TRANSCRANIAL MAGNETIC STIMULATION AS A DIAGNOSTIC TOOL FOR ASSESSING MOTOR IMPAIRMENT OF SPINAL CORD INJURED INDIVIDUALS

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By

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Abstract

Clinical diagnosis, classification of injury and the reliable and detailed description of a patient's neurological status are key factors in determining intervention, rehabilitation programs and predicting recovery. The American Spinal Injury Association (ASIA) impairment scale (AIS) is a standardized method for spinal cord injury (SCI) classification and neurologic status examination. Studies have revealed the AIS classification to be a general assessment tool that fails to explain the varying degrees and patterns of neurological damage, especially in individuals with incomplete injuries. In addition, intra-group variability can be attributed to inaccuracies in examinations and improper assessment tools that have limited research findings. Transcranial Magnetic Stimulation (TMS) has been used as a non-invasive method of evaluating the integrity of the motor nervous system. The primary purpose of this study was to evaluate TMS as an assessment tool to describe motor impairment of SCI individuals. A second purpose of this study was to assess AIS accuracy and sensitivity to muscle activation by using surface electromyographic (sEMG) techniques during clinical examinations. Six incomplete SCI participants were clinically assessed to obtain their individual motor scores from key muscles following AIS assessment criteria. TMS was then used to stimulate the motor cortex to elicit motor evoked potentials (MEPs) in 4 key muscles. MEPs correlated with motor scores, where significantly higher and lower MEPs corresponded to the highest and lowest motor scores, respectively. Of the 48 muscles analyzed, 18 received a motor score of zero; however MEPs were obtained in 7 of these 18 muscles. In general, MEPs paralleled motor function as assessed by the AIS. Results suggest that TMS may provide information on the relationship between corticospinal integrity and the quality of motor function. In addition, TMS demonstrated adequate validity and sensitivity to SCI individual differences. MEPs provided additional information regarding the existence of spared neuronal pathways not identified by standard clinical evaluations. The therapeutic potential of these motor pathways has yet to be explored. EMG activity was significantly correlated to motor scores and MEPs however; EMG analysis revealed some inaccuracies in muscle examinations and supported MEP data. Results suggest that the implementation of electrophysiological assessment tools may be more sensitive to detect motor damage, adaptive movement patterns and overall muscle activation that may be misinterpreted during clinical examinations.

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Table of contents

Abbreviation List

AIS	ASIA impairment scale
ANOVA	Analysis of variance
ASIA	American Spinal Injury Association
Bi	Biceps brachii
BWSTT	Body weight support treadmill training
CNS	Central nervous system
CPA	Canadian Paraplegic Association
ECR	Extensor carpi radialis
ECR L	Left extensor carpi radialis
ECR R	Right extensor carpi radialis
EMG	Electromyography
Ext. Dig.	Extensor digitorium
FCR	Flexor carpi radialis
FDS	Flexor digitorium superficialis
FDS L	Left flexor digitorium superficialis
FDS R	Right flexor digitorium superficialis
FIM	Functional Independence Measurement
GA	Gastrocnemius
HSD	Honest significant difference
LEMS	Lower extremity motor scores
M1	Primary Motor Cortex
MEP	Motor evoked potential
MSO	Maximum stimulator output
MVC	Maximum voluntary contraction
NASCIS	National Acute Spinal Cord Injury Study
nRMS	Normalized root mean square
NSCIA	National Spinal Cord Injury Association
RMS	Root mean square
SCI	Spinal cord injury
sEMG	Surface electromyography
SMN	Spinal motor neuron
SOL	Soleus
SOL L	Left soleus
SOL R	Right soleus
TA	Tibialis anterior
TA L	Left tibialis anterior
TA R	Right tibialis anterior
TMS	Transcranial Magnetic Stimulation
Tri	Triceps brachii
UEMS	Upper extremity motor scores
VL	Vastus lateralis
WISCI	Walking index for spinal cord injury

1.0 Introduction

1.1 Anatomy and Physiology of the Cortical and Spinal Motor Neuronal System

1.1.2 The Cortical Motor System

All human behaviours are mediated by the central nervous system (CNS). In the human brain, motor function originates from, and is processed by, interconnected anatomical regions (Weber & Eisen, 2002) including the primary motor cortex (M1, or Brodmann area 4); the pre-motor cortex (Brodmann area 6); supplementary motor cortex; basal ganglia; thalamus; cerebellum; brain stem; and the reticular formation (Amaral, 2000a, 2000b; Tortora & Grabowski, 2003). The primary motor cortex is different from the other motor areas in that it is thicker and contains a lower cell density. The main output cells are small pyramidal cells in lamina III, the *external pyramidal cell layer*, and larger cells in lamina V, the *internal pyramidal cell layer* (see Figure 1.1) (Amaral, 2000a, 2000b; Tortora & Grabowski, 2003). These cortical motor neurons (upper motor neurons) are also accompanied by interneurons (stellate or basket cells) that modulate excitatory and inhibitory responses (Weber & Eisen, 2002). The dendrites of these interneurons are oriented radially, parallel to the axis of the precentral gyrus and the primary motor cortex (Weber & Eisen, 2002).

M1, located in the dorsal part of the precentral gyrus, is the final site in the cortex for processing motor commands and it is arranged in areas that correspond to muscle activity of the body (Penfield & Jasper, 1954) (Amaral, 2000a, 2000b; Terao & Ugawa, 2002). Axons from M1's pyramidal neurons (from lamina V) directly synapse with motor neurons or interneurons in the ventral horn of the spinal cord (Ghez & Krakauer, 2000; Weber & Eisen, 2002). These motor axons, crossing from the cerebral cortex to the spinal cord, form the corticospinal (or pyramidal) tract (Amaral, 2000a; Ghez & Krakauer, 2000). A large proportion of the corticospinal fibers (about 80%) descend through the brain stem and cross over to the contralateral side in the pyramidal decussation at the medulla and spinal cord junction (Amaral, 2000a, 2000b). Their axons terminate in the ventral horn of the spinal cord to form monosynaptic connections with motor neurons of distal muscles (lower motor neurons). These monosynaptic

connections are of particular importance for the execution of movements that require a high degree of voluntary control (e.g., the distal musculature of the hand). The crossed fibers make up the *lateral corticospinal tract* whereas the rest of the fibers (about 20%) remain uncrossed until reaching the spinal cord and then descend as the *ventral corticospinal tract* into the medial and ventral area of the spinal cord to make polysynaptic connections with motor neurons of proximal and axial muscles (Figure 1.2). In all, about 40 % of the corticospinal tract fibers originate in the motor cortex (Amaral, 2000a).

There are several other pathways in addition to the pyramidal tract which contribute to the extrapyramidal motor system however, not all of the cell groups from these pathways receive descending fibers form motor cortex. Thus, this system primarily supports voluntary movement and helps control posture and muscle tone (Ghez & Krakauer, 2000). Broadly speaking, the pyramidal tract and the extrapyramidal motor system operate jointly to mediate impulses from the cerebral cortex to the spinal cord and cranial nerves. Most movements are controlled by motor signals from the pyramidal tract and are influenced by extrapyramidal cell groups (Ghez & Krakauer, 2000; Weber & Eisen, 2002).

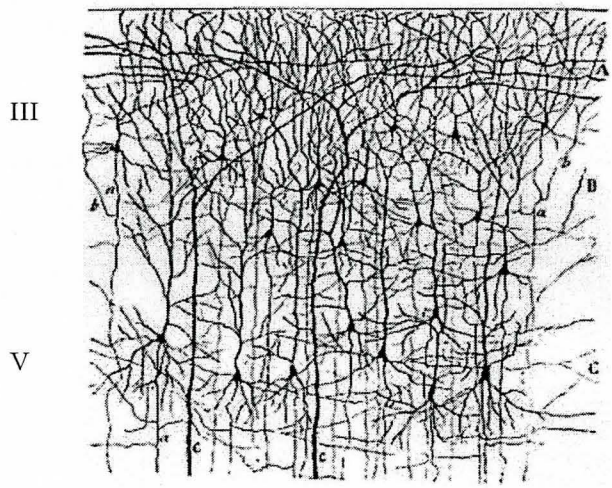

Figure 1.1 Cell layers of the cerebral cortex. Layer III contains different kinds of neurons, most of which, are pyramidally shaped and project to other parts of the neocortex (e.g. cells of lamina V since M1 has essentially no cells in layer IV). Projections to subcortical regions originate in layer V and IV. In addition to *projection neurons*, the cerebral cortex also has *local interneurons* located in all layers. Figure from Heimer 1994.

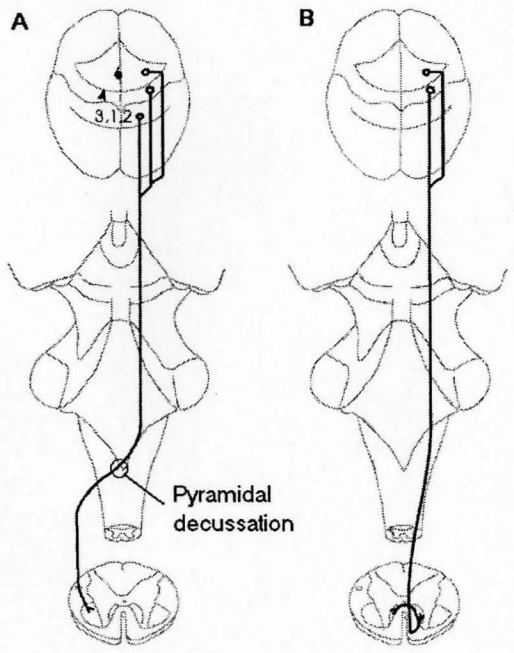

Figure 1.2 Descending pathways to the spinal cord.
A) The lateral corticospinal tract originates from the premotor cortex (area 6), M1 (area 4) and the somatosensory (areas 3, 2 & 1). Fibers extend through the dorso-lateral column, cross over in the medulla oblongata *(pyramidal decussation)* and terminate in spinal gray matter.
B) The ventral corticospinal tract originates in two motor areas (Brodmann's areas 4 & 6) and projects bilaterally to the ventro-medial cell column in the spinal cord. (Adapted from Ghez & Krakauer, 2000).

Both motor and sensory function follows a hierarchical process. The higher, more specialized levels of the motor neuronal system originate in the large pyramidal cells in the motor cortex (upper motor neurons). These cells synapse with interneurons that make connections with lower motor neurons, which exit the spine through a ventral root and branch until they enter a muscle. In order to fully understand the complexity and mechanism of the motor system and the loss of motor function, it is necessary to describe the organization of this interconnection between the upper and lower levels of the motor system: the spinal cord.

1.1.3 Spinal Cord

The spinal cord is a delicate structure localized within the canal of the vertebral column. It is protected by bony vertebra, meninges, cerebrospinal fluid and ligaments.

These structures support the spinal cord and protect it from shock and displacement (Amaral, 2000a; Harkey, White, Tibbs, & Haines, 2003; Tortora & Grabowski, 2003). However, the disruption of any of these structures may result in spinal cord injury.

The spinal cord does not extend throughout the vertebral column. Rather, it extends from the medulla oblongata (in brain stem) to approximately the level of the second lumbar vertebra or L2, growing only about 16 to 18 inches at maturity (Harkey et al., 2003; Somers, 2001). For this reason, in injury, the affected bony vertebra does not necessarily coincide with the spinal cord level (e.g. 7 cervical vertebra vs. 8 cervical spinal segmental levels, see Figure 1.3). The spinal cord is divided into four regions whose spinal nerves innervate certain body structures (Amaral, 2000a, 2000b). The *cervical* level innervates muscles in the back of the head, neck and arms to regulate both, sensory and motor function. The *thoracic* segment innervates muscles in the trunk. The *lumbar* and *sacral* levels supply muscles of the pelvis, lower back and legs (see also Figure 1.3).

The "inner" spinal cord is composed of grey matter (which corresponds to the darker "H" shape), surrounded by white matter. The grey matter is subdivided into dorsal and ventral horns, and contains nerve cell bodies that receive and integrate incoming and outgoing information (Amaral, 2000a, 2000b; Blam, Ehrler, Rauschning, & Vaccaro, 2003). The dorsal horns comprise groups of sensory neurons (sensory nuclei) and the ventral horns contain motor nuclei, whose myelinated axons in white matter innervate skeletal muscles. The spinal cord's white matter is also subdivided into bundles of axons, called tracts (i.e. ascending and descending tracts) which conduct impulses to and from the brain. All dorsal, lateral and ventral columns of the cord's white matter contain ascending axons. The descending motor axons are located in the lateral and ventral columns innervating interneurons and motor neurons in the spinal cord (Figure 1.4) (Amaral, 2000b). The axons exit and enter the spinal cord from the spinal nerves. There are 31 pairs of spinal nerves, which are considered mixed nerves because they contain both motor and sensory roots (Amaral, 2000b). The dorsal roots consist of sensory axons that transmit impulses from skin receptors and muscles to the CNS. The ventral roots consist of exiting motor axons that carry impulses from the CNS to effectors (muscles) and are considered the final common pathways of the complex motor system (also see Figure 1.4) (Amaral, 2000b). The shape and size and the proportion of grey and white matter of the spinal cord varies at each segmental level, depending on the structures

innervated. For example, at higher levels like the cervical segments, the number of ascending and descending tracts is larger; therefore there is more white matter than at sacral levels. Also, the ventral and dorsal horns are larger at segments where there are more motor neurons exiting and sensory neurons entering the spinal cord for the control of more complex movements (i.e., segments innervating the arms and legs) (Amaral, 2000b).

Major ascending and descending systems contained along the spinal cord are derived from muscle, skin, organs in the body, different parts of the cerebral cortex and spinal levels (e.g., the spinovestibular system originates from lower spinal levels, terminates in the medulla and controls postural reflexes) (Pearson & Gordon, 2000). These different pathways or "tracts" carry diverse types of information such as pain, temperature, proprioception, vibration, pressure, and motor responses to help modulate simple reflexes and complex movements. Conditions resulting in spinal cord damage are varied and complex and their severity is determined by the spinal cord's anatomical levels and function (Pearson & Gordon, 2000).

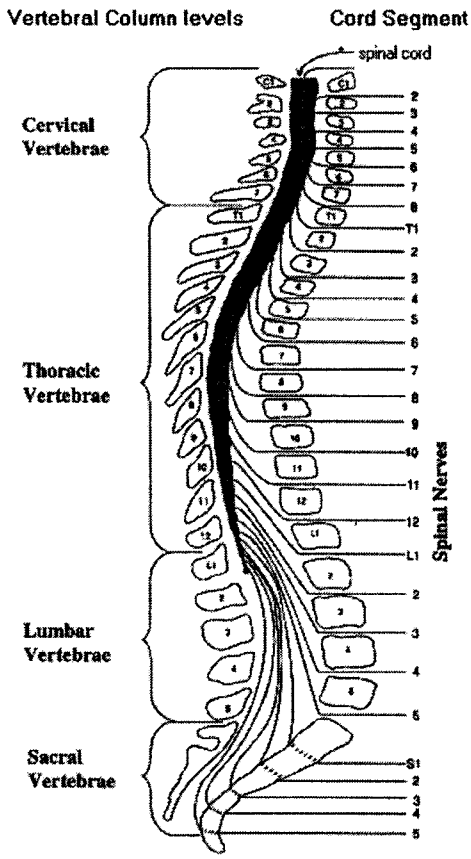

Figure 1.3. The bony vertebral column is also divided into cervical (1-7), thoracic (1-12), lumbar (1-5) and sacral (1-5) (left side). The spinal nerves branch out from each spinal segmental level between each vertebra to innervate the periphery. The figure also shows the size of the cord compared to the vertebral column.

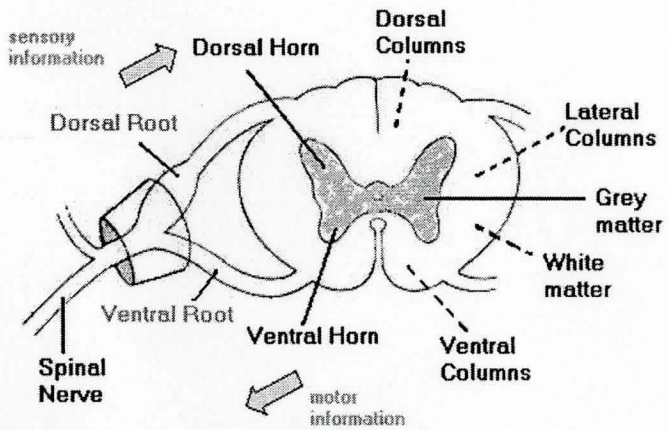

Figure 1.4. Cross-section of the spinal cord. The grey matter is divided into horns that contain sensory and motor nuclei. White matter is structured in columns and contains ascending and descending bundles of myelinated axons.

The spinal cord has been a subject of interest for many years in the area of motor control. It was presumed to be a simple pathway that connected the periphery to the higher centers of the brain. Presently, we know that the spinal cord is functionally superior to that of a simple connecting conduit. Although it is considered the lower level of the motor system, including motor neurons (common pathway for motor output) and interneurons (integrators of sensory feedback), the spinal cord is capable of supporting "automatic" movements such as reflexes and even more complex multi-joint and multi-limb responses. Reflexes are considered coordinated, involuntary motor responses to an external sensory stimulus, with the purpose of either initiating a movement or maintaining a motor pattern. Although the details of these mechanisms are not yet well known, it is apparent that the higher levels of the brain modulate the transmission of spinal reflexes.

In the early 1900's, Brown observed that the spinal cord was capable of independently generating rhythmic patterns (e.g., locomotion). He noted cyclic alternating contractions in the hindleg muscles of deafferented cats (i.e., no involvement of higher motor centers in the brain) (Prochazka, Mushahwar, & Yakovenko, 2002). Soon after, the term of central patter generators in the spinal cord emerged. How spinal, supraspinal and interneuronal systems are involved in initiating these centrally generated motor commands remains a focus of research (Dietz & Harkema, 2004; Prochazka et al., 2002). Some researchers claim to have found such oscillators in human spinal cords, through spinal cord injury research (i.e., step-like movement in incomplete spinal cord

injury (see Calancie et al., 1999; Dietz & Harkema, 2004). There is still controversy in the motor control field regarding the role of the spinal cord in movement as researchers are not able to reach a consensus on the mechanisms surrounding voluntary and reflex motor responses (Prochazka et al., 2002). However, it is unquestionable that the spinal cord plays an integral role in the motor systems function. Understanding the functional roles of the motor system and its components help localize alterations in motor patterns as a result of damage or disease to the central nervous system, which is important in the diagnosis of individuals with neurological disorders.

1.2 Spinal Cord Injury

Spinal cord injury is a general term that refers to damage to the spinal cord resulting in loss of motor and/or sensory function. Injuries to the spinal cord are complex, life changing and differ from person to person. Prognoses and functional outcomes depend on the type and severity of the injury, as well as physiological assessments that will lead to specific interventions at the time of injury and later on in life.

1.2.1 Pathophysiology

Damage to the spinal cord resulting in neurological dysfunction is caused by two major factors: (1) the initial mechanical insult delivered to the spinal cord, or *primary injury;* and (2) the cascade of pathobiological events that occur shortly after, known also as *secondary injury*, which further damage the spinal cord's anatomy and function (Blam et al., 2003; Harkey et al., 2003; Karlet, 2001; Lee & Green, 2002; Lou, Lenke, Ludwig, & O'Brien, 1998). The primary injury is considered a passive process occurring immediately after the impact to the spinal cord's structure, causing cord transection, compression or disruption of neuronal tissue (Karlet, 2001). Neurological deficit following primary injury is determined by the force and the mechanism of the impact and the level of the injury, as well as individual-specific factors such as the space available for the spinal cord within the compressed column (Karlet, 2001; Lee & Green, 2002) and the person's position at the time of injury (Somers, 2001).

Secondary injuries involve complex cellular and molecular processes which appear to be active during the first minutes, hours, days and weeks post injury, causing additional nerve cell death (Karlet, 2001). Shortly after trauma, swelling occurs as a result of localized haemorrhage and edema at the injury level (Karlet, 2001). Edema rapidly moves from the central grey matter toward the periphery of the spinal cord within the rigid vertebral canal (Blam et al., 2003; Karlet, 2001). The rising pressure halts capillary perfusion resulting in poor oxygenation of tissue which in turn leads to ischemia (Blam et al., 2003; Karlet, 2001; Lee & Green, 2002). Chemical and metabolic mechanisms are then triggered continuing neuronal destruction. Some post-injury cellular responses resulting in further damage to nerve cells include: the release of local "free radicals" or oxidizing agents; excessive release of neurotransmitters and programmed cell death (i.e., necrosis and apoptosis), that cause cell fragmentation; and myelin breakdown involving most of the cross-sectional area of the spinal cord (Blam et al., 2003; Karlet, 2001; Lou et al., 1998). These acute metabolic changes in the spinal cord last from approximately 48 hours to 1 week (Harkey et al., 2003; Karlet, 2001). During the subsequent three to four weeks, degenerated tissue is absorbed as interstitial edema decreases and resorption of the haemorrhage occurs (Blam et al., 2003; Karlet, 2001). Throughout the following months, clogged vessels are re-canalized and the traumatized spinal cord is replaced by scar tissue (Blam et al., 2003; Karlet, 2001). The damaged area usually extends from 1 to 3 segments of the cord. However, the damage to additional above and below segments diminishes in severity and depends on the initial trauma (Somers, 2001).

Spinal cord injury is not always a result of trauma. As with traumatic SCI, non traumatic injuries (e.g., haematoma, infection, arachnoiditis, etc.) interrupt the spinal cord's blood flow thereby initiating the secondary events that lead to ischemia and necrotic cell death (Somers, 2001).

Secondary damage is a destructive process believed to be the major factor responsible for the irreversible damage after spinal cord injury (Blam et al., 2003). Currently, the goal of clinical management of acute SCI is to fully understand these secondary events in order to lessen their effects and promote neuronal survival in the acute stages following injury (see Table 1.2). Research is presently focused on tissue damage mediators (e.g., growth factors, inflammation, calcium complexes, ischemia, superoxide radicals, etc.) and their manipulation to improve neurological outcome and yield new potential treatments for patients (Karlet, 2001; Lou et al., 1998).

Table 1.2. *Acute Management of SCI*

1. Maintenance of blood pressure
2. Early diagnosis by plain radiography
3. Drug therapy: Methylprednisolone to reduce inflammation and suppress activation of immune cell responses to SCI
4. Immediate traction and reduction for fracture and dislocation
5. Spinal Imaging: MRI and/or CT
6. Surgery, if necessary, for cord structure instability due to fracture or residual cord compression

Adapted from: Delamarter RB and Coyle J. Acute management of spinal cord injury. J Am Acad Orthop Surg 1999; 7:166-175.

1.2.2 Incidence, prevalence, progression and mortality

Secondary injury effects have been reduced as a result of new developments in acute clinical management. In spite of such advancements, spinal cord injury still constitutes a devastating physical, emotional and financial event affecting approximately 35,000 Canadians ("Overview on sci and its consequences", 2006). The CPA estimates that around 1,050 Canadians per year sustain a spinal cord injury. Overall, approximately 50% of injuries result in quadriplegia and 80% of injured individuals are male. The majority of these injuries are caused by car collisions (35%) followed by falls (17%) (see Figure 1.5). In the United States, the National Spinal Cord Injury Association (NSCIA) reports that since 2001, the incidence of SCI is about 11,000 new cases each year with a total of 250,000 individuals living with SCI. As in Canada, the majority of the SCI patients are men (82%). Both the CPA and the NSCIA report an increase in incomplete injuries (incomplete injuries corresponding to 52% of all injuries according to the NSCIA).

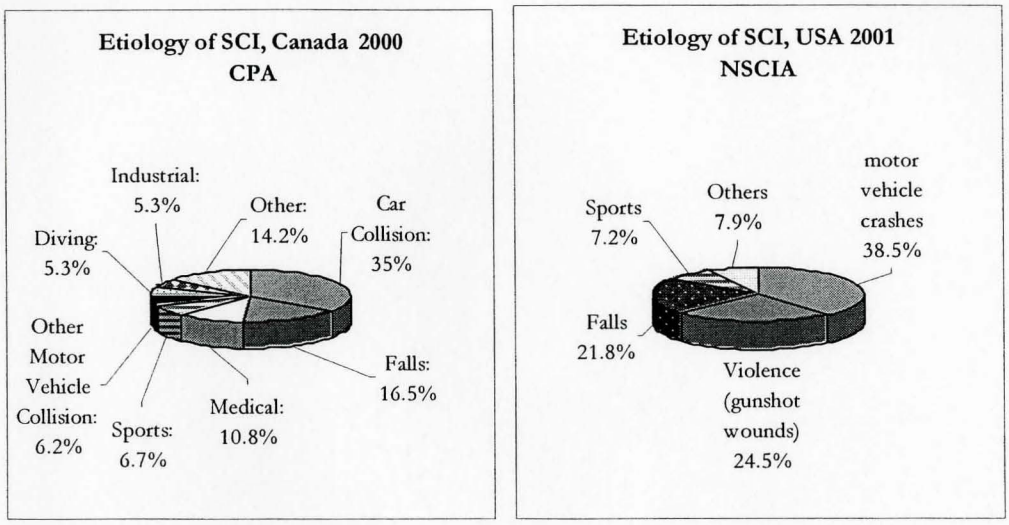

Figure 1.5. Causes of SCI in Canada and the United States. According to the NSCIA (right figure), the causes for injury vary slightly in the United States, with violence accounting for the second leading cause. The CPA (left figure) reports the incidence of non-traumatic causes, which account for more than 10% of injuries (Nobunago, Go, & Karunas, 1999, "Overview on SCI and its consequences", 2006).

Early interventions, such as immobilization and stabilization of the spinal column, decompression of the spinal cord, as well as physiologic homeostasis techniques have a profound positive effect on an individual's functional outcome (Finley, Rodgers, Rasch, McQuade, & Keyser, 2002; Karlet, 2001). In addition, advances in the medical management of SCI have increased life expectancy of injured individuals (Ballinger, Rintala, & Hart, 2000). This has meant that individuals with SCI are living longer (Hicks, Martin, Ditor, Latimer, Craven, Bugaresti et al., 2003) (see Table 1.3). Still, life after trauma is associated with other long-term complications. Co-morbidities following SCI impair the rehabilitation process, increase hospital stay duration and further contribute to a debilitating cycle among SCI individuals (i.e., changes in metabolism, contractures, increased pain, posture and pressure complications due to inactivity) (Finley et al., 2002). The most common secondary complications include pressure sores, muscle atrophy, urinary tract infections, lowered aerobic capacity, respiratory disorders, osteoporosis, renal dysfunction, musculoskeletal disorders (e.g., shoulder impingement, bursitis, contractures, etc.), cardiovascular diseases and metabolic changes (e.g., decreased resting metabolic rate) (Finley et al., 2002; Grange, Bougenot, Groslambert, Tordi, & Rouillon, 2002; Noreau & Shephard, 1995). During the first year post-injury, respiratory and cardiac-related causes account for over half of all deaths ("About spinal cord injury",

2006). Mortality after one year post injury has steadily decreased (according to the NSCIA, 1998), yet heart disease (18.8%), followed by respiratory complications (18%) remain the top causes of death during this period ("About spinal cord injury", 2006; Marino, 2003).

Table 1.3. Life expectancy of SCI individuals, after one year post injury

Age at Injury	*No SCI*	*Motor Functional at any level*	**Para*	*Low +Tetra (C5-C8)*	*High +Tetra (C1-C4)*	*Ventilator Dependent at any Level*
20 yrs	58.2	53.2	45.9	41.4	37.8	23.1
40 yrs	39.3	34.7	28.3	24.4	21.5	10.9
60 yrs	22.0	18.1	13.3	10.6	8.7	3.0

* Paraplegia refers to impairment or loss of motor and/or sensory function in the thoracic, lumbar or sacral, but not cervical segments of the spinal cord, affecting lower limb function; and +Tretraplegia refers to impairment or loss of function in the cervical segments affecting arms, trunk legs and pelvic organs (Maynard, 1997).
Table from the NSCI Statistical Center. Spinal cord injury: Facts and Figures at a Glance. Birmingham, AL: University of Alabama, 2000.

1.2.3 Recovery of function

Complete transection of the spinal cord is rare (Somers, 2001). Usually, some neurons passing at the injured level survive damage, resulting in an incomplete injury. Unfortunately, transection of the cord is not the only cause of irreversible damage. Compression of the cord during secondary injury, or by cysts and cavities post injury, can also result in non-recovery of function in surviving neurons (Somers, 2001). The spared neurons below the lesion level can function but may not be connected with higher motor levels (i.e., brain and brain stem). In this case, the individual exhibits spinal reflexes but lacks voluntary motor control and/or sensory function (Somers, 2001).

Incomplete spinal cord injuries have a significantly better prognosis than complete injuries (Harkey et al., 2003). With incomplete injuries, ascending and descending tracts may be partially or completely damaged at the injured level of the spinal cord (Somers, 2001). Because of this variability in neurological damage patterns, the spectrum of functional recovery in incomplete injuries varies from minimal preservation of distal function, to almost normal function (Harkey et al., 2003; Somers, 2001).

Recovery of function occurs after spinal shock subsides. Spinal shock is a temporary physiologic paralysis of the spinal cord occurring shortly after trauma (Karlet, 2001; Somers, 2001). During spinal shock, spinal reflexes, voluntary motor and sensory function, as well as autonomic control below the injury level are absent (Somers, 2001). Motor recovery occurs gradually after spinal shock (first 6 months to 1 year post injury, greatest rate within 3 months and slower rate for up to 2 years) (Kirshblum, Millis, McKinley, & Tulsky, 2004; Somers, 2001). Data corresponding to late recovery (1-2 years post injury) is limited (Kirshblum et al., 2004). Studies of late neurological improvement often take into account the level and type of injury, as well as different injury classification scales, muscle examinations or the resumption of function of a specific muscle, as prognostic indicators to determine recovery (Kirshblum et al., 2004). Inconsistencies in these studies, such as improper initial diagnosis (Maynard et al., 1997), intra and inter-rater reliability, changes and updates in classification scales, variability within a classification scale and between scales (Kirshblum et al., 2004), has limited significant findings, therefore undermining signs of recovery after 1 year post-injury.

Neurological recovery is usually considered to represent the recuperation of voluntary motor function or sensation below the injury level recuperated after injury and can occur due to nerve root and/or spinal cord functional recovery (Somers, 2001). Nerve roots are often damaged during SCI, but have the capacity of regenerating and resuming function (Somers, 2001). The functional recovery of neurons within the spinal cord may result from decompression of the cord, re-canalization of blood vessels, or regeneration and sprouting of neurons (Somers, 2001). However, the mechanisms for the recovery of neuron connections within the spinal cord are not completely understood and do not occur as often as root recovery (Somers, 2001). For these reasons, the degree of neurological recovery is difficult to predict. Thus, prognostic information is given when significant neurological function is observed and evaluated (initial assessment of injury about 3 days to 1 month post-injury) (Somers, 2001). Late recovery is not only dependant on the extent of neurological preservation, it also depends on interventions that are based on prognostic information and initial neurological evaluations, to prevent secondary complications and further enhance function (Kirshblum et al., 2004; Somers, 2001).

