Practice Related Plasticity: Functional and Cortical Changes in Individuals with Spinal Cord Injury Following Four Different Hand Training Interventions

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PRACTICE RELATED PLASTICITY: FUNCTIONAL AND CORTICAL CHANGES IN INDIVIDUALS WITH CERVICAL SPINAL CORD INJURY FOLLOWING FOUR DIFFERENT HAND TRAINING INTERVENTIONS.

By

Larisa Reed Hoffman

A DISSERTATION

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PRACTICE RELATED PLASTICITY: FUNCTIONAL AND CORTICAL CHANGES IN INDIVIDUALS WITH CERVICAL SPINAL CORD INJURY FOLLOWING FOUR DIFFERENT HAND TRAINING INTERVENTIONS.

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Injury to the cervical spinal cord results in complete or partial loss of arm and hand function, severely limiting the performance of daily activities. Deficits in hand function in individuals with cervical spinal cord injury (SCI) are primarily due to a loss of descending motor pathways that are vital for fine control of the hand and fingers. In addition to these deficits, secondary plastic reorganization may create further loss of function. This thesis will explore the following questions: 1. What are the similarities and differences between cortical organization of muscles affected by a cervical SCI to those not affected by the injury?; 2. Do individuals with cervical SCI improve in hand function and cortical organization after an intensive hand training intervention?; 3. Which physical therapy intervention provides the optimal conditions by which to improve hand function following cervical SCI?

In chapter 2 we compare cortical motor maps of transcranial magnetic stimulation (TMS) evoked responses of muscles rostral and caudal to the injury to those of ND
individuals. The cortical maps of the biceps brachii or the thenar muscles were constructed, and compared between ND individuals and individuals with SCI. The motor threshold (MT) for the thenar muscles in individuals with SCI was significantly higher than ND individuals.

The purpose of the study described in chapter 3 was to compare the functional and cortical changes associated with two different interventions: unimanual or bimanual massed practice training, both combined with somatosensory stimulation. There was a significant difference between pre- and post-intervention scores on tests measuring unimanual hand function, bimanual hand function, and sensory function. This difference was associated with a difference between pre- and post-intervention cortical map area.

The purpose of the study described in chapter 4 was to compare clinical and cortical changes associated with either a delayed intervention control period or a combined intervention of massed practice training with electrical stimulation. Participants were randomly assigned to one of two groups: delayed intervention control group or immediate intervention group. Participants were also randomly assigned to one of four groups: unimanual training with somatosensory stimulation, bimanual training with somatosensory stimulation, unimanual training with functional electrical stimulation, or bimanual training with functional electrical stimulation. There was a significant difference between the control and immediate intervention group on the test measuring unimanual hand function. Participants in the bimanual group performed significantly better on the test measuring bimanual hand function. There was a significant difference between the control group and immediate intervention group in cortical map area.
In chapter 5 we discuss the clinical relevance of the results of the studies described in three prior chapters. Conclusions drawn include the idea that cortical maps of muscles caudal to the level of injury in individuals with SCI have higher motor thresholds than ND participants. Individuals with tetraplegia can improve in hand function and sensation with a physical therapy intervention of massed practice training combined with somatosensory stimulation. Finally, the type of training (unimanual massed practice or bimanual massed practice) influences the type of improvements gained, however the type of electrical stimulation does not influence the clinical outcome.
This dissertation is dedicated to all of the wonderful research participants who dedicated their time, effort, and heart into participating in these research studies. I cannot thank these individuals enough for the enormous amount of time and effort they put forth during both the intervention and evaluation portions of these studies. Research cannot occur without the dedication of those individuals who are willing to give to science.
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CHAPTER 1: ETIOLOGY OF UPPER EXTREMITY DYSFUNCTION AND INTERVENTIONS THAT OPTIMIZE ARM AND HAND FUNCTION IN INDIVIDUALS WITH CERVICAL SCI

The most common form of spinal cord injury (SCI) is injury to the cervical spinal cord\(^1\). Cervical SCI commonly results in impaired arm and hand function which impacts an individual’s ability to participate in self care, work, and recreational activities. Many individuals with tetraplegia cite recovery of arm and hand function as the most important goal during rehabilitation\(^2,3\). In a survey of 681 individuals with chronic SCI, 48.7% of the individuals with tetraplegia stated that regaining arm and hand function would be the single factor that would most improve their quality of life\(^2\). In another report, 77% of individuals with tetraplegia stated they expected a significant change in their quality of life if they regained hand function\(^3\). Therefore, improving arm and hand function should be a compelling goal for rehabilitation specialists working with individuals with cervical SCI. Strategies designed to improve arm and hand function should address sensorimotor impairments and activity limitations associated with cervical SCI, but should also address the neurophysiological changes that accompany the injury.

On the surface, the mechanisms underlying upper extremity dysfunction following SCI seem unambiguous. Information from the cortex is essential for functional arm and hand movement, and damage to the spinal tracts limits the amount and rate of transmission of information from the cortex to the muscle\(^4\). Damage to spinal tracts then leads to impaired activation of intrinsic hand muscles, impaired sensory perception of the arm and hand, and disrupted modulation of muscle tone\(^5,7\). However, beyond damage to the spinal tracts, evidence suggests that maladaptive plastic reorganization of the central nervous system is associated with upper extremity dysfunction in individuals with
cervical SCI\textsuperscript{5,6,8-10}. It is possible plastic reorganization decreases the effectiveness of the remaining corticospinal tract connections. We define neuroplastic reorganization as a neuroanatomical or neurophysiological change in the nervous system associated with injury or learning.

**Cortical Reorganization in Individuals with Cervical SCI**

*Learned Non-use.* Learned non-use is a phenomenon most commonly associated with stroke. It is the result of failed attempts to use the more affected arm early after injury when the state of the nervous system is such that there is hypotonicity of the extremities. Later, the nervous system begins to recover from the insult and some upper extremity function might be possible, but the individual does not attempt to use the arm since prior attempts were unsuccessful. In those with cortical damage, decreased use is associated with cortical reorganization wherein the hand region of the motor cortex is invaded by areas representing more proximal arm control\textsuperscript{11,12}. This reorganization may be detrimental to function. There is much evidence now available to indicate that this detrimental cortical reorganization is reversible through mechanisms of practice-dependent plasticity.

