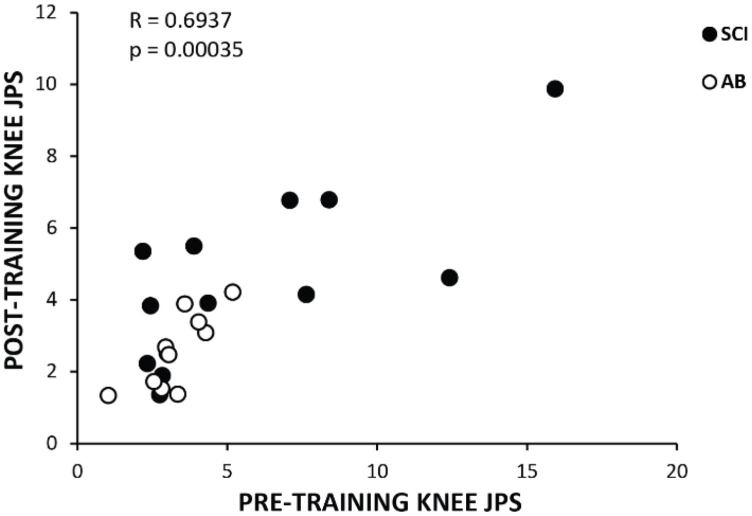

Figure 8 Scatterplot of Post-training knee JPS scores as a function of Pre-training scores. Inset values represent the Spearman's rank correlation coefficient between Pre-training and Post-training knee JPS values.

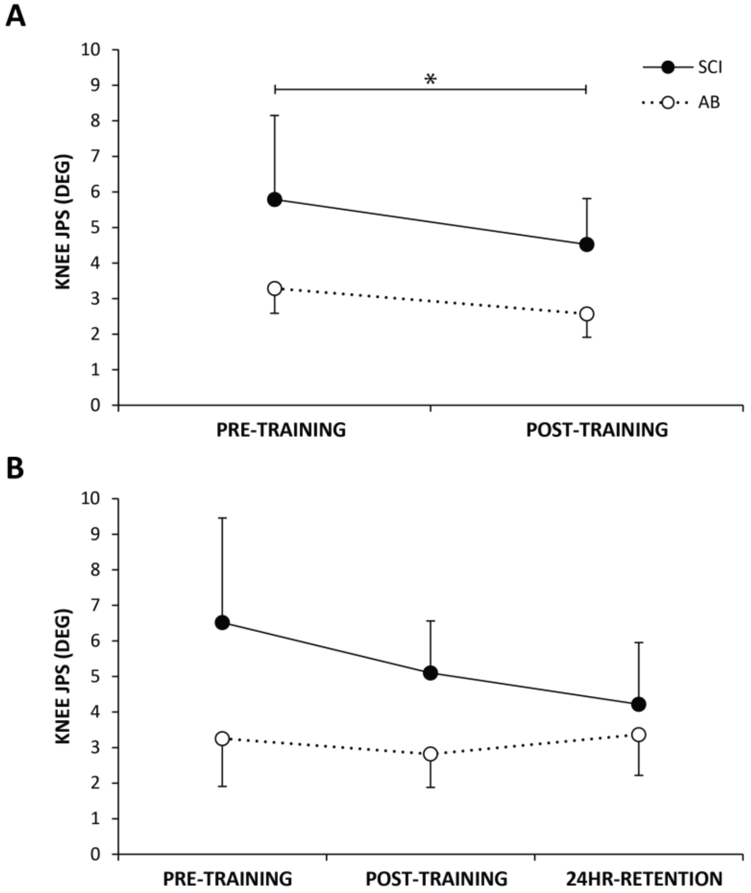

Figure 9 Knee JPS for SCI and AB participants. A) Knee JPS scores from Pre-training and Post-training (n = 13 SCI, 10 AB). B) Knee JPS from Pre-training, Post-training and 24Hr-retention in the subset of participants who completed retention testing (n = 10 SCI, 5 AB). Error bars represent the 95% confidence interval. Significant differences are indicated by asterisk.

3.4 Heel End-Point Discrimination

Spearman's correlation indicated a significant relationship (Spearman's rho = 0.5295, p=0.011) between Pre-training Heel EPD and Post-training Heel EPD (Figure 10). There was a significant main effect of time on heel EPD ($F_{1,20} = 4.40$, p=0.049). Heel EPD significantly improved from Pre-training (M = 0.523, SD = 0.26) to Post-training (M = 0.720, SD = 0.25). There was no main effect of group on heel EPD scores ($F_{1,20} = 0.00$, p=0.969) nor were there any significant interaction effects ($F_{1,20} = 0.01$, p = 0.923) (Figure 11).

In the subset of subject who completed the 24Hr-retention assessment, there was no significant effect of time on heel EPD ($F_{1,13} = 2.67$, p=0.088). There was no main effect of group on heel EPD scores ($F_{1,13} = 0.04$, p=0.849) nor were there any significant interaction effects ($F_{1,13} = 0.65$, p=0.528) (Figure 11). Appendix D contains the raw proprioception assessment values for each participant.

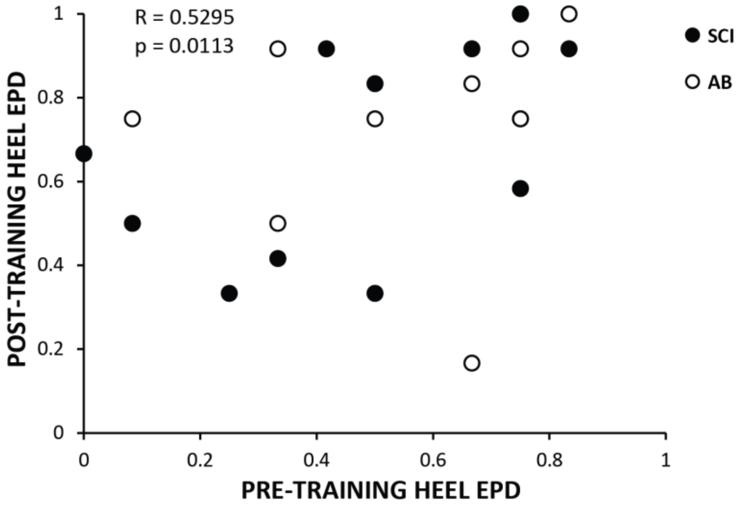

Figure 10 Scatterplot of Post-training heel EPD scores as a function of Pre-training scores. Inset values represent the Spearman’s rank correlation coefficient between Pre-training and Post-training heel EPD values.