1.2.4 Injury level and Impairment

The degree of impairment in the SCI population varies greatly and is related to the damaged segmental level of the spinal cord (i.e., injury level) and damage to motor and/or sensory nerve fibers. Identifying motor and sensory loss facilitates the recognition of focal lesions within the spinal cord and other external compressive lesions below the injury level (Table 1.4) (Pearson & Gordon, 2000). The most common symptoms in muscles affected, associated with motor root injury, are weakness, fasciculation (small involuntary muscle twitches), wasting (muscle atrophy) and loss of tendon reflexes (Pearson & Gordon, 2000). When descending motor tracts are also damaged, the symptoms include: weakness, increased tendon reflexes and spasticity (increases in muscle tone which causes exaggerated tendon reflexes and involuntary muscle group co-contraction) (Pearson & Gordon, 2000).

Neurological level of injury is determined by sensitivity and muscle strength tests post injury. These tests also help determine the completeness of an injury and thus, classify an individual's spinal cord injury. Discrepant diagnoses in injury level often result from different neurological and rehabilitation definitions (Young, 2003). For instance, some neurologists assign the neurological level of the injury as the first segmental level with abnormal function and some physiotherapists define the injury level as the lowest level with normal function. For example, an individual who suffered a fracture of the C5 vertebra has damaged C6 segmental level of the cord (vertebra levels don't always coincide with the spinal segmental levels, see figure 1.3), C5 segmental level and roots exiting between C5 and C6 vertebra, in addition to C4 roots exiting the spinal cord between C4 and C5 vertebra. Such injury would cause sensory and motor damage to C4 (deltoids), C5 (biceps) and function below C6 (wrist extensors) would be severely compromised. After spinal shock, it is possible that C4 roots and C5 spinal cord and roots would recover over time (spinal root recovery and decompression of spinal cord. A neurologist would likely conclude that the individual had a C5 vertebra injury (X ray diagnosis) and initially had a C4 neurological injury level, which progressed to a C6 injury level. A physiotherapist, on the other hand, would assess the injury initially as a C3 injury level that progressed to a C5 level (Young, 2003).

Table 1.4 Indicators of motor level lesions

Spinal nerve root	*Motor Function affected*	**Reflex loss*
Cervical 1-4	Diaphragm	
Cervical 5	Deltoid, Biceps	Biceps
Cervical 6	Wrist extensors	
Cervical 7	Triceps	Triceps
Cervical 8	Finger Flexors	
Thoracic 1-10	Finger abductor, Intercostals muscles	
Lumbar 2-4	Hip flexors, Quadriceps, ankle dorsi flexors	Knee jerk
Lumbar 5	Great toe extensor	
Sacral 1-3	Plantar flexors	Ankle jerk
Sacral 4-5	Rectal sphincter	

*Damage or disease of the CNS can alter the strength of spinal reflexes. Identifying the pattern of these changes can help in an individual's diagnosis (table adapted from Karlet, 2001; Pearson & Gordon, 2000).

The spinal vertebra and the spinal cord become more discrepant at lower levels and thus diagnoses become more conflicting. For this reason, to avoid confusion some orthopaedic surgeons tend to refer to the injury level as the damaged vertebra level. Classification standards have been established to avoid discrepancies in determining injury level and the resulting impairments. However, standards are often used exclusively by physiotherapists and a patient may have been assessed by more than one classification scale. Identification of the injury level provides information of motor and sensory impairment. However, in incomplete injuries where individuals may have the same neurological level but varied patterns of motor and sensory function, labelling these individuals by injury level has limited value (Somers, 2001).

1.3 SCI Classification

Clinical diagnosis of patients with SCI and the classification of injury are key factors in determining treatment, establishing rehabilitation protocols and predicting outcome. A detailed and reliable assessment of a patient's neurological status is necessary to define the individual's functional limitations and to facilitate communication with care givers to establish rehabilitation goals ("Clinical assessment after acute cervical spinal cord injury", 2002). In addition, accurate and reproducible neurological evaluations, together with reliable measurement tools, determine the functional significance of new interventions for SCI by accurately measuring improvement after implementation (Somers, 2001). Numerous assessment scales have been developed to evaluate and describe the neurological status of individuals after SCI and are divided into two general classifications: 1) Scales that evaluate neurological status by assigning motor and sensory values or grades (i.e., letters or numbers) that are used in acute and chronic assessments; and 2) Scales that evaluate an individual's functional abilities and independence, usually used to describe chronic functional status ("Clinical assessment after acute cervical spinal cord injury", 2002). These scales are used in research as a way to compare therapeutic trials however, in some cases, within specific research studies and/or treatment evaluations; one type of scale is preferred over the other. As a result, researchers, and clinicians, are often left with an incomplete picture as to either the motor abilities or functional capabilities of specific patients. The implementation, and subsequent clinical interpretation, of both scales (i.e., neurological examination scores as well as functional outcome scores) is important for a complete assessment and management of SCI.

Some of the assessment systems more commonly used include the Frankel scale, the Yale scale, the National Acute Spinal Cord Injury Study (NASCIS) scale, the Functional Independence Measurement (FIM), the International Medical Society of Paraplegic (IMSOP) standards, the modified Barthel index (MBI), motor index score (MIS), the walking index for spinal cord injury (WISCI), the quadriplegic index of function (QIF), the functional ambulatory inventory (FAI) and the American Spinal Injury Association (ASIA). These assessments are strictly neurological evaluations (Frankel scale, Yale scale, NASCIS, IMSOP, MBI, MIS and ASIA) or functional outcome scales (WISCI, QIF, FAI, FIM). For research purposes, assessments are often compared and tested and correlations between scoring methods have been generated to provide

information regarding their accuracy and validity. Consequently, several assessment scales have been refined and their ability to evaluate and document a patient's neurological status and functional capabilities, before and after treatment, has improved. Ideally, clinical neurological evaluations of SCI should be consistent, reproducible, thorough and easy to apply ("Clinical assessment after acute cervical spinal cord injury", 2002). Currently, the American Spinal Injury Association (ASIA) approach has been widely used and adopted by almost every major organization related to SCI ("Clinical assessment after acute cervical spinal cord injury", 2002; Young, 2003).

1.3.1 ASIA classification of SCI

Clinical assessment that grades neurologic deficit in patients with SCI was first provided by Frankel and colleagues in 1969. Their scoring approach included a five-grade scale that defined SCI individuals (SCIs) with respect to functional ability. Specifically, (A) corresponded to no function below the injury level, (B) indicated sensory function only, (C) indicated some sensory and motor function, (D) grade described useful motor function and (E) graded patients had normal function ("Clinical assessment after acute cervical spinal cord injury", 2002; Young, 2003). The Frankel scale only described motor and sensory function and differentiation between patients was imprecise, especially when describing patients scored at grades C and D (Young, 2003). The lack of sensitivity of the scale led to the development of a variety of more detailed neurological assessment scales that were more sensitive to improvements (i.e, patients that advanced grades) over time and more accurate in describing neurological status ("Clinical assessment after acute cervical spinal cord injury", 2002; Young, 2003). In the early 1980's, ASIA published their first neurological classification system, based on clinical neurological examinations (Cohen, Ditunno, Donovan, & Maynard, 1998). The neurological assessments used a 6 point scale to grade 10 muscle groups and incorporated the Frakel scale to evaluate functional abilities. After revisions in 1988, these standards did not show reliability between clinical examinations and Frankel grades and showed difficulty in transferring the input from examinations to the classification of a patient (Cohen et al., 1998). In 1991, after redefinition of motor and sensory scores and inclusion of zones of partial preservation in 1989 (Cohen et al., 1998), Priebe and Waring (1991) tested inter-rater reliability of the revised ASIA standards by giving out patient examples as quizzes (Priebe

& Waring, 1991). Priebe and Waring (1991) concluded that although variability had decreased with the 1989 revisions, the interobserver reliability was "less than optimal" and further revisions were necessary (Priebe & Waring, 1991). In 1992, major revisions to the ASIA standards were made based on Priebe and Waring's (1991) recommendations, wherein the Frankel scale was modified to generate the ASIA impairment scale (Cohen et al., 1998). The degree of disability is quantified by the ASIA Impairment Scale (AIS) generating a grade of A for a complete injury, B for motor complete and sensory incomplete, C or D for a motor incomplete injury with different motor and sensory scores relative to preserved function, and finally a grade E for a normal motor and sensory function (Ditunno, Young, Donovan, & Creasey, 1994; Maynard et al., 1997). Several studies tested the reliability of the 1992 ASIA standards (Cohen et al., 1998; El Masry, Tsubo, Katoh, El Miligui, & Khan, 1996; Jonsson, Tollback, Gonzales, & Borg, 2000). Although ASIA resulted in a superior tool in predicting and describing function than other scales, findings from these studies also indicated ASIA's limitations ("Clinical assessment after acute cervical spinal cord injury", 2002). Overall, ASIA was still not sensitive enough to detect individual differences and presented weak inter-rater reliability for scoring incomplete SCI (Cohen et al., 1998; Jonsson et al., 2000). Further revisions were made in 1996 and 2000 to address the issues in complete and incomplete classification and degree of "incompleteness". The modifications included the redefinition of motor incomplete injuries where the patient must have sacral (S4-S5, anal sphincter contraction) sparing with motor function of more than three levels below the injury level (Kirshblum, Memmo, Kim, Campagnolo, & Millis, 2002). Kirshblum et al. (2002) examined the effects of these changes in the classification and the prognosis for recovery (1 yr post injury) and found no significant differences between the 1996 and the revised 2000 standards. They reported that the modifications to the scale were still not sensitive enough to detect changes in classification of ASIA B and C and did not improve the prognosis for neurological recovery after 1 year (Kirshblum et al., 2002). Sacral sparing made the classification of incomplete injury more stable since few patients gain sufficient function to transfer from an incomplete to a complete injury and also, a SCI individual with no S4-5 sparing rarely exhibits significant spontaneous recovery (Kirshblum et al., 2002). However, not exhibiting function in S4-5 does not mean that there are no axons across the injury level and that such a patient will not benefit from treatment (Young, 2003). In addition, S4-5 function may predict early recovery, but does

not reflect injury severity and does not give information on the functional capabilities of an individual with incomplete SCI for the implementation of treatment. In general, the AIS based on a motor and a sensory clinical examination provides information used for planning an individual's rehabilitation. It is important for these measurements to correctly explain a patient's neurological status for the prescription of treatment that will maximize function and independence (Somers, 2001).

1.3.2 ASIA standard neurological examination: motor components

Neurological examinations provide information on motor and sensory function. These evaluations are then interpreted to classify an individual's SCI, determining completeness of injury, motor level, and the AIS (A, B, C, D or E; see figure 1.5). Motor scores are obtained by testing the muscle strength of 10 key muscles in each myotome (i.e., the collection of muscle fibers innervated by the motor axons within each segmental nerve or root, see Figure 1.6). Key muscles below the injury level in each myotome are graded using a 6 point scale (0-5) ranging from no visible or palpable contraction; to contraction against full resistance (Figure 1.7) (Ditunno et al., 1994; Maynard et al., 1997). The examination produces two motor grades for right and left side, which are then summed to produce a single motor score. This single score is often used to describe motor function and recovery. The motor level is defined by the lowest key muscle grade, provided the motor grades of the segments above that level are judged as normal. The use of a total motor score has limited usefulness to explain impairment, especially in incomplete injuries (Somers, 2001). For example, a patient with a complete paraplegia may have the same total motor score as a person with incomplete quadriplegia. A number of combinations from the muscle scores could be summed to obtain a total motor score that does not provide specific information on a patient's functional status and where his or her functional limitations are located. Also, labeling the motor level alone will fail to identify the varying degrees and patterns of neurological damage in the incomplete spinal cord injured population (Somers, 2001).

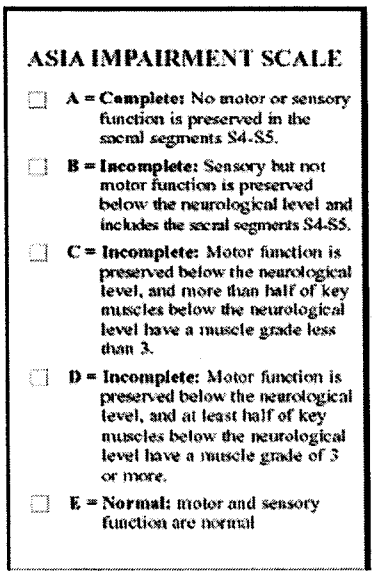

Figure 1.6. Degree of impairment scale based on key muscle grade and sensory point function (from Maynard et al., 1997).

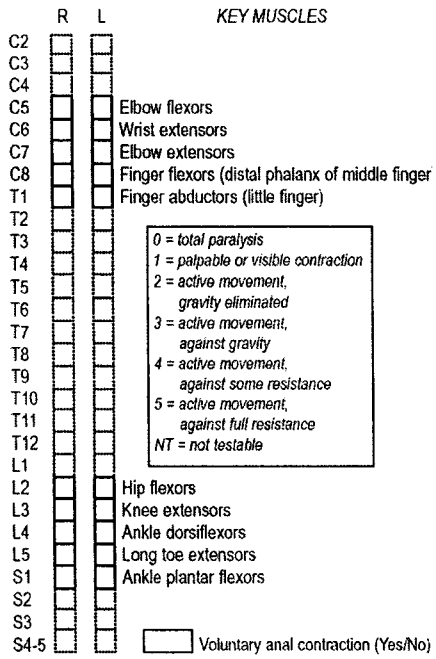

Figure 1.7. Key muscles tested in the 10 paired myotomes, graded on a six-point scale. C1 to C4, T1 to L1 and S2 to S5 myotomes are not clinically testable by manual muscle exam (from Maynard et al., 1997).

Clinical examinations of motor function rely upon the examiner's judgments and may present a number of factors that can have an adverse effect on the accuracy and/or reliability of the resultant score and the AIS. For example, some patients may inhibit a full effort during clinical testing due to pain, improper positioning, hypertonicity and disuse (Curt, Keck, & Dietz, 1998). Furthermore, SCI individuals quickly learn to compensate for, or even substitute, impaired muscle function when performing the movement and can give the false appearance that the key muscle has some or regular

function (Somers, 2001). Other factors that can also influence muscle test results are reflexive contractions (spasticity) which can make the muscle appear to function or to be stronger than it is; and poor stabilization of the musculature, when the patient is unable to do so and to isolate the key muscle, making the muscle appear weaker than it really is (Somers, 2001). In other cases (e.g., an unconscious patient state due to trauma, uncooperative behaviours resulting from psychiatric disorders or drugs, or patient comprehension barriers due to language or age, etc.) clinical examinations, and the resultant ASIA scores, are of limited value (Curt et al., 1998). Motor grade variations within a specific classification have a direct effect upon assessing the extent of an injury and level of SCI. Variations in diagnosis may affect recovery after SCI. For this reason, alternative measurements should be explored to fully assess the functional capabilities of an individual with SCI and properly prescribe treatment. The potential for one such alternative is described below.

1.4 Transcranial Magnetic Stimulation

Human cortical magnetic stimulation was first developed and applied successfully in the mid 1980s by Barker et al. (Terao & Ugawa, 2002). Barker and colleagues developed a compact stimulator used to activate neurons in the motor cortex and evaluate conduction of the motor tracts by evoking muscle activity (Kobayashi & Pascual-Leone, 2003). Transcranial magnetic stimulation (TMS) was developed to excite the cerebral cortex non-invasively and less painfully unlike previous techniques using electrical stimulation (Kobayashi & Pascual-Leone, 2003; Terao & Ugawa, 2002). Since its introduction, TMS has been used extensively to stimulate motor pathways, to assess upper and lower motor neuron dysfunction, document plasticity, evaluate the effects of rehabilitation techniques, locate damage and understand the effects of disease (Clarke, Modarres-Sadeghi, Twomey, & Burt, 1994; Kobayashi & Pascual-Leone, 2003). TMS delivers a brief magnetic pulse to activate neurons in nearby biological tissue. When stimulating motor pathways (motor cortex or peripheral nerves), the resulting response is muscle activation. A detailed description of the TMS technique is described as follows.

1.4.1 Basic principles of TMS technique

TMS consists of a source of current that charges an energy storage capacitor and when triggered, the capacitor discharges sending electric current to a coil of wire (Nollet, Van Ham, Deprez, & Vanderstraeten, 2003; Weber & Eisen, 2002). The flowing current in the coil produces a brief magnetic field perpendicular to the plane of the coil, which passes unimpeded through skin and bone, inducing an electrical current, flowing parallel to the surface of the coil, in nearby nerve cells, lasting approximately 100 μsec (Terao & Ugawa, 2002; Weber & Eisen, 2002). Specifically, the magnetic field, when strong enough, induces a differential potential in nerve cells which influences ion flow, resulting in a local depolarization of the neurons (see Figure 1.8).

In the M1, TMS activates the major output cortical cells (pyramidal neurons) that synapse directly and indirectly with spinal motor neurons (SMN) which innervate specific muscles in the body (Di Lazzaro et al., 2001; Weber & Eisen, 2002). The coil is placed on the skull over an area of M1 corresponding to a targeted muscle. The activation of the cortical cells that leads to a brief contraction of the targeted muscle is called a motor evoked potential (MEP) (see Figure 1.8). MEPs are typically recorded using electromyographic (EMG) techniques and measurements include: amplitude of the signal (μV peak to peak) and the time between the stimulus and the onset of the muscle burst, known as latency (msec) (Weber & Eisen, 2002).

Studies have shown that TMS stimulates pyramidal neurons in the motor cortex trans-synaptically resulting in I waves or indirect waves, compared to D waves or direct waves obtained by electrical stimulation (see Figure 1.8) (Di Lazzaro et al., 2001; Di Lazzaro et al., 1998; Weber & Eisen, 2002). However, it has been suggested that at high intensities, TMS is capable of stimulating pyramidal neurons directly at the axon hillock, resulting in D waves conducted down the pyramidal tract (Di Lazzaro et al., 2001; Di Lazzaro et al., 1998). There is still debate as to which motor cortical structures are activated using TMS, particularly when stimulating lower limb muscles (Di Lazzaro et al., 1998). Still, TMS is preferred over electrical stimulation in the clinical and research realm since it is a non-invasive technique that requires little preparation and it is easy to locate different areas of the motor cortex (Nollet et al., 2003).

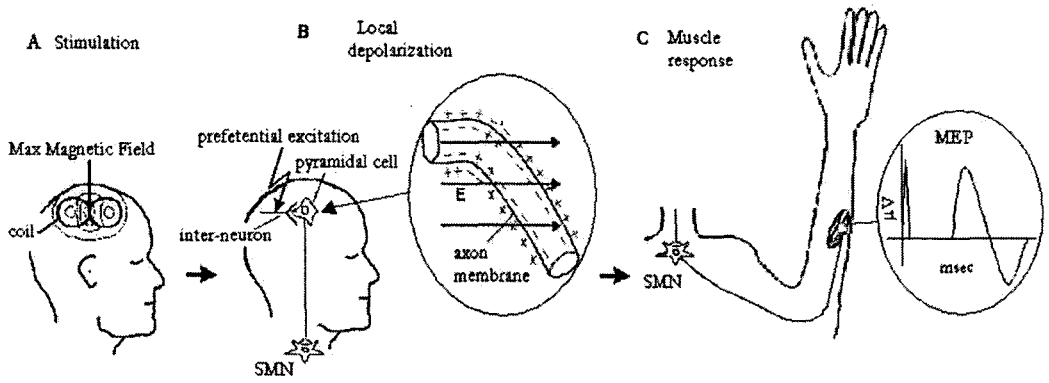

Figure 1.8. TMS technique. A) The center of the fi gure eight coil (max magnetic field) is positioned over the M1 area corresponding to forearm muscle contraction. B) The electric current flows parallel to the surface of the brain, preferentially exciting inter-neurons that are horizontally oriented. The pyramidal cell is then indirectly stimulated. C) When cortical threshold is achieved, the motor pathway is stimulated (pyramidal cell synapses with the SMN), resulting in a brief contraction of the targeted muscle (Weber and Eisen, 2002).

The current inductors (coils) used are capable of activating neurons located a few centimeters (4-5 cm; about 2 cm from scalp and about 2 cm in neural tissue) below the stimulation site (Nollet et al., 2003; Terao & Ugawa, 2002) but the stimulus becomes attenuated at deeper sites (e.g., basal ganglia) (Nollet et al., 2003). Circular coils induce current around the entire coil winding and produce a magnetic field that can stimulate deep cell pools (Terao & Ugawa, 2002; Weber & Eisen, 2002). Because the magnetic field in circular coils is distributed through a larger area, the resulting stimulus is non-focal (Weber & Eisen, 2002). In contrast, figure eight coils contain two wire loops side by side on the same plane (Terao & Ugawa, 2002) and thus, the intensity of the magnetic stimulus is maximal in the intersection site of the two circular wire loops, resulting in a more focal stimulation (Nollet et al., 2003; Weber & Eisen, 2002). However, the figure eight coil contains two circular coils that are smaller and is not capable of producing strong and penetrating magnetic stimuli (Weber & Eisen, 2002). A double cone coil also consists of two coils that are usually larger than figure eight coils and its two circular coils are placed in a 90° angle which does not allow the magnetic field to dissipate (Nollet et al., 2003; Terao & Ugawa, 2002). This allows for a stronger and more penetrating magnetic field that can reach deeper structures such as lower limb muscles in the motor cortex (Weber & Eisen, 2002). Focal stimulation results in a more accurate map of the stimulation site and decreases the variability of the TMS technique (i.e., variability due to location and orientation of the coil on the stimulated surface) (Weber & Eisen, 2002).

Another way of decreasing variability of MEPs is to facilitate responses, by voluntarily contracting the muscle (Bondurant & Haghighi, 1997; Mills & Kimiskidis, 1996; Weber & Eisen, 2002). When the target muscle is contracted prior to stimulation, the cortical threshold decreases, MEP latency is shortened and the amplitude increases (Weber & Eisen, 2002). It has been suggested that voluntary contraction of the targeted muscle raises motor cortex excitability, increasing the size and number of descending volleys that evoke a muscle response (Mills & Kimiskidis, 1996; Nollet et al., 2003). When an individual cannot contract the targeted muscle, alternative procedures can be used such as simply thinking about a movement, contracting the antagonist muscle, contracting the muscle of the opposite limb, implementing afferent electrical stimulation of the target muscle, and electrical stimulation of the peripheral nerve (Hayes, Allatt, Wolfe, Kasai, & Hsieh, 1991);(Kasai, Hayes, Wolfe, & Allatt, 1992; Nollet et al., 2003; Weber & Eisen, 2002). The mechanisms of these facilitatory effects are not entirely understood but have shown to be effective neurological reinforcements for minimizing negative interpretations of MEPs by decreasing MEP variability through increased cortical and spinal excitability (Hayes et al., 1991; Kiers, Cros, Chiappa, & Fang, 1993; Mills & Kimiskidis, 1996).

1.4.2 TMS and SCI

TMS has been used successfully in the past as a viable diagnostic tool to assess damage of descending motor tracts (Nollet et al., 2003) since MEPs are thought to reflect the structural integrity of the corticospinal tract, nerve roots and peripheral motor pathways (Hayes et al., 1991; Kobayashi & Pascual-Leone, 2003). Studies have shown that after SCI and other motor tract damage or disease, MEP characteristics change in correspondence to the clinical status of the individual (Hayes et al., 1991; Kobayashi & Pascual-Leone, 2003; Weber & Eisen, 2002). These changes in MEP characteristics include a higher threshold for activation, smaller amplitude, at times polyphasic waveforms, and prolonged latencies possibly due to demyelinated axons (reduced axonal conduction velocities) at the injury site or by weakened muscles (Alexeeva, Broton, & Calancie, 1998; Hayes et al., 1991). In addition, it had been reported that MEPs with these characteristics were only present in individuals with incomplete injuries and that MEPs could not be evoked in individuals with motor complete injuries (see Bondurant &

Haghighi, 1997; Hayes et al., 1991), supporting the clinical diagnosis for complete paralysis of descending motor tracts and some preserved but not normal function (incomplete paralysis). However, later findings on individuals with acute and chronic (>1yr) complete motor paralysis revealed that MEPs were possible to obtain by implementing facilitation techniques (i.e., target muscle contractions, cutaneous stimulation, remote muscle contraction) (see Dimitrijevic, Eaton, Sherwood, & Van der Linden, 1988; Hayes et al., 1991). Although MEPs were found in very few subjects (see Dimitrijevic et al., 1988; Hayes et al., 1991), these findings suggest the possibility of the existence of preserved motor pathways that were spared from injury which, for some reason, cannot be accessed by the individual to generate movement (Dimitrijevic et al., 1988; Hayes et al., 1991). Another important implication from these findings is that TMS was able to detect spared motor pathways in various muscles where conventional clinical examinations could not and thus offer the potential for a more complete injury diagnosis (Hayes et al., 1991). The potential for recovery of spared motor pathways supports the need for additional electrophysiological measurements such as MEPs generated from TMS. As well, the efficiency of the TMS technique for explaining neurological status, evaluating motor function, and monitoring recovery will demonstrate the significance of electrophysiological recordings as diagnostic information capable of broadening the clinical assessment of SCI patients (Curt & Dietz, 1999; Hayes et al., 1991).

A study by Clarke et al., (1994) assessed whether TMS was able to predict functional improvement in individuals with acute (15 days post injury) complete (n=7) and incomplete (n=3) spinal cord injury. Clarke and colleagues (1994) observed that, in complete injuries, TMS failed to predict recovery but was able to measure the functional improvements after 6 months (reappearance of MEPs after recovery of some function). In contrast, MEPs from biceps brachii, abductor pollicis brevis and tiabialis anterior were obtained from 2 out of 3 incomplete injured patients in the acute phase and continued to appear (after 6 months) after significant recovery and moderate recovery. In addition, motor function was measured as the total motor score from standard neurological assessments. Clarke et al. (1994) observed that in incomplete SCI, motor scores did not translate into an equivalent functional improvement. For example, one participant's total motor score increased by 66 points after 6 months but continued to exhibit little useful function (Clarke et al., 1994). In contrast, MEPs from this participant showed constant

amplitudes and slightly improved latencies. Clarke et al. (1994) concluded that TMS may be a useful tool for explaining motor function in patients with incomplete SCI.

Another study by Curt et al. (1998) examined how MEPs and motor scores predicted improvements in hand function and ambulatory capacity in patients with acute (n= 36) and chronic (n= 34) SCI with C1 to T1 neurological levels of lesion. Ambulatory capacity and hand function were clinically assessed using a 4 point scale (no capacity to full capacity with little disturbance ,see Crozier et al., 1992) and three types based on functional capability of grasping objects (see also Curt & Dietz, 1996) respectively. Curt et al. (1998) found that standard neurological assessments (motor scores) were significantly correlated to hand function and ambulatory capacity, as well as improvements after 6 months in the acute patients, when the scores were separated into upper extremity motor scores (UEMS) and lower extremity motor scores (LEMS); UEMS explaining improvements in hand function and LEMS in ambulatory capacity (also see Marino & Graves, 2004). Curt and colleagues (1998) also showed that MEP recordings of upper limbs (abductor digiti mini and biceps brachii) and lower limbs (quadriceps femoris and tibialis anterior) correlated to hand function and ambulatory capacity respectively and were as sensitive as motor scores (UEMS and LEMS) in predicting and measuring functional recovery in 90% of SCI subjects (Curt et al., 1998). They also concluded that the appearance of MEPs was a positive indicator of functional recovery.

A more recent study by Thomas and Gorassini (2005) examined whether the recovery of locomotor function after intensive BWSTT also increased the excitability and function of spared corticospinal tracts in chronic SCI, assessed through a TMS technique. Previous studies had examined MEPs potential of describing "spontaneous" recovery in acute SCI individuals. In Thomas and Gorassini's (2005) study, 8 individuals with chronic ($\geq$ 1yr) incomplete SCI (with some function below the injury level: AIS C and AIS D) received intensive treadmill training and were tested to obtain bilateral MEP recordings from tibialis anterior (TA) or vastus lateralis (VL) muscle, while contracting (10% of maximum voluntary contraction) the target muscle, before and after training. Participants trained until improvements were measured according to the WISCI II scale (21 point scale measuring the distance walked in 6 min) and EMG activity (Thomas & Gorassini, 2005). Motor scores were also measured pre and post training, and corticospinal function

was measured as MEP amplitude (peak to peak) as a function of threshold, intermediate and high stimulation intensities (Thomas & Gorassini, 2005). As in previous studies with individuals with some voluntary muscle function (Dietz, Colombo, & Jensen, 1994; Wernig & Muller, 1992), improvements in locomotor function were observed in most participants (except for one). More interesting, Thomas and Gorassini (2005) also found that MEPs evoked at intermediate and high intensities showed higher amplitudes and shorter latencies after training and were significantly correlated to the recovery of locomotor function, as assessed by the WISCI II scale. Thomas and Gorassini (2005) concluded that the enlarged MEPs indicated an increase in corticospinal connectivity and function. These results demonstrated that training can improve function of spared corticospinal tracts after chronic SCI and also provided more in depth information on the role of the corticospinal tract in locomotion (Thomas & Gorassini, 2005).

2.0 Summary and purpose of study

The current goal in the rehabilitation of individuals with spinal cord injury has moved beyond increasing life expectancy to maximizing functional capabilities, promoting independence and improving quality of life (QOL) (Hicks et al., 2003). The most important part of a patient's treatment begins with the assessment of the injury and continues with effective monitoring of recovery (Vaccaro, 2003). Currently, the only way to predict functional recovery, as well as evaluate neurological impairment, is by clinical examination (Clarke et al., 1994). The most common method of this evaluation is the AIS, an assessment technique that estimates muscle strength based on observations that characterize visible or palpable movement (Lee, Lim, McKay, Priebe, Holmes, & Sherwood, 2004; Lim, Lee, McKay, Priebe, Holmes, & Sherwood, 2005). Although the AIS scale provides a useful description of voluntary function without the use of instrumentation, it is limited in its ability to describe how muscles are recruited and it provides little information regarding the integrity of the corticospinal pathways (Lim et al., 2005; Hayes et al., 1991). Furthermore, in spite of numerous revisions over the past years, the AIS is still somewhat compromised by the rather subjective nature of its grading technique. Evidence of these limitations in AIS are indicated by both inter- and intra- rater variability that are due, in large part, to an inherent lack of sensitivity to issues of motor control in the grading procedures (Lim et al., 2005; Lee et al., 2004). As new

interventions emerge in the field of SCI rehabilitation (e.g., BWSTT and functional electric stimulation, FES), the need for more objective measurement techniques that are sensitive to changes in motor function becomes apparent (Lim et al., 2005). The combination of clinical examinations with electrophysiological measurements, or the use of electrophysiological recordings alone, such as surface EMG and TMS, could, in certain circumstances (e.g., in uncooperative patients), prove to be better methods of assessing SCI recovery and motor function (Curt & Dietz, 1999; Lee et al., 2004).

The purpose of this study, therefore, was to assess whether TMS can be used as an assessment tool to further describe motor function of SCI individuals by providing an enhanced capability to detect the existence of potentially spared motor pathways than would be possible using ASIA scores alone. It was hypothesized that MEP responses would provide superior information regarding neurological damage (i.e., through the existence of impulse transmission of descending motor tracts) and will thus provide an assessment technique that is more sensitive in describing actual motor function by assessing activity of each muscle individually. The second purpose of this study was to examine whether simple electrophysiological recordings, such as surface EMG, could provide a more accurate measurement of voluntary motor function assessed during standard clinical examination. In this case it was hypothesized that muscle activity recordings would provide information on the sensitivity of the ASIA technique to detect and quantify voluntary muscle activity and would also reveal muscle recruitment strategies.