*Decreased Cortical Motor Representation.* Investigations with functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS), and electroencephalography (EEG) have identified profound cortical reorganization in individuals with SCI\textsuperscript{4,13-20}. Neuroimaging techniques have demonstrated that individuals with tetraplegia have significantly less activation of cortical motor areas than either individuals with paraplegia or non-disabled (ND) individuals\textsuperscript{16}. Further, individuals with
greater upper extremity deficits have less activation of supplementary motor area, sensorimotor area, and ipsilateral cerebellum\textsuperscript{16}. Not only is there less total cortical motor activity, muscles distal to the injury have less cortical motor representation\textsuperscript{19}, and the more proximal musculature expand into the areas that typically control more distal muscles\textsuperscript{13}. Thus, individuals with tetraplegia have smaller cortical motor arm and hand representation relative to both non-disabled individuals and individuals with paraplegia.

\textit{Decreased Cortical Motor Excitability}. Neurophysiologic investigations have established that muscles affected by the SCI have less cortical motor excitability\textsuperscript{10}. This decreased cortical motor excitability in individuals with SCI may be due to the combination of deafferentation and deafferentation. Studies investigating the impact of blocking afferent input\textsuperscript{21,22} or voluntary movement of the arm\textsuperscript{23} in non-disabled individuals have both demonstrated that decreased sensory input and decreased movement are associated with less cortical excitability. Blocking afferent input through either local anesthetic block\textsuperscript{21} or ischemic nerve block\textsuperscript{22} decreases the cortical motor excitability of the muscles associated with that segment\textsuperscript{21,22}. Likewise, reducing movement also results in decreased cortical motor excitability. Immobilization of the wrist due to an orthopedic injury, results in decreased excitability in the motor cortex for the region of the affected segment\textsuperscript{23}. One of the consequences of decreased movement is decreased movement-related afferent input to the sensory cortex, which may contribute to decreased cortical motor excitability. Individuals with cervical SCI have varying degrees of deafferentation due to the damage of ascending pathways, decreased voluntary movement due to the damage of the descending pathways, as well as loss of movement.
related afferent information; all of which are associated with decreased cortical motor excitability.

**Impaired Somatosensory System.** Disrupted sensory input and decreased movement related afferent information, also induces cortical reorganization within the sensory cortex, specifically S1\(^24\). Individuals with cervical SCI have significantly less gray matter in the hand and leg region within S1 compared to non-disabled individuals\(^25\). It is thought that the atrophy of this region is a secondary plastic change due to the decrease in afferent input and not a direct result of the injury\(^25\). In addition to the atrophy of S1, the secondary sensory association areas (S2 and S3) also undergo plastic reorganization, such that the more proximal sensory regions of the sensory cortex (such as the face) invade the more distal regions (such as the arm and hand)\(^26\). This reorganization is similar to that which is seen in the cortical motor system, and like the motor system, may be modifiable with rehabilitation interventions.

**Cortical Representations are Located in a More Posterior Location.** In addition to the reduction in size of the hand region of the sensorimotor cortices, there is evidence from EEG to suggest that the location of the cortical representations is more posterior in individuals with SCI, compared to non-disabled individuals. It is possible that individuals with SCI may rely more heavily on other cortical areas that contribute to the corticospinal tract, such as the sensory cortex\(^17,18\). In intact animals, the sensory cortex makes a considerable contribution to the corticospinal tract\(^27,28\). While the purpose of projections from the sensory cortex to the corticospinal tract are primarily to modulate proprioceptive information\(^39\), the system may demonstrate plasticity by utilizing these spared projections in the absence of a more direct pathway from motor areas. Further,
there is evidence that with recovery, the hand representation shifts back to its more
typical anterior position\textsuperscript{18}.

\textit{Impaired Cortical Drive.} The cortical motor reorganization that occurs after SCI
also negatively affects muscle recruitment patterns, specifically in the hand musculature.
In non-disabled individuals, low levels of muscle contraction (10\% maximum voluntary
contraction) of hand musculature significantly increase the motor output from the motor
cortex, but further increases in muscle contraction do not increase cortical motor
excitability\textsuperscript{10}. In individuals with cervical SCI, the increase in motor response is not seen
until a much larger muscle contraction is created (50\% maximum voluntary
contraction)\textsuperscript{10}. It is possible that those muscles with less voluntary drive are not able to
recruit all motoneurons available for that muscle\textsuperscript{30} such that it requires more voluntary
effort to produce the same level of force as non-disabled individuals. Therefore
individuals with tetraplegia must use greater effort over a similar force range than non-
disabled individuals.

\textit{Decreased Intracortical Inhibition.} As a consequence of their injury, individuals
with incomplete cervical SCI have less cortical drive\textsuperscript{10} which may also lead to adaptive
changes in inhibitory cortical circuits\textsuperscript{9}. Compared to non-disabled individuals, individuals
with incomplete cervical SCI have less intracortical inhibition to the corticospinal tract,
specifically to intrinsic hand muscles\textsuperscript{9}. It has been suggested that a decrease in
intracortical inhibition is an adaptive mechanism at the level of the cortex to increase the
descending cortical drive\textsuperscript{31}. Further support for this conclusion is provided from
individuals with stroke who also exhibit loss of intracortical inhibition in both the
affected and non-affected cortex\textsuperscript{32,33}, with greater loss of intracortical inhibition seen in
the affected hemisphere\textsuperscript{32}. While the role of intracortical inhibition is not known, it has been hypothesized that this inhibitory network is involved in the plastic changes of muscle representation that occur within the motor cortex\textsuperscript{32}.