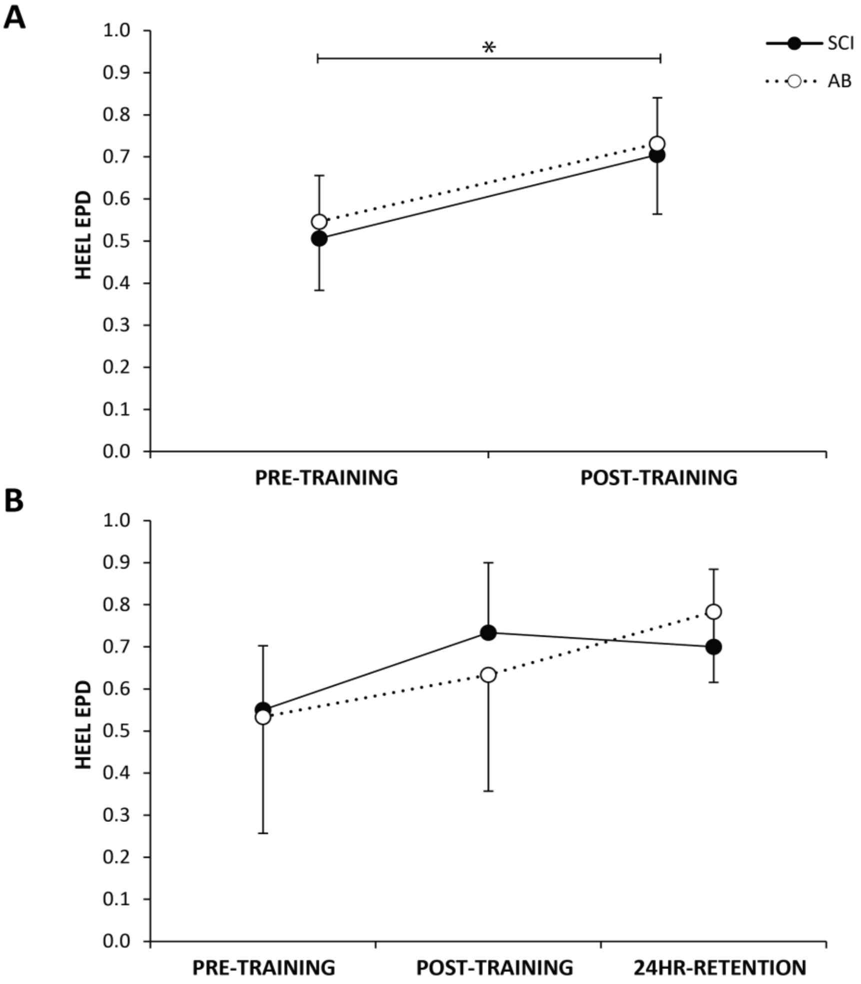

Figure 11 Heel EPD in SCI and AB participants. A) Heel EPD scores from Pre-training and Post-training sessions (n = 13 SCI, 9 AB). B) Heel EPD from Pre-Training, Post-training and 24Hr-retention in the subset of participants who completed retention testing (n = 10 SCI, 5 AB). Error bars represent the 95% confidence interval. Significant differences are indicated by asterisk.

3.5 Skilled Walking

Out of the 13 SCI subjects only 7 were able to complete the skilled walking task (Figure12). There was a significant reduction in skilled walking performance from Pre-training (M = 18.69 mm, SD = 8.76 mm) to Post-training (M =14.91 mm, SD = 7.80 mm) (p = 0.019). There was no significant difference in CoV of skilled walking performance between Pre-training and Post-training (p = 0.462) (Figure13). The average error of the first 5 steps also showed no significance between Pre-training and Post-training (p = 0.868).

For the 4 participants who completed the 24Hr-retention test, there was a significant effect of time on performance error ($F_{1,3} = 5.91$, p = 0.038). However, pairwise comparison displayed no significant difference between any time points on performance error. There was no significant effect of time on CoV of the performance error ($F_{1,3} = 0.79$, p = 0.495) (Figure 13). The average error of the first 5 steps also showed no significance across all skilled walking assessments ($F_{1,3} = 3.24$, p = 0.111).

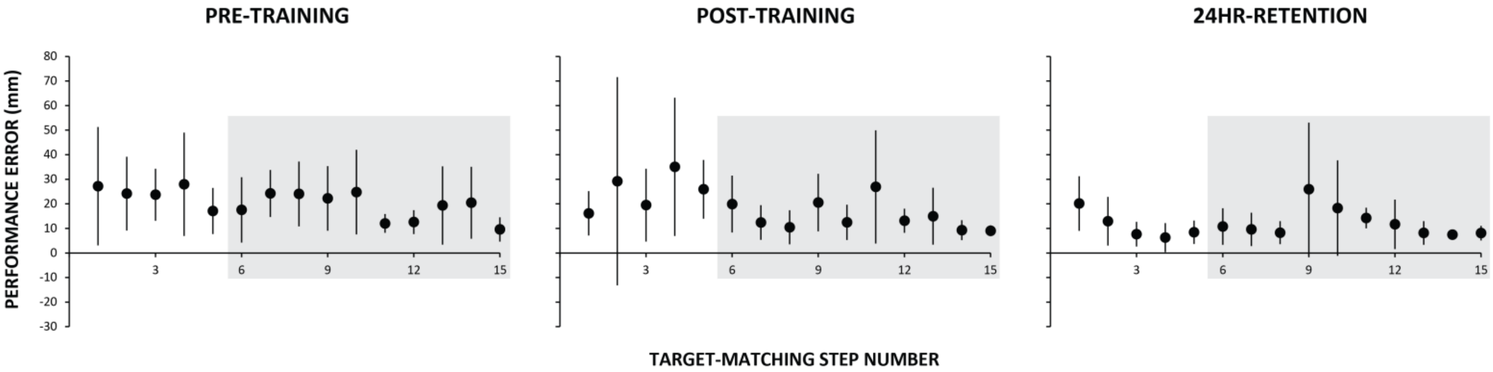

Figure 12 Skilled walking task performance. Average error for each step across all participants is displayed for Pre-training, Post-training and 24Hr-retention. Error bars represent the 95% confidence interval. The grey box outlines the points used to calculate performance scores (last 10 target-matching steps).