3.0 Methods

3.1 Participants

Six individuals with chronic incomplete spinal cord injury (iSCI) participated in this study with informed consent (see Table 3.1). Inclusion criteria consisted of individuals: with incomplete SCI; previously diagnosed and classified (AIS grade B, C or D); not in acute stages (more than one year post-injury); no limb fractures or joint dislocations and; with no brain injuries or other medical contraindications to TMS testing (e.g., magnetic reactive metal planting in the head, use of heart implant, etc., see medical history questionnaire, Appendix A) (Wassermann, 1998; Weber & Eisen, 2002). Five participants were recruited from the rehabilitation center at McMaster University, through the "MacWheelers" exercise program with the remaining participant recruited through the Chedoke Hospital SCI rehabilitation program. Ethics approval for this study was obtained from the Research Ethics Board of St. Joseph's Healthcare Hamilton, Hamilton Health Sciences/McMaster University, Faculty of Health Sciences and other affiliated institutions.

Table 3.1. Participant pre-testing detailed information.

participant	*age*	*sex*	*Time post-injury in years (yrs)*	*Level of Injury (Sensory & motor)*	**Cause of injury*	*AIS*
S1	33	M	9	C5	T	C
S2	59	M	8	C5	T	C
S3	28	M	9	C5	T	B
S4	33	M	13	C5-C6	T	B
S5	60	M	2	T1	NT	B
S6	49	M	2	T10	NT	D

age = 43.67 ± 14.16 yrs; mean ± standard deviation (SD), time = 7.3 ± 4.4 yrs
*The majority of injuries (4 out of the 6 participants in this study) were the result of trauma (T), while only two participants suffered non traumatic (NT) SCI.

All participants had incomplete injuries according to AIS criteria. Three participants had an AIS B classification (i.e., motor complete but preserved sensory function below the injury level). AIS B classified participants were included to assess whether TMS could find activity where AIS examinations could not. Participants also reported being diagnosed and classified at the time of injury and had not had a follow up examination one year post-injury (as recommended by the International ASIA classification Standards, Kirshblum et al., 2002). In addition, S3, S4 and S5 (AIS grade B) have been participating in the rehabilitation program (MacWheelers) for three years, one year and four years respectively. Improvements in motor function are possible to observe at this time (recovery > 5yrs post-injury) (Kirshblum et al., 2004) and would be revealed by the AIS assessments in this study.

3.2 General Procedure

All six individuals with iSCI participated in this two part study. In Part 1, participants were clinically assessed by a professional physiotherapist to obtain individual motor scores in all 20 key muscles (10 on the right and 10 on the left side of the body) according to ASIA neurological and functional classification standards ("Clinical assessment after acute cervical spinal cord injury", 2002). During the AIS muscle grading examinations, electromyographic (EMG) activity was recorded from 12 key muscles (six on the right and six on the left side of the body) using surface EMG equipment. In addition, M-waves from six key muscles (three on the right and three on the left side of the body) were obtained to assess peripheral neurological damage. Part 1 of this study was completed in one session of about three hours with a 15 min break between M-wave testing and clinical muscle evaluations. In Part 2, participants received magnetic stimulation, using TMS, to elicit MEPs from the same eight key muscles that were also scored following the AIS protocol. TMS testing was divided into two sessions of about one hour and 30 min. Experimental procedures are detailed as follows.

3.3 ASIA assessments

Participants were carefully transferred from a seated position in their wheelchair to a supine position on a clinical bed (0.77m wide x 2 m long x 0.55 m high) where all muscle testing was performed. A physiotherapist, with SCI rehabilitation experience, performed motor examinations of key muscles (one on the right and one on the left side of body) of the 10 paired myotomes (C5-8, T1, L2-5 and S1) for all six participants. A total of 20 muscles (10 right and 10 left) were tested and graded on a six-point scale (0-5) based on both their strength and their ability to perform the movement (Ditunno et al., 1994; Maynard et al., 1997). In addition, individual motor grades from upper and lower limbs and from right and left side of the body were summed across to obtain a total motor score. Based on these motor evaluations, each participant's motor level was characterized (e.g., C5, T1, T10, etc.) and subjects were classified using the AIS (A, B, C, D or E). The motor level, according to ASIA international standards, corresponds to the lowest key muscle that has a grade of at least 3, given that the segments above are scored 5 (Kirshblum et al., 2004; Maynard et al., 1997). All key muscles were examined through grades 0 or 1 (i.e., visible or palpable muscle contraction) to 5 (i.e., movement against full resistance, which tests maximum muscle strength), regardless of their resulting motor score. For example, a muscle was evaluated for a score of 0/1 to 5 even though the final given grade was 1 (AIS typical protocol). Participants key muscle grades, total motor grade, AIS and motor level are reported in Appendix B.

3.4 EMG recordings for ASIA assessments

During clinical evaluations, sEMG activity was recorded from 12 key muscles (6 on the right and 6 on the left side of the body) using an 8 channel Delsys System (Delsys Systems, model Bagnoli-4EMG System, Boston, MA). Surface 3 x 2 cm electrodes (2 contacts of 1 x 0.1 cm and spacing of 1 cm) were positioned and secured with electrode interfaces and additional tape, over the muscle bellies of biceps brachii (Bi), triceps brachii (Tri), flexor digitorium superficialis (FDS), extensor carpi radialis (ECR), tiabialis anterior (TA), soleus (SOL) and gastrocnemius (GA). Prior to electrode placement, the skin surface over each muscle belly was shaved, cleaned with alcohol and allowed to dry. EMG signals were processed by the Delsys System's main amplifier unit with a bandpass

of 20 ± 5 Hz – 450 ± 50 Hz and a selected gain of 1000. DataQ hardware (DataQ instruments, Model D1-220) and software (WindaQ, version 2.09, DataQ instruments) was used to digitize, record EMG activity at a channel sample rate of 2000 Hz/sec, and display the data in real time on a personal computer.

During each key muscle examination, additional EMG activity was collected from other muscles to observe muscle recruitment strategies such as co-contraction of synergistic muscles or antagonist activation. Four channels (ch) recorded and displayed activity from the upper limb and three channels recorded lower limb activity during evaluations (see Table 3.2). For example, when evaluating myotomes C5 (elbow flexor), the key muscle graded corresponded to biceps brachii (channel 1), while additional EMG activity was recorded from triceps brachii (channel 2), FDS (channel 3) and ECR (channel 4).

Table 3.2. Fixed sEMG set up during muscle evaluations.

Upper limb			*Lower Limb*		
Channel	**Key Muscle*	*Level/ myotome*	*Channel*	**Key Muscle*	*Level/ myotome*
Ch1	Bi	C5-elbow flexors	Ch1	TA	L4 -ankle dorsiflexors
Ch2	Tri	C7-elbow extensors	Ch2	SOL	S1-ankle plantar flexors
Ch3	FDS	C8-finger flexors	Ch3	GA	S1-ankle plantar flexors
Ch4	ECR	C6-wrist extensors			

*Electrodes were switched from right to left side of the body in accordance with AIS evaluations.

Muscle activity was recorded from key muscles and additional muscles involved, when evaluating grades 0 to 5. Participants were asked to attempt to activate the key muscle (according to the AIS motor examination guidelines) and relax after each grade trial (when testing for grades 0-1 to 5). After the 5 grade trials (0-1 to 5), a motor score was given to the key muscle. In the WindaQ display window, markers were placed by the experimenter at the beginning and end of the trial to distinguish activity between grades and exclude activity due to a change in positions when switching between grade trials (e.g., when moving with gravity eliminated and changing the position of the limb to move

against gravity). Resting activity was recorded (10 sec) from each key muscle and the additional muscles prior to examinations. After all key muscles received a motor score; tape and electrodes were carefully removed and the participant was transferred back to his wheelchair.

3.5 Peripheral nerve stimulation: M-waves

Nerve stimulation was performed on the six individuals with iSCI with the purpose of identifying damage to the peripheral motor pathway. Participants remained in their wheelchair for the duration of the testing session. M-waves from 3 key muscles: FDS, TA and SOL on the right and the left side of the body, were elicited by surface electrical stimulation of the median, the common peroneal and tibial nerves respectively. No M-waves were elicited from ECR (wrist extensors) due to excessive levels of pain experienced when the peripheral nerve (radial nerve) was stimulated. Single pulse electrical current to the nerves was applied using a Medical Systems stimulator (Medical Systems Corp, type 3072, Miami, FL), which delivered rectangular voltage pulses ranging from 0 to 100 V (set at 4x of output) through 2 Ag/Ag electrodes (2 cm diameter) fixed accordingly and filled with conductive gel (Table 3.3). The intensity of the stimulation was increased by 5 volts until there was no peak-to-peak increase of the M-wave. Pulse width varied between 100 and 500 μsec. Inter-stimulus intervals were about 8-10 sec and were controlled by the experimenter. Surface EMG was collected from each key muscle using a UFI Fetrode system amplifier (gain of 10) (model 2283FT/i, Morro Bay, CA). Ag/AgCl electrodes (1 cm diameter) were placed over the muscle motor point and near the tendon, along the longitudinal midline, parallel to the length of muscle fibers (see Table 3.3). The ground electrode was positioned between the stimulating electrodes and the recording electrodes on a "non-involved" muscle or a bony prominence. EMG signals were recorded and displayed by a custom made LabVIEW software program (National Instruments, version 7.0, Austin, TX), which sampled the data at 4000 Hz. Only the peak M-wave amplitude was recorded, measured in mV peak-to-peak and the latency (i.e., the time between the end of stimulation artifact and the on-set of muscle activation) of the signal was measured in msec.

Table 3.3. Electrode Positioning.

Muscle	*Ag/AgCl EMG recording electrodes*	*Ag/Ag stimulating electrodes*
FDS	Electrode 1: muscle belly (halfway between medial epicondyle and end point of ulna). Electrode 2: on distal tendon (wrist joint). Ground: on medial epicondyle.	Cathode and anode on median nerve, underneath distal biceps.
TA	Electrode 1: muscle belly (one-third of the way laterally between tibial tuberosity and medial malleolus). Electrode 2: on distal tendon (lateral to medial malleolus). Ground: beneath head of fibula.	Cathode over the head of the fibula and anode below the patella (on patellar ligament).
SOL	Electrode 1: muscle belly (halfway between the popitleal fossa and the calcaneal tuberosity, below GA). Electrode 2: on distal tendon (over calcaneal tendon). Ground: beneath head of Fibula.	Cathode and anode fixed over the popitleal fossa.

* The skin surface over each muscle, where electrodes were positioned, was shaved, cleaned with alcohol and allowed to dry, prior to electrode placement.

3.6 TMS

All six iSCIs participated in 2-3 TMS sessions (of 1 hour and 30 min). Each session was scheduled on the same day and same time of day for each participant. Prior to experimental trials, participants answered a medical questionnaire (see Appendix A), which followed the International Workshop on Safety of TMS suggested guidelines (Wassermann, 1998).

3.6.1 Apparatus

TMS was delivered using a single pulse, Magstim 200 stimulator (Magstim Company, Wales, UK) that delivered 100 μsec pulses of up to 2.2 Tesla in strength. A figure-eight coil (7 cm diameter, type 9925) was used to stimulate M1 and elicit MEPs from the upper limb muscles and a double-cone coil (9 cm diameters each, type 9902) was used to stimulate muscles of the lower limbs. Double cone coils can achieve a better depth of penetration and are capable of stimulating the areas of M1 that activate muscles of lower limbs (Nollet et al., 2003; Weber & Eisen, 2002). Magnetic pulse intervals were controlled by the experimenter and delivered at most every 3 sec to allow the Magstim 200 to recharge.

3.6.2 Experimental Protocol

TMS was used to obtain MEPs in 8 key muscles (4 on the right and 4 on the left side of the body): the ECR, FDS, TA and SOL. Participants remained in their wheelchair for the testing sessions.

Prior to experimental trials, optimal coil location and orientation, as well as stimulation threshold were established. To determine the optimal coil location, the scalp was marked over the M1 regions (right and left hemispheres) corresponding to the 4 key muscles (Figure 3.1). To elicit responses in ECR and FDS muscles, the figure-eight coil was positioned tangentially to the scalp on the contralateral hemisphere approximately 4.5 cm lateral to the vertex following a 45° angle, around C4-F4 and C3-F5 measured according to the 10/20 International System (Figure 3.2) (Brasil-Neto, McShane, Fuhr, Hallett, & Cohen, 1992; Weber & Eisen, 2002). To obtain MEPs from TA and SOL, the double cone coil was positioned above the vertex, Cz measured according to the 10/20 International System (Figure 3.2) (Curt et al., 1998; Weber & Eisen, 2002). Each participant's vertex measurements were recorded to ensure similar coil locations for subsequent testing sessions.

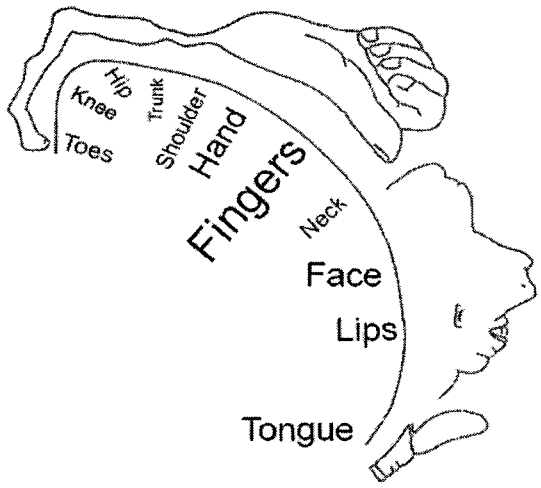

Figure 3.1. Map of M1 in left hemisphere. Representation of lower limbs is located deeper (Cz), compared to a more superficial representation of upper limbs (adapted from Penfield and Rasmussen, 1950)

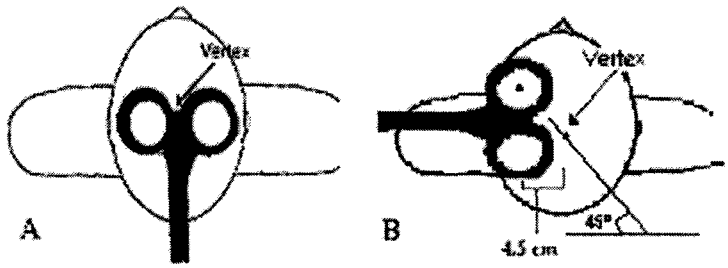

Figure 3.2. Coil location. A) Double cone coil located at vertex (Cz) to stimulate lower limb; B) figure eight coil located 4.5 cm at 45° from vertex to stimulate muscles of the forearm on contralateral side.

Once the coil was positioned over the recommended M1 region for each muscle, magnetic stimuli were delivered at a low intensity (approximately 30% of the maximum available stimulus intensity for the Magstim 200, below motor threshold), to find the optimal site or "hot spot" (i.e., where the best signal and sometimes muscle activation was observed) for each participant. The "hot spot" was identified through facilitation techniques (i.e., asking the participant to think about or attempt to activate the muscle using minimal force, just enough strength to overcome gravity) and marked on the scalp. Coil location and orientation was frequently checked throughout the experiment.

After identifying optimal coil location, magnetic stimuli were delivered over this "hot spot" starting at a low intensity (e.g., 35% of maximum stimulator output, MSO)

and slowly increasing by 5-10% of MSO, until threshold was established for each muscle. Threshold was defined as the stimulus intensity required to evoke reproducible peak to peak responses of about 50μV in amplitude in half of 10 trials (Weber & Eisen, 2002). The same facilitation techniques as those used to locate the "hot spot" were used when MEPs were not found when the muscle was relaxed.

After recording MEPs at threshold intensity, two additional muscle conditions were established for experimental trials: key muscle at rest and at 20% of maximum voluntary contraction (MVC) (see EMG recordings for TMS section). In both conditions stimuli were delivered at 115% of the identified threshold intensity. Twenty consecutive stimuli were thus delivered when the participant was at rest and twenty stimuli were delivered when the participant was voluntarily contracting the key muscle. To avoid fatigue during the 20% of MVC condition, stimulation was divided in two sets of 10 consecutive stimuli with a one minute rest period in between. Participants who could not voluntarily activate the key muscle tested, were asked to attempt contraction nonetheless (for FDS: flex fingers; for ECR: extend wrist; for TA: flex foot towards shin; and for SOL: extend foot downwards) or to contract the antagonist muscle when possible. In addition, participants had visual feedback of their muscle activity, used as a facilitation technique, throughout the experiment.

FDS MEPs were obtained with the arm in a supinated position and resting on a cushion. A small soft rounded object was positioned in the hand to monitor finger flexion during stimulation and ensure FDS activation. ECR MEPs were elicited when the arm was rested in a pronated position and extension of the wrist was observed during stimulation. When stimulating Cz (TA and SOL), the legs were extended and rested on a small footstool. Participants rested for five minutes between each key muscle experimental trial. Stimulation was kept at a minimum and intensities were less than 100% of stimulator, to minimize participant discomfort.

3.7 EMG recordings for TMS

Surface EMG was recorded from right and left key muscles: ECR, FDS, TA and SOL, using a using a 4 channel Delsys System (Delsys Systems, model Bagnoli-4EMG System, Boston, MA). Surface 3 x 2 cm electrodes (2 contacts of 1 x 0.1 cm and spacing of 1 cm) were placed over muscle bellies (reference electrode in bony prominence) after

the skin surface was shaved, cleaned with alcohol and allowed to dry. EMG signals were processed by the Delsys System's main amplifier unit with a band pass of 20 ± 5 Hz – 450 ± 50 Hz and a selected gain of 1000. A custom made LabVIEW software program (National Instruments, version 7.0, Austin, TX) digitized, at a sampling rate of 4000 Hz, recorded, displayed and analyzed EMG data.

The stimulators discharge pulse served as an external trigger, which started the sweep to display and record the motor response of a key muscle. The LabVIEW™ program displayed and recorded two channels corresponding to muscle activity of the key muscle tested and its corresponding antagonist. For example, when testing for motor activity in TA (channel 1), a second electrode (channel 2) was also placed over the soleus muscle to detect any antagonist activation. Recording antagonist activity led to a more precise coil location and optimal stimulation of the key muscle. A third channel in the LabVIEW program displayed background activity of the key muscle for the 20% of MVC condition, in real time. Prior to stimulation of a key muscle, participants practiced performing MVC of that key muscle. MVC activity was rectified and low pass filtered with a cut off frequency of 3Hz (Thomas & Gorassini, 2005). The EMG envelope, stored and played back when attempting contraction, was used as feedback for the participants so they could maintain key muscle contraction or a signal that corresponded to 20% of their MVC.

MEPs from threshold, rest and 20% of MVC trials were stored for each key and antagonist muscle. In addition, the custom LabVIEW program generated Excel files containing the amplitude (μV peak-to-peak) and latency (msec) of all MEPs (channel 1 and 2). The stimulus artifact had a latency of ~0.004 msec. The five largest MEPs (μV peak-to-peak, chosen out of a range of ~10 trials) from threshold and from each condition (rest and 20% of MVC) were chosen for analysis.

3.8 Statistical Analyses

Data from clinical evaluations and TMS testing sessions were analyzed using Statistica software ('99 edition, StatSoft Inc., Tulsa, OK). Significance levels were established at a p level of 0.05. EMG data were represented as means and standard

deviations (SD). Data, including MEPs, motor scores, muscle activity during clinical examinations, and M-waves were analyzed for each participant.

3.8.1 ASIA motor scores and EMG recordings

EMG data from clinical examinations were analyzed using DIAdem software (version 10.0, National Instruments, Austin, TX) where the data were filtered through a band pass with a low and high cut off frequency of 20-450 Hz. Motor grading experimental trials had different time durations. For example, the duration of a trial for a motor score of 0/1 (a simple movement from the key muscle was observed) was shorter than a trial to measure for a motor score of 5 (the muscle is capable of moving with full resistance). All grade trials were at least 2 sec long. The root mean square (RMS) of each grade trial (0/1-5) and channel (key muscle and additional channels, 4 in total) was calculated over 2 sec intervals. RMS from resting trials (baseline) was also calculated. The RMS values were then normalized to baseline to obtain muscle activity as a fold increase from baseline and make comparisons between grade trials and participants. A repeated measures 2-way analysis of variance (ANOVA) was used to determine the degree of difference between the 6 key muscles' (Bi, Tri, ECR, FDS, TA and SOL) normalized RMS (nRMS) values and activity with respect to side of the body. Comparisons between key muscle nRMS values (right and left side) and the corresponding AIS motor scores (right and left side) were performed using Spearman's rho correlations ($p < 0.05$).

Muscle activity recorded from additional muscles during each key muscle assessment (e.g., EMG activity recorded from Bi, ECR and FDS muscles during Tri key muscle assessment) was compared to baseline (zero) using an ANOVA to identify whether other muscles were active during the muscle test.

3.8.2 MEPs

The peak values (μV peak-to-peak) of the 5 MEPs selected from threshold (th) and from each condition (rest and 20% of MVC) were averaged. The three means for each of the 4 key muscles (ECR, FDS, TA and SOL) were then analyzed and compared. A repeated measures three-way ANOVA was used to determine the degree of difference between key muscle MEPs, side of the body (right and left) and motor responses at each

condition (th, rest and 20% of MVC). Post-hoc tests (Tukey-HSD) were used to determine significant pair-wise comparisons ($p = 0.05$). Antagonist muscle activation during key muscle stimulation was analyzed and compared to agonist MEPs bilaterally and in all conditions. MEP latency values from upper and lower limb muscles across conditions were also analyzed and compared using a 2 way ANOVA.

Correlationss between key muscles MEPs (right and left sides and all conditions) and the corresponding AIS motor scores were assessed using Spearman's rho correlation coefficients. MEPs were also analyzed based on muscle grade (MEPs at grade 5, MEPs at grade 4, etc). The existence and amplitude of the MEPs at a certain grade was measured. A one factor ANOVA was used to make comparisons between MEP amplitudes at different motor grades.

A Pearson correlation was used to examine associations between evoked muscle activity (MEPs) and voluntary motor function recorded during AIS assessments (nRMS values) across all conditions.

4.0 Results

4.1 M-waves, clinical evaluations and participants post-testing information

Peripheral nerve stimulation suggested lower motor neuron damage and/or possible changes in motor neuron innervation (nerve sprouting) in participant S4 who exhibited no muscle activity in TA and SOL muscle during either M-wave, clinical assessment or TMS testing sessions (Table 4.1). M-waves, as well as MEPs, from all participants were present when testing FDS muscle. FDS M-wave from participant S4 had the lowest amplitude size and did not exhibit visual or palpable movement during clinical examinations (motor score of zero, also see Table 4.1).

Clinical evaluations determined total motor scores (summed across all 10 key muscles) and motor level. Only left finger abductor (T1) from S2 was not testable due to contractures of finger muscles. This participant may have lost 5 points in the total motor score due to contractures (Table 4.2, also see appendix B for individual motor grades). During muscle strength grading, S1, S3, S5 and S6 exhibited spasticity in lower limbs. S2 exhibited mild contractures and stiffness of the lower limbs.

Table 4.1. M-wave amplitude and latency measurements.

	FDS		*TA*		*SOL*	
Subject	*Amplitude (mV)*	*Latency (ms)*	*Amplitude (mV)*	*Latency (ms)*	*Amplitude (mV)*	*Latency (ms)*
S1	20.79 ± 3.15	3.88 ± 0.53	8.76 ± 2.44	1.63 ± 0.18	17.41 ± 2.57	5.25 ± 0.35
S2	23.85 ± 2.7	3.00 ± 0.35	3.62 ± 0.13	2.13 ± 0.53	11.81 ± 2.76	5.88 ± 0.18
S3	12.50 ± 1.75	2.63 ± 0.18	3.80 ± 1.2	1.25	13.62 ± 4.41	3.00
S4	6.12	2.75 ± 1.06	0	--	0	--
S5	15.98 ± 0.07	2.50	6.36 ± 1.02	4.23 ± 0.74	12.54 ± 0.30	4.38 ± 0.18
S6	25.38 ± 0.62	2.88 ± 0.18	10.96 ± 1.45	1.88 ± 0.18	11.75 ± 0.21	4.23 ± 0.74

Overall, mean amplitude size of TA (6.7 ± 3.18 mV) was significantly smaller from SOL (13.42 ± 3.18 mV) and FDS (17.44 ± 3.18 mV) ($F_{2,8}$= 17.22, $p < 0.05$).

Table 4.2. Participants post-testing information.

subject	*Time post-injury (yrs)*	*Level of Injury*	*Motor level*	*UEMS**	*LEMS**	*Total motor score*	*AIS*
S1	9	C5	C6	27	10	37	C
S2	8	C5	T1	45	10	55	C
S3	9	C5	C6	24	1	25	B
S4	13	C5	C6	20	0	20	B
S5	2	T1	T1	50	0	50	B
S6	2	T10	T1	50	40	90	D

S2 motor level was lower than expected and could be due to functional recovery since the time of injury. Also, S2 left finger abductor was not testable while the right finger abductor had normal function. Overall, the highest motor score corresponded to the lowest injury and motor level, as well as the participant with an AIS grade D. In addition, a low motor score corresponded to a high injury and motor level and an AIS grade B. (*) UEMS= upper extremity motor scores (sum of motor scores); LEMS = lower extremity motor scores (sum of scores). Total motor score = UEMS + LEMS.

4.2 MEPs of key muscles

Overall, stimulation intensities ranged from 40% - 90% of MSO for stimulating upper limb muscles (54 ± 14.7% MSO) and 42% - 100% of MSO for lower limb muscles (79 ± 22.2% MSO). Stimulus intensities of 100% of MSO were reached when trying to evoke lower limb muscle responses in participants S4 and S5 (both AIS grade B and total lower limb motor scores were zero) and in spite of high stimulation intensities, no MEPs were elicited. The cortical threshold of S3 (AIS grade B, lower limb motor score of 1) was also high (92.5 ± 5% MSO) and small MEPs were obtained in lower limb muscles. S6 had the lowest cortical threshold for lower limb muscle activation (44.75 ± 3.77% MSO) and had the highest lower limb motor score (40) while MEPs were obtained in all muscles tested. In upper limbs, participant S4 had the lowest motor score (20) yet the cortical threshold (S4 = 47.25 ± 1.5% MSO) was comparable to the thresholds from participants (S2 = 41.75 ± 2.36% MSO, S5 = 48.25 ± 6.65% MSO and S6 = 43 % MSO) who had higher motor scores (total upper motor scores of 45, 50 and 50) as assessed by clinical examinations.

All 6 participants tolerated TMS sessions except participant S1, who terminated the session due to discomfort when stimulating the left lower limb muscles. During this testing session (for S1 left lower limb), reliable and repeatable MEPs from left TA and left SOL could not be elicited during the duration of the trial, although some sporadic SOL muscle activation was observed in only two trials. This participant was excluded from further testing. None of the remaining participants experienced side effects or pain during testing.

Cortical stimuli were administered to elicit at least 5 MEPs which were recorded bilaterally from each key muscle (ECR, FDS, TA and SOL) in every condition: at threshold stimulation intensity (th), at 115% of th with the muscle at rest (rest), and at 115% of th when contracting the target muscle (20% of MVC). Not all participants exhibited MEPs in TA and SOL muscle (e.g., MEPs were not obtained in TA and SOL muscles from S4 and S5 at any condition, see Table 4.3). The amplitudes (μV peak to peak) and latencies (msec) of the MEPs found at each condition were measured and averaged. Side of the body was considered an independent measure and introduced into the analysis since activity of agonist muscles on opposite sides of the body is produced by separate corticospinal pathways (Thomas & Gorassini, 2005).

Latencies of the 5 MEPs were measured across condition (th, rest and 20% of MVC) from upper and lower limb muscles (overall, upper limb = 16.27 ± 2.11 msec and lower limb = 45.05 ± 5.14 msec). Latencies of responses evoked when using facilitation techniques (voluntary or attempted muscle contraction at th = 30.04 ± 13.51 msec and at 20% of MVC = 30.28 ± 15.11 msec) were significantly shorter than those MEPs when the muscle was resting (rest = 31.66 ± 13.51 msec) ($F_{2,2}$= 41.23, $p<0.05$).

Amplitude analysis revealed significant differences between condition ($F_{2,10}$= 7.43, $p<0.05$) wherein the largest MEPs were obtained at 20% of MVC (648.17 ± 640.85 μV), followed by MEPs obtained at rest (207.7 7± 197.77 μV) and were approximately 6 times and 3 times larger respectively than those evoked at threshold condition (93.28 ± 62.76 μV). The 3-way ANOVA (muscle x side x condition) also revealed no significant differences between MEPs on right and left side of the body, but showed muscle group differences ($F_{3,15}$= 7.43, $p<0.05$). Overall, MEPs of the wrist extensor muscles (ECR) (866.36 ± 753.03 μV) and finger flexors (FDS) (309.6 ± 313.04 μV) had significantly larger amplitude sizes than those obtained in SOL (51.82 ± 74.67 μV) and TA (37.84 ±

61.11 μV) muscles (see Table 4.3). More specifically, comparisons across all conditions revealed significantly larger MEPs in wrist extensor muscles in the 20% of MVC condition (1861.35 ± 1638.83 μV, from interaction, $F_{6,30}$= 4.88, $p<0.05$) than any other muscles under any condition (Table 4.3).

Table 4.3. Participants MEPs at th, rest and 20% of MVC (μV) collapsed across side.

	Threshold (μV)				*Rest (μV)*				*20% of MVC (μV)*			
	ECR	*FDS*	*TA*	*SOL*	*ECR*	*FDS*	*TA*	*SOL*	*ECR*	*FDS*	*TA*	*SOL*
S1	146	43	58	42	370	59	0	0	459	80	95	38
S2	132	156	50	90	627	336	0	141	1486	405	63	285
S3	292	125	0	0	244	166	0	0	1132	338	15	12
S4	159	80	0	0	1172	110	0	0	4479*	155	0	0
S5	107+	96+	0	0	174+	142+	0	0	384+	645+	0	0
S6	242+	232+	104	85	763+	462+	128	93	3229+*	1941+	169	147

Largest MEPs corresponded to activity of ECR muscles, especially from participants S4 (AIS grade B, mean = 1936.42 ± 2259.14 μV) and S6 (AIS grade D, mean= 1411.16 ± 1595.57 μV). ECR MEPs from S4 and S6 exhibited large amplitude values while contracting (*), while MEPs at th were similar to those of other subjects. No MEPs were obtained from TA and SOL muscles from S4 and S5 (both ASIA B) and low amplitude responses were observed from S3 (ASIA B) and S1 (ASIA C), where MEPs were only obtained from right TA and right SOL when attempting to contract the target muscle. Although S3 lower limb MEP amplitudes were below the threshold level, they appeared to be reproducible and reliable data throughout the trials. S5 and S6 upper limb MEPs correspond to muscles with normal function (+, above injury level).

Antagonist muscle activation (channel 2 during TMS target muscle testing) was also measured, averaged (on the same 5 trials chosen for agonist MEP analysis) and compared to agonist MEPs. A 3-way ANOVA was used to determine differences between muscle group (agonist vs. antagonist) of right and left side of the body under all conditions.