**Spinal Cord Reorganization in Individuals with Cervical SCI**

*Impaired Modulation of Spinal Reflexes.* Following cervical SCI, hyperreflexia or spasticity in the upper extremities is detrimental to upper limb function both limiting performance of activities and causing pain. Spasticity is most frequently defined in the literature as “a motor disorder characterized by a velocity dependent increase in tonic stretch with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex”\textsuperscript{7,34,35}. However, an increase in stiffness does not completely describe the impairments, as the presence of spasticity is also related to the loss of motor functions such as muscle power and coordination\textsuperscript{7}. In an investigation including 354 individuals with SCI, problematic spasticity was correlated with incomplete cervical SCI; of these individuals, 60% experienced spasticity in their upper extremities\textsuperscript{7}. The mechanisms behind spasticity are thought to be partially related to the loss or disruption of normal supraspinal influence over multiple spinal reflexes including reciprocal inhibition, presynaptic inhibition, and recurrent inhibition\textsuperscript{34-36}.

*Decreased Excitability of Spinal Motoneurons.* In addition to the disruption of spinal reflex circuits, there is decreased excitability of the spinal motor neuron\textsuperscript{37}. This change in excitability at the spinal level, in individuals with cervical SCI, may contribute to upper extremity weakness; thereby decreasing arm and hand function.
Lower Motoneuron Damage. Injury to the cervical spinal cord may also result in damage to the motoneuron or final common pathway. In a study investigating the integrity of the peripheral motor nerve in individuals with cervical SCI, more than 50% had a reduced or absent muscle response to maximal stimulation to the peripheral nerve (m-wave)\textsuperscript{37}. The reduced motor response is likely related to damage to the motoneuron or spinal nerve root. With recovery of injury, residual motoneurons may sprout new connections to compensate for the loss\textsuperscript{30}. However, sprouting of new connections results in the creation of large motor units, and decreases the number of motoneurons per muscle fiber\textsuperscript{38,39}. Maintaining a high ratio of motoneurons to muscle fibers is vital for grading muscle force\textsuperscript{40}, and altering this ratio may result in the inability to grade of movement\textsuperscript{41}.

Implications from Cortical and Spinal Reorganization in Individuals with Cervical SCI. Many neurological factors appear to contribute to the deficits in arm and hand function in individuals with cervical SCI, and some maybe modifiable with practice and motor learning. To determine the mechanism by which recovery of function occurs in individuals with cervical SCI, we must measure the neurophysiological responses that are hypothesized to be most responsive to practice.

Influence of Severity of Injury on Arm and Hand Function in Individuals with Cervical SCI

For individuals with cervical SCI, factors used to identify prognosis of recovery of arm and hand function include severity of injury and the neurological level of injury\textsuperscript{42}. As would be expected, individuals with incomplete cervical SCI demonstrate greater motor recovery than individuals with complete SCI\textsuperscript{6,43}. Recovery of upper limb function is almost two times greater in individuals with incomplete SCI than individuals with
complete SCI\textsuperscript{43}. It is possible that individuals with motor complete injury have less recovery because they are less likely to have voluntary control over intrinsic hand muscles, which are important indicators of future hand function\textsuperscript{5,6}.

\textit{Motor Incomplete Cervical SCI.}

\textbf{Functional Recovery in Individuals with Motor Incomplete Cervical SCI.} Of individuals who have tetraplegia, individuals with motor incomplete cervical SCI have the greatest potential for recovery of upper extremity function\textsuperscript{42-44}, and recovery of function at the next caudal level occurs much faster in individuals with motor incomplete SCI\textsuperscript{45}. Waters et al.\textsuperscript{46} found in individuals with motor incomplete cervical SCI, muscles that had a score of two out of five at one month post-injury were 100\% likely to be move against gravity at one year post-injury. Further, 73\% of muscles that had an initial score of one out of five were able to move against gravity at one year post-injury, and 20\% of muscles that had an initial score of zero out of five were able to move against gravity at one year post-injury\textsuperscript{46}. In these individuals, functional recovery of the upper extremities plateaus around nine to twelve months\textsuperscript{44,47}.

\textit{Incomplete Syndromes.} Individuals with incomplete cervical SCI can be further characterized according to the distribution of their sensorimotor scores and classified into syndromes: Central Cord, Brown-Sequard, and Anterior Cord\textsuperscript{48,49}. Earlier versions of the International Classification System for Individuals with Spinal Cord Injury also included Posterior Cord syndrome and Mixed syndrome, but these were eliminated due to the low incidence of posterior cord syndrome and indefinable nature of Mixed syndrome\textsuperscript{48}. Among individuals with incomplete SCI, those individuals classified as having either
central cord syndrome or Brown-Sequard syndrome have the best prognosis for recovery.\textsuperscript{50}

Central cord syndrome is characterized by greater upper extremity than lower extremity dysfunction.\textsuperscript{48} Many individuals that fall into this classification make dramatic improvements in their ASIA sensorimotor scores.\textsuperscript{51} One investigation of 112 individuals with central cord syndrome found that two years post-injury, the average ASIA motor score was 92 out of a total 100.\textsuperscript{51} While the prognosis for functional recovery is good for individuals with central cord syndrome, the pattern is such that intrinsic hand function is the last to recover.\textsuperscript{52,53} Further, many individuals with only minor impairment in sensorimotor scores demonstrate moderate to severe limitations in the performance of functional activities.\textsuperscript{51} In individuals with central cord syndrome, many factors influence the amount of motor recovery, return of functional skills, and perceived health-related quality of life. Factors that predict recovery in individuals with central cord syndrome include: level of education, presence of spasticity, and age; where a higher level of education, absence of spasticity, and younger age was positively correlated with improved functional outcome.\textsuperscript{51} It is possible that individuals with higher level of education, who are older, are more likely to seek out intensive rehabilitation; whereas individuals of lower education who are also younger have fewer resources. The influence of spasticity on arm and hand function may be particularly devastating as medical interventions that are effective in the lower limb are not as effective in the upper limbs.