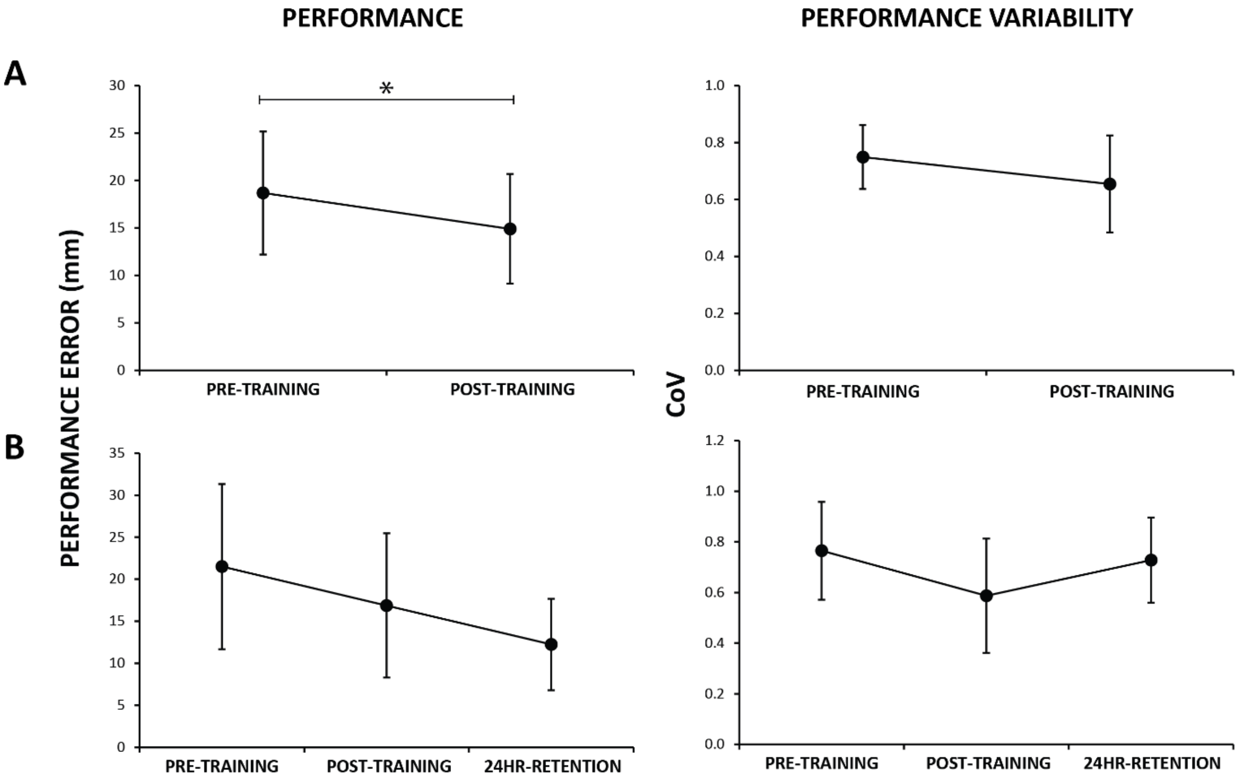

Figure 13 Skilled walking performance and its variability. A) Skilled walking performance (left panel) and performance variability (right panel) during Pre-training and Post-training sessions (n = 7). B) Skilled walking performance (left panel) and performance variability (right panel) during Pre-training, Post-training, and 24Hr-retention in the subset of participants who completed retention testing (n = 4). Error bars represent the 95% confidence interval. Significant differences are indicated by asterisk.

Chapter 4: Discussion

In this study, we developed a novel robotic-based sensory training tool and showed that lower limb proprioceptive acuity could be improved. Both Knee JPS and Heel EPD were improved after proprioceptive training, and the extent of improvement was associated with baseline proprioceptive sense. Moreover, the data indicated that improvements persisted 24 hours after training in a subset of our sample. We also found that skilled walking performance improved after proprioception training in the SCI group. Our findings indicate that proprioceptive acuity can be improved in both SCI and AB individuals.

4.1 Specificity and Generalization of Sensory Training

Previous work has demonstrated that it is possible for proprioceptive acuity to change based on the targeted training given (Nourouzpour et al. 2014, Wong et al. 2011). Nourouzpur et al. (2014) gave participants a novel reaching task while they received distorted visual feedback. Participants gradually adjusted their visuomotor skills to accommodate for the distorted feedback. It was found that after learning this new task, a corresponding perceptual shift in the location of the arm was also seen to a similar degree. This indicates that proprioceptive acuity can be manipulated within the workspace in which a specific training was employed. Similarly, Wong et al. (2011) also showed that training participants in a novel upper limb reaching task resulted in enhanced upper limb proprioceptive acuity within the training workspace. In our study, it could be inferred that training performance in the Med trials and the corresponding improvement in the heel EPD test represent analogous improvement in the specific sensory 'workspace'.

Our results indicate that the intervention not only improved end-point foot position sense, but also improved single joint position sense. This data demonstrates that even though improvements are seen in one form of proprioceptive acuity, it was able to generalize to enhancing single joint position sense accuracy, specifically knee JPS. Considering the role of the knee joint in mediating changes in foot height during gait adjustment (Winter 1992), it may not be surprising that training heel EPD could transfer to knee JPS. During walking there is a complex interplay between various joints, especially for skilled tasks such as obstacle crossing or stepping over a curb. Small changes at individual joints can account for adaptations in foot clearance to successfully navigate these tasks. Winter (1992) showed that changes in knee joint angle (knee flexion) accounted for much of the vertical height displacement during regular over ground walking, and certainly more when compared to the swing hip (hip flexion). Moreover, in gait adaptations from level walking to obstacle crossing, McFadyen and Carnahan (1997) demonstrated that changes in vertical foot displacement is associated more with changes at the knee joint while changes in hip strategy are more associated with anterior-posterior changes. Collectively, these studies suggest the important role of the knee joint in obstacle avoidance and its contribution to modulation of foot position. Our results are consistent with the notion that knee joint proprioceptive sense can serve as a measure to gauge whether any changes in proprioception occurred as a result of vertical change detection training.

Our data also indicate that improvements in skilled walking performance may be realized following the 2-day sensory training intervention. Previous studies have shown the critical role of proprioceptive sense during walking. Deafferented patients who have lost proprioceptive sense due to large-fiber neuropathy experience a high degree of difficulty controlling their movements (Cole 2009). Even though their motor systems are spared, their ability to walk is compromised due to the lack of sensory input. Additionally, our previous work in able-bodied participants has shown a relationship between lower limb joint position sense and performance in a skilled walking task identical to the one used here (Qaiser et al. 2016). The current data further extend these findings to indicate a potential contribution for training effects in proprioceptive sense that could translate to improvements in skilled walking performance. The data from the 4 individuals who were able to perform the skilled walking task at 24Hr-retention also point to possible longer term transfer effects of sensory training on motor performance, but of course the small sample size precludes any firm conclusions.

Although SCI and AB subjects have varying levels of proprioceptive acuity, we found that both groups can benefit from proprioception training. Our results strongly indicate that the effectiveness of the training intervention can be predicted by the baseline knee JPS, where individuals who had greater deficits in proprioceptive acuity showed larger improvements in knee JPS following training. Lesser improvements were observed if knee proprioceptive acuity was already accurate, even though training was tailored to each subject. Williams et al. (2002) similarly showed a relationship between baseline status and training. Participants were trained to control an oncoming ball with their foot, a task which required high levels of integration of lower limb proprioceptive acuity. Results showed that individuals who initially scored lower levels of ball control improved to a greater extent than those who had higher baseline scores.

Our findings also suggest that changes in proprioceptive acuity are not only transient, but could be retained for at least 24 hours after the completion of training. It has been suggested that delayed retention is a better indicator of motor skill learning in comparison to assessments of skill performance immediately post-training (Kantak and Winstein 2011). It is postulated that motor memory consolidation offline is critical for motor learning. Robertson et al. (2005)

trained participants in a patterned reaction time task. Following training, repetitive transcranial magnetic stimulation (rTMS) was applied to disrupt the anterior M1 motor cortex of these individuals. It was found that when TMS is applied immediately after training, learning effects were not seen during reassessment. However, if the rTMS was provided after an interval of sleep, deficits in learning were not seen. This suggests that a period of time away from practice might be integral for motor skill consolidation and if disrupted, can prevent skill acquisition. Savion-Lemieux and Penhune (2005) has shown that skills can be retained for as long as 8 weeks post training. Thus, it is indicated that there are active post-practice neuronal processes such as motor consolidation that must be responsible for skill acquisition that allow for skill retention (Kantak and Winstein 2011; Robertson et al. 2005; Savion-Lemieux and Penhune 2005).

Retention is not only exclusive to motor skill, but can also be seen in sensory changes as well. The results from Nourouzpour et al. (2014) demonstrate how proprioceptive improvements in addition to motor skill can be retained following a motor learning. Nourouzpour et al. (2014) employed a reaching task in the upper limb with distorted visual feedback. The aim was to induce visuomotor adaptation within the upper limb so that participants learned to adjust to the displayed cursor when reaching for target positions. It was found that after learning the new task, a perceptual shift in the location of the arm was also seen to a similar degree. This proprioceptive recalibration persisted 24 hours after the completion of the training sessions. Thus it is important to investigate sensory retention in addition to immediate improvements to determine if changes can be long lived.