Analysis comparing key muscle ECR and antagonist muscle flexor carpi radialis (FCR) activity revealed significant differences between muscle group ($F_{2,5}$= 8.11, $p< 0.05$) wherein the activity from the antagonist (FCR = 107.41 ± 92.42 μV) muscle was not equivalent to the MEP size of the ECR muscle (significantly larger MEP size of 866.36 ± 1212.96 μV).

Comparisons between key muscle FDS and extensor digitorium muscle (Ext. Dig.) did not reveal significant differences between muscle group MEPs. These results suggest that the antagonist (ant) muscle (extensor digitorium) was activated during TMS testing and this evoked muscle activation was not significantly different to that of the targeted muscle (FDS = 309.6 ± 454.92 μV; ED_{ant}= 763.82 ± 1267.79 μV). MEPs were recorded in most participants during FDS stimulation and were most frequent, and exhibited larger sizes, during stimulation at the 20% of MVC condition. No significant differences were found in antagonist muscles when testing TA (TA = 37.84 ± 60.24 μV; SOL_{ant}= 55.58 ± 146.76 μV) and SOL (SOL = 51.82 ± 86.99 μV; TA_{ant}= 39.06 ± 94.68 μV). Overall, in lower limb muscles, antagonist MEPs were present together with agonist activation and more frequent when facilitation methods were used. Furthermore, regardless of MEP amplitude, antagonist activity always paralleled agonist MEPs with increases across threshold, rest and 20% of MVC conditions (e.g., Figure 4.1).

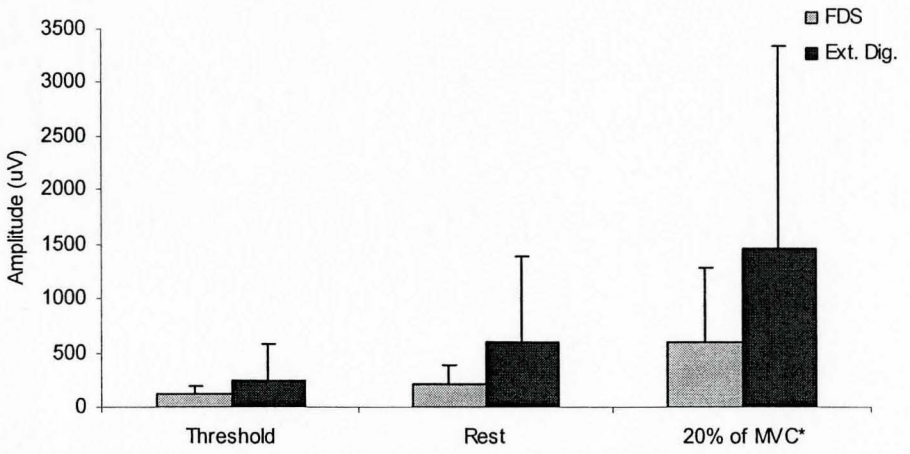

Figure 4.1. Average amplitude of MEPs evoked in FDS and antagonist Ext Dig muscles. All participants exhibited MEPs from antagonist muscle during FDS stimulation. As MEP amplitude from FDS muscle increased, simultaneous activity recorded from antagonist also increased throughout the conditions and MEPs from both muscle groups were significantly larger when attempting contraction of agonist muscle (*).

4.3 Correlation between MEPs and ASIA motor scores

Individual motor scores from the 4 key muscles ECR, FDS, TA and SOL (right and left side of the body) were analyzed separately and then compared to the corresponding averaged MEP. Similar to MEP amplitude analysis, the ASIA motor score analysis revealed no significant differences between muscle grades of the right and the left side of the body. In addition, ECR muscle received a significantly higher motor score (ECR = 4.67 ± 0.52; $F_{3,15}$= 10.77, $p<0.05$) compared to the other key muscles. The TA muscle had the lowest motor score (TA = 0.83 ± 1.6) with only two participants receiving a muscle score different from zero (see Table 4.4). The higher score from ECR was not surprising since at least 2 participants had a thoracic injury level (S5 and S6; also S2 with a motor level of T1) and had normal function at the cervical level where wrist extensor muscles are innervated. Also, most participants exhibited a motor level of C6, suggesting that the muscles innervated at that level must have had a motor score of at least 3. What is notable is that the largest mean MEPs corresponded with the highest motor score in the ECR muscle. MEPs from other muscles also seem to mirror motor scores in that large MEP correspond to high motor scores and small MEPs to low scores (Table 4.5). A Spearman rho tests revealed positive significant correlations between MEPs across all conditions and motor scores of key muscles (correlation coefficients at threshold $\varphi = 0.75$, at rest $\varphi = 0.72$, and at 20% of MVC $\varphi = 0.80$, $p<0.05$). However, individual muscle comparisons (e.g., MEPs vs. motor grades of FDS muscle) were not relevant due to the lack of score range (0-5) within the muscle grades. For example, all ECR muscles received a grade of either 5 or 4 only. In addition, a large number of zero scores of the TA and SOL, small sample size and large differences between MEPs limited the ability to make comparisons between scores and MEPs of a particular muscle (Figure 4.2 and 4.3).

Table 4.4. Participant's key muscle motor scores collapsed across side

subjects	*AIS*	*Level of Injury*	*Motor level*	*ECR*	*FDS*	*TA*	*SOL*
S1	C	C5	C6	4	1	1	0.5
S2	C	C5	T1	5	5	0	1
S3	B	C5	C6	5	0	0	0.5
S4	B	C5	C6	4	0	0	0
S5	B	T1	T1	5	5	0	0
S6	D	T10	T1	5	5	4	4

According to clinical examinations, only two participants (S1 and S6) exhibited some function of the TA muscle. Four participants received a muscle score different than zero of the SOL muscle, where two participants received a muscle score higher than zero only on the right side (SOLR, averaged 0.5). Function in lower limb was present in all ASIA C classified participants (motor incomplete), the ASIA D, and only one ASIA B participant (S3 motor score = 1 in SOLR muscle).

Table 4.5.MEPs from each muscle compared to motor scores collapsed across condition.

Muscle	*MEP (μv)*	*ASIA score*
ECR	**866.36 *** ± 766.03	**4.67 *** ± 0.49
FDS	309.60 ± 313.04	2.67 ± 2.46
SOL	51.82 ± 61.11	1 ± 1.53
TA	37.84 ± 74.67	0.83 ± 1.48

* ECR MEPs were significantly larger than SOL and TA MEPs, and the corresponding motor score was also significantly higher than MEPs and motor scores of other muscles. Overall, as MEPs decreased in size, the motor scores also declined, suggesting that large MEPs correspond to higher voluntary motor function and smaller MEPs reflect lower motor function.

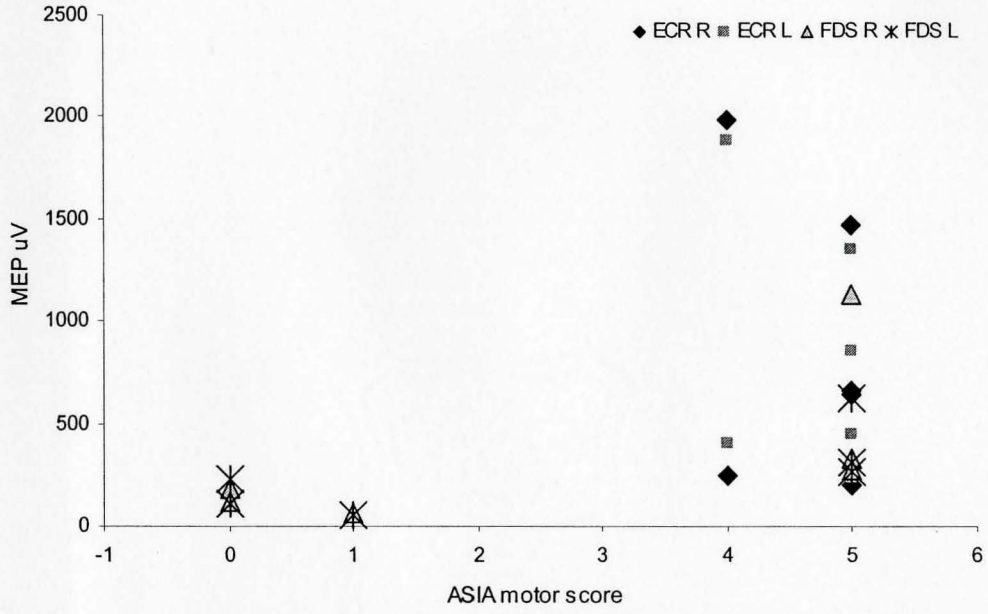

Figure 4.2. Averaged right (R) and left (L) MEPs of upper limb muscles of all participants at their corresponding motor score. The graph shows high variability between muscle responses (MEPs) of the same motor score. Not only is there high variability between muscles that were given a grade of 4 of muscle strength, but the graph also shows MEPs at a motor score of zero (finger flexors of the right (FDS R) and left (FDS L) side of the body).

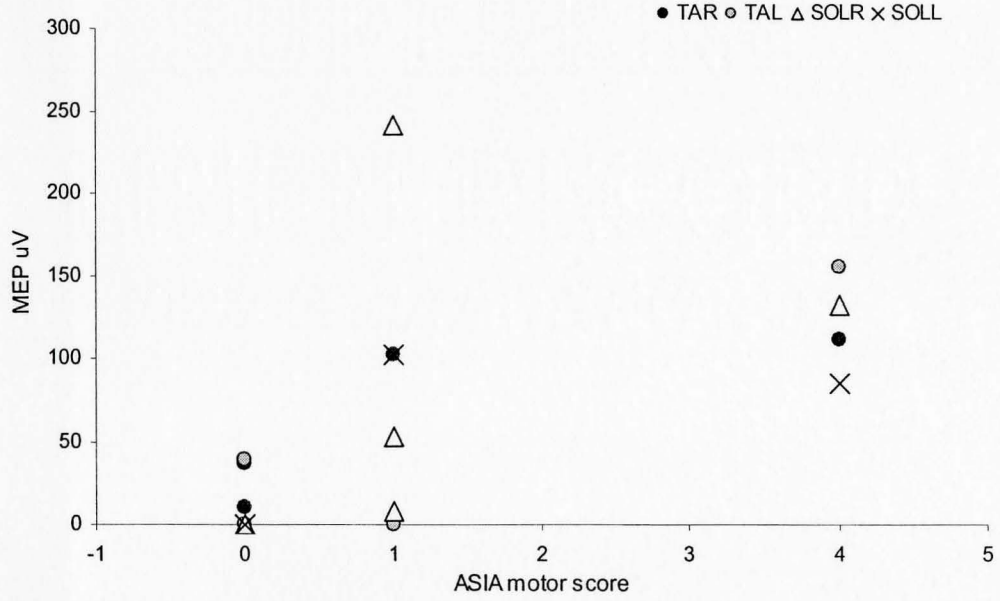

Figure 4.3. MEPs of lower limb muscles of all participants at their given motor score. This graph also shows high variability of MEPs within a score (motor score of 1) and the appearance of MEPs in muscles (TA and SOL) that were scored zero. Overall, MEP amplitude sizes ranged between 0 -186 μV at the zero score; 0 - 241 μV within a score of 1; 84 - 1986 μV at a score of 4; and 203 - 1468 μV within the maximum score of 5.

4.3.1 MEPs and their corresponding motor scores

There were a total of 48 muscle assessments or 48 muscles graded (4 muscles x 2 sides x 6 participants, same muscles from different side of the body and from different participants viewed as independent assessments and muscle grades) with their corresponding motor score under each condition. When rearranging the 48 motor scores by grade and their corresponding MEP amplitude response, assessment analysis revealed that 14 muscles received a grade of 5, 8 muscles were graded 4, 8 received a motor grade of 1 and 18 of those 48 muscles were graded zero. Furthermore, MEPs were obtained in assessments where the given muscle score was zero. More specifically, in 7 out of those 18 clinical assessments where the muscle received a grade of zero, MEPs were elicited when attempting to activate the muscle compared to 4 obtained with MEPs at rest and 6 at the threshold condition (Table 4.6). The evoked responses were found in upper and lower limb muscles: FDS R and FDS L under all conditions in participants S3 and S4 (both AIS grade B); in TA R and TA L muscles in S2 (AIS grade C) when attempting to contract the target muscle; and small responses were found in TA R muscle in S3 also when facilitating. These results suggest that MEPs were present with motor function and also revealed the existence of spared pathways when motor function was absent, according to clinical examinations (see Table 4.6).

Table 4.6. Mean MEPs under 20% of MVC condition at each given score

Assessments	*ASIA score*	*Number of MEPs found*	*Mean MEPs (μV)*
14	5	14	1317.37 ± 1008.7 *
8	4	8	1313.25 ± 2041
8	1	7+	127.23 ± 136.43
18	0	7	63.43 ± 116.54 * 163.28 ± 139.55 **

MEPs from S1 TAL muscle were not able to be elicited due to an unfinished trial (+). Mean MEPs with a motor score of 5 were significantly larger than those scored zero ($F_{3,44}$= 6.22, $p< 0.05$, unequal N HSD post hoc test)(*). This table also shows the mean MEPs from all the 18 assessments where a zero score was given (*, including zeros) and the mean amplitude of those 7 MEPs found (**). The 7 averaged MEPs ranged from 0 to 432 μV between participants classified as B (S3 and S4) and C (S2).

4.4 Key muscle EMG analysis of clinical examinations

Normalized RMS (nRMS) values were obtained bilaterally from EMG measurements of the 6 key muscles: Bi, Tri, ECR, FDS, TA and SOL while clinical assessments were performed. The nRMS values selected for analysis were those corresponding to the key muscle assessed and the grade given during clinical examinations. For example, when testing Bi muscle with a motor grade of 5, EMG activity was collected from all channels (additional muscle activity during the trial examination) and from all grade trials (0-5). Only the nRMS value of the key muscle at the given grade (e.g., Bi = 5) was selected to make comparisons with ASIA motor scores.

EMG analysis of nRMS values and ASIA motor scores of the 12 key muscles revealed no significant differences between muscle assessments of the different sides of the body. Comparisons between muscle activities revealed a significantly higher fold increase from baseline in the Bi muscle compared to FDS, TA and SOL (muscle effect, $F_{5, 25}=4.27$, $p<0.05$) (Table 4.3). Furthermore, ASIA assessment analysis revealed that the highest increase from baseline corresponded to the highest motor score compared to FDS, TA and SOL muscle (muscle effect, $F_{5, 25}=12.36$, $p<0.05$) (also see Table 4.7).

Table 4.7. Averaged nRMS values compared to mean ASIA motor scores.

Muscle/ myotome	*nRMS (fold increase from baseline)*	*ASIA motor score*
Bi (C5)	189.78 ± 196.64 *	5 *
ECR (C6)	111.76 ± 50.76	4.67 ± 0.49 **
Tri (C7)	46.54 ± 51	3.42 ± 1.73 **
FDS (C8)	17.83 ± 30.63	2.67 ± 2.46
SOL (S1)	4.41 ± 3.17	1 ± 1.48
TA (L4)	2.07 ± 6.61	0.83 ± 1.53

*Fold increase from baseline was significantly higher from Bi muscle across all participants and corresponded to the highest motor score. No significant differences were obtained between grades or EMG activity from Bi, ECR and Tri. Also, as with MEP amplitude sizes, nRMS values paralleled motor scores. As expected, due to motor level of C6 and T1, all participants received a motor score of 5 in Bi muscle (Bi muscle corresponds to C5 myotome). Bi motor score was higher than FDS, TA and SOL muscles (*). ECR and Tri motor scores were significantly higher than TA and SOL (**).

4.5 Correlation between nRMS of key muscles and ASIA motor scores

Comparisons between nRMS values and ASIA motor scores revealed a positive significant correlation of $\varphi = 0.85$ ($p<0.05$). Although not as much variability was observed in nRMs values as with MEPs, no individual key muscle and corresponding motor score comparisons were made due to small sample size, large number of zeros and lack of motor score range within a muscle (Figure 4.4). Still, comparisons between nRMS values and ASIA motor grades suggest that EMG techniques are reasonable when measuring muscle activity during clinical examinations. What is more, EMG measurements also revealed differences between nRMS values of the same muscles that received the same grade during the clinical diagnosis (Figure 4.4).

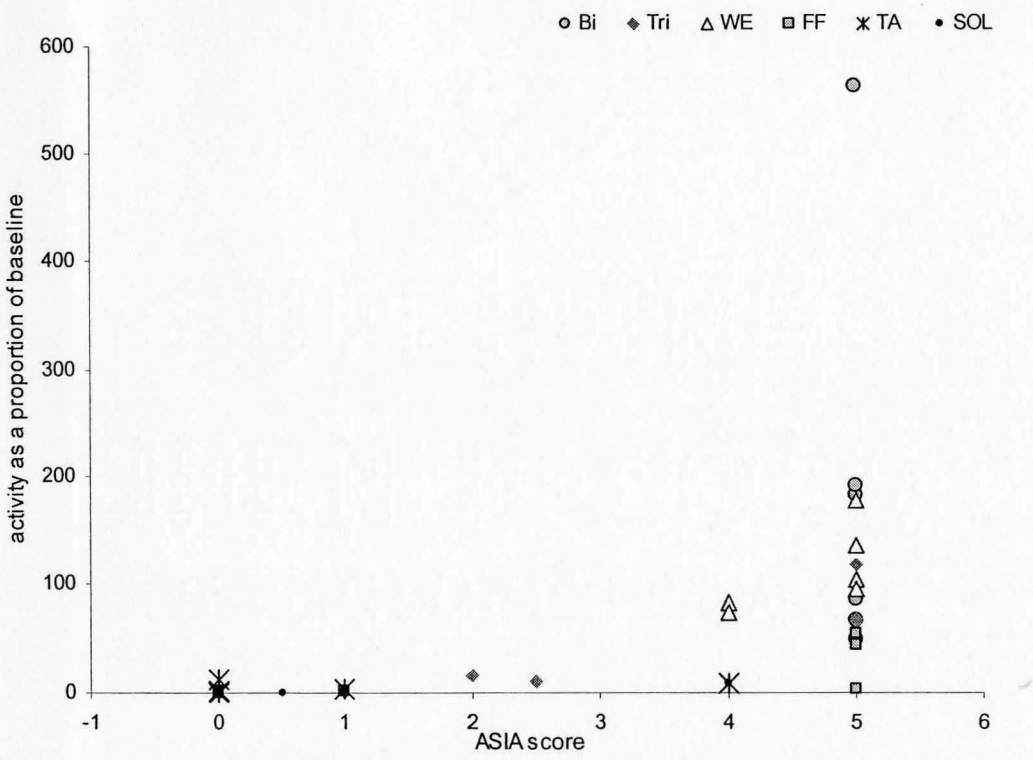

Figure 4.4. EMG activity (fold increase from baseline) of key muscles collapsed across side at their corresponding motor grade. Data shows a more congruent match between EMG and motor scores at zero. However, S2, who received a motor score of zero in strength in TA muscle, had a very similar nRMS value compared to S6, who received a motor score of 4 in the same muscle (fold increase from baseline of 11.62 ± 11.7 compared to 9.37 ± 8.5 respectively). Similarly, S1 received a motor grade in TAR of 1 with an nRMS value of 7.53, while S6 received a motor grade of 4 in the same muscle with an nRMS value of 3.39. FDS muscles of S6 and S5 were graded 5, however nRMS values were not similar (fold increase from baseline of 4.16 ± 0.87 and 43.41 ± 3.28 respectively).

4.5.1 Additional muscle analysis during clinical examinations

EMG activity was recorded from the key muscle and from additional muscles. Additional muscle nRMS values from all participants were analyzed and compared to baseline activity using a repeated measures ANOVA during clinical examinations of the 6 key muscles (right and left Bi, Tri, ECR, FDS, TA, and SOL). The EMG activity used for this analysis also consisted of the nRMS values (of the additional muscles in this case) at the given grade of the key muscle tested.

During Bi examination, activity was recorded from the antagonist (Tri), FDS and ECR muscles. Only the averaged nRMS values from FDS (32.94 ± 32.33 fold increase from baseline) and ECR (30.56 ± 24.59) muscles were different from baseline ($F_{3,33}$= 8.31, $p<0.05$), suggesting no muscle activity from antagonist (Tri). All participants received a muscle grade of 5 in Bi muscle. Consequently, all participants exhibited significant muscle activity in FDS muscle during this test.

No significant antagonist (Bi) or FDS activity was recorded during Tri assessments. During this test, some ECR muscle activity (18.49 ± 13.93 fold increase; $F_{3,33}$= 6.85, $p<0.05$) was recorded. The average motor grade for Tri was 3.4 ± 1.8 where 3 participants (S2, S5 and S6) exhibited normal function (motor score of 5). ECR activity during Tri examination was observed in participants (S1, S3 and S4) who exhibited some weakness at that level (C7, Tri). From these participants, ECR muscle activation was mostly noted in S1 (ECR 19.93 ± 0.006 fold increase compared to Tri = 10.78 ± 13.27 fold increase) and S4 (ECR = 20.15 ± 26.8 and Tri = 0.78 ± 0.002).

Additional muscle activity analysis, when testing the ECR key muscle, revealed significant differences ($F_{3,33}$= 6.27, $p<0.05$) from baseline in the Bi muscles (9.32 ± 9.75 fold increase from baseline) and FDS (8.25 ± 5.75). The mean ECR motor score was 4.7 ± 0.52, suggesting that EMG activity was recorded when performing wrist extension against some and full resistance which may explain additional muscle activity (although not comparable to that of the key muscle tested, ECR = 111.76 ± 50.76 fold increase from baseline).

During FDS muscle testing, activity from the ECR muscle was notable (24.2 ± 24.49 fold increase from baseline; $F_{3,33}$= 8.46, $p<0.05$) in participants S1 (ECR nRMS = 47.95 ± 37.87), S2 (21.35 ± 16.53), S5 (23.73 ± 25.46), and S6 (47.68 ± 7.71). Of these participants, only S1 had a low score of FDS (motor grade of 1), while the other

participants had normal function (motor score of 5, mean motor score for FDS muscle was 2.7 ± 2.58). The remaining participants S3 and S4 did not show any EMG activity of the FDS key muscle or ECR during FDS testing and both were the only participants to receive a motor score of zero in FDS muscle.

FDS muscle activity was present in almost all upper limb key muscle examinations. S1, S3 and S4 FDS motor scores were low (1, zero, and zero respectively) and the EMG activity recorded from that key muscle test was in accordance with those low muscle grades. However, when testing for other key muscles, activity from the FDS muscle was higher than that obtained when FDS was tested as a key muscle (Table 4.8).

Table 4.8. FDS activity (nRMS fold increase from baseline) during FDS key muscle examination and as additional muscle activity during ECR, Tri and Bi muscle examinations.

subject	*FDS nRMS*	*ASIA score*	*FDS during ECR*	*FDS during Tri*	***FDS during Bi***
S1	**1.98** ± 0.27	**1**	**5.85** ± 2.39	**9.3** ± 12.64	**36.9** ± 14.32*
S2	55.36 ± 64.62	5	8.76 ± 8.19	31.81 ± 41.98	45.46 ± 51.22
S3	**1.94** ± 0.4	**0**	**11.11** ± 0.54	**3.29** ± 1.32	**57.48** ± 71.54*
S4	**0.15** ± 0.18	**0**	**2.99** ± 1.9	**0.65** ± 0.89	**19.64** ± 2.81*
S5	4.15 ± 0.87	5	11.38 ± 12.71	1.87 ± 0.45	5.83 ± 1.82
S6	43.4 ± 3.29	5	9.45 ± 3.75	7.65 ± 0.83	32.32 ± 12.45

The table shows FDS nRMS values and their corresponding motor scores during FDS assessments. FDS activity, from S1, S3 and S4 (who had low motor scores), was higher in ECR, Tri and Bi key muscle assessments (*). The remaining participants also had high nRMS values during the Bi test, however, nRMS values are similar to those of FDS muscle during FDS examination and their muscle strength was considered normal.

During TA key muscle examination, SOL and GA muscle activity were collected. Additional muscle activity analysis revealed some muscle activity from SOL and GA during TA assessments (1.71 ± 1.64 and 1.5 ± 1.56 respectively, $F_{2,22}$= 8.89, $p<0.05$). This antagonist activity was mostly seen in participants S1, S2 and S6 and accompanied agonist activity (TA muscle) during TA key muscle examination (Table 4.9). Participants with no TA muscle activity did not exhibit antagonist activation (Table 4.9). In this

analysis S2 exhibited some TA muscle activity but received a motor score of zero in TA key muscle test. This TA activity from S2 was also present during SOL key muscle assessment. Furthermore, TA activity, during TA key muscle assessment increased throughout the grade trials (0-5) (participant S2 TA L nRMS values increased to 112.36 fold increase from baseline at grade trial 5).

Table 4.9. TA and antagonist activity (nRMS fold increase from baseline) during TA muscle examination and SOL, and antagonist activity (nRMS fold increase from baseline) during SOL muscle testing.

subjects	*TA Key muscle*	*ASIA score (TA)*	*SOL during TA*	*SOL Key muscle*	*ASIA score (SOL)*	*TA during SOL*
S1	4.06 ± 4.9	1	**3.35 ± 0.25 +**	**0.65 ± 0.69 +**	0.5	2.83 ± 2.71
S2	**11.62 ±11.74***	0	3.79 ± 2	2.29 ± 1.81	1	**17.72 ± 8.87***
S3	0.10 ± 0.14	0	0.56 ± 0.51	0.58 ± 0.7	0.5	0.04 ± 0.06
S4	0.29 ± 0.03	0	0.29 ± 0.02	0.37 ± 0.01	0	0.15 ± 0.06
S5	1.03 ± 0.57	0	0.32 ± 0.35	0.46 ± 0.09	0	0.88 ± 0.49
S6	9.37 ± 8.47	4	1.93 ± 0.65	8.07 ± 3.84	4	0.95 ± 0.61

SOL activity during TA assessments was present in participants with some TA activity. S2 exhibited activity of TA in both TA and SOL muscle tests and was given a motor score of zero (*). S1 exhibited higher SOL muscle activity during TA muscle test than during assessment of SOL as a key muscle (+).

4.5.2 nRMS values and their corresponding motor scores

When comparing nRMS values by grade, analysis showed significant differences between muscle EMG activity graded 5 and values corresponding to a motor score of zero ($F_{5,66}$= 5.45, $p< 0.05$) (Table 4.10). No significant differences were seen between other grades (4 approaching significance, no significant differences between grades 3, 2, 1 and zero).

Table 4.10. Averaged nRMS values across ASIA motor scores.

Assessments	*ASIA score*	*Mean nRMS (Fold increase from baseline)*
32	5	125.41 ± 135.38 *
8	4	43.80 ± 49.58
1	3	20.15
3	2	10.83 ± 8.55
10	1	1.95 ± 2.19
18	0	1.84 ± 4.6

Comparisons between nRMS values at the different motor scores revealed differences between grades 5 and 0 ($p<0.05$, unequal N HSD post hoc test).

4.6 Voluntary vs. stimulated muscle activation

There was a significant correlation between nRMS values and MEPs of the 4 key muscles (right and left ECR, FDS, TA and SOL) under all conditions (at threshold r = 0.74, at rest r = 0.54, and at 20% of MVC r = 0.52, $p<0.05$). The correlation was strongest at th condition and around low MEP amplitudes in muscles that presented little or no activity (nRMS and no MEPs). When attempting muscle contraction and the relationship between these two variables was poor and most evident as MEPs and nRMS values increased (Figure 4.5).

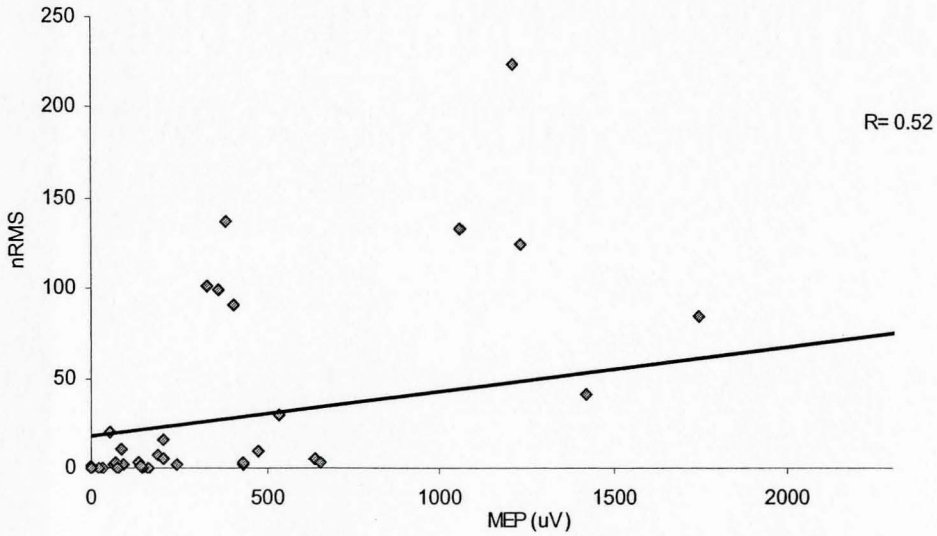

Figure 4.5. Correlation between MEPs and nRMS values at 20% of MVC condition.

5.0 Discussion

Since early 1980's, the AIS evaluations have served as the primary determinant of function in individuals with spinal cord injury. Although these clinical assessment techniques have proven extremely useful in providing a general indication of motor function, issues of inter-assessor reliability as well as a marked lack of sensitivity in isolating specific muscle function have limited their overall effectiveness. Therefore, in this study electrophysiological recordings were used to examine whether alternative assessment tools would provide a greater degree of information on preserved pathways as well providing insight into the relationship between corticospinal integrity (MEPs) and motor function (motor scores); and whether these measurements, if obtained during standard clinical examinations (sEMG), would provide a more sensitive method for quantifying motor function in individuals with incomplete spinal cord injury.

It is important to acknowledge that although the actual pathways investigated through TMS technique remain unknown, previous research has suggested that TMS mainly activates fast conducting pathways including the corticospinal tracts (Nollet et al., 2001).

5.1 Appearance of MEPs and the effects of facilitation techniques

As expected, and in accordance with previous studies, increased MEP amplitudes and shorter latencies were associated with the implementation of facilitation techniques and suprathreshold stimulating intensities (see Boundurant & Highighi, 1997; Hayes et al., 1991; Kobayashi & Pascual-Leone, 2003; Weber & Eisen, 2002; Nollet et al., 2003). Presumably, facilitation techniques such as voluntary muscle contraction may increase the number and size of the descending volleys evoked by TMS, recruiting larger and faster spinal motor neurons than would typically be recruited with the muscle at rest (Nollet et al., 2003). In this study, apart from target muscle contraction or when simply thinking about a movement, participants always had visual feedback during TMS trials which can also contribute to the facilitation of MEP responses (Hayes et al., 1991; McKay, Lee, Lim, Holmes & Sherwood, 2005). In addition, background EMG provided information of spasticity and the state of muscle contraction or relaxation, helping the participants to relax their key muscle when necessary. The largest amplitude together with shortest

latency was obtained when participants attempted muscle contraction (i.e., 20% of MVC condition). Also, the probability of MEP appearance was increased when facilitating than when the target muscle remained relaxed during stimulation (i.e., rest condition) (Hayes et al., 1991). MEPs were obtained in 75% of the 48 muscles assessed (4 right and 4 left muscles X 6 participants) at 20% of MVC condition, followed by about 71% at threshold and 63% at rest conditions. MEPs at the threshold condition had similar latencies compared to the 20% of MVC condition and were present in more muscles (4) than in the "rest" condition. This was possibly due to the implementation of facilitating techniques such as thinking about contracting the target muscle (e.g., wrist extension, dorsiflexion, etc.) or trying to slightly activate the agonist (only force necessary to overcome gravity). These neurological reinforcement techniques were necessary in muscles that appeared to have little or no motor function and were clinically tested as having severe or total motor paralysis (i.e., motor score of zero or 1).