Brown-Sequard syndrome is characterized by ipsilateral hemiplegia, ipsilateral hypoesthesia, and contralateral hemianalgesia, and frequently caused by a penetrating injury.\textsuperscript{48} These clinical findings can be explained by the organization of the spinal
pathways, within the spinal column, where the cortical spinal tract and the dorsal column medial lemniscus decussate at the level of the brainstem, whereas the spinal thalamic pathway decussates at the root level where the nerves exit. Thus, for an individual who has Brown-Sequard syndrome, the pathways that carry light touch, deep pressure, and proprioceptive information, as well as motor information will be disrupted on the same side as the injury; whereas the pathways that carry pain and temperature will be disrupted on the opposite side of the injury. Most individuals classified under this syndrome have a relative asymmetry of symptoms and not a pure form of Brown-Sequard syndrome\textsuperscript{48}. One of the most important factors impacting functional recovery in individuals with Brown-Sequard syndrome is the preservation of motor function in the dominant hand\textsuperscript{54}.

Anterior cord syndrome is characterized by loss of function of anterior pathways (including motor function and sensation of pain and temperature), but relative preservation of the dorsal columns (including proprioception, light touch, and deep pressure)\textsuperscript{48}. Among individuals who are classified with an incomplete cervical SCI syndrome, those with anterior cord syndrome demonstrate less recovery than other incomplete syndrome classifications\textsuperscript{50}.

Implications from Individuals with Incomplete Cervical SCI. Individuals with incomplete SCI plateau in recovery around nine months. Therefore to investigate the impact of a physical therapy intervention, we should include individuals with chronic injury, as we can expect further recovery of function to be due to the intervention and not simply spontaneous neurological recovery. Further, individuals with incomplete SCI demonstrate the greatest potential for recovery and should be a target population for intervention studies.
**Motor Complete Cervical SCI.**

Functional Recovery in Individuals with Complete Cervical SCI. Individuals with complete cervical SCI frequently recover at least one level of sensory or motor function, with the greatest rate of recovery occurring within the first three months\(^43\). The level of injury may determine the relative amount of sensory or motor recovery in individuals with complete tetraplegia. Individuals with complete C4 SCI have much less likelihood of regaining sensorimotor function at the level C5 compared to individuals with a complete C5 SCI, who have a greater likelihood of regaining sensorimotor function at C6\(^55\). Further, the presence of initial voluntary muscle activation indicates the probability of achieving antigravity muscle strength for that muscle\(^43\). Only 27% of individuals with complete cervical SCI who initially had a motor score of zero out of five at the next caudal level, regained antigravity muscle activation at one year post-injury; whereas 97% of individuals with complete cervical SCI who initially had a motor score of one out of five at the next caudal level regained antigravity muscle strength\(^56\). In individuals with complete cervical SCI, functional recovery of upper limb function begins to plateau around 12-18 months\(^47,55,56\).

Functional Recovery in Individuals with Sensory Incomplete Cervical SCI. The presence of sensation at a motor level improves the probability of motor return at that level, especially if perception of pain is intact\(^57\). It is thought that the close proximity of the lateral spinal thalamic tract to the lateral corticospinal tract may indicate that if one is preserved the other may also be preserved. Thus, preservation of the perception of pain,
which would be relayed through the lateral spinal thalamic pathway may, indicate that other pathways that travel in the lateral columns may also be preserved.\textsuperscript{54}

**Implications from Individuals with Complete Cervical SCI.** Individuals with complete injury do demonstrate recovery of arm and hand function, but the amount of recovery is dependent on the presence of at least minimal voluntary control in those muscles targeted for improvement.\textsuperscript{5,6} Therefore, individuals with complete injury can be included in investigations of interventions, provided they have voluntary control over muscles targeted for the intervention (i.e.: intrinsic hand muscles).

**Physical Therapy Interventions**

In the presence of abnormal cortical and spinal organization, the cortex is likely to be less effective in activating the spared descending pathways. Therefore, interventions that focus on the reversal of the maladaptive plastic reorganization may improve the effectiveness of the remaining corticospinal connections in individuals with SCI. In the subsequent section, the effect physical therapy intervention strategies and their impact on function and cortical neurophysiology will be discussed.

**Interventions Aimed to Improved Function.** In task-oriented training, the goal is to practice and improve performance of the task. There are several different strategies that can be implemented that achieve this goal, but this discussion is limited to massed practice training including unimanual and bimanual training, and functional electrical stimulation (FES).

**Massed Practice Training.** Massed practice is a form of task-oriented training that involves repetitive practice of discrete motor tasks. The most thoroughly investigated
type of massed practice training is constraint-induced movement therapy in individuals with stroke. Constraint-induced movement therapy involves intensive, repetitive practice of task-oriented activities and shaping of the more affected upper extremity while the less affected upper extremity is constrained. However, some investigators believe it is the intensity of the practice that accounts for the greatest improvement in arm and hand function. Most constraint-induced movement therapy protocols require an intense training schedule: six hours per day, five days per week for two weeks. Beekhuizen and Field-Fote have investigated massed practice training in individuals with cervical SCI with a slightly less intensive training schedule: two hours per day, five days a week for three weeks. To ensure a variety of training activities, each session was divided into five, 20 minute sessions in which each 20 minute session was dedicated toward the performance of activities that focused on a different movement category. There were five movement categories: grip, grip with rotation, pinch, pinch with rotation, and gross motor. Following massed practice training, individuals with tetraplegia demonstrated improvements in arm and hand function.

**Changes in Function Following Massed Practice Training.** In individuals with hemiplegia due to stroke, massed practice training (combined with shaping) is associated with functional improvement as indicated by improvements on functional outcome measures. Likewise, individuals with cervical SCI who received massed practice training alone or in combination with somatosensory stimulation demonstrated improvements in sensory function, pinch grip force and timed unimanual tasks. Understanding the neurophysiological changes that are associated with skill acquisition in
different groups of participants can provide insight as to the mechanism in which individuals with SCI demonstrate functional recovery.