4.2 Attributes of Sensory Training

During training, trials were tailored to each participant's Pre-training sensory acuity. On average, participants had better correct response rates on higher versus lower trials during training. Similarly, higher trials had less variability in response rates than the lower trials. These data indicate that participants had an easier time distinguishing positions that were displaced higher than lower ones regardless of trial difficulty. One reason could be that people might be predisposed or more sensitive towards heel adjustments in the upward direction since in everyday life, trajectory modifications of the lower limb typically occur in the upward direction, e.g. actions associated with clearing environmental hazards. Indeed, in a survey of daily ambulation tasks, Musselman and Yang (2007) found that tasks requiring lifting the foot higher, such as to walking over rough surfaces, clearing obstacles or navigating steps were among the most common. There also appeared to be a slight pattern of improvement over the course of training only in the Med trials. Recall that the Med heights corresponded to Pre-training Knee JPS error. The apparent improvement in ARS in Med trials, which was not as apparent in the Easy or Hard trials, could suggest that the current training protocol could be targeting changes associated with the detection threshold. Easy trials may have been too easy for subjects to discern. For the Hard trials, it is possible that these targets were well below participants' detection threshold levels which could have made it difficult for meaningful training effects to occur even in the presence of visual feedback.

It is critical that for learning to occur, knowledge of results be provided to the trainee (Abdollahipour et al. 2014; Wong et al. 2012). This allows the person to consolidate their attempts and adjust their behaviour so that the desired learning effect can be achieved. One such method of demonstrating knowledge of results is through visual feedback after each attempt.

Abdollahipour et al. (2014) provided 2 groups with a motor task of throwing a dart on a target. One group received knowledge of results as visual feedback after every attempt while the other group received no such feedback. It was determined that those who received visual feedback acquired the target task faster and more effectively than those who didn't. Batcho et al. (2016) reported similar results when employing a novel upper arm reaching task with resistance. Individuals who received constant online visual feedback about the location of their index finger displayed faster learning and a reduction in movement end-point error. Not only can visual feedback help with motor learning, it has shown to improve sensory perception. Van beers et al (1996) examined how localizing the tip of the index finger at various locations on a table was more precise when individuals were provided visual feedback of their fingertip compared to proprioception alone. Similarly, Wong et al. (2012) showed that subjects who received visual feedback about the location of their arm during passive movements were better able to reproduce such motions and also showed improved proprioceptive acuity. Our results similarly show that appropriate visual feedback can be used to improve foot position sense, as shown by the increases in correct response rates that were observed during training, and that this effect carried over to improved knee joint proprioceptive acuity and heel detection, as shown through the Post-training test of the knee JPS and heel EPD (respectively) in the absence of visual feedback.

4.3 Why Use End-Point Based Training?

There is compelling evidence that shows the ability of the nervous system to be more sensitive to detecting end-point differences versus single joint. Bosco and Poppele (1997) examined how neurons have a distinct direction bias where the discharge rates are higher in some directions versus others in cats. Bosco and Poppele (1997) further explain how these discharge biases are strongly correlated to the end-point position of the limb in contrast to specific joint angles or muscle lengths. In humans, Soechting (1982) investigated the proprioceptive relationship in end-point versus single joint within the upper limb. It was determined that participants are more accurate at matching position of the whole limb in comparison to specific joint angles at individual joints. This data among others suggests that humans are more suitable at discerning end-point limb positions than individual joints as it is more applicable for daily functionality (eg. reaching) (Soechting 1982; van Beers 1998).

Kinematic studies of human locomotion show that foot trajectory (end-point position) is strongly conserved across multiple forms of walking (Ivanenko et al. 2002; Grasso et al. 1998; Grasso et al. 2000). For example, Ivanenko et al. (2002) showed that even among varying levels of body weight support (manipulating contact sensation), which results in dramatic changes in muscle activity patterns during walking, foot trajectory profiles remained fairly consistent. Grasso et al. (1998) showed that end-point foot kinematics are conserved even with the reversal of gait direction, such as walking backwards. Furthermore, Grasso et al. (2000) assessed foot trajectory as subjects walked with various postural constraints such as with a crouched posture with knee and trunk flexion. In spite of dramatic changes in posture, the end-point foot trajectory of each limb remained very similar across different postures. These findings collectively show the priority the nervous system places on conserving end-point location.

4.4 Neural Changes Associated With Proprioception Training

The underlying neural mechanism driving proprioceptive changes are unclear. When individuals learned a reaching task under force field perturbation of the upper limb, Ostry et al. (2010) showed that there were subsequent perceptual changes in proprioceptive acuity. However, if participants experienced identical reaching movements, but through passive motion, no such proprioception changes were seen. As a result, it was deduced that movement alone (eg. manipulating only peripheral receptors) cannot result in proprioception changes. Thus it was reasoned by Ostry et al. (2010) and Goble and Anguera (2010) that changes in proprioceptive acuity must be the result of alteration of central nervous system rather than changes in neural firing from the peripheral receptors. Naito et al. (2005) examined the brain regions associated with proprioception perception by recording brain activity using the fMRI during extensor carpi ulnaris muscle tendon vibration. During vibration, there was not only activation of the main proprioceptive area 2 of the somatosensory cortex, but also a wide spread activation within the cortical motor areas, making these areas candidates for sites of plasticity associated with improved proprioceptive acuity.

Nudo (2006) explains that since the sensory and motor systems share a strong cortical connection, changes in one system can affect the other. There is evidence showing that the PPC is responsible for integrating proprioceptive, visual and cutaneous input that aids in motor task performance (McVea and Pearson 2007a; McVea and Pearson 2007b; Marigold et al. 2011; Andujar et al. 2009). More specifically, Padberg et al. (2010) showed that lesion to the area 5 of the PPC led to an inability of monkeys to reach and grab food pellets. However, plasticity of neighboring regions were able to compensate to allow for functional recovery. Our data suggests that skilled walking performance improved following proprioception training. Given the role of area 5 of the PPC in sensory motor integration, it is possible that our training could have elicited changes within this brain region.

Cortical motor changes have also been associated with lack of proprioceptive input. Friel et al. (2005) examined how lesion to the anterior M1 hand region results in deficits in reaching actions in monkeys because of a disruption of proprioceptive information to the motor cortical region. The current study saw changes within lower limb proprioceptive acuity in addition to skilled walking motor performance. It is possible that our proprioception training could have resulted in changes not only to the somasosensory region such as area 2 or area 5 of PPC, but also to the motor cortical representations namely lower limb M1 region of the brain.

4.5 Methodological Considerations

4.5.1 Length of proprioception training

It is possible that the number of trials employed during training sessions were insufficient to induce a prominent learning effect for the Hard trials. For sensory training, Wong et al. (2012), employed a total of 320 training trials over 3 days. In our study, participants performed 96 training trials over 2 days. However, despite the lower volume of training, our results indicate that we could improve lower limb proprioception. Moreover, unlike previous studies, our training required participants to be supported in a harness while strapped to the Lokomat, as opposed to previous studies where subjects could be comfortably seated while performing upper limb tasks. Thus the nature of the training posed greater risk of fatigue, which we had to counterbalance against training volume. Datla (2016) showed that individuals who experienced induced fatigue within the upper limb were unable to acquire a skill that required them to position the arm in a certain location in space. Datla (2016) argued that such lack of on skill acquisition could be in part due to degraded proprioceptive feedback as a result of fatigue. Thus having a prolonged training session within the current study could have led to fatigue that would render our training ineffective. As a result, we selected a protocol to balance the amount of training against the risk of fatigue.

4.5.2 Type of feedback during proprioception training

As discussed earlier, Wong et al. (2012) demonstrated effective training of proprioception based on meaningful feedback of limb trajectory during a passive motion. In the current study, feedback was given only after the participant announced their response and represented a static position in space, as opposed to an aspect of movement trajectory. It would be ideal to also incorporate a dynamic feedback based on foot trajectory motion during training. This variation in feedback could potentially provide sufficient information to the trainee which could allow them to better consolidate the current motion of their lower limb. Such form of training might present improvements in gait trajectories that are transferred over when the participant actively walks again and during a skilled walking task.