The increase of stimulus intensity from threshold (115%) without combining muscle contraction (i.e., rest condition) did not make a difference between the overall MEP amplitudes at threshold and rest (no significant difference), revealed longer latencies, and did not increase the probability of MEP appearance in lower limb muscles. However, an overall increase in MEP amplitude was observed from the threshold to "rest" condition and subsequently at 20% of MVC where amplitudes were the highest. This was especially true in upper limb muscles. Furthermore, MEPs of FDS muscle in all participants were elicited under all conditions despite the motor score received during clinical examination (zero, 1 or 5). This trend was only observed in lower limb muscles of S6, who exhibited motor function in TA and SOL (motor scores of 4), and in S2 SOL muscle (motor score of 1). These muscles exhibited MEPs throughout the conditions and their size increased accordingly. Some MEPs that did appear at the threshold condition (TA of S2; and TA and SOL of S1) failed to be elicited at rest but reappeared when muscle contraction was attempted. These failed responses at rest were of low amplitude (42 – 58 μV peak to peak) at threshold compared to those MEPs that appeared with muscle contraction (85-104 μV peak to peak). This suggests that increasing the stimulus intensity (115% of th) has a greater impact on upper limb MEP amplitude than in lower limb responses. The difference may be due to the deeper location of lower limbs in motor cortex compared to the more superficial map of upper limb musculature (Hayes et

al., 1991). Therefore, the deeper areas may require a greater stimulation increase to evoke the same effect. It is also possible that simple facilitation techniques could have given a false threshold and therefore the increase of stimulus intensity was not sufficient to evoke a response in resting muscle. In addition, the fact that these lower limb muscles seemed to have little to no motor function suggests that in these cases, neurological reinforcement is the only technique that can evoke a muscle response when activating descending motor tracts.

The loss of MEP responses in relaxed muscle was also observed by Wolfe, Hayes, Potter and Delaney (1996). In that study, participants with some preserved motor function (AIS C) exhibited small amplitude and long latency MEPs only when the target muscle was contracted (Wolfe et al., 1996). However in this study, MEPs were obtained in two of three participants (S3 and S4) with motor complete paralysis (AIS grade B). These two participants had cervical injuries (C5) unlike S5, also AIS B, who had a thoracic injury and thus normal function in upper limbs. S3 and S4 exhibited FDS muscle responses at threshold, small MEPs at rest and larger MEPs when attempting to contract. Only one of these AIS grade B participants (S3) exhibited small, long latency MEPs in lower limb muscles when facilitating. According to clinical examinations, this participant had no detectable motor function below C7, but did exhibit remote muscle contraction of the right SOL muscle (motor score of 1) that could have facilitated small responses in right lower limb TA and SOL muscles.

Antagonist activity was collected during key muscle stimulation to observe facilitation and inhibition effects on agonist muscle (Hayes et al., 1991) and to improve coil location and orientation based on activation of the specific area in motor cortex corresponding to distal lower limb muscles (SOL and TA) or forearm muscles (ECR, FDS and their corresponding antagonists). During S3 right TA stimulation, low background EMG antagonist (SOL) muscle activity was observed, however MEPs from the antagonist were not clearly identifiable. Antagonist activation during target muscle cortical stimulation has been previously reported (see Hayes et al., 1991; and Thomas & Gorassini, 2005) and was also seen in participants with greater motor function in both upper and lower limb muscles (S1, S2 and S6). In the study by Hayes et al., (1991) co-contraction and thus simultaneous MEPs from the antagonist occurred despite attempts from participants to maintain a quiet antagonist during agonist stimulation. Antagonist activation occurred during forearm muscle stimulation (ECR and FCR) and was most

apparent during agonist contraction (Hayes et al., 1991). In the current study, like in Hayes et al. (1991), MEPs from antagonists were also seen in upper limb muscles during FDS stimulation, where antagonist MEPs were not significantly different from agonist MEPs; and during ECR stimulation, where MEPs from antagonist were present although MEPs from ECR were significantly larger. Regardless of whether the overall antagonist MEPs were significantly different or comparable from agonist, increases in antagonist MEP amplitude paralleled those of agonist throughout the conditions and in all muscle groups (also see Hayes et al., 1991). Thomas and Gorassini (2005) also observed increased antagonist evoked activity in lower limb muscles that accompanied large MEPs from agonist muscles. Although inhibitory effects, and thus attenuated MEPs, may be attributed to antagonist activation (Hayes et al., 1991), they may also increase overall cortical excitability of the motor neuron pool associated with the area of the target muscle (Thomas & Gorassini, 2005). Therefore, S3 contraction of SOL could have also increased cortical and spinal excitability of the motor neuron pool associated with distal lower limb muscles, thus facilitating TA muscle activation. In addition, stimulating coils are not focal enough (Weber & Eisen, 2002) to activate only the site for the agonist muscle and high intensity stimuli may activate otherwise silent muscles.

There is extensive evidence suggesting evoked potentials following occurring as a result of cortical magnetic stimulation is only present in individuals with motor incomplete injuries that have preserved corticospinal innervation to yield volitional motor function (Boundurant & Haghighi, 1997; Clarke et al., 1994; Curt et al., 1998). However, evidence to the contrary, such as that obtained in this study, has also been previously reported by others (e.g., Dimitrijevic et al., 1988; and Hayes et al., 1991). Facilitated MEPs exhibited by motor complete participants (AIS grade B) may suggest the existence of preserved descending tracts that are able to activate the corresponding muscle (Wolfe et al., 1996). Although, impulse transmission through descending motor tracts does not always imply useful function (Wolfe et al., 1996), it may provide information of neurological impairment as a relationship between corticospinal tract integrity and quality of voluntary motor function through MEP appearance and wave characteristics.

5.2 Comparisons between MEPs and motor scores

It has been suggested that the latency, shape and amplitude of an MEP reflect the integrity of the corticospinal tract and that an abnormal MEP may indicate damage at any level along the descending pathway (Kobayashi & Pascual-Leone, 2003; Nollet et al., 2003). Small amplitudes, high motor thresholds, polyphasic and dispersed waveforms, as well as long latencies are MEP characteristics associated with SCI (Alexeeva et al., 1998; Hayes et al., 1991; Kobayashi & Pascual-Leone., 2003; Weber & Eisen, 2002). In this study, cortical magnetic stimulation of upper and lower limb musculature revealed MEPs with such characteristics.

Latencies from upper and lower limbs were similar to those previously observed in the SCI population (Bondurant and Haghighi, 1997; Clarke et al., 1994; Curt et al., 1998; Hayes et al., 1991; Thomas and Gorassini, 2005). Small differences may be attributed to the severity of the injuries of the participants in this study (e.g., longer latencies due to more AIS grade B participants than in previous studies). The delayed effects in muscle responses may also be related to spinal excitability. The TMS evoked response is suggested to slow down at the injury site where the number of innervated tracts is decreased and axonal distribution ranges from normal to slow conducting fibers due to demyelination (Kobayashi & Pascual-Leone 2003; Nollet et al., 2003; Wolfe et al., 1996). MEP amplitude may be influenced by the number and firing rate of motor neurons along the descending motor pathway (cortical, spinal, peripheral nerve, neuromuscular junction, and muscle) (Kobayashi & Pascual-Leone, 2003).

Procedures such as peripheral nerve stimulation additional to TMS are not uncommon since TMS alone cannot specify whether abnormal responses reflect upper or lower motor neuron damage (Carroll, Riek & Carson, 2001; Curt & Dietz, 1999; Kobayashi & Pascual-Leone, 2003; Thomas & Gorassini, 2005, Weber & Eisen, 2002). Generally, TMS is suggested as a method to assess upper central motor pathways in addition to electrophysiological measurements that are performed to determine lower motor neuron involvement (Nollet et al., 2003). TMS can also be used to stimulate peripheral nerves, however current coil designs fail to deliver a controlled focal stimulus and the technique presents difficulty in eliciting a maximum response unlike conventional electrical stimulation (Weber & Eisen, 2002). As well, other examinations such as spinal root stimulation can be achieved through TMS by positioning the coil over the

lumbosacral or cervical spine. The latency of the response to spinal root stimulation is then subtracted from the onset latency of the MEP from cortical stimulation. This is called the central motor conduction time (CMCT) and long latencies are also related to central motor deficits (Kobayashi & Pascual-Leone, 2003; Weber & Eisen, 2002). However, electrical stimulation of peripheral nerve (M-waves and F-waves) is preferred over TMS because it can better estimate the conduction time from the spinal motor neuron, not the spinal root like with TMS (Weber & Eisen, 2002). In this study, to determine that absence of MEPs was a result of corticospinal characteristics of each participant, percutaneous electrical stimulation was preferred over TMS peripheral stimulation, and delivered to the corresponding peripheral nerve of each target muscle (with the exception of ECR). M-waves revealed possible peripheral damage in participant S4 SOL and TA, as well as small responses of the FDS muscles. This participant had a C5 injury and reported no lower limb reflexes or muscle spasms. In addition, some muscle weakness was observed in the FDS muscle and small muscle mass was also noted in the TA and SOL. Furthermore, although no MEPs were obtained in lower limbs, FDS MEPs were present in all conditions.

In addition to the differences found in the three conditions, amplitude analysis revealed a muscle effect. Overall, ECR cortical stimulation revealed the largest amplitude ($p<0.05$) followed by FDS muscle ($p<0.05$). TA exhibited the lowest overall amplitude not only due to the lack of MEP appearance, but also due to small amplitude responses when MEPs were present. It is interesting to note that not only did ECR muscle exhibit the largest MEP, but also received the highest mean motor score (individual scores ranged from 4 to 5). High overall motor score from ECR muscle was not surprising due to participants' motor level. Some participants had a low injury level (thoracic) and thus, normal ECR strength (motor score of 5). The remaining participants had a C6 motor level, although some participants had normal function and some exhibited some damage at that segmental level (received an ECR motor sore of 4). The AIS considers a muscle with a motor grade of at least 3 as fully innervated by at least one segment. For instance if C6 has a motor score of 3 and the segment above C5 is graded as 5 and the segment C7 below is less than normal (≥ 3), then the motor level corresponds to C6, the spinal level innervating the muscle with the motor score of 3 (motor level = most caudal level with

normal function). This can cause some confusion when determining motor level and discrepancies if participants are to be selected by their motor level.

In general, MEP amplitudes seemed to parallel motor function, as assessed by clinical examinations, in that, the largest MEPs corresponded to the muscle with higher motor function (i.e., ECR with significantly higher scores) and the smallest MEPs corresponded to the muscle with severe or absent motor function (i.e., TA muscle). Correlations suggest that MEPs may reflect preserved functional corticospinal connectivity (Thomas & Gorassini, 2005) that translates to useful or voluntary motor function. In addition to finding these functional pathways, TMS detected spared descending tracts that, for some reason, cannot be accessed by the individual to produce volitional movement.

Although one must exercise a certain degree of caution when intimating that the existence of spared pathways suggests a greater potential for functional recovery, it can be argued that such a possibility exists. A recent study by Thomas and Gorassini (2005), examining the effects of training chronic incomplete SCI individuals on corticospinal tract function, showed significant training (BWSTT) induced changes in MEPs that paralleled muscle strength scores and recovery of locomotor function (assessed using the WISCI scale) (Thomas & Gorassini, 2005). They concluded that the changes in MEPs after training where central in origin and due to a generalized increase in connectivity of preserved corticospinal pathways (Thomas & Gorassini, 2005). The significance of these findings is that MEPs were able to assess corticospinal integrity and correlate to the degree of motor function (ASIA and WISCI). Furthermore, function of spared pathways could be enhanced even in individuals with chronic injuries (Thomas and Gorassini, 2005). In addition to increases in agonist and overall locomotor function, they also observed enhanced muscle responses from antagonist muscle which had been previously electrically silent (i.e., no MEPs were evoked and no background EMG was observed). This constitutes further evidence to suggest that spared pathways have the potential for recovery. In the current study, correlations from key muscle MEPs with their corresponding motor score strongly supported Thomas and Gorassini's findings.

Positive significant correlation between MEPs and motor scores support the hypothesis that corticospinal integrity, as described by TMS, reflects motor function as assessed by standard clinical examinations. Other studies have examined the relationship between motor function and corticospinal integrity through MEP measurements. For

example, Clarke and colleagues (1994) examined MEPs from individuals with very acute (15 days post-injury) incomplete and complete SCI individuals. Improvements according to clinical examinations (total motor scores) were compared 6 months after with simultaneous MEP measurements (biceps brachii, abductor pollicis brevis and TA) (Clarke et al., 1994). They showed that MEPs (CMCT and amplitude) paralleled motor function improvements. In addition, the appearance of MEPs in the incomplete population, and later recovery, indicated the prognostic value of MEPs in this population (Clarke et al., 1994). In participants with complete injuries, individuals with quadriplegia (2/4) exhibited MEPs after 6 months together with some recovery of muscle strength and this recovery preceded a favorable outcome (Clarke et al., 1994). Another study by Curt et al., (1998) examined the significance of MEPs (amplitude and latencies) and ASIA total, upper limb and lower limb motor scores in the outcome of hand function and ambulatory capacity. MEPs were not only related to neurological deficit and motor function, but were also significantly correlated to lower and upper limb function (hand function and ambulatory capacity) in the acute and chronic SCI participants (Curt et al., 1998). Curt and colleagues (1998) concluded that MEPs may be as sensitive as ASIA scores in describing motor functional deficit in the SCI population. However, when follow up tests were performed (6 months after) in the acute individuals, motor function increased but there was no significant differences between pre and post MEPs. Curt et al., (1998) suggested that improvements in motor function may not be related to increased corticospinal tract connectivity. Smith et al., (2000) also observed changes in motor scores and no significant differences in MEPs of the thenar muscle in acute individuals. MEPs were obtained using a circular coil which is considered to elicit a larger magnetic field that is non focal (Weber & Eisen, 2002). In addition, thenar muscles are not directly tested by the AIS. Smith and colleagues (2000) suggested that no changes in MEPs over time, and therefore no significant correlations between MEPs and motor function, occurred probably because changes in corticospinal tracts had already happened and functional changes are delayed (Smith et al., 2000). These findings imply that in the acute population, the timing for implementing electrophysiological techniques for assessing neurological deficit and spontaneous recovery requires further study. In addition, comparisons between only one muscle (in the case of Smith et al., 2000) and the total motor score from 10 muscles (bilaterally) may not be appropriate and may limit results.

It is suggested that larger MEPs are associated with a greater corticospinal connectivity and nerve cell firing rate (Nollet et al., 2003; Thomas & Gorassini, 2005). However, several studies have indicated that MEP amplitude may be of limited clinical value due to inter-trial and intra-individual differences owing to factors such as stimulation intensity and coil positioning (Nollet et al., 2003; Weber & Eisen, 2002). However, TMS technique research has shown that increases in intensity from threshold and facilitation techniques reduce inter-trial variability (Brasil-Neto et al., 1992; Kiers et al., 1993) as seen in the reliable and repeatable MEPs across all participants. Also, the use of a large stimulating coil, such as the double cone coil used to stimulate lower limb muscles, has been shown to elicit MEPs that are not sensitive to small changes in coil position (Thomas & Gorassini, 2005). A study by Carroll et al., (2001) examined the day to day variability of the input–output properties of the corticospinal pathways using TMS, and concluded that this relationship can be measured reliably through MEPs. In this study, comparisons between MEPs and motor scores also revealed that amplitude can be a descriptive factor of descending tract damage (also see Thomas & Gorassini, 2005).

5.3 Summary and clinical applications: TMS as an assessment tool

In this study, detection of MEPs in upper and lower limbs was enhanced by facilitation methods suggested to elevate spinal and cortical motor neuron excitability and thus activate a greater number of descending fibers. Increases in stimulus intensity alone without the involvement of the patient were not as effective, therefore it is recommended that when patients are uncooperative, more aggressive facilitation methods need to be used such as paired- pulse TMS, percutaneous or peripheral nerve stimulation. The implementation of these techniques, as well as conventional facilitation techniques help reduce MEP variability, increase probability of appearance of evoked responses and thus avoid misinterpretations of corticospinal function.

As MEP amplitude is thought to reflect the sum of upper and lower motor neuron activity, changes in peripheral nerve (Weber & Eisen, 2002), neuromuscular junction and muscle (Kobayashi & Pascual-Leone, 2003) may also have an effect on MEP characteristics. TMS together with other electrophysiological tools and assessment techniques can further describe and localize damage at any level of the descending motor

tracts and changes occurring after SCI. AIS information of patients injury level, total motor score and completeness of injury is limited and does not provide a complete picture. New interventions targeting motor function should be aware of the location, characteristics of the injury, and consequently the changes occurring in the CNS occurring after SCI. TMS is a more direct measurement of a pathway or segment innervating a muscle and may provide objective pre and post measurements of individual segments in iSCI patients that will fully describe the variety of neurological damage patterns characteristic of this population. AIS assessments are more indirect in that the key muscle might be the "prime mover" for the assessment, but the movement is affected by multiple muscles and multiple pathways related to sensory, motor and perceptual function. Therefore MEPs are of clinical value since they provide superior localized assessments of neurological motor function and sensitivity to different damage patterns, unlike the AIS. MEPs were obtained in participants with motor incomplete and motor complete chronic injuries. The incomplete spinal cord injured participants (B, C and D) exhibited different patterns of corticospinal damage and results suggest that MEPs were sensitive enough to display their individuality.

In general, and consistent with previous research, MEPs were obtained wherever motor function was observed during AIS assessments. A very significant finding from this study was that TMS revealed spared pathways that were not detected through clinical examinations. These pathways require further consideration in SCI diagnosis and new interventions targeting recovery of neuron connectivity. It has been previously suggested that the existence of MEPs is a positive indicator of motor function recovery and thus, the potential for recovery and characteristics of these pathways needs to be examined. Overall, this study has demonstrated that TMS has the potential of assessing motor function in incomplete spinal cord injured individuals and may also provide objective markers for assessing neurological function as well as quantify motor function related to corticospinal integrity.

5.4 nRMS and motor scores

The implementation of sEMG techniques for motor control analysis in SCI population has been previously examined (Lee et al., 2004; Sherwood, McKay and Dimitrijevic, 1996). Recent studies have used sEMG as objective measurements of

voluntary function and recovery of function in the motor incomplete spinal cord injured population (see Lee et al., 2004; Lim et al., 2005; and McKay et al., 2005). In these studies, multi-channel sEMG techniques were used to develop a measurement of voluntary activity (voluntary response index or VRI) of several muscles (including some of the key muscles defined by ASIA) and the simultaneous activation of other muscles involved in defined voluntary movements under strictly controlled conditions (Lee et al., 2004). The VRI not only provided information on total muscle activity but also provided qualitative analysis of EMG patterns and seemed to be sensitive enough to detect functional improvements after BWSTT (Lee et al., 2004). Lim et al., (2005) examined the relationship between their EMG measurements (VRI) and the AIS and individual motor scores in lower limb muscles. Significant correlations revealed that sEMG techniques can be sensitive to injury severity as measured by the AIS (Lim et al., 2005).

In the current study, EMG activity was measured during standard voluntary movements performed throughout ASIA assessments thus no separate voluntary movement trials were used. Therefore, multi-channel sEMG was not only employed to measure motor function but also to assess the sensitivity and accuracy of the ASIA motor grading technique.

Overall, key muscle nRMS values were significantly correlated to ASIA motor scores. As with MEPs, mean nRMS values from key muscles paralleled motor scores. Correlation between nRMS and motor grades support previous findings and suggest that sEMG techniques can be effective in adding a quantitative measurement of muscle activty in the AIS clinical examination. The range of nRMS values of the same muscle within a motor score (e.g., Bi) suggest variability of the assessments, but it may also explain the variability within individuals with incomplete SCI (i.e., different nRMS at different grades). As with MEPs, sEMG is also a more direct measurement than AIS of spinal segment integrity, however and unlike MEPs, sEMG recordings may explain voluntary muscle recruitment. It is suggested that sEMG measurements can provide superior information of key muscle strength, not only through direct measurements of volitional key muscle recruitment, but also by recording additional muscle activity involved in an AIS assessment. The AIS measures key muscle strength, but it does not consider synergistic recruitment of other musculature that may produce assessments that do not fully describe a patients true motor function and therefore may have an effect on treatment prescription and the rehabilitation goals.

5.5 sEMG revealed inconsistencies during clinical assessments

In general and as previously described, MEP amplitudes correlated with motor scores. However, some discrepancies between MEPs and motor scores were observed. For instance, S4 (AIS grade B, C6) exhibited very large MEPs in ECR muscle, especially when facilitating (muscle x condition interaction). S4 MEPs were the largest at rest and when contracting; however, muscle strength was scored as 4. If large and fast MEPs are associated with high levels of motor function and are suggested to reflect a greater amount of corticospinal connectivity, then S4 ECR assessed as having less than normal muscle strength (ECR muscle score of 4) represents a discrepancy. It is difficult to say whether changes in axon connectivity (i.e., cortical and spinal plasticity which can elevate excitability and the number of descending volleys, and/or nerve sprouting which can send all activity to a particular muscle) occurring after trauma may account for ECR activity (Côté & Gossard, 2004; Perez, Lungholt, Nyborg & Nielsen, 2004). In this case, activity may be high but the quality of the movement may not be normal and therefore give the impression that its function is less than 5 (Schouenborg, 2004). However, variability within the AIS and resulting motor scores has been previously reported (Cohen et al., 1998) and may account for discrepancies between MEPs and motor scores.

During the ECR muscle test in S4 (motor score of 4), sEMG recordings revealed that muscle activity kept increasing from grade 4 to grade 5. Normalized RMS values from right and left ECR at grade trial 4 corresponded to 47.41 and 101.2 fold increase from baseline; however, when assessing right and left ECR for grade trial 5, nRMS values increased another 22.62 and 13.21 fold, respectively. This suggests that the subjective assessment may have resulted in an inaccurate score although it is difficult to say whether the increases in nRMS values from grade trial 4 to 5 are significant enough to warrant a higher score. Another discrepancy between motor scores and EMG activity recorded during grade trials was observed in the TA assessments of S2. During clinical examination, this participant exhibited no motor function of the dorsiflexors (TA score of zero), but exhibited some EMG activity. While the right TA muscle activity remained constant from baseline throughout grade trials (19.91- 18.57, from grades 0/1-5), left TA EMG activity increased from grade trial 0/1 (3.3 fold increase from baseline) to grade trial 5 (112.36 fold increase). In addition, activity increased when gravity was eliminated

(170.85 fold increase at grade trial 2). This muscle activity also suggests inaccuracies during clinical examinations. This participant (S2) exhibited some stiffness of the lower limbs due to mild contractures which could have limited range of motion and give the impression that the muscle did not have motor function. Small MEPs were obtained from these dorsiflexor muscles in S2. The appearance of MEPs in this case indicates spared pathways not identified by clinical examinations and thus were assessed as non functional, as previously described. However, evidence of muscle activity (nRMS) may suggest a functional pathway strong enough to elicit muscle contraction.

Statistical analysis of EMG activity from different grade trials was not possible due to a small sample size as well as a small number of muscles or muscle groups with the same grade. However, indications of enhanced muscle activity from the nRMS values seen at the given motor score could be identified in at least one muscle assessment in 4 of 6 participants. In addition to nRMS values increases in S2 TA and S4 ECR, S1 triceps muscle activity was higher at grade trial 5 than at the grade trials (3 fro right and 2 for left TRI) for motor scores given to that specific muscle. Right Tri muscle had a muscle grade of 3 and a nRMS value of 20.2 fold increase from baseline which increased to 72.28 at grade 5, while left Tri muscle exhibited a muscle strength graded 2 and a nRMS value 1.38 that increased to 23.6 at grade trial 5. Also, S1 right TA (motor score of 1) activity increased from grade 1 to grade 5 (7.5 to 22.9 fold increase). The same trend was observed in S3 right triceps (nRMS at grade trial 2 = 18.03 to grade trial 5 = 34.59) and left FDS (1.6 to 10.94) which were assessed as not functional. These findings may indicate that clinical assessments are not sensitive enough to detect increases in activity from grade trial to grade trial, which may also explain the lack of intermediate scores (scores of 2 or 3). The AIS may be sensitive enough to detect no muscle activity and normal muscle activity, but the subjective technique may be limited in determining different muscle strengths (between 2, 3 and 4). This is alarming since a motor score of 3 may determine a patient's neurological level and completeness of injury. It is suggested that sEMG activity recorded during muscle grade trials may help assess the sensitivity and accuracy of current standard clinical examinations. Muscle activity recordings may help avoid misinterpretations of absent muscle strength due to contractures or improper positioning and identify spasticity and the presence of muscle tone, which can give the impression of enhanced muscle strength. In addition, sEMG techniques can provide

superior information regarding motor control issues (Lim et al., 2005) such as compensation and overall muscle recruitment (also discussed in the next section).

5.6 Additional muscle activity during key muscle tests

Multi-channel sEMG recordings revealed additional muscle activity during key muscle assessments that may describe muscle recruitment strategies in iSCI participants. Considering that voluntary movement control is achieved by synergistic muscle activity and coordination of complex mechanical interactions such as joint movement, then it would be difficult to assert that, even for simple movements such as those used for AIS assessments, performing the task only requires the activation of the key muscle during the muscle test. In addition, participants exhibited or attempted full effort during muscle exams where recruitment of other muscles may not be uncommon. For example, Bi muscles had normal motor function (i.e., motor score of 5) and exhibited additional activity from FDS and ECR muscles (comparisons from nRMS values at grade trial 5 or movement against full resistance). However, recruitment of additional musculature may also imply muscle weakness. For instance, S1 and S4 exhibited ECR activity (overall significantly increased activity from baseline of ECR $p<0.05$) during Tri examination and both had low scores of Tri muscles (S1 Tri= 2.5 $\pm$ 0.71; S4 Tri= 1). In addition, S1 displayed higher ECR muscle activity on the weaker side (left Tri motor score = 2) and ECR muscle activity increased across grade trials on both sides, suggesting that in this case, ECR was used as compensation for Tri weakness.

During FDS muscle assessments, EMG activity was not different from baseline in participants S4 and S3, which corresponded with the assessed motor score (both of zero). Also, no significant ECR activity was observed during finger flexion. S1 FDS also exhibited activity that corresponded to the given motor score (nRMS = 1.98 $\pm$ 0.027, motor score of 1). However, FDS muscle activity recorded in other key muscle tests revealed enhanced FDS nRMS values in these participants. Substantial FDS muscle activity from all participants was exhibited during Bi examinations (significantly different from baseline, $p<0.05$). When comparing FDS activity during FDS examination and during Bi examination, not much change was observed in muscle activity from participants who exhibited normal function (S2, S5 and S6 had a motor score of 5 in FDS muscle). However, those participants who did not show function of the FDS muscle

revealed enhanced activity during Bi test (e.g., S1 FDS nRMS during Bi test = 36.9 ± 14.32). This muscle activity suggests that these participants were not able to voluntarily activate their FDS key muscle during FDS examination but were able to unintentionally exhibit more activation when attempting to contract another muscle (Bi) at full effort (for a grade trial of 5). FDS activity may support MEP appearance and thus the existence of a preserved pathway in these participants. This may also imply changes below the injury level that the individual cannot control. It may be possible to train an individual and provide feedback on how to access this spared pathways, since the motor nervous system is not hardwired and can re-learn through stimulation (i.e., plasticity).

This additional activity during Bi testing may also contribute to background activity from other muscles, a well known limitation of sEMG technique. Wrist flexor muscles (i.e., flexor carpi radialis, FCR; and flexor carpi ulnaris, FCU) are superficial muscles unlike FDS, which is located in the intermediate layer of the forearm. It is possible that during full effort of Bi contraction, the surface electrodes picked up signals not only from FDS but from nearby muscles such as wrist flexors.

Multi-channel analysis also revealed additional muscle activity during lower limb assessments. Specifically, antagonist activity during assessments was observed which may have inhibited aginist activity. For example, S2 exhibited activity in TA not only when TA was the key muscle examined and increased from grade trial 0 to 5, as previously mentioned, but was also active during SOL assessments. S2 TA was assessed as not functional while the SOL muscle received a score of 1, despite exhibiting a lower increase from baseline. As described, the incongruent relationship between nRMS and motor score in this case might be a result of muscle contractures and may explain the appearance of MEPs. These findings not only reveal changes in movement patterns after SCI such as antagonist activation, but also provide further evidence of inconsistencies in AIS standard clinical examinations.

5.7 Evoked vs. voluntary muscle activity

A positive significant correlation between nRMS values and MEPs was found. This might be considered a more direct comparison between MEPs and muscle contraction since in both methods; electrodes were placed directly on the key muscles.

The relationship between evoked and voluntary muscle activity was weaker at higher levels of muscle activity. TMS stimulus intensities and thus, MEPs were controlled to obtain a response around a certain amplitude (~ 50 μV peak to peak). In addition, when participants exhibited motor function, muscle contraction was also controlled (20% of MVC) and those participants that did not exhibit motor function were attempting to contract with full effort only to facilitate a small response. In addition to controlled MEPs, TMS alone is not capable of eliciting maximum responses (Nollet et al., 2003). Therefore, nRMS values corresponding to activity during full effort, especially from participants with normal function, were separated from the evoked vs. voluntary response relationship. This was typically observed in ECR muscles that had normal function (and therefore high voluntary muscle activity) but their MEPs were not maximum responses. The TMS technique is limited to stimulus strengths and therefore may not be able to activate all corticospinal neurons responsible for activating a target muscle (McKay et al., 2005) and therefore differences between a muscle that is fully innervated and activated could be observed.

As in McKay et al.'s (2005) study, where MEPs were compared to a key muscle VRI, a relationship between corticospinal integrity and the quality of voluntary motor function, as assessed by the AIS, was found.

5.8 Summary and clinical applications: sEMG during AIS assessments

To explore the potential of electrophysiological recordings to improve SCI diagnosis, sEMG was used to measure voluntary muscle activity during standard clinical evaluations. Muscle activity recorded (nRMS) confirmed some inconsistencies observed between MEP data and the corresponding motor score. Comparisons between nRMS values and motor scores also revealed variability between muscle activity within the same motor score, which may indicate that the AIS assessment may be accurate enough to detect high motor function and no motor function (5 or 0: Bi or TA), but it is not sensitive enough to detect activity within intermediate grades.

In the AIS, the assessment of a key muscle is a simplified way of describing damage of nerve segments (Maynard et al., 1997). It is suggested that the AIS individual muscle assessments describe a total output of muscle activity, joint torque and force

rather than localizing and quantifying contraction of one muscle, like in EMG and MEP techniques. Thus, it is questionable whether the AIS motor scores should be considered a measure of function of a particular pathway. Although the key muscles assessed are prime movers of the simple voluntary tasks required, additional musculature involvement is disregarded but may have an effect on the key muscle (e.g., inhibition effect from antagonist and /or compensation from other muscles involved in the movement), as damage to the spinal cord disrupts normal movement patterns.