**Changes in Cortical Neurophysiology Following Massed Practice Training.**

Learning new specialized skills of fine motor movements is thought to be related to plastic reorganization of the motor cortex\textsuperscript{64}. Cortical motor reorganization can be investigated by measuring the motor response to a cortical stimulus (using transcranial magnetic stimulation (TMS))\textsuperscript{65,66}. An increase in the amplitude of the motor response in response to the same stimulus intensity would suggest an increase in cortical excitability. Likewise, a decrease in the required stimulus intensity to elicit a minimal motor response would also suggest an increase in cortical excitability\textsuperscript{65,66}. In non-disabled individuals, participation in a four week protocol of skill training has been shown to be associated with increased amplitude of biceps maximum motor evoked potential and decreased response threshold (level of stimulus required to elicit a minimum motor evoked potential)\textsuperscript{67}. This suggests that skill training is associated with increased corticospinal excitability, which may be important for improvements in performance.

Similar mechanisms are thought to underlie functional recovery in individuals with sensorimotor impairment. Several different investigations have provided evidence that the reversal of associated abnormalities in cortical organization is the mechanism underlying the effectiveness of massed practice training in individuals with stroke\textsuperscript{58,59,68,69}. Similar to the results seen in individuals post stroke, individuals with SCI who participated in massed practice training demonstrated cortical reorganization following the training. Beekhuizen and Field-Fote\textsuperscript{63,70} have shown that individuals with cervical SCI who were trained with either massed practice training, or with a combination
approach using massed practice with somatosensory stimulation, demonstrated increased
cortical excitability following the training.

**Implications from Massed Practice Training.** Learning new fine motor tasks is
thought to be related to cortical reorganization in non-disabled individuals and
individuals with impaired motor function. Therefore measuring cortical changes
associated with a task-oriented training intervention may explain any improvements in
function associated with the intervention.

**Bimanual Massed Practice Training.** Prior studies of massed practice training
have been limited to primarily unimanual task-oriented training\textsuperscript{63,70}. However,
individuals with SCI frequently have deficits in both upper limbs, and therefore may
benefit from bimanual training. In bilateral upper extremity tasks, the central nervous
system must control a greater number of degrees of freedom, resulting in greater cortical
activation\textsuperscript{71-73}. There is evidence that suggests bilateral movements may increase cortical
excitability, and thereby facilitate movement in non-disabled individuals\textsuperscript{74,75}, and those
with impaired movement\textsuperscript{76}. When the contralateral homologous muscle is contracted, the
motor output to the muscle is greater\textsuperscript{74,75}. Further, there are more cortical motor areas
active during bimanual tasks than unimanual tasks, even when the tasks are similar\textsuperscript{71}.
Finally, in individuals with sensorimotor impairment, the peak velocity is greater during a
bilateral symmetrical ballistic movement than a unilateral movement\textsuperscript{77}. If bimanual
activities are associated with greater cortical drive, then bilateral massed practice training
may be a strategy to improve functional arm and hand use in individuals with bilateral
upper extremity dysfunction.
Using unimanual massed practice training as a model, a bimanual massed practice training model has been proposed\textsuperscript{78}. This protocol utilizes a similar intensive training schedule of five days per week, two hours per day, for three weeks. Like the unimanual massed practice training, bimanual training divides each session into five movement categories: pinch, pinch with rotation, grip, grip with rotation, and finger isolation (Figure 1.1).

**Changes in Function Following Bimanual Massed Practice Training.** Bimanual massed practice training has not been investigated in individuals with cervical SCI; however, several studies explored the effects of bimanual training on both unimanual skill performance and bimanual skill performance in individuals with stroke. Mudie and Matyas\textsuperscript{79} found individuals with hemiplegia due to stroke who participated in a bimanual training program demonstrated improvements in unimanual reaching and grasping tasks. Cauraugh et al.\textsuperscript{80} investigated the effects of a training program that incorporated either bimanual or unimanual active wrist extension in conjunction with neuromuscular electrical stimulation in individuals with stroke. They noted those in the bimanual group had a greater improvement in performance of unimanual skills including greater hand manipulation, faster reaction times, and sustained voluntary muscle contractions. However some studies have found limited effectiveness of a bimanual training program. Lewis and Byblow\textsuperscript{81} investigated the effects of a unimanual training program followed by a bimanual training program. The researchers found limited additional benefit from the bimanual training.

**Changes in Cortical Neurophysiology Following Bimanual Massed Practice Training.** Bimanual massed practice training is associated with changes in cortical
neurophysiology. Following bimanual task-oriented training in non-disabled individuals, Smith and Staines\textsuperscript{82} found increases in amplitude in the movement-related potentials measured with EEG. The authors suggest the increase in movement potentials may reflect an increase in supplementary motor area excitability. Individuals with impaired movement also demonstrate changes in cortical activation following a bimanual training intervention. Luft \textit{et al.}\textsuperscript{83} found that individuals with stroke who participated in a bilateral training program had greater activation of the contralateral hemisphere as measured by fMRI. However, other studies investigating bimanual training found only small changes in cortical reorganization\textsuperscript{84} or inconsistent responses to the training\textsuperscript{81}. Thus it is possible unimanual training (where the individual is focused on improving one limb alone) is necessary to induce cortical reorganization.

\textbf{Implications from Bimanual Massed Practice Training.} Individuals with SCI frequently have deficits in both upper extremities and therefore may benefit from a bimanual training intervention. Further, cortical activity during bimanual practice may be greater than during unimanual practice. Bimanual massed practice should be compared to massed practice interventions that have been previously investigated.

\textit{Transcutaneous Functional Electrical Stimulation.} Functional Electrical Stimulation (FES) systems are electrical stimulating devices used to stimulate intact peripheral nerves or muscles during the performance of functional tasks. Factors influencing recovery of function with use of FES include integrity of the peripheral nerve (or lower motoneuron), and volitional control of proximal limb muscles (FES systems are generally utilized for stimulating the distal extremity)\textsuperscript{85}. There are many surface stimulation devices that are used to improve grasp in individuals with SCI including the
Rebersk and Vodovnik FES unit, the Hand Master, the Bionic Glove, the Belgrade Grasping System, and the ActiGrip System. The primary differences between the systems are the type of grasp elicited (due to the stimulating electrode placement) and the switch that triggers the electrical stimulation.