4.5.3 Length of skilled walking task

Skilled walking performance was assessed from a trial consisting of 15 target-matching steps. Our previous work with the same task has shown that, on average, AB individuals reach a plateau in skill walking performance after approximately 25 steps (Qaiser et al. 2016). While it is possible that the skilled walking trials could have provided a practice effect, we noted that there was no significant differences in performance error averaged across the first 5 target-matching steps between sessions. This suggests that at Post-training and 24Hr-retention, participants performed at the same level as during Pre-training and that there were no carry-over effects to subsequent testing sessions.

4.5.4 Task attention and motivation

It is also possible that the level of attention or motivation could have affected the training outcomes. Goble et al. (2011) investigated the role of attention and proprioceptive acuity within the upper limb. Participants were tasked to encode a target elbow position and were asked to replicate it from a starting position. It was determined that individuals who were given a secondary task of counting up by 3s during encoding phase were less accurately able to reproduce the target angle. This data indicates that when participants are lacking attention or prioritize something other than encoding joint position, their working memory is affected and that can compromise accuracy of conscious proprioceptive acuity.

Motivation can also have an impact. Reckless et al. (2013) used fMRI to measure functional activity in brain regions associated with decision making (detect pictures of an animal among other distractors) and showed that motivation, through monetary incentives, resulted in increased activity in dorsolateral prefrontal cortex (a region of the brain responsible for perceptual decision making). As a result of heightened dorsolateral prefrontal cortex, they found that these individuals showed faster and more selective response patterns. There is also evidence that level of motivation can also affect motor learning. Suksudaj et al. (2011) reported a mild association between intrinsic motivation and fine motor performance in dental students performing cavity-filling procedures. In a study of motor cortical responses during a reaction timed task, Meadows et al. (2016) showed that prior to movement, beta frequency readings in the contralateral motor cortex decrease. This ‘beta suppression’ is associated with faster reaction times. Meadows et al. (2016) showed that individuals who received motivation through monetary incentives, displayed heighted beta suppression which was associated with faster reaction times. These studies collectively explain the role of motivation on skill performance. Although we screened for baseline deficits in cognitive function (e.g. attention, memory) using the MOCA, we did not assess the level of attention or motivation during the training sessions. As the nature of our training set-up could have posed higher risk of cognitive fatigue (as specified above), it is possible that participants became less attentive or motivated over the course of the training trial.

Chapter 5: Conclusion

It is apparent that proprioception plays a paramount role in the control of complex movements such as walking. The current study demonstrated that in individuals who have a proprioception deficit, such as those seen after SCI, a passive robotic based intervention could help improve proprioceptive acuity and may translate to improved motor performance (in a walking task). Our findings could have clinical implications for the development of new training strategies to improve proprioceptive acuity, and concomitantly, motor performance in functional tasks. Future studies should explore the potential benefits of sensory training with constant feedback about limb position during a dynamic task, as well as investigate longer-term training protocols (e.g. over weeks or months) to determine lasting training effects.

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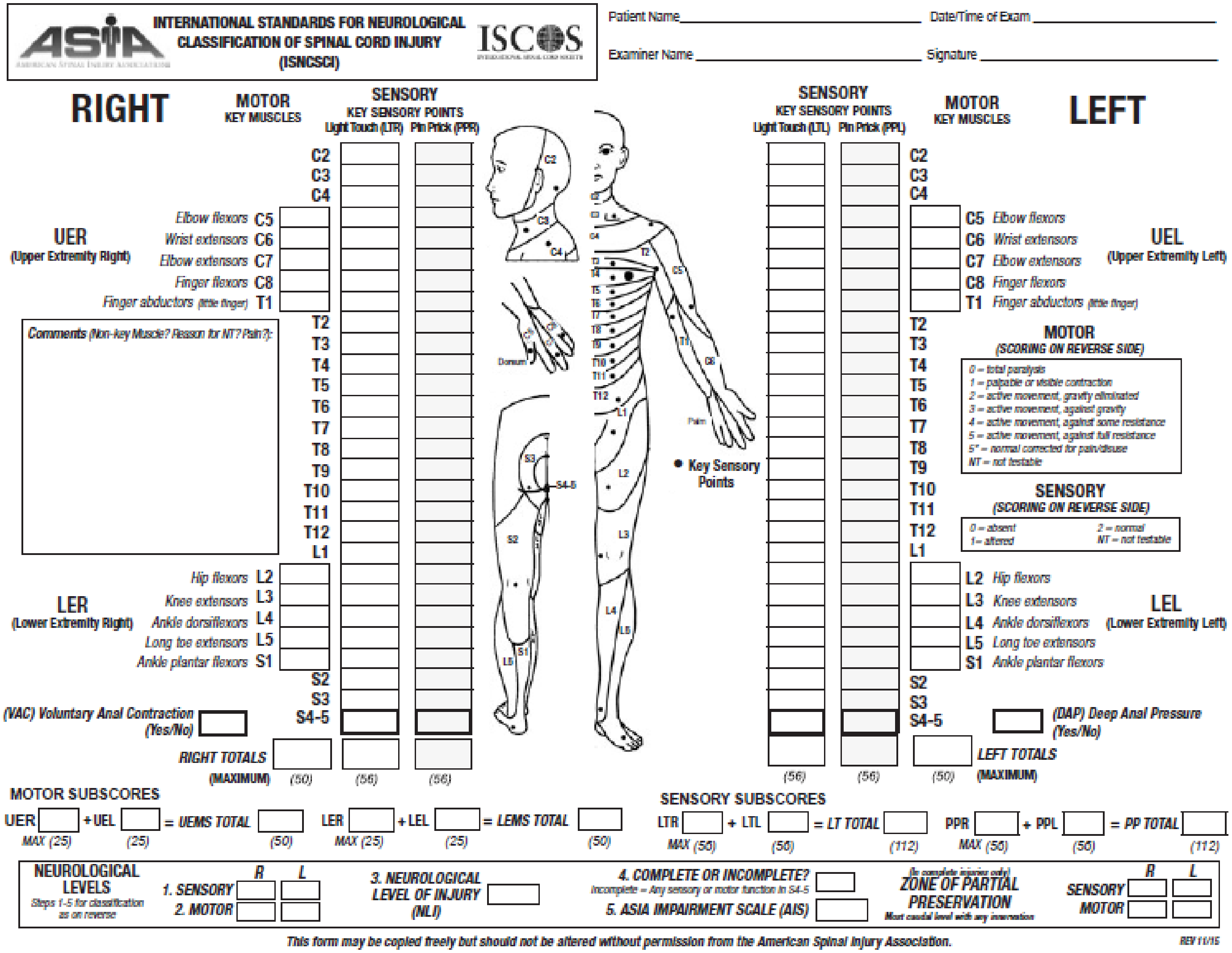
Appendices

Appendix A International Standards for Neurological Classification of Spinal Cord Injury



INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY (ISNCSCI)

Patient Name________________ Date/Time of Exam ________________

Examiner Name ________________ Signature ________________

RIGHT

MOTOR KEY MUSCLES			SENSORY KEY SENSORY POINTS Light Touch (LTR)	Pin Prick (PPR)
	C2			
	C3			
	C4			
Elbow flexors	C5			
Wrist extensors	C6			
Elbow extensors	C7			
Finger flexors	C8			
Finger abductors (little finger)	T1			
	T2			
	T3			
	T4			
	T5			
	T6			
	T7			
	T8			
	T9			
	T10			
	T11			
	T12			
	L1			
Hip flexors	L2			
Knee extensors	L3			
Ankle dorsiflexors	L4			
Long toe extensors	L5			
Ankle plantar flexors	S1			
	S2			
	S3			
	S4-5			
RIGHT TOTALS (MAXIMUM)		(50)	(56)	(56)