Inaccuracies in muscle scores may have an effect on an individual's motor level (e.g., S4 ECR muscles may have had higher motor score and therefore a lower motor level) or on the overall AIS grade (motor complete: A - B or incomplete: C - D), which is dependent on motor function found below the injury level. EMG recordings may be more sensitive to motor patterns and overall muscle activation that, as seen in this study, may be misinterpreted during AIS clinical examinations.

6.0 Limitations of study and persisting issues

Although it is suggested that the facilitation techniques used in this study were sufficient to obtain reliable and reproducible MEPs, factors other than participants' individual differences may account for some MEP variability. It has been suggested that minimal angulation of a figure eight coil may change the characteristics of a response (Weber and Eisen, 2002). In contrast, the double cone coil is said to be less sensitive to coil shifts, but the stimulation in this coil is non focal and thus can activate inhibiting mechanisms or other nearby muscles affecting the characteristics of the observed MEP. Currently, improvements in coil design and positioning are being developed (Nollet et al., 2003). Location of lower limb musculature may have also contributed to variability in that the probability of failing to evoke a response in this area is greater than that in upper limb musculature (Hayes et al., 1991). In addition, participants were not in supine position when stimulating lower limb muscles and would have affected impulse transmission.

Sample size also presents a limitation, especially given the heterogeneity of the incomplete SCI population. Given the different degrees and patterns of damage, it is difficult to match participants into the same category. Currently, the AIS is used for this purpose. However, as previously suggested, this scale might not describe individual differences thereby limiting significant findings. In this study, comparisons between

individual muscle MEPs and their corresponding motor scores were difficult to perform due to the lack of score range within the same muscle across participants. Having a greater number of muscles with varying scores (e.g., ECR with scores ranging from 0 to 5) would better determine the relationship between MEPs and motor function. This was also a limiting factor when attempting individual muscle nRMS comparisons and their corresponding grade. In this case correlations would improve when having more score range on the same muscle (i.e., in this study there was a lack of grades 2 and 3). As well, having more muscles with the same grade would allow for comparisons between recorded muscle activity at different grade trials (e.g., Bi nRMS at grade trial 0 to grade trial 5). However, small sample size and heterogeneity has been a limiting factor in most SCI research which is one reason why better assessment techniques, such as those proposed in this research, are needed.

Apart from the inherent limitations of sEMG techniques (e.g., noise, crosstalk and volume conduction), variability within the clinical assessment techniques was also observed. Inconsistencies in the duration and timing of movements between participants and between grade trials (where maximum bursts at different times and with different durations were observed); a variable range of motion allowed when performing the movement (isotonic or isometric movements); and inconsistent stabilization positions between participants may all have affected nRMS values. In addition, no practice of movement tasks was provided which suggests that participants did not effectively reach a maximum voluntary contraction. For example, a participant may have had more muscle strength than expected and thus full resistance was not provided. This would have allowed the participant to complete full range of motion whereas other, weaker participants could not complete the movement. It is suggested that more controlled and restricted movement tasks would minimize these limitations of sEMG techniques. In addition, more consistent assessments would not only provide more reliable EMG data, but a more accurate clinical diagnosis.

Muscle tone and spasticity are a SCI characteristic that may also affect sEMG recordings during TMS testing and AIS assessments, therefore it is important to take these factors into consideration when analyzing MEPs and muscle activity. As demonstrated in this study, EMG feedback may be an appropriate method of achieving muscle relaxation and minimizing spasticity. Also, during TMS testing, spasticity was

identified from voluntary activity by asking the participant to contract and relax the muscle and determining if muscle activity was voluntary (on and off EMG activity).

Comparisons between EMG data from control groups may be helpful in determining AIS assessment movement patterns and total muscle activity to make comparisons with the SCI population. Also, having a larger sample size would help examine the increases in motor output necessary for jumping from one grade to another, as assessed by AIS. In addition, force and torque measurements could provide more information on AIS assessments and motor function.

A very significant finding in this study was the appearance of MEPs in individuals with motor complete injuries and in muscles that, as assessed by clinical examinations, had no motor function. These findings support the importance of implementing alternative assessment tools to further describe neurological status in the incomplete spinal cord injured population. However, TMS alone cannot describe whether MEP characteristics are due to upper motor neuron damage or lower motor neuron damage or both. For this reason, additional tests are required to assess motor tract damage and thus, TMS becomes a more involved diagnostic method compared to the AIS, which is a simple method used to describe voluntary motor function without the use of instrumentation (Lee et al., 2004).

Another issue arising from MEP findings is whether those preserved axon connections reflect a spared pathway. If a spared pathway is considered as preserved corticospinal connections capable of impulse transmission, then it is important to clarify that this spared pathway does not necessarily mean useful function (Wolfe et al., 1996). However, the potential for this pathway to benefit from intervention has yet to be explored and in this case, all aspects of impulse transmission through descending motor tracts should be explored. For example, the number of motor units activated before and after an intervention should be assessed, as well as cortical and spinal excitability to determine how big and how excitable a pathway needs to be for recovery of corticospinal connectivity and function. This will also support the relationship between MEPs and motor function.

7.0 Conclusion

Previous research has examined the manner in which TMS activates descending motor pathways, analyzed and implemented effective ways of improving impulse transmission to activate all possible neural connections and has addressed the potential of TMS to improve diagnosis, monitor recovery and assess the significance of new treatments in the SCI population. This study has provided additional evidence that facilitating techniques can improve impulse transmission and MEP appearance in the iSCI population. Furthermore, TMS revealed spared pathways that were not identified by standard clinical examinations thereby suggesting that cortical magnetic stimulation may provide superior information regarding a patient's neurological status. The correlation between MEPs and motor scores of key muscles also supports TMS as a diagnostic tool that was also sensitive enough to assess injury severity and describe individual differences often seen in the iSCI population. The implementation of TMS techniques in the assessment of SCI may also provide insights into the relationship between corticospinal integrity (described by MEPs) and the quality of voluntary motor function (described by clinical examination). This relationship may be useful in the development of new interventions that target axon connectivity for the recovery of motor function. Although, some of the mechanisms of TMS need to be further addressed (e.g., pathways involved in MEP modulation, cortical and spinal excitability differentiation, and axon stimulation) before introducing MEP technique into the clinical realm, the need for alternative assessment tools for SCI is evident.

8.0 References

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APPENDIX A

MEDICAL HISTORY QUESTIONNAIRE

VOLUNTEERS PARTICIPATING IN STUDIES INVOLVING TRANSCRANIAL MAGNETIC OR TRANSCUTANEOUS STIMULATION

SURNAME:..... GIVEN NAMES:.....

DATE OF BIRTH:..... SEX:.....

HOME PHONE:..... WORK PHONE:.....

---

1. When was the last time you had a physical examination?
2. If you are allergic to any medications, foods or other substances, please name them.
3. If you have been told that you have any chronic or serious illnesses, please name them.
4. Have you been hospitalized in the past three years? Please give details.
5. During the past twelve months:

Has a physician prescribed any form of medication for you?	Y/N
Has your weight fluctuated by more than a few kilograms?	Y/N
If yes, did you attempt to bring about this weight change through diet and/or exercise?	Y/N
Have you experienced any faintness, light-headedness, blackouts?	Y/N
Have you occasionally had trouble sleeping?	Y/N
Have you had any severe headaches?	Y/N
Have you experienced unusual heartbeats such as skipped beats or palpitations?	Y/N
Have you experienced periods in which your heart felt as though it were racing for no apparent reason?	Y/N

7. At present: Do you experience shortness of breath or loss of breath while walking? Y/N

Do you experience sudden tingling numbness or loss of feeling in your arms, hands, legs, feet or face? Y/N

Do you experience swelling in your feet and ankles? Y/N

Do you get pains or cramps in your legs? Y/N

Do you experience pain or discomfort in your chest? Y/N

Do you experience any pressure of heaviness in your chest? Y/N

Do you have diabetes? Y/N

If yes, how is it controlled? dietary means... insulin injector... oral medication... uncontrolled...

7. Have you ever been told that your blood pressure was abnormal? Y/N

8. Have you ever had asthma? Y/N

9. How often would you characterize your stress level as being high? occasionally... frequently... constantly...

10. Have you ever undergone electro-convulsive-therapy (ECT)? Y/N

11. If you are female, are you pregnant? Y/N

12. Have you ever experienced seizures or fainting spells? Y/N

13. Have you ever been told that you have any of the following illnesses?

myocardial infraction... arteriosclerosis... heart disease... heart block... coronary thrombosis... rheumatic heart... heart attack... aneurism... coronary occlusion... angina... heart failure... heart murmur... Y/N

14. Has any member of your immediate family been treated for or suspected of having any of the following conditions? Please identify their relationship to you (e.g., father, mother, etc.)

(a) Epilepsy
(b) Stroke
(c) Diabetes
(d) Heart disease
(e) High blood pressure
(f) Memory loss
(g) Dementia Y/N

15. Please list all operations or surgical procedures of any kind performed in the last 15 years.

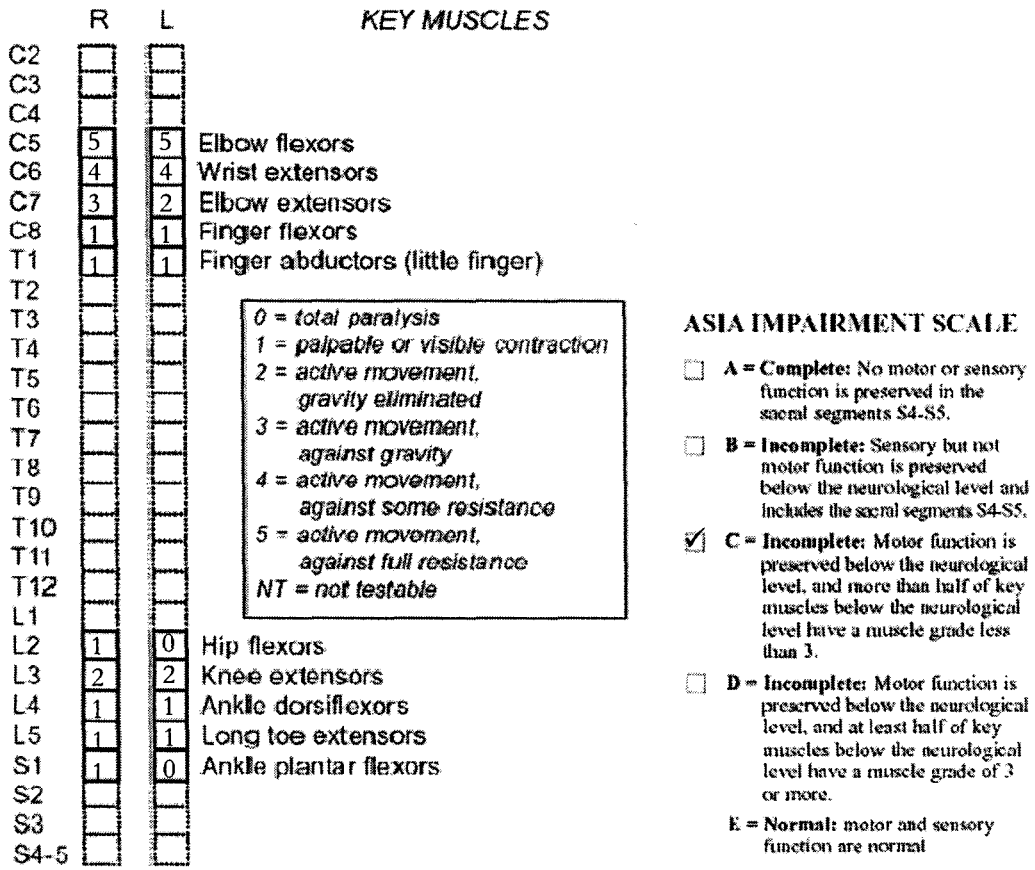
16. Have you ever been injured by any metallic foreign body (e.g. bullet, shrapnel, etc.)? Y/N

17.	Have you ever engaged in metal grinding?	Y/N
	If yes, could metal fragments be present near your eyes?	Y/N
18.	Is there any history of head trauma with loss of consciousness?	Y/N
19.	Please indicate if you have any of the following:	
	1. Cardiac pacemaker	Y/N
	2. Aneurism clips	Y/N
	3. Implanted cardiac defibrillator	Y/N
	4. Any type of bio-stimulator	Y/N
	5. Any type of internal electrodes (e.g., cochlear implant)	Y/N
	6. Insulin pump	Y/N
	7. Any type of electronic, mechanical or magnetic implant	Y/N
	8. Hearing aid	Y/N
	9. Any type of intravascular coil filter (e.g., IVC filter)	Y/N
	10. Artificial heart valve prosthesis	Y/N
	11. Orbital/eye prosthesis	Y/N
	12. Any type of surgical clip or staple	Y/N
	13. Intraventricular shunt	Y/N
	14. Artificial limb or joint	Y/N
	15. Dentures	Y/N
	16. Any implanted orthopedic item (e.g., pins, rods, screws, nails, clips, plates, wire)	Y/N
	17. Any other implanted item	Y/N

APPENDIX B: Individual AIS assessments

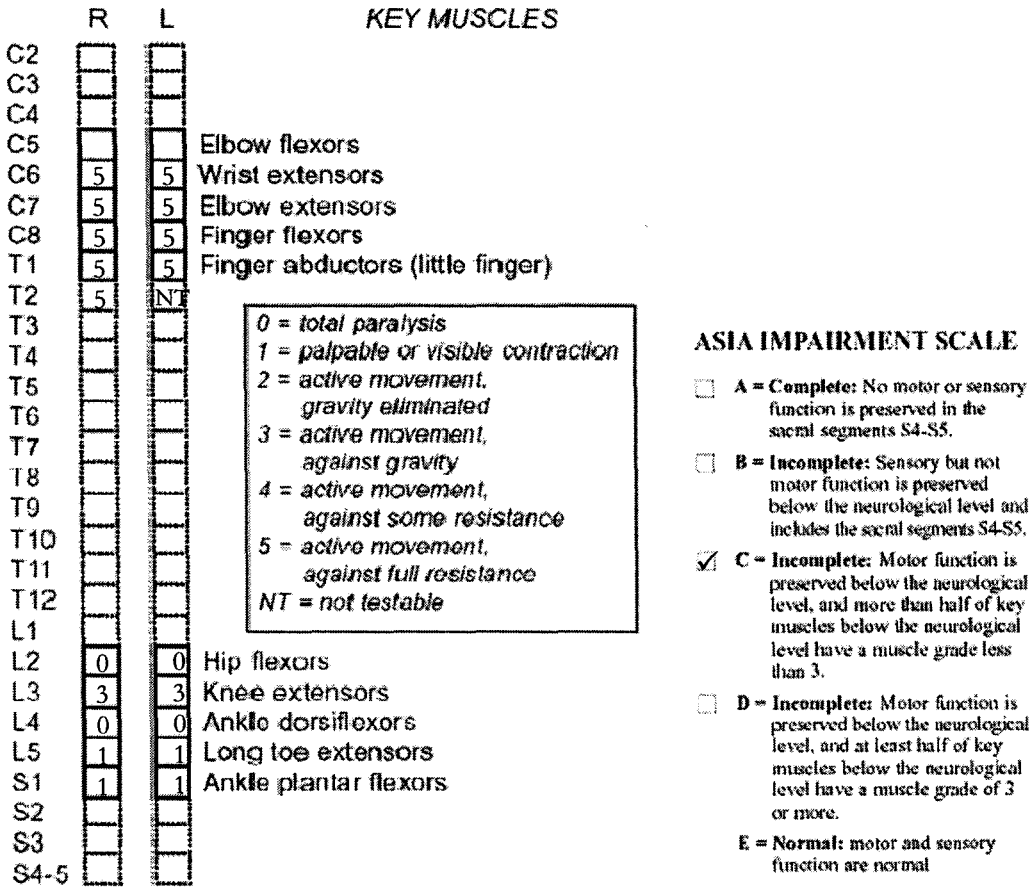
- Individual right and left motor scores
- Motor level
- AIS
- Total motor scores

Participant S1



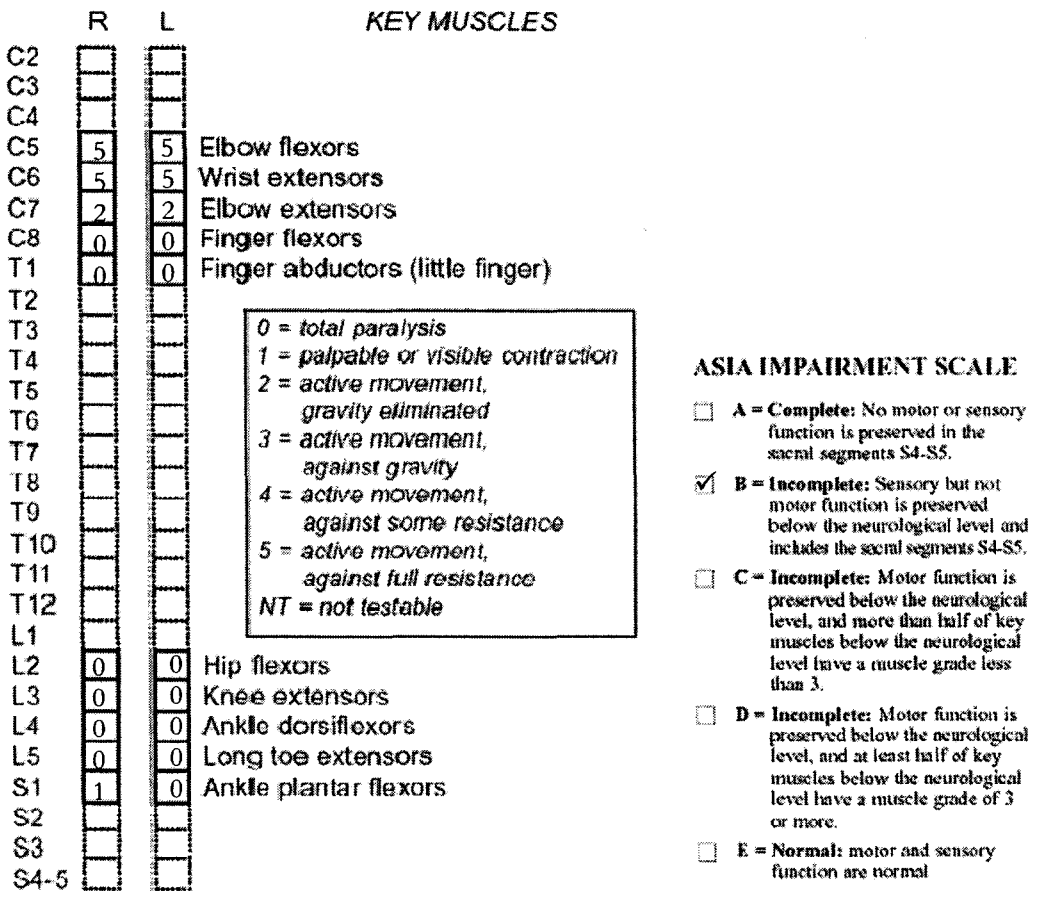
MOTOR LEVEL	C6
ASIA right side score	20
ASIA left side score	17
ASIA upper limb score	27
ASIA lower limb score	10
ASIA TOTAL motor score	37

Participant S2



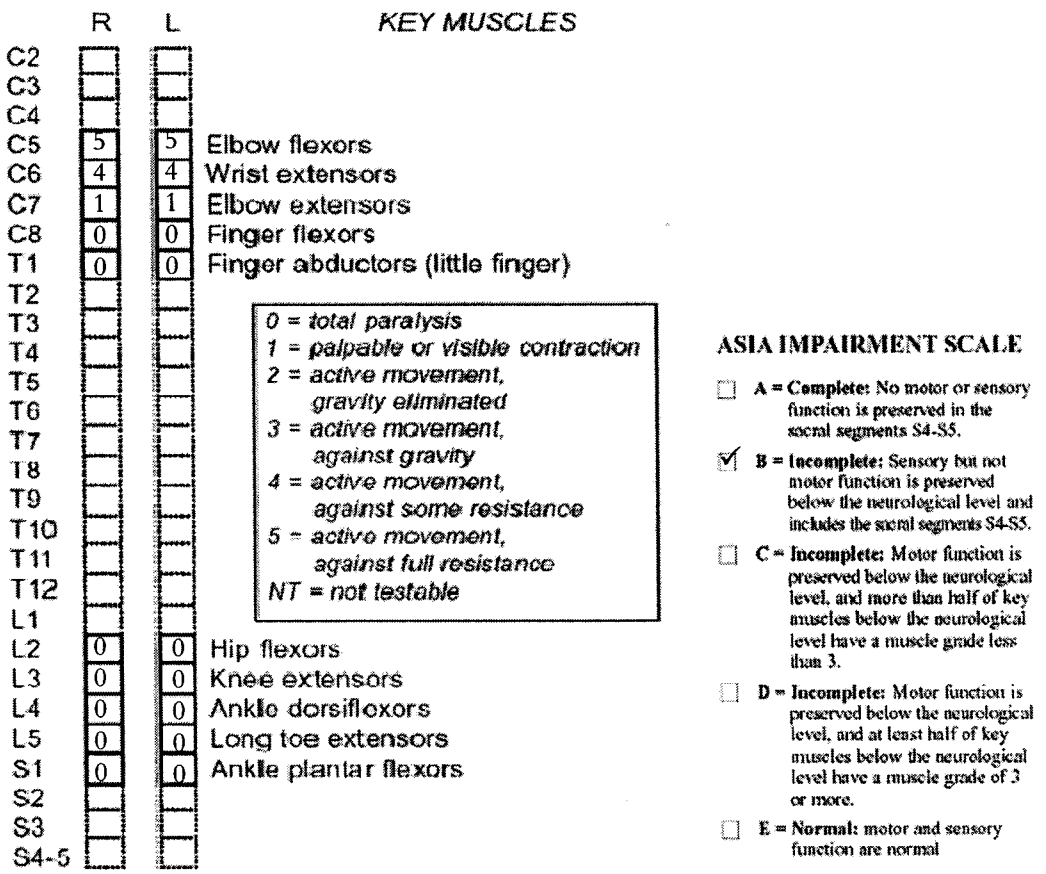
MOTOR LEVEL	T1
ASIA right side score	30
ASIA left side score	25
ASIA upper limb score	45
ASIA lower limb score	10
ASIA TOTAL motor score	55
observations	Stiffness Could not complete full ROM Contracture on left finger

Participant S3



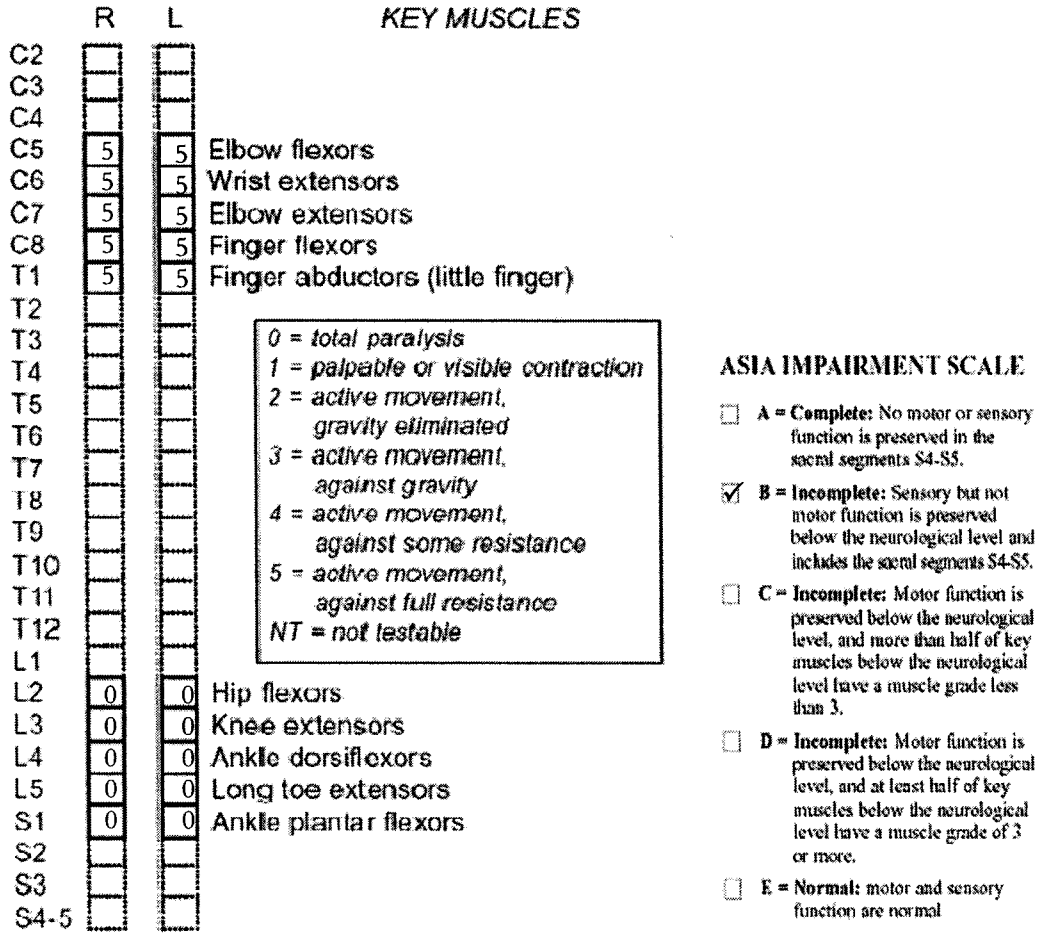
MOTOR LEVEL	C6
ASIA right side score	12
ASIA left side score	13
ASIA upper limb score	24
ASIA lower limb score	1
ASIA TOTAL motor score	25
observations	Spasms Could not complete full ROM

Participant S4



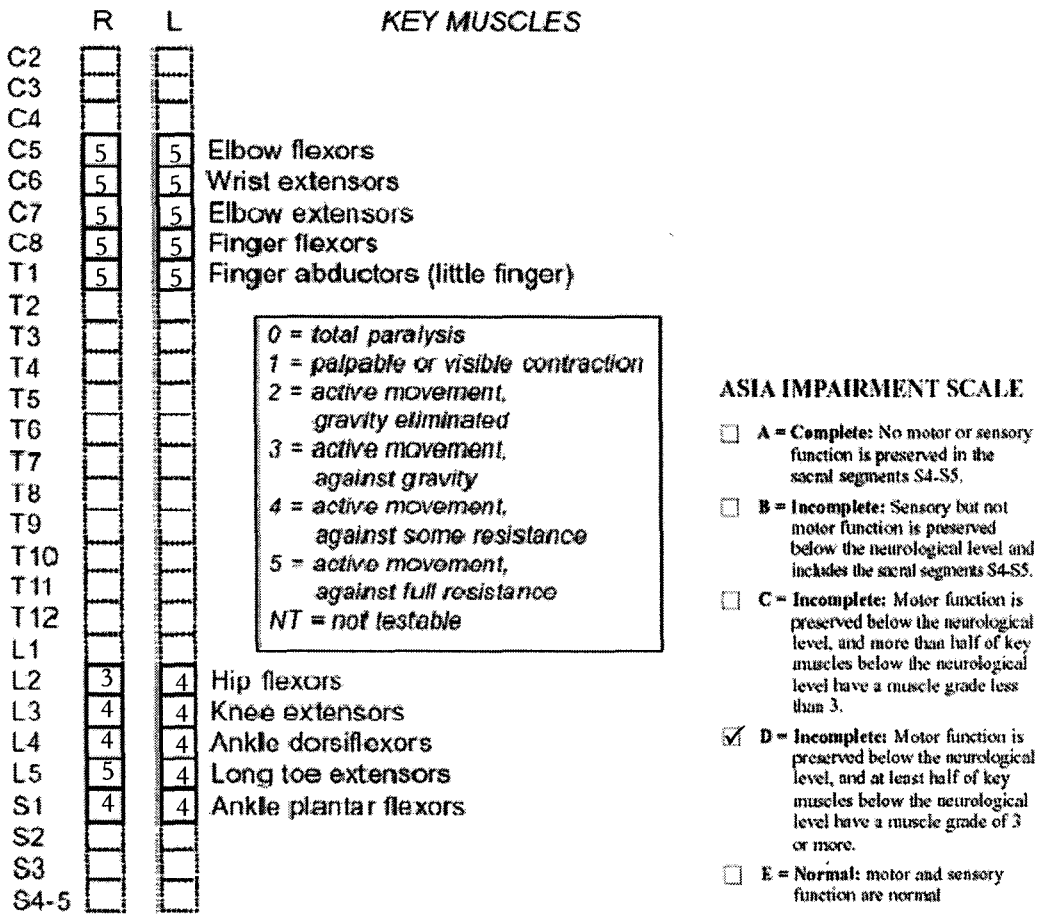
MOTOR LEVEL	C6
ASIA right side score	10
ASIA left side score	10
ASIA upper limb score	20
ASIA lower limb score	0
ASIA TOTAL motor score	20
observations	No Spasms in lower limbs

Participant S5



MOTOR LEVEL	T1
ASIA right side score	25
ASIA left side score	25
ASIA upper limb score	50
ASIA lower limb score	0
ASIA TOTAL motor score	50
observations	Spasticity stiffness

Participant S6



MOTOR LEVEL	T1
ASIA right side score	45
ASIA left side score	50
ASIA upper limb score	50
ASIA lower limb score	40
ASIA TOTAL motor score	90
observations	Spasticity on right leg

APPENDIX C: Data

1. M-waves
    - amplitude (mV) and latency (msec)

2. MEPs
    - Amplitude (μV peak to peak) analysis: across each condition and collapsed.
    - Mean MEPs vs. AIS motor scores (4 key muscles)
    - Stimulator intensities (% of MSO)
    - MEPs by grade
    - Latency (msec)
    - Antagonist MEPs (μV peak to peak)

3. nRMS
    - nRMS (fold increase from baseline)
    - Mean nRMS vs. AIS motor scores (6 key muscles)
    - nRMS by grade
    - nRMS from additional channels (additional muscle analysis)
    - Individual data

4. MEPs vs. nRMS

1. M-waves

M-waves: amplitude (mV)								
	ECR		FDS		TA		SOL	
S	R	L	R	L	R	L	R	L
1	18.56	23.01	7.03	10.48	15.59	19.23	18.56	23.01
2	21.94	25.76	3.71	3.53	13.76	9.86	21.94	25.76
3	13.72	11.28	4.64	2.95	10.5	16.73	13.72	11.28
4	6.12	6.12	0	0	0	0	6.12	6.12
5	15.93	16.03	5.64	7.08	12.33	12.72	15.93	16.03
6	25.81	24.94	9.93	11.98	11.89	11.6	25.81	24.94
M	17.01	17.86	5.16	6.00	10.68	11.69	17.01	17.86
SD	6.85	8.04	3.33	4.66	5.51	6.68	6.85	8.04