**Changes in Function Following Functional Electrical Stimulation.** Many FES systems function as neuroprosthetic devices improve hand grasp in individuals with SCI. Notably, incorporating these systems as part of a training intervention may result in improved hand function even when the device is not in use. This form of training has been shown to be effective in improving arm and hand function in individuals with cervical SCI and stroke. While stimulation parameters will vary depending on the device and tissue stimulated, Popovic et al. advocate biphasic pulse, with an intensity between 8-50 milliamps, duration of 250 microseconds, and frequency of 20-70 Hertz. Using these parameters, and a training schedule of 45 minutes per session for six weeks, individuals practiced functional tasks, repeating the activity 35-50 times per session. Following this intervention, individuals demonstrated gains on the Functional Independence Measure and the Spinal Cord Independence Measure. The treatment effect, however, appears to be dependent on severity of injury, where individuals with less hand function demonstrate greater gains after use of FES than individuals with more incomplete injuries. It may be that individuals with more severe injuries may require greater assistance (such as that provided by FES) to complete the motor task, which provides the central nervous system with greater sensorimotor feedback required for motor learning.
Changes in Cortical Neurophysiology Following Functional Electrical Stimulation. Cortical neurophysiology associated with improvements in grasping function induced by FES have not been investigated, however changes in cortical excitability following FES to the lower limb have been investigated. Kido et al. investigated the changes in cortical excitability following 30 minutes of FES assisted walking. The investigators found increased cortical motor excitability of the tibialis anterior after the intervention. Thus, it is likely that training the upper limb through an intervention that utilizes FES will also result in increased cortical excitability.

Implications from Functional Electrical Stimulation. FES can induce changes in function in both individuals with complete and incomplete cervical SCI. Therefore, both groups of individuals should be included in future research studies. To determine the mechanism by which recovery is occurring, the cortical reorganization associated with FES should be measured.

Interventions Aimed to Increase Cortical Excitation. As described earlier, individuals with cervical SCI have decreased cortical motor excitability related to both their sensory and motor impairment. However, increased cortical excitability is associated with the early signs of neural plasticity and learning. Thus, interventions that focus on increasing cortical excitability essentially may be preparing the system for cortical reorganization and motor learning. Physical therapy interventions that are associated with increasing cortical excitability include: somatosensory stimulation, vibration, and motor imagery. Of these interventions, the intervention that is associated with improved function is somatosensory stimulation.
Somatosensory Stimulation. Somatosensory stimulation has been shown to increase cortical excitability in both non-disabled individuals and individuals with sensorimotor impairment due to stroke and SCI. This type of stimulation is thought to preferentially activate the large sensory fibers associated with type I muscle afferents. It is possible activity of muscle afferent information plays a critical role in inducing cortical reorganization. The disruption of cutaneous and joint afferents alone does not result in a reduction in the corresponding cortical excitability; whereas the disruption of muscle, joint, and cutaneous afferents has been found to decrease cortical excitability. Thus, prolonged somatosensory stimulation may lead to increased cortical motor excitability.

In individuals with stroke, one of the consequences of decreased movement is decreased movement-related afferent information to the sensory cortex. In individuals with SCI, the consequences of decreased movement are further complicated by varying degrees of central deafferentation due to the damage to ascending pathways that convey sensory information to the supraspinal centers. Consequently, in both populations, loss of afferent input to the sensory cortex may contribute to cortical changes that are detrimental to function.

Changes in Function Following Somatosensory Stimulation. In individuals with impaired grasping function due to stroke, two hours of somatosensory stimulation applied to the median nerve induced increases in pinch grip strength. In individuals with weakness in their upper extremities due to SCI, two hours of somatosensory stimulation applied to the median nerve, five days per week, for three weeks was found to increase pinch grip strength, improve somatosensory function, and improve functional measures associated with upper extremity use. However, if the somatosensory stimulation is
applied in conjunction with task-oriented training, such as massed practice training, the combination produces a powerful effect on function, greater than either intervention in isolation.\(^{63}\)

**Implications from Somatosensory Stimulation.** Somatosensory stimulation is known to improve function and increase cortical excitability; however it has not been compared to other electrical stimulation interventions. It is possible any form of electrical stimulation is sufficient to improve function and increase cortical excitability. Therefore, future studies should compare different parameters of electrical stimulation and the effects on both function and cortical organization.

**Implications for Research**

Based on this literature review, we know that cortical reorganization occurs after injury and appears to be related to use (or lack of use)\(^{64,96}\). However, it is not known if the reorganization after SCI is more dependent on the injury itself or lack of use of the upper limbs. This leads us to research question number one, are cortical maps different for muscles affected by the injury and muscles not affected by the injury?

*Hypothesis 1a: The injury leads to cortical reorganization, thus muscles spared by the injury are similar in cortical organization to non-disabled individuals.*

*Hypothesis 1b: The cortical reorganization is due to non-use, thus other upper extremity muscles spared by the injury are more similar to those affected by the injury.*

If muscles spared by the injury are more similar to those of non-disabled individuals, then hypothesis 1b is rejected. If muscles not affected by the injury are more similar to those
affected by the injury, then hypothesis 1a is rejected. Chapter two is designed to address research question number one.

Individuals with chronic SCI begin to plateau in functional improvements nine to twelve months after their injury\textsuperscript{31,44}. However, recent studies suggest intensive, task-oriented training focusing on a single upper extremity can induce both improvements in function and cortical organization\textsuperscript{62,63}. Yet, individuals with SCI frequently have deficits in both limbs, and therefore may benefit from a bimanual training intervention. The question remains: Do individuals with SCI who participate in a bimanual massed practice training program receive similar benefits to those who participate in a unimanual massed practice training program?

*Hypothesis 2a*: Individuals with SCI receive similar or greater benefit from a bimanual massed practice training program in terms of functional skills and cortical organization than those who receive unimanual massed practice training.

*Hypothesis 2b*: Individuals with SCI receive less benefit from a bimanual massed practice training program in terms of functional skills and cortical organization than those who receive unimanual massed practice training.

If addressing functional deficits in both limbs simultaneously results in better outcomes, then hypothesis 2b is rejected. However, if focusing on the functional deficits of one limb alone results in better outcomes, then hypothesis 2a is rejected. Research question number two is addressed in chapter three and four, using two different bimanual training programs.