UER (Upper Extremity Right)

LER (Lower Extremity Right)

Comments (Non-key Muscle? Reason for NT? Pain?):

(VAC) Voluntary Anal Contraction (Yes/No) ☐

● Key Sensory Points

LEFT

SENSORY KEY SENSORY POINTS Light Touch (LTL)	Pin Prick (PPL)		MOTOR KEY MUSCLES	
		C2		
		C3		
		C4		
		C5		*Elbow flexors*
		C6		*Wrist extensors*
		C7		*Elbow extensors*
		C8		*Finger flexors*
		T1		*Finger abductors* (little finger)
		T2		
		T3		
		T4		
		T5		
		T6		
		T7		
		T8		
		T9		
		T10		
		T11		
		T12		
		L1		
		L2		*Hip flexors*
		L3		*Knee extensors*
		L4		*Ankle dorsiflexors*
		L5		*Long toe extensors*
		S1		*Ankle plantar flexors*
		S2		
		S3		
		S4-5		
(56)	(56)		(50)	*LEFT TOTALS* (MAXIMUM)

UEL (Upper Extremity Left)

LEL (Lower Extremity Left)

MOTOR
(SCORING ON REVERSE SIDE)

0 = total paralysis
1 = palpable or visible contraction
2 = active movement, gravity eliminated
3 = active movement, against gravity
4 = active movement, against some resistance
5 = active movement, against full resistance
5 = normal corrected for pain/disuse*
NT = not testable

SENSORY
(SCORING ON REVERSE SIDE)

0 = absent
1= altered
2 = normal
NT = not testable

(DAP) Deep Anal Pressure (Yes/No) ☐

MOTOR SUBSCORES

UER ☐ + UEL ☐ = *UEMS TOTAL* ☐ — *MAX (25)* (25) (50)

LER ☐ + LEL ☐ = *LEMS TOTAL* ☐ — *MAX (25)* (25) (50)

SENSORY SUBSCORES

LTR ☐ + LTL ☐ = *LT TOTAL* ☐ — *MAX (56)* (56) (112)

PPR ☐ + PPL ☐ = *PP TOTAL* ☐ — *MAX (56)* (56) (112)

NEUROLOGICAL LEVELS
Steps 1-5 for classification as on reverse

	R	L
1. SENSORY		
2. MOTOR		

3. NEUROLOGICAL LEVEL OF INJURY (NLI) ☐

4. COMPLETE OR INCOMPLETE? ☐
Incomplete = Any sensory or motor function in S4-5

5. ASIA IMPAIRMENT SCALE (AIS) ☐

(In complete injuries only)
ZONE OF PARTIAL PRESERVATION
Most caudal level with any innervation

	R	L
SENSORY		
MOTOR		

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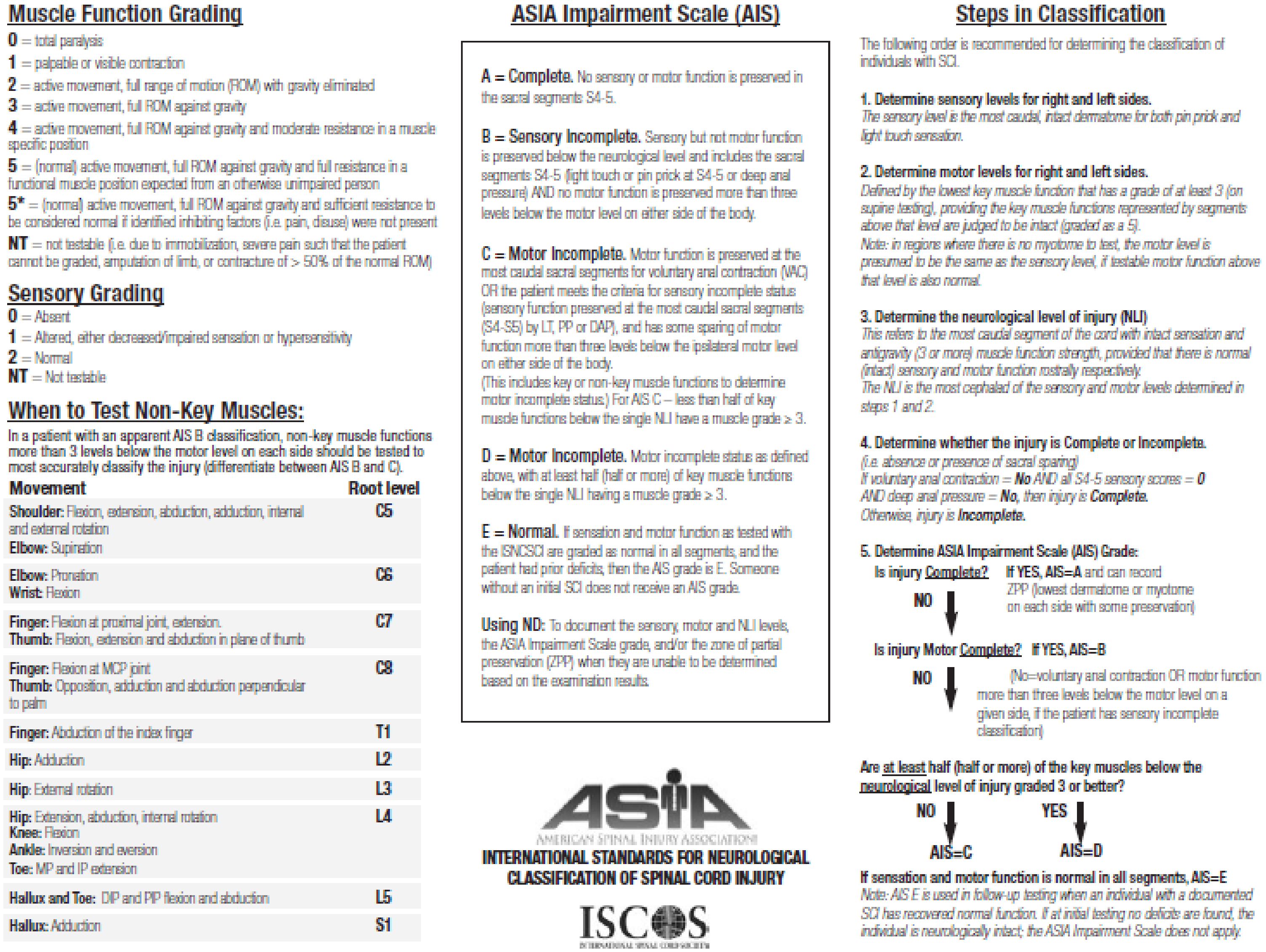
REV 11/15



Muscle Function Grading

0 = total paralysis
1 = palpable or visible contraction
2 = active movement, full range of motion (ROM) with gravity eliminated
3 = active movement, full ROM against gravity
4 = active movement, full ROM against gravity and moderate resistance in a muscle specific position
5 = (normal) active movement, full ROM against gravity and full resistance in a functional muscle position expected from an otherwise unimpaired person
5* = (normal) active movement, full ROM against gravity and sufficient resistance to be considered normal if identified inhibiting factors (i.e. pain, disuse) were not present
NT = not testable (i.e. due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of > 50% of the normal ROM)

Sensory Grading

0 = Absent
1 = Altered, either decreased/impaired sensation or hypersensitivity
2 = Normal
NT = Not testable

When to Test Non-Key Muscles:

In a patient with an apparent AIS B classification, non-key muscle functions more than 3 levels below the motor level on each side should be tested to most accurately classify the injury (differentiate between AIS B and C).