M-waves: latency (msec)								
	ECR		FDS		TA		SOL	
S	R	L	R	L	R	L	R	L
1	4.25	3.5	1.5	1.75	5	5.5	4.25	3.5
2	3.25	2.75	1.75	2.5	6	5.75	3.25	2.75
3	2.75	2.5	1.25	1.25	3	3	2.75	2.5
4	3.5	2	0	0	0	0	3.5	2
5	2.5	2.5	3.7	4.75	4.5	4.25	2.5	2.5
6	3	2.75	3.7	4.75	1.75	2	3	2.75
M	3.21	2.67	1.98	2.50	3.38	3.42	3.21	2.67
SD	0.62	0.49	1.46	1.92	2.23	2.21	0.62	0.49

2. MEP data

- **MEPs under each condition**

THRESHOLD (uV)

	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	172.06	119.72	47.12	39.52	116.15	0	83.59	0
2	109.10	154.36	201.08	111.82	54.26	45.87	105.35	74.10
3	388.09	195.50	154.63	96.34	0	0	0	0
4	136.51	180.59	78.19	82.31	0	0	0	0
5	83.92	130.19	65.64	126.25	0	0	0	0
6	213.36	270.51	228.79	235.81	74.54	132.84	82.15	87.40
M	183.84	175.14	129.24	115.34	40.82	29.79	45.18	26.92
SD	110.04	54.89	76.30	66.10	48.97	53.72	50.17	41.91

REST (uV)

	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	179.57	560.36	64.91	52.49	0	0	0	0
2	592.80	660.46	313.14	359.38	0	0	187.16	94.45
3	377.78	110.69	160.49	172.12	0	0	0	0
4	272.74	2071.56	109.34	111.39	0	0	0	0
5	163.36	184.30	128.85	154.51	0	0	0	0
6	929.63	595.72	709.04	214.67	125.37	130.05	106.84	79.58
M	419.31	697.18	247.63	177.43	20.89	21.68	49.00	29.00
SD	295.54	710.82	241.41	104.90	51.18	53.09	80.05	45.18

20% OF MVC (uV)

	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	384.61	533.20	93.35	66.25	189.36	0	75.71	0
2	1228.39	1743.77	477.23	331.94	56.00	70.77	430.85	139.92
3	1207.55	1055.54	244.45	431.79	29.83	0	24.38	0
4	5550.93	3406.19	163.54	146.61	0	0	0	0
5	362.85	405.40	639.44	651.12	0	0	0	0
6	3261.93	3195.82	2463.44	1418.76	133.36	203.72	206.60	87.39
M	1999.38	1723.32	680.24	507.75	68.09	45.75	122.92	37.89
SD	2035.42	1311.48	897.11	492.45	77.27	82.40	169.69	61.00

- **MEPs collapsed across condition vs. Motor scores**

	MEP uV								AIS motor scores							
	ECR		FDS		TA		SOL		ECR		FDS		TA		SOL	
S	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
1	245	404	68	53	102	0	53	0	4	4	1	1	1	1	1	0
2	643	853	330	268	37	39	241	103	5	5	5	5	0	0	1	1
3	658	454	187	233	10	0	8	0	5	5	0	0	0	0	1	0
4	1987	1886	117	113	0	0	0	0	4	4	0	0	0	0	0	0
5	203	240	278	311	0	0	0	0	5	5	5	5	0	0	0	0
6	1468	1354	1134	623	111	156	132	85	5	5	5	5	4	4	4	4
M	867.5	865.2	352.4	266.8	43.3	32.4	72.4	31.3	4.7	4.7	2.7	2.7	0.8	0.8	1.2	0.8
SD	712.2	640.9	395.0	199.7	50.8	62.3	96.9	48.8	0.5	0.5	2.6	2.6	1.6	1.6	1.5	1.6

- **Averaged MEPs vs. Motor scores**

	MEP uV				AIS motor scores			
s	ECR	FDS	TA	SOL	ECR	FDS	TA	SOL
1	324.92	60.61	50.92	26.55	4	1	1	1
2	748.15	299.10	37.82	171.97	5	5	0	1
3	555.86	209.97	4.97	4.06	5	0	0	1
4	1936.42	115.23	0	0	4	0	0	0
5	221.67	294.30	0	0	5	5	0	0
6	1411.16	878.42	133.31	108.33	5	5	4	4
M	866.4	309.6	37.8	51.8	4.7	2.7	0.8	1.0
SD	672.5	294.5	51.4	72.0	0.5	2.6	1.6	1.5

- **Averaged stimulation intensities**

	% of MSO							
	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	52	80	80	90	60	90	75	90
2	40	42	40	45	70	70	55	48
3	70	75	60	60	90	90	90	100
4	45	48	48	48	100	100	100	100
5	46	40	52	55	100	100	100	100
6	43	43	43	43	42	42	50	45
M	49.33	54.67	53.83	56.83	77.00	82.00	78.33	80.50
SD	10.88	17.95	14.62	17.45	23.62	22.45	22.06	26.64

- **MEPs by grade: MEPs at grade 0**

MEPs uV	ASIA motor scores
1418.76	5
651.12	5
2463.44	5
639.44	5
477.23	5
3195.82	5
405.40	5
1055.54	5
1743.77	5
3261.93	5
362.85	5
1207.55	5
1228.39	5
331.94	5
87.39	4
206.60	4
203.72	4
133.36	4
3406.19	4
533.20	4
5550.93	4
384.61	4
139.92	1
24.38	1
430.85	1
75.71	1
0	1
189.36	1
66.25	1
93.35	1
0	0
0	0
0	0
0	0
0	0
0	0
0	0
0	0
0	0
70.77	**0**
0	0
0	0
29.83	**0**
56.00	**0**
146.61	**0**
431.79	**0**
163.54	**0**
244.45	**0**

- **MEP latencies**

	THRESHOLD (msec)							
	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	17.00	14.50	14.00	13.25	43.25		43.40	
2	17.25	17.70	15.00	16.25	40.20	42.00	38.50	49.80
3	17.10	13.80	16.00	14.00				
4	12.20	15.75	14.00	13.60				
5	14.65	13.30	13.00	13.20				
6	19.70	14.90	15.80	14.60	44.00	37.90	52.00	45.00
M	16.32	14.99	14.63	14.15	42.48	39.95	44.63	47.40
SD	2.57	1.58	1.17	1.15	2.01	2.90	6.83	3.39

	REST (msec)							
	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	15.25	14.50	14.25	11.50				
2	19.50	19.50	15.25	15.25			41.25	49.30
3	16.00	14.00	15.70	13.95				
4	16.00	15.25	13.70	13.25				
5	13.30	14.40	11.50	12.00				
6	15.80	14.90	18.00	15.35	52.00	36.65	54.40	48.90
M	15.98	15.43	14.73	13.55	52.00	36.65	47.83	49.10
SD	2.01	2.04	2.17	1.61			9.30	0.28

	20% OF MVC (msec)							
	ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L
1	11.00	11.00	11.25	10.00	36.00		43.50	
2	19.50	16.75	18.40	13.00	42.40	41.25	40.25	49.25
3	14.00	14.80	14.70	13.70	47.00		50.25	
4	15.00	14.35	11.00	12.50				
5	14.00	12.40	12.90	12.10				
6	15.60	14.25	14.50	13.70	52.00	40.50	48.40	44.70
M	14.85	13.93	13.79	12.50	44.35	40.88	45.60	46.98
SD	2.77	2.00	2.74	1.38	6.81	0.53	4.56	3.22

- **Antagonist MEPs**

THRESHOLD (uV)

	FCR		Ext. Dig.		SOL		TA	
s	R	L	R	L	R	L	R	L
1	11.51	12.48	103.39	1617.80	24.38	0	141.17	0.00
2	65.18	136.81	18.00	347.32	508.18	328.61	31.92	17.42
3	59.08	83.44	119.81	18.64	0	0	0	0
4	40.10	68.66	103.97	98.91	0	0	0	0
5	25.17	39.52	110.72	163.54	0	0	0	0
6	134.61	28.62	154.82	71.42	12.32	17.10	21.09	55.42
M	55.94	61.59	101.79	386.27	90.81	57.62	32.36	12.14
SD	43.49	45.10	45.27	613.95	204.70	132.93	54.97	22.32

REST (uV)

	FCR		Ext. Dig.		SOL		TA	
s	R	L	R	L	R	L	R	L
1	11.54	18.99	182.13	699.83	0	0	0	0
2	102.66	236.76	55.97	536.07	0	0	96.46	16.72
3	155.09	103.72	23.92	30.24	0	0	0	0
4	47.27	98.38	2569.10	1787.30	0	0	0	0
5	36.07	97.75	262.90	287.72	0	0	0	0
6	366.97	223.63	285.87	377.59	22.20	14.44	61.04	139.20
M	119.93	129.87	563.32	619.79	3.70	2.41	26.25	25.99
SD	131.62	83.93	988.34	615.30	9.06	5.90	42.18	55.86

20% OF MVC (uV)

	FCR		Ext. Dig.		SOL		TA	
s	R	L	R	L	R	L	R	L
1	9.25	32.14	529.20	664.55	27.22	0	534.54	0
2	35.77	502.81	346.00	733.70	504.94	489.87	88.65	21.70
3	100.70	73.02	1163.27	97.14	0	0	0	0
4	116.36	113.31	6370.12	4134.20	0	0	0	0
5	27.22	274.54	781.19	746.73	0	0	0	0
6	275.42	102.10	837.01	1067.51	32.93	18.60	70.25	110.47
M	94.12	182.99	1671.13	1240.64	94.18	84.75	115.57	22.03
SD	98.48	177.15	2318.88	1452.11	201.78	198.61	208.99	44.19

- **Averaged agonist MEPs vs. antagonist MEPs**

	Upper limb muscle groups (agonist /antagonist uV)				Lower limb muscle groups (agonist /antagonist uV)			
	ECR	FCR	FDS	Ext Dig	TA	SOL	SOL	TA
MEAN	866.36	107.41	309.60	763.82	37.84	55.58	51.82	39.06
SD	676.53	96.63	297.32	1005.64	56.57	125.50	72.86	71.42

3. nRMS data (fold increase from baseline)

	BI		Tri		ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L	R	L	R	L
1	640.49	486.77	20.15	1.38	137.04	29.90	1.79	2.17	7.53	0.59	0.17	1.14
2	49.21	315.22	28.58	101.43	124.37	84.36	9.66	101.05	19.91	3.32	3.57	1.01
3	71.52	61.32	18.03	13.06	223.24	133.26	2.23	1.66	0.00	0.19	1.07	0.09
4	41.15	130.52	0.78	0.78	47.41	101.19	0.03	0.28	0.31	0.27	0.36	0.38
5	30.11	67.19	53.87	83.09	98.65	90.25	4.78	3.54	1.43	0.63	0.53	0.39
6	161.16	222.70	165.31	72.03	162.53	108.89	45.74	41.09	3.39	15.36	5.36	10.79
M	165.61	213.95	47.79	45.30	132.21	91.31	10.70	24.96	5.43	3.40	1.84	2.30
SD	237.40	165.26	60.13	45.26	59.34	34.61	17.49	40.45	7.62	5.98	2.13	4.18

- **AIS scores from 6 key muscles**

	BI		Tri		ECR		FDS		TA		SOL	
s	R	L	R	L	R	L	R	L	R	L	R	L
1	5	5	3	2	4	4	1	1	1	1	1	0
2	5	5	5	5	5	5	5	5	0	0	1	1
3	5	5	2	2	5	5	0	0	0	0	1	0
4	5	5	1	1	4	4	0	0	0	0	0	0
5	5	5	5	5	5	5	5	5	0	0	0	0
6	5	5	5	5	5	5	5	5	4	4	4	4
M	5	5	3.5	3.33	4.67	4.67	2.67	2.67	0.83	0.83	1.17	0.83
SD	0	0	1.76	1.86	0.52	0.52	2.58	2.58	1.6	1.6	1.47	1.6

- **Averaged nRMS vs motor scores**

	nRMS (fold increase from baseline)						AIS motor scores					
s	Bi	Tri	ECR	FDS	TA	SOL	Bi	Tri	ECR	FDS	TA	SOL
1	563.63	10.77	83.47	1.98	4.06	0.65	5	3	4	1	1	0.5
2	182.22	65.01	104.37	55.36	11.62	2.29	5	5	5	5	0	1
3	66.42	15.55	178.25	1.94	0.10	0.58	5	2	5	0	0	0.5
4	85.83	0.78	74.30	0.15	0.29	0.37	5	1	4	0	0	0
5	48.65	68.48	94.45	4.16	1.03	0.46	5	5	5	5	0	0
6	191.93	118.67	135.71	43.41	9.37	8.07	5	5	5	5	4	4
M	189.78	46.54	111.76	17.83	4.41	2.07	5	3.42	4.67	2.67	0.83	1
SD	192.75	45.52	38.87	24.76	4.97	3.03		1.8	0.52	2.58	1.6	1.52

- **nRMS values by AIS motor grade (for correlation analysis)**

nRMS	motor score
640.49	5
49.21	5
71.52	5
41.15	5
30.11	5
161.16	5
486.77	5
315.22	5
61.32	5
130.52	5
67.19	5
222.70	5
28.58	5
53.87	5
165.31	5
101.43	5
83.09	5
72.03	5
124.37	5
223.24	5
98.65	5
162.53	5
84.36	5
133.26	5
90.25	5
108.89	5
9.66	5
4.78	5
45.74	5
3.54	5
41.09	5
101.05	5

nRMS	Motor score
137.04	4
47.41	4
29.90	4
101.19	4
3.39	4
15.36	4
5.36	4
10.79	4
20.15	3
18.03	2
1.38	2
13.06	2
0.78	1
0.78	1
1.79	1
2.17	1
7.53	1
0.59	1
0.17	1
3.57	1
1.07	1
1.01	1
2.23	0
0.03	0
1.66	0
0.28	0
19.91	0
0.00	0
0.31	0
1.43	0
3.32	0
0.19	0
0.27	0
0.63	0
0.36	0
0.53	0
1.14	0
0.09	0
0.38	0
0.39	0

- **nRMS from additional channels**

Key muscle assessed: Bi

	Bi		Tri		FDS		ECR	
s	R	L	R	L	R	L	R	L
1	640.49	486.77	8.16	11.61	47.03	26.77	93.95	53.30
2	49.21	315.22	1.07	10.84	9.24	81.68	32.05	38.61
3	71.52	61.32	6.00	4.42	6.90	108.07	16.91	8.58
4	41.15	130.52	14.39	8.98	17.66	21.63	6.92	30.75
5	30.11	67.19	2.05	2.36	4.54	7.12	17.68	14.49
6	161.16	222.70	5.36	8.30	41.34	23.32	13.19	40.34
M	189.78		6.96		32.94		30.56	
SD	196.64		4.15		32.33		24.59	

Key muscle assessed: Tri

	Tri		Bi		FDS		ECR	
s	R	L	R	L	R	L	R	L
1	20.15	1.38	7.86	7.53	18.24	0.37	19.94	19.93
2	28.58	101.43	1.45	8.54	2.13	61.50	23.12	30.11
3	18.03	13.06	4.31	1.33	2.35	4.22	11.55	3.03
4	0.78	0.78	0.80	0.94	0.02	1.28	1.20	39.10
5	53.87	83.09	6.49	4.97	1.55	2.19	45.19	12.00
6	165.31	72.03	4.75	4.32	8.24	7.07	9.13	7.58
M	46.54		4.44		9.10		18.49	
SD	50.76		2.81		17.26		13.93	

Key muscle assessed: ECR

	ECR		Tri		Bi		FDS	
s	R	L	R	L	R	L	R	L
1	137.04	1.38	1.87	1.43	35.38	13.25	4.16	7.54
2	124.37	101.43	0.90	2.08	2.41	8.96	2.97	14.55
3	223.24	13.06	13.66	7.20	5.33	3.91	10.73	11.50
4	47.41	0.78	0.90	0.15	0.97	1.71	1.59	4.28
5	98.65	83.09	0.24	3.05	9.13	1.30	2.39	20.37
6	162.53	72.03	4.17	3.41	12.77	16.67	12.10	6.80
M	111.76		3.26		9.32		8.25	
SD	51.00		3.83		9.75		5.72	

Key muscle assessed: FDS

	FDS		Tri		Bi		ECR	
s	R	L	R	L	R	L	R	L
1	1.79	2.17	0.00	0.63	16.80	13.38	21.17	74.73
2	9.66	101.05	1.35	8.84	27.09	35.92	9.67	33.04
3	2.23	1.66	2.00	1.15	0.53	0.00	4.19	2.69
4	0.03	0.28	1.27	0.00	0.07	0.07	1.13	0.90
5	4.78	3.54	0.00	0.28	0.06	0.43	41.74	5.74
6	45.74	41.09	0.17	0.07	3.64	3.34	53.13	42.22
M	17.83		1.31		8.44		24.20	
SD	30.63		2.46		12.26		24.49	

Key muscle assessed: TA

	TA		SOL		GA	
s	R	L	R	L	R	L
1	7.53	0.59	3.52	3.17	2.68	3.21
2	19.91	3.32	5.20	2.37	2.02	1.04
3	0.00	0.19	0.92	0.20	0.76	0.00
4	0.31	0.27	0.27	0.30	0.38	0.63
5	1.43	0.63	0.57	0.08	0.58	0.19
6	3.39	15.36	2.39	1.47	5.30	1.14
M	4.41		1.71		1.50	
SD	6.61		1.64		1.56	

Key muscle assessed: SOL

	SOL		TA		GA	
s	R	L	R	L	R	L
1	0.17	1.14	4.75	0.92	0.02	0.57
2	3.57	1.01	11.45	24.00	1.89	1.44
3	1.07	0.09	0.00	0.08	0.41	0.00
4	0.36	0.38	0.19	0.11	0.32	0.54
5	0.53	0.39	1.22	0.53	0.86	0.27
6	5.36	10.79	1.38	0.51	13.49	5.16
M	2.07		3.76		2.08	
SD	3.17		7.16		3.86	

- **Individual nRMS data**

subject 1

		Right				Left			
	test	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR
key muscle ECR	1 or 0	0.920	0.012	1.481	**48.580**	0.699	0.077	8.842	**29.723**
	2	0.872	0.099	1.432	**34.438**	0.961	0.293	10.886	**32.089**
	3	0.975	0.003	2.263	**74.586**	0.653	0.128	9.684	**23.291**
	4	**35.381**	**1.870**	**4.159**	**137.043**	**13.252**	**1.429**	**7.544**	**29.899**
	5	33.492	3.117	1.652	**186.278**	19.552	1.978	8.693	**39.877**
key muscle FDS	**1 or 0**	**16.797**	**0.046**	**1.788**	**21.169**	**13.378**	**0.634**	**2.168**	**74.728**
	2	0.553	0.076	**1.461**	49.411	17.630	0.492	**1.630**	62.529
	3	0.085	0.149	**1.470**	11.007	11.203	0.347	**2.832**	64.790
	4	6.255	0.513	**1.470**	11.232	10.141	0.510	**2.803**	60.812
	5	120.744	0.694	**1.564**	80.803	12.491	0.677	**3.226**	63.820
key muscle TRI	1 or 0	33.242	**1.070**	1.519	18.594	7.829	**1.189**	0.463	15.765
	2	18.845	**0.744**	1.563	19.194	**7.528**	**1.384**	**0.368**	**19.927**
	3	**7.865**	**20.153**	**18.237**	**19.936**	5.712	**5.229**	5.887	43.732
	4	8.090	**45.450**	18.322	35.524	8.896	**13.995**	14.509	42.922
	5	8.411	**72.286**	38.496	23.731	13.278	**23.599**	11.887	27.492
key muscle BI	1 or 0	**497.920**	5.715	16.785	103.625	**136.335**	2.335	15.052	49.065
	2	**530.784**	9.426	22.880	523.698	**94.578**	1.568	7.117	44.672
	3	**269.080**	6.401	57.985	272.071	**298.604**	4.959	14.409	21.056
	4	**411.203**	4.808	20.181	156.394	**479.303**	9.005	19.310	35.809
	5	**640.495**	**8.157**	**47.030**	**93.947**	**486.766**	**11.608**	**26.773**	**53.301**

		Right			Left		
	test	ch1: TA	ch2: SOL	ch3: GA	ch1: TA	ch2: SOL	ch3: GA
key muscle TA	**1 or 0**	**7.528**	**3.524**	**2.684**	**0.594**	**3.168**	**3.210**
	2	**2.168**	0.708	0.093	**0.829**	3.411	1.921
	3	**3.650**	0.517	1.975	**0.883**	1.098	0.576
	4	**14.067**	0.121	0.013	**0.471**	1.927	0.386
	5	**22.882**	0.316	0.087	**0.354**	0.558	0.279
key muscle SOL	**1 or 0**	**4.755**	**0.165**	**0.016**	**0.915**	**1.139**	**0.567**
	2	14.045	**0.203**	2.463	0.954	**1.472**	0.545
	3	10.664	**0.319**	0.037	0.808	**0.991**	0.454
	4	1.456	**2.500**	0.339	0.496	**0.985**	0.371
	5	1.769	**1.885**	0.210	0.502	**2.610**	1.753

subject 2

		Right				Left			
	test	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR
key muscle ECR	1 or 0	4.646	5.362	16.805	**51.464**	8.986	4.046	73.406	**32.403**
	2	5.245	5.518	11.125	**30.826**	2.319	3.739	8.085	**21.873**
	3	0.256	2.978	2.152	**42.548**	1.626	2.458	34.231	**39.370**
	4	0.222	2.453	1.257	**79.752**	10.004	1.090	2.849	**74.246**
	5	**2.411**	**0.902**	**2.968**	**124.374**	**8.963**	**2.085**	**14.554**	**84.362**
key muscle FDS	1 or 0	2.421	0.238	**2.669**	7.455	21.742	7.054	**26.750**	28.642
	2	1.714	0.004	**2.531**	7.707	18.267	6.502	**71.108**	27.704
	3	15.125	0.145	**4.043**	10.339	14.746	5.053	**47.368**	8.377
	4	17.196	0.055	**3.659**	3.801	27.675	5.115	**52.757**	11.128
	5	**27.088**	**1.347**	**9.662**	**9.670**	**35.924**	**8.840**	**101.051**	**33.042**
key muscle TRI	1 or 0	1.962	**8.513**	0.193	6.962	6.158	**12.717**	6.037	2.108
	2	3.919	**7.003**	0.565	4.813	9.930	**13.314**	9.400	1.431
	3	1.486	**13.398**	1.322	4.010	3.185	**15.908**	3.826	1.437
	4	0.686	**18.079**	1.741	7.831	5.771	**124.180**	16.273	5.712
	5	**1.454**	**28.582**	**2.128**	**23.121**	**8.537**	**101.433**	**61.499**	**30.109**
key muscle BI	1 or 0	**4.880**	0.212	3.494	2.030	**111.933**	2.707	31.271	19.723
	2	**12.524**	6.311	0.741	8.597	**8.608**	0.695	4.307	16.114
	3	**7.288**	8.504	1.166	0.901	**21.241**	1.434	35.701	6.343
	4	**45.836**	1.042	7.633	17.994	**12.120**	2.001	13.295	9.048
	5	**49.210**	**1.074**	**9.237**	**32.054**	**315.223**	**10.836**	**81.681**	**38.610**

		Right			Left		
	test	ch1: TA	ch2: SOL	ch3: GA	ch1: TA	ch2: SOL	ch3: GA
key muscle TA	**1 or 0**	**19.914**	**5.203**	**2.017**	**3.316**	**2.369**	**1.042**
	2	**13.076**	3.587	0.330	**170.854**	1.538	0.613
	3	**16.567**	5.282	0.939	**49.585**	1.149	0.810
	4	**18.748**	4.892	0.655	**143.372**	1.338	0.990
	5	**18.567**	4.990	0.656	**112.362**	0.926	0.999
key muscle SOL	**1 or 0**	**11.451**	**3.571**	**1.895**	**23.997**	**1.009**	**1.440**
	2	0.135	**4.740**	1.632	1.364	**1.548**	1.241
	3	110.128	**3.342**	1.575	241.656	**0.904**	1.153
	4	5.961	**8.152**	2.923	13.467	**3.014**	2.290
	5	30.397	**8.995**	2.226	64.361	**3.402**	1.712

subject 3

		Right				Left			
	test	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR
key muscle ECR	1 or 0	1.901	15.029	8.471	**140.505**	1.924	3.344	27.696	**27.509**
	2	1.513	12.376	7.877	**124.081**	1.447	2.160	23.972	**23.145**
	3	1.253	11.409	10.212	**112.285**	0.791	7.994	25.127	**27.551**
	4	1.557	9.855	8.177	**135.790**	0.770	5.849	18.459	**58.143**
	5	**5.327**	**13.660**	**10.726**	**223.238**	**3.914**	**7.200**	**11.495**	**133.265**
key muscle FDS	**1 or 0**	**0.525**	**1.999**	**2.228**	**4.192**	**0.018**	**1.155**	**1.656**	**2.689**
	2	0.561	1.319	**1.441**	4.745	2.663	1.875	**13.715**	2.568
	3	0.638	2.929	**2.578**	5.407	0.003	0.160	**9.338**	0.425
	4	0.856	2.052	**2.537**	8.010	0.003	0.136	**8.914**	1.577
	5	0.812	2.671	**2.548**	6.826	0.025	0.170	**10.937**	0.410
key muscle TRI	1 or 0	2.847	**22.850**	1.982	9.902	2.181	**13.176**	2.724	3.066
	2	**4.309**	**18.035**	**2.353**	**11.551**	**1.326**	**13.060**	**4.223**	**3.025**
	3	3.100	**32.170**	6.679	89.596	2.021	**13.006**	10.214	11.397
	4	4.224	**35.675**	2.211	106.600	2.995	**15.897**	5.069	22.778
	5	4.662	**34.586**	2.711	130.083	3.166	**14.260**	5.652	32.702
key muscle BI	1 or 0	**3.561**	7.709	3.578	15.365	**3.754**	3.593	26.774	3.236
	2	**2.682**	7.957	2.188	11.604	**2.403**	3.182	13.202	3.486
	3	**11.972**	2.448	8.724	9.226	**16.427**	3.366	32.955	5.418
	4	**40.145**	2.313	6.709	11.320	**26.532**	3.180	33.835	6.166
	5	**71.523**	**6.000**	**6.896**	**16.911**	**61.315**	**4.424**	**108.074**	**8.582**

		Right			Left		
	test	ch1: TA	ch2: SOL	ch3: GA	ch1: TA	ch2: SOL	ch3: GA
key muscle TA	**1 or 0**	**0.000**	**0.923**	**0.763**	**0.193**	**0.204**	**0.001**
	2	**0.036**	1.127	1.019	**0.170**	0.387	0.004
	3	**0.021**	1.204	0.984	**0.179**	0.219	0.188
	4	**0.066**	2.152	1.627	**0.107**	0.092	0.051
	5	**0.048**	2.143	1.608	**0.089**	0.086	0.065
key muscle SOL	**1 or 0**	**0.014**	**1.069**	**0.406**	**0.084**	**0.086**	**0.059**
	2	0.102	**0.715**	0.776	0.176	**0.135**	0.052
	3	0.049	**0.418**	0.649	0.128	**0.215**	0.070
	4	0.125	**0.982**	0.967	0.086	**0.071**	0.083
	5	0.105	**0.935**	0.815	0.075	**0.049**	0.097

subject 4

		Right				Left			
	test	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR
key muscle ECR	1 or 0	0.105	1.201	2.670	**6.396**	0.664	0.074	3.235	**61.771**
	2	0.268	1.211	3.789	**18.371**	0.543	0.053	3.342	**53.938**
	3	0.197	0.926	1.180	**18.319**	1.094	0.064	2.965	**57.339**
	4	**0.968**	**0.903**	**1.595**	**47.408**	**1.713**	**0.149**	**4.275**	**101.193**
	5	5.492	1.662	1.540	**70.030**	1.769	0.328	4.782	**114.406**
key muscle FDS	**1 or 0**	**0.073**	**1.266**	**0.027**	**1.129**	**0.075**	**0.137**	**0.282**	**0.902**
	2	0.176	1.451	**0.191**	2.940	0.104	0.143	**0.253**	0.222
	3	0.590	1.262	**0.460**	2.910	1.822	0.072	**1.441**	13.312
	4	0.939	1.541	**0.481**	3.675	1.048	0.114	**1.110**	9.098
	5	2.405	1.836	**0.350**	2.279	1.823	0.117	**0.738**	5.149
key muscle TRI	**1 or 0**	**0.796**	**0.780**	**0.227**	**1.201**	**0.936**	**0.783**	**1.285**	**39.099**
	2	0.499	**0.160**	0.015	4.688	1.104	**1.141**	1.200	40.049
	3	3.372	**0.583**	18.570	50.528	5.875	**0.557**	4.306	88.838
	4	4.344	**0.637**	11.475	35.958	50.467	**0.846**	4.796	85.923
	5	29.787	**2.970**	9.056	103.107	67.738	**1.276**	5.161	104.089
key muscle BI	1 or 0	**1.659**	0.385	5.080	3.569	**8.307**	0.610	1.271	10.874
	2	**1.693**	0.280	1.525	1.477	**2.472**	0.623	1.190	15.854
	3	**28.810**	6.080	32.264	2.912	**88.069**	6.131	6.212	10.163
	4	**33.428**	12.792	15.432	6.669	**100.809**	8.582	18.647	21.068
	5	**41.149**	**14.393**	**17.656**	**6.923**	**130.516**	**8.977**	**21.632**	**30.749**

		Right			Left		
	test	ch1: TA	ch2: SOL	ch3: GA	ch1: TA	ch2: SOL	ch3: GA
key muscle TA	**1 or 0**	**0.310**	**0.273**	**0.385**	**0.270**	**0.299**	**0.629**
	2	**0.259**	0.414	0.404	**0.247**	0.312	0.602
	3	**0.238**	0.339	0.443	**0.241**	0.439	0.612
	4	**0.203**	0.295	0.380	**0.127**	0.370	0.653
	5	**0.210**	0.251	0.440	**0.181**	0.208	0.649
key muscle SOL	**1 or 0**	**0.189**	**0.364**	**0.321**	**0.108**	**0.384**	**0.536**
	2	0.082	**0.434**	0.100	0.050	**0.335**	0.453
	3	0.160	**0.398**	0.246	0.165	**0.359**	0.415
	4	0.090	**0.361**	0.212	0.068	**0.289**	0.320
	5	0.142	**0.266**	0.174	0.119	**0.218**	0.006

subject 5

		Right				Left			
	test	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR
key muscle ECR	1 or 0	0.074	0.899	8.562	**13.408**	0.764	1.583	20.225	**51.513**
	2	0.052	0.851	16.666	**11.499**	3.538	0.294	44.142	**47.057**
	3	0.198	0.948	5.221	**57.537**	0.247	1.878	12.935	**43.977**
	4	2.322	0.065	3.677	**67.629**	0.471	1.411	20.514	**77.777**
	5	**9.127**	**0.244**	**2.389**	**98.651**	**1.300**	**3.054**	**20.368**	**90.248**
key muscle FDS	1 or 0	0.065	0.016	**2.146**	41.738	0.427	0.277	**4.487**	5.737
	2	0.069	0.010	**4.493**	42.871	0.458	0.286	**5.184**	7.171
	3	15.069	0.048	**1.964**	47.986	0.425	0.271	**7.108**	7.915
	4	14.544	0.072	**3.038**	72.307	0.448	0.432	**2.729**	14.861
	5	**12.318**	**0.101**	**4.777**	**87.895**	**3.487**	**0.323**	**3.540**	**16.985**
key muscle TRI	1 or 0	3.968	**3.523**	1.918	51.246	1.362	**8.623**	0.403	8.466
	2	4.768	**4.219**	1.647	71.105	6.787	**11.206**	2.503	13.664
	3	2.444	**9.888**	1.804	65.980	2.889	**25.552**	3.069	14.419
	4	2.457	**29.574**	0.835	27.448	5.495	**82.259**	4.747	31.890
	5	**6.490**	**53.870**	**1.549**	**45.189**	**4.970**	**83.090**	**2.187**	**12.004**
key muscle BI	1 or 0	**1.832**	0.140	0.576	6.688	**4.814**	0.487	0.962	7.193
	2	**1.259**	0.204	0.284	5.167	**5.309**	0.514	0.781	6.043
	3	**8.447**	0.800	1.314	25.467	**31.678**	2.124	29.697	10.911
	4	**52.001**	2.371	6.395	32.923	**51.011**	2.546	11.736	16.183
	5	**30.108**	**2.048**	**4.543**	**17.678**	**67.189**	**2.357**	**7.121**	**14.490**