Finally, electrical stimulation augments functional changes associated with task-oriented training. However, it is not known if the type of nerve fiber targeted (sensory or
motor) provides a more optimal environment than the other. Further, it is not known if the timing of the electrical stimulation is a critical factor in improving hand function. Thus, comparing different electrical stimulation paradigms may provide evidence supporting one intervention over another. Research question number three is do individuals with SCI receive greater benefit from continuous SS or task-related FES?

_Hypothesis 3a: Individuals with SCI receive more benefit from somatosensory stimulation than functional electrical stimulation; therefore continuous sensory stimulation provides a more optimal environment over task-specific motor stimulation._

_Hypothesis 3b: Individuals with SCI receive less benefit from somatosensory stimulation than functional electrical stimulation; therefore task-specific motor stimulation provides a more optimal environment over continuous sensory stimulation._

_Hypothesis 3c: Individuals with SCI receive similar benefit from somatosensory stimulation than functional electrical stimulation, therefore simply providing electrical stimulation provides sufficient input into the nervous system to induce functional changes._

If individuals with SCI demonstrate greater functional gains with somatosensory stimulation then hypothesis 3b and 3c are rejected. If individuals with SCI demonstrate greater functional gains with functional electrical stimulation then hypothesis 3a and 3c are rejected. Finally, if individuals make similar gains following both interventions, then hypothesis 3a and 3b are rejected. Chapter four is designed to addresses this research question.
Summary. Injury to the cervical spinal cord affects arm and hand function which results in activity limitations and participation restrictions. Additional cortical reorganization associated with upper extremity dysfunction may decrease the effectiveness of the remaining corticospinal tract connections. Individuals with chronic SCI plateau in recovery of function after nine to twelve months; however, it may be possible to induce recovery of function and cortical reorganization in these individuals with different physical therapy interventions. This dissertation will explore the different cortical organization patterns of individuals with SCI and investigate whether these cortical changes are responsive to changes with physical therapy interventions.
Figure 1.1: List of training activities for massed practice training.

<table>
<thead>
<tr>
<th>Finger Isolation</th>
<th>Grasp</th>
<th>Grasp with Rotation</th>
<th>Pinch</th>
<th>Pinch with Rotation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Keyboard:</strong> Typing on a keyboard with both hands, type a specified sequence of keys without activating multiple buttons.</td>
<td><strong>Extension Cords:</strong> Plug 2 extension cords together and separate them using both hands.</td>
<td><strong>Can Opener:</strong> Squeeze the handle of a can opener together with one hand, while rotating the lever with the other hand.</td>
<td><strong>Thread and Needle:</strong> Using one hand to stabilize the knitting needle, thread the yarn into the needle.</td>
<td><strong>Tying Knots:</strong> Using both hands, tie different knots according to diagrams.</td>
</tr>
<tr>
<td><strong>Phone:</strong> Stabilizing the phone with one hand, punch in a list of phone numbers without depressing multiple buttons.</td>
<td><strong>Scissors:</strong> Stabilize a piece of paper with one hand and cut out shapes with the other hand.</td>
<td><strong>Rubik’s Cube:</strong> Stabilizing the Rubik’s Cube with one hand, while rotating the object with the other hand.</td>
<td><strong>Pipecleaner Shapes:</strong> Using both hands, orient the pipecleaners to create preset shapes.</td>
<td><strong>Lace Up Cards:</strong> Stabilizing the cards with one hand, thread the shoelace into the holes with the other hand.</td>
</tr>
<tr>
<td><strong>Calculator:</strong> Stabilizing the calculator with one hand, press the buttons of the calculator to calculate the solutions to set of math problems.</td>
<td><strong>Glue:</strong> Using both hands, squeeze glue out of a large bottle to create preset designs on paper.</td>
<td><strong>Scooping:</strong> Stabilizing the container with one hand, scoop sugar out of the container and into another container.</td>
<td><strong>Ziploc:</strong> Using one hand to stabilize the Ziploc bag, open and close it with the other hand.</td>
<td><strong>String Beads:</strong> Stabilizing the bead with one hand, thread string into bead with the other hand.</td>
</tr>
<tr>
<td><strong>Punch Pad:</strong> Stabilizing a video game with one hand, press the buttons to play the game with the other hand.</td>
<td><strong>Nesting Boxes:</strong> Using both hands, separate out nesting boxes and place inside each other.</td>
<td><strong>Containers:</strong> Stabilizing a container with one hand, unscrew the lid of the container with the other hand.</td>
<td><strong>Buttons:</strong> Button and unbutton different sized buttons on a strip.</td>
<td><strong>Twist Ties:</strong> Stabilize the bag with one hand and twist the twist tie around the bag with the other hand.</td>
</tr>
<tr>
<td><strong>Clay:</strong> Poke holes into clay using each finger individually and using both hands simultaneously.</td>
<td><strong>Building:</strong> Using both hands, separate Legos and attach together.</td>
<td><strong>Measuring Cups:</strong> Pour a predetermined amount of liquid into a measuring cup.</td>
<td><strong>Braiding Yarn:</strong> Braid 3 pieces of yarn.</td>
<td><strong>Nuts and Bolts:</strong> Stabilize the bolt with one hand and twist the nut on and off with the other hand.</td>
</tr>
<tr>
<td><strong>Piano:</strong> Press individual keys on the piano without pressing several at one time.</td>
<td><strong>Clay:</strong> Using both hands, shape clay into predetermined shapes.</td>
<td><strong>Flipping Cans:</strong> Using 2 soda cans at one time, rotate both cans upside down simultaneously.</td>
<td><strong>Bubble Wrap:</strong> Using both hands, pop bubbles in bubble wrap.</td>
<td><strong>Key and Padlock:</strong> Using one hand to stabilize the lock, use the key with other hand to open the lock.</td>
</tr>
</tbody>
</table>
CHAPTER 2: COMPARISON OF CORTICAL MOTOR MAPS IN INDIVIDUALS WITH SPINAL CORD INJURY AND NON-DISABLED INDIVIDUALS: A PILOT STUDY

Following an injury to the cervical spinal cord, the central nervous system undergoes rapid reorganization due to the disruption of afferent and efferent pathways. Reorganization of the cortical motor system has been identified with imaging techniques wherein the cortical motor representations of muscles unaffected by the injury are much larger and more excitable than either representation of muscles affected by the injury or those in non-disabled (ND) individuals\textsuperscript{19,97}. This plastic reorganization is associated with loss of arm and hand function\textsuperscript{5,6}.