Movement	Root level
Shoulder: Flexion, extension, abduction, adduction, internal and external rotation **Elbow:** Supination	C5
Elbow: Pronation **Wrist:** Flexion	C6
Finger: Flexion at proximal joint, extension. **Thumb:** Flexion, extension and abduction in plane of thumb	C7
Finger: Flexion at MCP joint **Thumb:** Opposition, adduction and abduction perpendicular to palm	C8
Finger: Abduction of the index finger	T1
Hip: Adduction	L2
Hip: External rotation	L3
Hip: Extension, abduction, internal rotation **Knee:** Flexion **Ankle:** Inversion and eversion **Toe:** MP and IP extension	L4
Hallux and Toe: DIP and PIP flexion and abduction	L5
Hallux: Adduction	S1

ASIA Impairment Scale (AIS)

A = Complete. No sensory or motor function is preserved in the sacral segments S4-5.

B = Sensory Incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-5 (light touch or pin prick at S4-5 or deep anal pressure) AND no motor function is preserved more than three levels below the motor level on either side of the body.

C = Motor Incomplete. Motor function is preserved at the most caudal sacral segments for voluntary anal contraction (VAC) OR the patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segments (S4-S5) by LT, PP or DAP), and has some sparing of motor function more than three levels below the ipsilateral motor level on either side of the body.
(This includes key or non-key muscle functions to determine motor incomplete status.) For AIS C – less than half of key muscle functions below the single NLI have a muscle grade ≥ 3.

D = Motor Incomplete. Motor incomplete status as defined above, with at least half (half or more) of key muscle functions below the single NLI having a muscle grade ≥ 3.

E = Normal. If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

Using ND: To document the sensory, motor and NLI levels, the ASIA Impairment Scale grade, and/or the zone of partial preservation (ZPP) when they are unable to be determined based on the examination results.

AMERICAN SPINAL INJURY ASSOCIATION

INTERNATIONAL STANDARDS FOR NEUROLOGICAL
CLASSIFICATION OF SPINAL CORD INJURY

ISCOS
INTERNATIONAL SPINAL CORD SOCIETY

Steps in Classification

The following order is recommended for determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
The sensory level is the most caudal, intact dermatome for both pin prick and light touch sensation.

2. Determine motor levels for right and left sides.
Defined by the lowest key muscle function that has a grade of at least 3 (on supine testing), providing the key muscle functions represented by segments above that level are judged to be intact (graded as a 5).
Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level, if testable motor function above that level is also normal.

3. Determine the neurological level of injury (NLI)
This refers to the most caudal segment of the cord with intact sensation and antigravity (3 or more) muscle function strength, provided that there is normal (intact) sensory and motor function rostrally respectively.
The NLI is the most cephalad of the sensory and motor levels determined in steps 1 and 2.

4. Determine whether the injury is Complete or Incomplete.
(i.e. absence or presence of sacral sparing)
If voluntary anal contraction = ***No*** *AND all S4-5 sensory scores =* ***0***
AND deep anal pressure = ***No****, then injury is* ***Complete.***
Otherwise, injury is ***Incomplete.***

5. Determine ASIA Impairment Scale (AIS) Grade:

Is injury Complete? **If YES, AIS=A** and can record ZPP (lowest dermatome or myotome on each side with some preservation)

NO ↓

Is injury Motor Complete? **If YES, AIS=B**

NO ↓ (No=voluntary anal contraction OR motor function more than three levels below the motor level on a given side, if the patient has sensory incomplete classification)

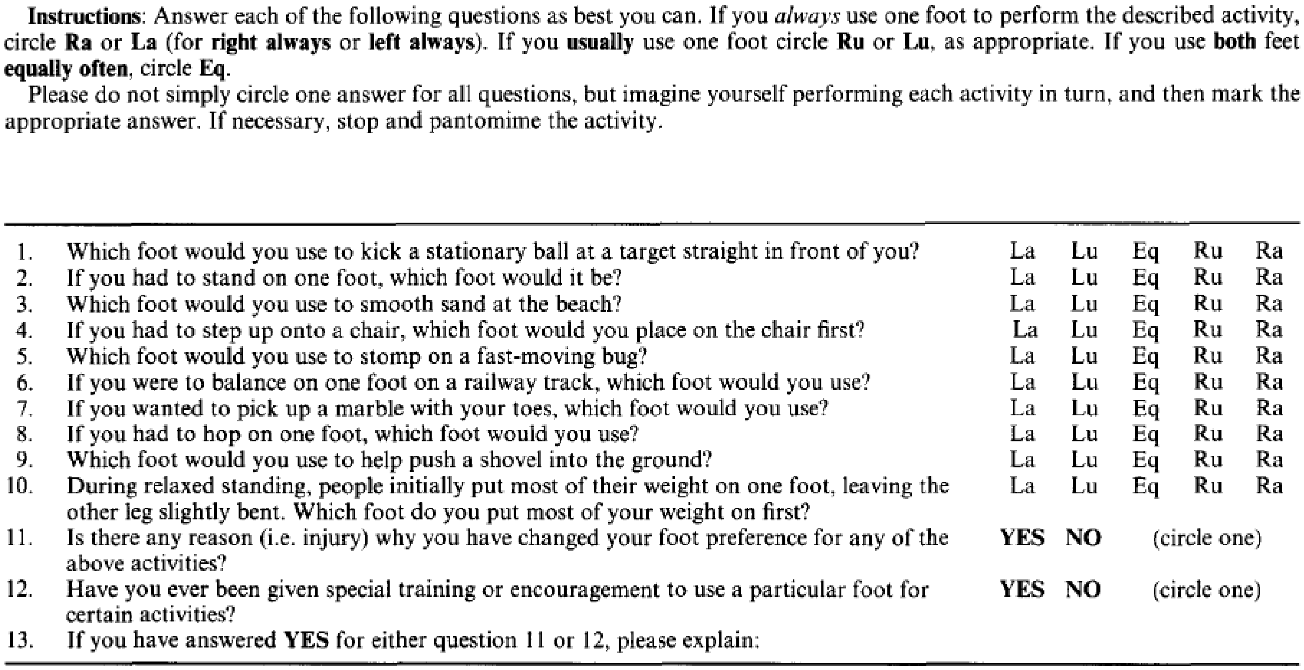
Are at least half (half or more) of the key muscles below the neurological level of injury graded 3 or better?

NO ↓ **AIS=C**

YES ↓ **AIS=D**

If sensation and motor function is normal in all segments, AIS=E
Note: AIS E is used in follow-up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact; the ASIA Impairment Scale does not apply.