		Right			Left		
	test	ch1: TA	ch2: SOL	ch3: GA	ch1: TA	ch2: SOL	ch3: GA
key muscle TA	**1 or 0**	**1.434**	**0.571**	**0.581**	**0.634**	**0.076**	**0.195**
	2	**1.416**	0.608	0.890	**0.621**	1.487	0.243
	3	**1.406**	0.520	0.601	**0.621**	0.397	0.121
	4	**1.496**	0.655	0.731	**0.611**	0.320	0.152
	5	**1.507**	0.597	0.705	**0.643**	0.288	0.206
key muscle SOL	**1 or 0**	**1.223**	**0.528**	**0.863**	**0.534**	**0.395**	**0.266**
	2	1.239	**0.578**	0.942	0.530	**0.369**	0.305
	3	1.298	**0.558**	0.017	0.107	**0.002**	0.241
	4	1.288	**0.584**	0.034	0.121	**0.044**	0.256
	5	1.205	**0.508**	0.220	0.124	**0.247**	0.292

subject 6

		Right				Left			
	test	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR	ch1: BI	ch2: TRI	ch3: FDS	ch4: ECR
key muscle ECR	1 or 0	11.160	9.958	18.369	**137.135**	7.351	0.376	10.428	**85.470**
	2	10.544	8.931	10.376	**138.184**	6.189	0.245	9.536	**73.320**
	3	11.099	6.739	14.632	**146.073**	7.431	0.411	4.831	**86.875**
	4	12.242	3.513	10.223	**157.378**	9.373	2.212	6.630	**106.794**
	5	**12.767**	**4.173**	**12.103**	**162.529**	**16.672**	**3.412**	**6.800**	**108.891**
key muscle FDS	1 or 0	3.637	0.175	**29.036**	53.131	3.343	0.071	**13.170**	42.224
	2	4.299	0.154	**15.896**	61.331	4.235	0.109	**17.192**	52.869
	3	2.216	8.500	**4.766**	31.864	0.968	0.099	**20.688**	15.067
	4	3.441	9.348	**25.765**	47.195	2.547	0.233	**30.852**	25.634
	5	**5.842**	**8.398**	**45.737**	**78.679**	**12.497**	**0.454**	**41.090**	**29.984**
key muscle TRI	1 or 0	0.614	**4.426**	0.596	6.556	13.849	**0.298**	0.950	3.871
	2	0.790	**0.694**	0.335	7.769	12.939	**2.753**	0.249	5.732
	3	0.932	**33.156**	1.109	3.196	1.138	**25.608**	3.765	3.889
	4	2.505	**58.915**	2.515	7.739	3.077	**57.317**	3.655	6.368
	5	**4.752**	**165.314**	**8.235**	**9.132**	**4.317**	**72.034**	**7.069**	**7.578**
key muscle BI	1 or 0	**5.180**	0.138	2.428	21.375	**9.773**	0.189	0.199	13.541
	2	**2.161**	0.579	2.140	12.364	**9.497**	0.137	1.977	10.832
	3	**11.673**	6.221	23.355	13.561	**8.864**	9.083	29.403	11.592
	4	**71.590**	3.684	2.399	8.886	**35.678**	6.406	17.061	27.993
	5	**161.159**	**5.361**	**41.341**	**13.188**	**222.700**	**8.300**	**23.316**	**40.343**

		Right			Left		
	test	ch1: TA	ch2: SOL	ch3: GA	ch1: TA	ch2: SOL	ch3: GA
key muscle TA	1 or 0	**1.410**	1.026	1.343	**10.323**	2.217	1.527
	2	**2.072**	1.559	1.453	**9.537**	1.715	1.196
	3	**1.965**	2.358	3.803	**9.197**	1.409	1.116
	4	**3.386**	**2.391**	**5.300**	**15.364**	**1.467**	**1.140**
	5	**4.957**	2.653	4.083	**13.614**	1.617	1.100
key muscle SOL	1 or 0	0.754	**3.830**	12.331	1.656	**4.687**	4.168
	2	0.730	**4.375**	11.963	0.335	**4.469**	3.883
	3	1.938	**3.295**	4.671	1.767	**6.648**	1.882
	4	**1.379**	**5.358**	**13.493**	**0.513**	**10.787**	**5.161**
	5	1.868	**5.893**	10.003	1.149	**10.115**	7.483

4. MEP vs. nRMS (data for correlation)

muscle	subject	MEPs (uV)	nRMS
ECR R	1	245.412	137.043
	2	643.433	124.374
	3	657.807	223.238
	4	1986.725	47.408
	5	203.379	98.651
	6	1468.306	162.529
ECR L	1	404.429	29.899
	2	852.864	84.362
	3	453.908	133.265
	4	1886.114	101.193
	5	239.960	90.248
	6	1354.017	108.891
FDS R	1	68.461	1.788
	2	330.485	9.662
	3	186.523	2.228
	4	117.025	0.027
	5	277.976	4.777
	6	1133.756	45.737
FDS L	1	52.755	2.168
	2	267.712	101.051
	3	233.418	1.656
	4	113.434	0.282
	5	310.628	3.540
	6	623.081	41.090
TA R	1	101.837	7.528
	2	36.753	19.914
	3	9.944	0.000
	4	0.000	0.310
	5	0.000	1.434
	6	111.089	3.386
TA L	1	0.000	0.594
	2	38.879	3.316
	3	0.000	0.193
	4	0.000	0.270
	5	0.000	0.634
	6	155.538	15.364
SOL R	1	53.101	0.165
	2	241.119	3.571
	3	8.128	1.069
	4	0.000	0.364
	5	0.000	0.528
	6	131.866	5.358
SOL L	1	0.000	1.139
	2	102.824	1.009
	3	0.000	0.086
	4	0.000	0.384
	5	0.000	0.395
	6	84.788	10.787

APPENDIX D: Analysis

1. MEP analysis (ANOVA and post-hoc tests)
    - MEPs by motor score
    - Latency analysis
    - MEPs vs. AIS motor scores correlation: Spearman test
    - Antagonist MEP analysis

      ECR vs. FCR

      FDS vs. Ext. Dig.

      TA vs. SOL

      SOL vs. TA
2. AIS motor scores (ANOVA and post-hoc tests)
    - 4 key muscles
    - 6 key muscles
3. nRMS analysis (ANOVA and post-hoc tests)
    - nRMS by motor score
    - nRMS vs. AIS motor scores correlation: Spearman test
    - Additional muscle activity (Channel analysis)
4. MEPs vs. nRMS correlation: Pearson test

1. MEP analysis

REPEATED MEASURES ANOVA
1-MUSCLE, 2- SIDE OF THE BODY R/L, 3-CONDITION

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**3**	**5401273.000**	**15**	**726834.313**	**7.43123**	**0.00281**
2	1	43971.703	5	24237.305	1.81422	0.23583
3	**2**	**4119638.500**	**10**	**519924.781**	**7.92353**	**0.00867**
12	3	12728.335	15	30461.520	0.41785	0.74278
13	**6**	**1994764.750**	**30**	**408536.313**	**4.88271**	**0.00137**
23	2	108242.734	10	91691.773	1.18051	0.34652
123	6	48705.891	30	99262.500	0.49068	0.81007

Probabilities for Post Hoc Tests

Tukey HSD test
MAIN EFFECT: MUSCLE

	ECR 866.3629	FDS 309.6045	TA 37.83672	SOL 51.81887
ECR		0.06163108	**0.0045867**	**0.005241513**
FDS	0.06163108		0.54605019	0.587060094
TA	**0.0045867**	0.54605019		0.999884367
SOL	**0.00524151**	0.58706009	0.99988437	

Tukey HSD test
MAIN EFFECT: CONDITION

	TH 93.28427	REST 207.7656	20% OF MVC 648.1673
TH		0.7244668	**0.00946522**
REST	0.7244668		**0.03325427**
20% OF MVC	**0.00946522**	**0.03325427**	

Tukey HSD test

INTERACTION: MUSCLE X CONDITION

	ECR			FDS			TA			SOL		
	TH	REST	20% MVC	TH	REST	20% MVC	TH	REST	20% MVC	TH	REST	20% MVC
	179.5	558.3	1861.4	122.3	212.5	594.0	35.3	21.3	56.9	36.0	39.0	80.4
	1	2	3	4	5	6	7	8	9	10	11	12
1		0.94	**1.5E-04**	1	1	0.9	1	1	1	1	1	1
2	0.94		**1.3E-03**	0.87	0.97	1	0.69	0.65	0.74	0.69	0.7	0.79
3	**1.5E-04**	**1.3E-03**		**1.4E-04**	**1.6E-04**	**1.8E-03**	**1.4E-04**	**1E-04**	**1.4E-04**	**1.4E-04**	**1.4E-04**	**1.4E-04**
4	1	0.87	**1.4E-04**		1	0.8	1	1	1	1	1	1
5	1	0.97	**1.6E-04**	1		0.94	1	1	1	1	1	1
6	0.9	1	**1.8E-03**	0.8	0.94		0.6	0.57	0.65	0.6	0.61	0.71
7	1	0.69	**1.4E-04**	1	1	0.6		1	1	1	1	1
8	1	0.65	**1.4E-04**	1	1	0.57	1		1	1	1	1
9	1	0.74	**1.4E-04**	1	1	0.65	1	1		1	1	1
10	1	0.69	**1.4E-04**	1	1	0.6	1	1	1		1	1
11	1	0.7	**1.4E-04**	1	1	0.61	1	1	1	1		1
12	1	0.79	**1.4E-04**	1	1	0.71	1	1	1	1	1	

- **MEPs according to motor score**

1 WAY ANOVA

1-MEPs between score analysis

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**3**	**6043448.5**	**44**	**971553.5**	**6.220397**	**0.001290349**

Probabilities for Post Hoc Tests

Unequal N HSD

MAIN EFFECT: MEP

	MEPs at 0 score 63.49947	MEPs at 1 score 127.4796	MEPs at 4 score 1313.251	MEP at 5 score 1317.371
MEPs at 0 score		0.99926782	0.06823117	**0.00846374**
MEPs at 1 score	0.99926782		0.09083581	0.089212358
MEPs at 4 score	0.06823117	0.09083581		0.999999821
MEP at 5 score	**0.00846374**	0.08921236	0.99999982	

- **MEP latency analysis**

REPEATED MEASURES ANOVA: LATENCY ANALYSIS
1-CONDITION, 2-UPPER / LOWER LIMB

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**2**	**3.0767E-06**	**2**	**7.46484E-08**	**41.2155952**	**0.023687929**
2	**1**	**0.00248508**	**1**	**1.1975E-05**	**207.522202**	**0.044121649**
12	2	1.8641E-06	2	6.06654E-07	3.07276082	0.245533705

Probabilities for Post Hoc Tests
Tukey HSD test
MAIN EFFECT: CONDITIO

	TH .0300375	REST .0316625	20% OF MVC .0302781
TH		**0.02534217**	0.53996718
REST	**0.02534217**		**0.03450489**
20% OF MVC	0.53996718	**0.03450489**	

Tukey HSD test
MAIN EFFECT: UPPER/LOWER LIMB MUSCLES

	UPPER LIMB .0162688	LOWER LIMB .0450500
UPPER LIMB		**0.04439944**
LOWER LIMB	**0.04439944**	

- **Correlation analysis: MEPs vs. AIS motor scores**

At threshold
Spearman Rank Order Correlations
MEPs & AIS

		N	Spearman R	t(N-2)	p-level
MEPs	**& AIS**	**48**	**0.74519449**	**7.57918024**	**1.24212E-09**

At rest
Spearman Rank Order Correlations
MEPs & AIS

		N	Spearman R	t(N-2)	p-level
MEPs	**& AIS**	**48**	**0.71901059**	**7.01665211**	**8.60298E-09**

At 20% of MVC
Spearman Rank Order Correlations MEPs & AIS

		N	Spearman R	t(N-2)	p-level
MEPs	**& AIS**	**48**	**0.79016227**	**8.74394035**	**2.42685E-11**

- **Antagonist MEPs analysis**

$ECR_{agonist}$ vs. $FCR_{antagonis}$

Repeated Measures ANOVA
Summary of all Effects
1-GROUP (agonist/antagonist), 2-CONDITION (th, rest, 20% of MVC), 3-SIDE (R/L)

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**1**	**10368262**	**5**	**1278849.5**	**8.10749149**	**0.035934553**
2	**2**	**5035171.5**	**10**	**745132.8125**	**6.75741434**	**0.01390884**
3	1	4759.75098	5	52707.92969	0.09030426	0.775884449
12	**2**	**4327042.5**	**10**	**758201.0625**	**5.70698547**	**0.022208231**
13	1	6198.13086	5	10529.2627	0.58865762	0.477584392
23	2	86032.9375	10	200635.5156	0.42880216	0.662719786
123	2	150773.047	10	164840.8281	0.91465843	0.431719512

Probabilities for Post Hoc Tests
Tukey HSD test: MEP
MAIN EFFECT: GROUP (agonist/antagonist)

	ECR	FCR
	866.3629	107.4067
ECR		**0.03612608**
FCR	**0.03612608**	

$FDS_{agonist}$ vs. Ext. $Dig._{antagonist}$

Summary of all Effects
1-GROUP, 2-CONDITION, 3-SIDE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	3713645.75	5	3005948.75	1.23543215	0.316921443
2	**2**	**4578016.5**	**10**	**983402.75**	**4.65528107**	**0.037241351**
3	1	59902.5039	5	278840.4375	0.21482717	0.662486374
12	2	847184.063	10	1207138	0.70181215	0.518543839
13	1	13956.1807	5	342695.125	0.04072477	0.848023713
23	2	297800.656	10	51506.99609	5.78175116	0.021448825
123	2	121754.641	10	111976.3359	1.08732474	0.373867452

Probabilities for Post Hoc Tests
Tukey HSD test
MAIN EFFECT: GROUP

	FDS	Ext Dig
	309.6045	763.8221
FDS		0.31711316
Ext. Dig	0.31711316	

$TA_{agonist}$ vs. $SOL_{antagonist}$

Summary of all Effects
1-GROUP, 2-CONDITION, 3-SIDE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	5665.29199	5	50632.76953	0.11188983	0.751577973
2	2	23510.1934	10	14293.80078	1.64478254	0.241238222
3	1	2928.30176	5	2369.806885	1.23567116	0.316879362
12	2	5883.84473	10	10261.29492	0.57340181	0.58109647
13	1	64.1000671	5	2128.270996	0.03011838	0.869029164
23	2	761.112549	10	1120.183716	0.67945337	0.528831482
123	2	464.26358	10	736.2206421	0.63060385	0.552173018

Probabilities for Post Hoc Tests
Tukey HSD test
MAIN EFFECT: GROUP

	TA	SOL
	37.83672	55.57758
TA		0.75174731
SOL	0.75174731	

$SOL_{agonist}$ vs. $TA_{antagonist}$

Summary of all Effects
1-GROUP, 2-CONDITION, 3-SIDE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	2931.601074	5	14086.10938	0.20812	0.667376161
2	2	15380.49512	10	4979.485352	3.08877206	0.090247884
3	1	28163.42578	5	11531.22949	2.44236112	0.178860053
12	2	7.282653332	10	4997.196289	0.00145735	0.998543918
13	1	42.9613533	5	6958.69043	0.00617377	0.940419614
23	2	11256.54102	10	4012.343994	2.80547762	0.107858062
123	2	327.6980591	10	4011.455322	0.08169056	0.922165632

Probabilities for Post Hoc Tests
Tukey HSD test
MAIN EFFECT: GROUP

	SOL	TA
	51.81887	39.05695
SOL		0.66755688
TA	0.66755688	

2. AIS motor scores

- **For 4 key muscles (comparisons with MEPs)**

REPEATED MEASURES ANOVA
Summary of all Effects
1-SIDE (R/L), 2-MUSCLES

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	0.083333336	5	0.033333335	2.5	0.174687803
2	**3**	**38.30555725**	**15**	**3.555555582**	**10.7734375**	**0.00049803**
12	3	0.083333336	15	0.033333335	2.5	0.099081926

Probabilities for Post Hoc Tests

Tukey HSD test
MAIN EFFECT: MUSCLE

	ECR 4.67	FDS 2.67	TA .83	SOL 1
ECR		**0.084493577**	**0.000992775**	**0.00141871**
FDS	**0.08449358**		0.123789668	0.178074837
TA	**0.00099277**	0.123789668		0.996326268
SOL	**0.00141871**	0.178074837	0.996326268	

- **For 6 ley muscles (comparisons with nRMS)**

REPEATED MEASURES ANOVA
1-MUSCLE score, 2-SIDE R/L

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**5**	**37.7472229**	**25**	**3.053888798**	**12.3603783**	**4.2105E-06**
2	1	0.125	5	0.058333334	2.14285707	0.203110695
12	5	0.058333334	25	0.031666666	1.84210527	0.140996695

Probabilities for Post Hoc Tests

Tukey HSD test
MAIN EFFECT: MUSCLE score

	Bi 5	Tri 3.42	ECR 4.67	FDS 2.67	TA .83	SOL 1
Bi		0.26453292	0.99691957	**0.03301102**	**0.00018126**	**0.00022876**
Tri	0.26453292		0.51256216	0.89567608	**0.01473248**	**0.02533132**
ECR	0.99691957	0.51256216		0.09000272	**0.00030577**	**0.00045401**
FDS	**0.03301102**	0.89567608	0.09000272		0.14246553	0.21750242
TA	**0.00018126**	**0.01473248**	**0.00030577**	0.14246553		0.99989837
SOL	**0.00022876**	**0.02533132**	**0.00045401**	0.21750242	0.99989837	

3. nRMS analysis

REPEATED MEASURES ANOVA
1-MUSCLE, 2-SIDE R/L

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**5**	**66962.10156**	**25**	**14068.73242**	**4.75964022**	**0.003424418**
2	1	155.5834656	5	4291.198242	0.03625642	0.856476486
12	5	2503.106201	25	1810.616821	1.38246036	0.264551461

Probabilities for Post Hoc Tests

Tukey HSD test
MAIN EFFECT: MUSCLE

	Bi 189.7794	Tri 46.54313	ECR 111.7584	FDS 17.83388	TA 4.411910	SOL 2.071140
Bi		0.065300643	0.59918189	**0.017373204**	**0.00901276**	**0.008023143**
Tri	0.06530064		0.75684011	0.990642369	0.95025063	0.938084543
ECR	0.59918189	0.75684011		0.403111875	0.26560187	0.245279431
FDS	**0.0173732**	0.990642369	0.403111875		0.99976462	0.99948436
TA	**0.00901276**	0.950250626	0.265601873	0.999764621		0.99999994
SOL	**0.00802314**	0.938084543	0.245279431	0.99948436	0.99999994	

- **nRMS according to motor score**

1 WAY ANOVA
1-nRMS at a given ASIA MOTOR SCORE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**5**	**48425.07813**	**66**	**8877.374023**	**5.45488739**	**0.000292114**

Probabilities for Post Hoc Tests

Unequal N HSD
MAIN EFFECT: nRMS by motor score

	nRMS at 0 1.842208	nRMS at 1 1.945429	nRMS at 2 10.82630	nRMS at 3 20.15289	nRMS at 4 43.80469	nRMS at 5 125.4091
grade 0			1 0.999997139	0.999993503	0.94748676	**0.002785265**
grade 1		1	0.999997258	0.999993682	0.94801706	0.050734043
grade 2	0.99999714	0.999997258		0.999999762	0.99812907	0.672156632
grade 3	0.9999935	0.999993682	0.999999762		0.99997681	0.968349278
grade 4	0.94748676	0.948017061	0.99812907	0.999976814		0.51602751
grade 5	**0.00278527**	0.050734043	0.672156632	0.968349278	0.51602751	

- **Correlation analysis: nRMS vs. AIS motor scores**

Spearman Rank Order Correlations

	N	Spearman R	t(N-2)	p-level
nRMS & AIS	**72**	**0.847160101**	**13.33963299**	**6.66005E-21**

- **Additional muscle activity analysis**

Bi assessment

Summary of all Effects
1-MUSCLE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**3**	**3305.5769**	**33**	**397.999329**	**8.30548382**	**0.000296877**

Tukey HSD test
MAIN EFFECT: MUSCLE

	baseline 0.000000	Tri 6.961158	FDS 32.94171	ECR 30.56466
		0.82789195	**0.00172448**	**0.00370425**
Tri	0.82789195		**0.01576728**	**0.03205723**
FDS	**0.00172448**	**0.01576728**		0.99125242
ECR	**0.00370425**	**0.03205723**	0.99125242	

Tri assessment

Summary of all Effects
1-MUSCLE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**3**	**751.594604**	**33**	**109.785736**	**6.84601307**	**0.00103305**

Tukey HSD test
MAIN EFFECT: MUSCLE

	baseline 0.000000	Bi 4.440002	FDS 9.096284	ECR 18.48920
		0.72871935	0.16595143	**0.00086439**
Bi	0.72871935		0.69895953	**0.0124349**
FDS	0.16595143	0.69895953		0.14553887
ECR	**0.00086439**	**0.0124349**	0.14553887	

ECR assessment

Summary of all Effects
1-MUSCLE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**3**	**228.199326**	**33**	**36.4027138**	**6.26874495**	**0.001735323**

Tukey HSD test
MAIN EFFECT: MUSCLE

	baseline	Bi	Tri	FDS
	0.000000	9.316259	3.256811	8.248010
		0.00342983	0.55583787	**0.01056862**
Bi	**0.00342983**		0.08552027	0.97228748
Tri	0.55583787	0.08552027		0.19915932
FDS	**0.01056862**	0.97228748	0.19915932	

FDS assessment

Summary of all Effects
1-MUSCLE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**3**	**1481.02954**	**33**	**175.123657**	**8.45705032**	**0.000262119**

Tukey HSD test
MAIN EFFECT: MUSCLE

	baseline	Bi	Tri	ECR
	0.000000	8.444434	1.313906	24.19601
		0.41307914	0.99490333	**0.0006063**
Bi	0.41307914		0.55729043	**0.03075057**
Tri	0.99490333	0.55729043		**0.00106627**
ECR	**0.0006063**	**0.03075057**	**0.00106627**	

TA assessment

Summary of all Effects
1-MUSCLE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	**2**	**10.3795233**	**22**	**1.16750836**	**8.89031982**	**0.00147999**

Tukey HSD test
MAIN EFFECT: MUSCLE

	baseline	SOL	GA
	0.000000	1.705606	1.495502
		0.00241482	**0.00722444**
SOL	**0.00241482**		0.88318008
GA	**0.00722444**	0.88318008	

SOL assessment

Summary of all Effects
1-MUSCLE

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	2	42.626564	22	22.5211887	1.89273155	0.17439146

Tukey HSD test
MAIN EFFECT: MUSCLE

	baseline	TA	GA
	0.000000	3.762438	2.080435
		0.15085399	0.53987962
TA	0.15085399		0.6655643
GA	0.53987962	0.6655643	

4. Correlation analysis nRMS vs. MEPs

MEPs at threshold vs. nRMS

Pearson correlation
Marked correlations are significant at p < .05000

	Mean	Std.Dv.	r(X,Y)	r^2	t	p	N
MEPS	93.28427083	86.96366102					
nRMS	34.01884463	54.177773	**0.741174921**	0.549340263	7.48816236	1.70E-09	48

MEPs at rest vs. nRMS

Pearson correlation
Marked correlations are significant at p < .05000

	Mean	Std.Dv.	r(X,Y)	r^2	t	p	N
MEPS	207.765646	353.099016					
nRMS	34.0188446	54.177773	**0.544066182**	0.29600801	4.397914565	6.4E-05	48

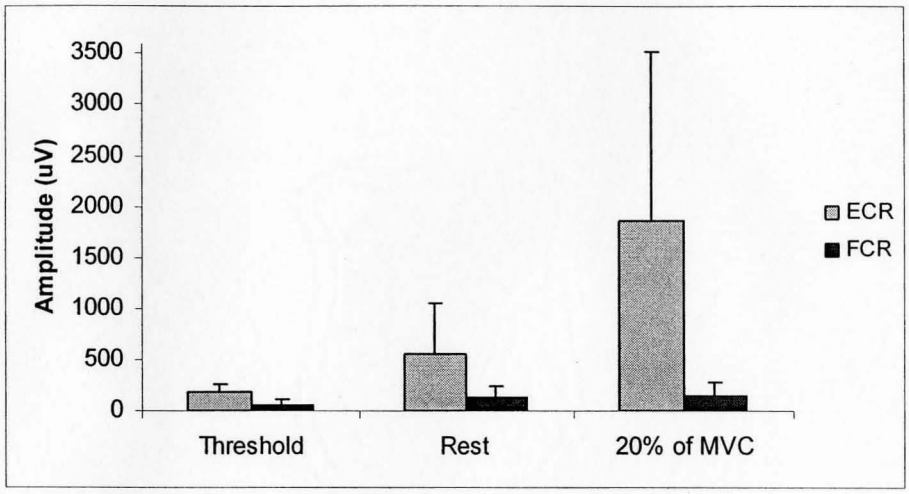
MEPs at 20% of MVC vs. nRMS

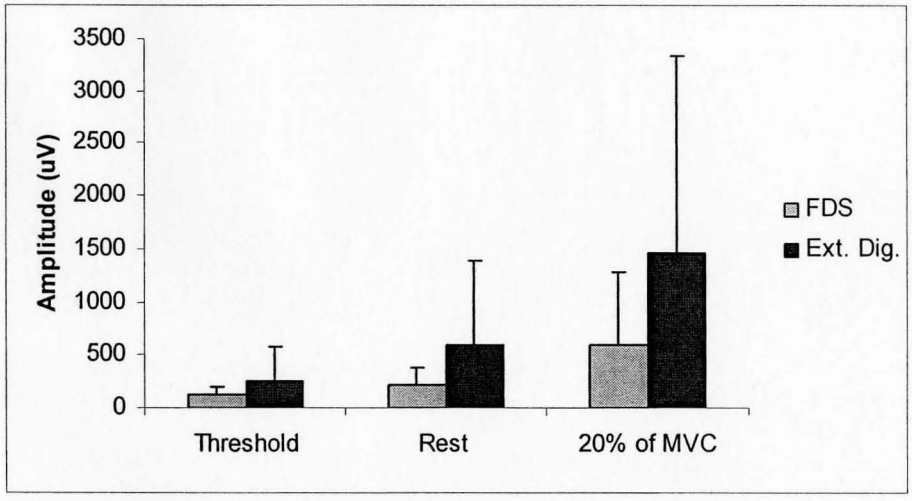
Pearson correlation
Marked correlations are significant at p < .05000

	Mean	Std.Dv.	r(X,Y)	r^2	t	p	N
MEPS	661.914713	1146.37657					
nRMS	34.7426453	54.5284072	**0.515578167**	0.265820846	4.03645161	2.E-04	48

APPENDIX E: Antagonist/Agonist MEPs

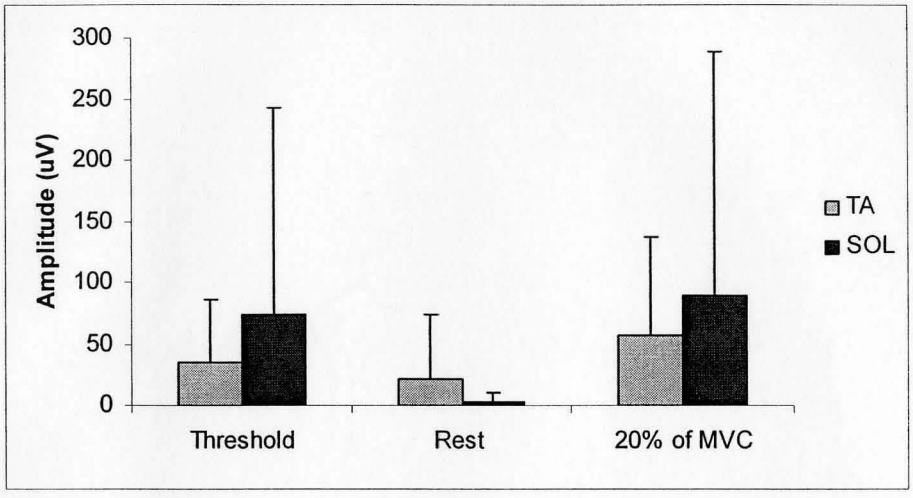
- Agonist/antagonist MEPs in upper limbs:

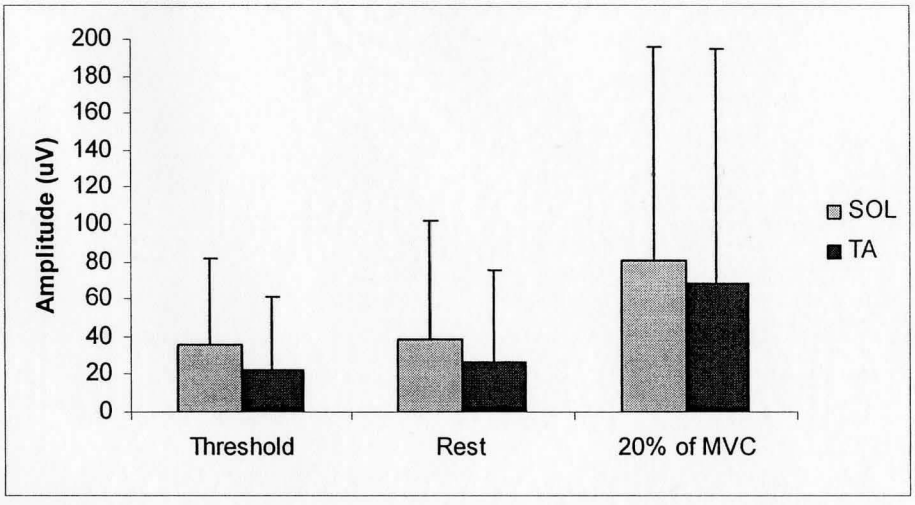




FCR or antagonist (■) activity during ECR or agonist (▨) stimulation was present throughout the trials, but was not significant. In contrast, antagonist Ext. Dig. MEPs were larger than the agonist MEPs across condition.

- Agonist/antagonist MEPs in lower limbs:





Antagonist (■) activity in lower limbs was always present and mirrored agonist (▨) MEPs.