Appendix B Edinburgh Footedness Questionnaire

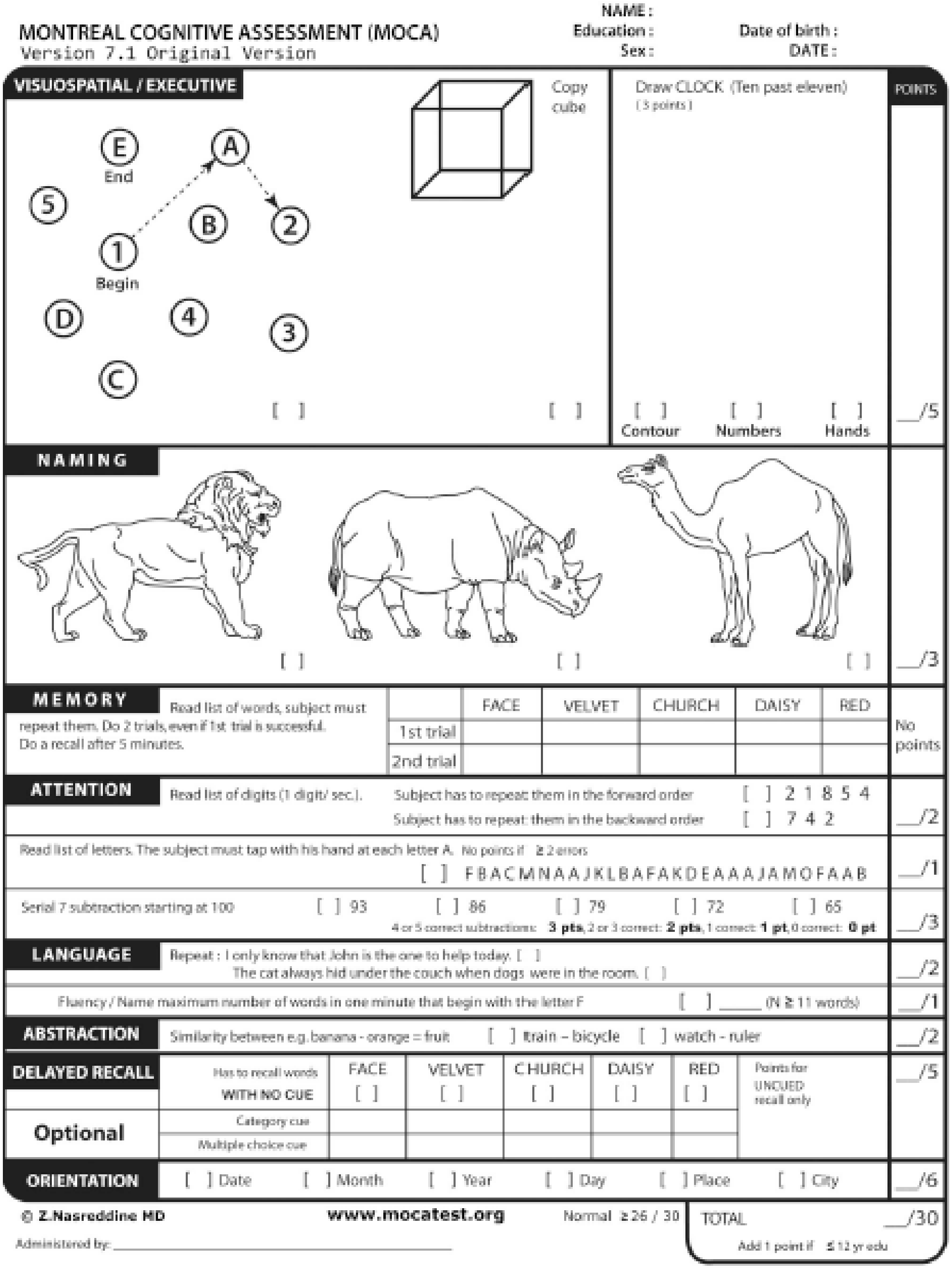


Instructions: Answer each of the following questions as best you can. If you *always* use one foot to perform the described activity, circle **Ra** or **La** (for **right always** or **left always**). If you **usually** use one foot circle **Ru** or **Lu**, as appropriate. If you use **both** feet **equally often**, circle **Eq**.

Please do not simply circle one answer for all questions, but imagine yourself performing each activity in turn, and then mark the appropriate answer. If necessary, stop and pantomime the activity.

1.	Which foot would you use to kick a stationary ball at a target straight in front of you?	La	Lu	Eq	Ru	Ra
2.	If you had to stand on one foot, which foot would it be?	La	Lu	Eq	Ru	Ra
3.	Which foot would you use to smooth sand at the beach?	La	Lu	Eq	Ru	Ra
4.	If you had to step up onto a chair, which foot would you place on the chair first?	La	Lu	Eq	Ru	Ra
5.	Which foot would you use to stomp on a fast-moving bug?	La	Lu	Eq	Ru	Ra
6.	If you were to balance on one foot on a railway track, which foot would you use?	La	Lu	Eq	Ru	Ra
7.	If you wanted to pick up a marble with your toes, which foot would you use?	La	Lu	Eq	Ru	Ra
8.	If you had to hop on one foot, which foot would you use?	La	Lu	Eq	Ru	Ra
9.	Which foot would you use to help push a shovel into the ground?	La	Lu	Eq	Ru	Ra
10.	During relaxed standing, people initially put most of their weight on one foot, leaving the other leg slightly bent. Which foot do you put most of your weight on first?	La	Lu	Eq	Ru	Ra
11.	Is there any reason (i.e. injury) why you have changed your foot preference for any of the above activities?	**YES**	**NO**	(circle one)		
12.	Have you ever been given special training or encouragement to use a particular foot for certain activities?	**YES**	**NO**	(circle one)		
13.	If you have answered **YES** for either question 11 or 12, please explain:					

Appendix C Montreal Cognitive Assessment



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE [ ] Copy cube [ ]	Draw CLOCK (Ten past eleven) (3 points) [ ] Contour [ ] Numbers [ ] Hands	POINTS ___/5
NAMING [ ] [ ] [ ]		___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED	
1st trial						No points
2nd trial						

ATTENTION Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2 ___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B ___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** ___/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] ___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) ___/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler ___/2

DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	___/5
Optional	Category cue							
	Multiple choice cue							

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City ___/6

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30 TOTAL ___/30
Add 1 point if ≤ 12 yr edu

Administered by: ____________________

Appendix D Average Participant Knee JPS and Heel EPD Values

	KNEE JPS			HEEL EPD		
	Pre-Training	**Post-Training**	**Retention**	**Pre-Training**	**Post-Training**	**Retention**
SCI 01	4.4	3.9	-	0.3	0.4	-
SCI 02	3.0	2.5	-	0.8	0.8	-
SCI 03	2.8	1.4	-	0.0	0.7	-
SCI 04	7.1	6.8	2.5	0.1	0.5	0.4
SCI 05	2.3	2.2	2.1	0.3	0.3	0.2
SCI 06	3.9	5.5	3.5	0.8	0.9	0.7
SCI 07	2.8	1.9	2.7	0.8	0.6	0.8
SCI 08	2.2	5.4	5.3	0.4	0.9	0.3
SCI 09	2.4	3.8	1.7	0.5	0.3	0.9
SCI 10	15.9	9.9	10.9	0.5	0.8	0.8
SCI 11	7.6	4.2	6.7	0.8	1.0	0.9
SCI 12	8.4	6.8	2.8	0.8	1.0	1.0
SCI 13	12.4	4.6	4.0	0.7	0.9	1.0
AB 01	2.8	1.5	-	0.3	0.9	-
AB 02	3.6	3.9	-	0.7	0.8	-
AB 03	3.4	1.4	-	0.5	0.8	-
AB 04	4.3	3.1	-	0.8	0.9	-
AB 05	2.6	1.7	-	-	-	-
AB 06	5.2	4.2	4.5	0.8	1.0	1.0
AB 07	4.1	3.4	3.0	0.1	0.8	0.9
AB 08	3.0	2.7	4.9	0.8	0.8	0.8
AB 09	1.0	1.3	1.8	0.3	0.5	0.8
AB 10	3.1	2.5	2.6	0.7	0.2	0.5