In addition to the reduction in size of the hand region in the cortical motor area, the movement potentials may be in a more posterior location compared to ND individuals\textsuperscript{17,18}. Green et al.\textsuperscript{17} investigated movement potentials, using electroencephalography (EEG), associated with finger movement in individuals with tetraplegia and toe movement in individuals with paraplegia. Movement potentials are the potential difference between electrodes placed on the scalp associated with movement. Using the international 10-20 system, the investigators found the potentials of muscles affected by the injury to be located more posteriorly compared to ND individuals. The authors suggest that individuals with SCI may rely more heavily (for movement) on cortical areas other than the motor cortex that contribute to the corticospinal tract, such as the sensory cortex\textsuperscript{17,18}. Following injury, individuals with SCI may utilize the contribution from the sensory cortex to the corticospinal tract as an alternative motor pathway when axons from the cortical motor area are damaged. In intact animals, the sensory cortex makes a considerable contribution to the corticospinal
tract to modulate afferent information\textsuperscript{27,28}. This pathway projects from the sensory cortex to the dorsal horn.

It is possible that the system may demonstrate plasticity utilizing descending tracts from the sensory cortex for movement. The exact pathway is not known, but many potential pathways can be hypothesized. It maybe that the descending projections from the sensory cortex utilize latent connections to the anterior horn, as evidence suggests that direct, invasive stimulation in humans (done during intraoperative procedures unrelated to the experiment) to the sensory cortex can induce movement\textsuperscript{98}. Alternatively, it is also possible that the nervous system sprouts new terminal projections creating a new pathway from the sensory cortex to the anterior horn, as the spinal cord is known to sprout new connections between sensory and motor neurons after injury\textsuperscript{99}. However, caution must be taken as these are only hypothesized pathways and not direct evidence for a connection between the sensory cortex and anterior horn cells.

The purpose of this study was to investigate the cortical organization of a muscle affected by the injury and a muscle spared by the injury in individuals with cervical SCI; and to compare the cortical maps in these individuals with those of ND individuals. We hypothesized that the MT of the cortical motor map of muscles affected by the injury measured by TMS would be of higher intensities compared to the same muscles in ND individuals, whereas muscles not affected by the injury would be unaffected. We further hypothesized that cortical map area, volume, and normalized map volume would be smaller in muscles affected by the injury, whereas muscles not affected by the injury would not be affected.
Methods

Ten individuals with cervical SCI and five ND individuals were recruited for this study. The inclusion criteria for the individuals with SCI were injury level between C5-7, at manual muscle test score of at least one out of five (an observable muscle twitch) in the thenar muscles and five out of five (normal strength) in the biceps brachii in the tested upper extremity. The inclusion criterion for ND individuals was no history of neuromuscular disorder. The exclusion criteria for all participants were history of brain injury, stroke, or metal implants in the cranium. All experimental procedures were approved by the Human Subjects Review Board of the University Of Miami Miller School of Medicine and participants gave written informed consent to participate.

The participant demographic information can be found in Table 2.1. The distribution of neurological level of injury, impairment classification (ASIA B or C), and time since injury, were comparable in the two groups of participants with SCI. The age and gender of the participants in all the groups was also similar.

Cortical motor maps of a muscle unaffected by the injury (biceps brachii) were compared to a muscle affected by the injury (thenar muscles) in response to TMS. The thenar muscles were chosen as these muscles were hypothesized to be important for grasping function in ND individuals, whereas individuals with SCI may utilize tenodesis for grasping function. The biceps muscle was chosen as this muscle is innervated at three segmental levels rostral to the thenar muscles, and is less likely to be affected by the spinal cord injury. In individuals with SCI, the cortical maps of either the biceps brachii or the thenar muscles in one upper extremity (UE) were constructed; whereas, in ND individuals the cortical maps of both muscles in one UE were constructed. The intensity
at which the cortical map is created in individuals with SCI is frequently at high
intensities, which can be uncomfortable, and the mapping procedure can require up to
200-300 stimuli. Therefore to reduce the discomfort, we mapped only one muscle in
participants with SCI. Monophasic TMS was delivered by a Magstim 200 stimulator\(^1\)
(maximum magnetic field strength = two Tesla) using a figure-eight coil. In individuals
with SCI, the muscle responses were recorded from the weaker limb based on their
American Spinal Injury Association (ASIA) UE motor score. For those who had
symmetrical injuries and ND individuals, the non-dominant limb was chosen.

Participants sat on a reclining table with hips at 120 degrees of flexion and knees
at zero degrees of flexion. A headrest was used to minimize head movement. A pillow
supported the test UE in a position of slight shoulder flexion and elbow flexion (Figure
2.1). Participants were fit with a tight-fitting plastic cap\(^2\) imprinted with a grid marking
one cm squares. Either the biceps brachii or the thenar muscles were palpated and the
overlying skin was abraded with an alcohol swab. Two surface Ag / Ag-Cl electrodes
(3.2 cm by 2.2 cm) were placed two cm apart in a muscle-tendon montage with a ground
electrode over the olecranon. To ensure the test muscle was at rest, electromyographic
(EMG) data were recorded 200 milliseconds before and 300 milliseconds after the
stimulus was applied. If the muscle was not at rest prior to the stimulus, the associated
MEP was not included in the analysis and a subsequent response was evoked and
included in the analysis. The EMG signals were amplified by 1000, band pass filtered

\(^1\) The Magstim Co Ltd, Spring Gardens, Whitland, Carmarthenshire, Wales, United Kingdom SA34 OHR.
\(^2\) The Bobby Co, 4807 Mercury St, San Diego, CA 92111.
(10-2KHz) (Grass P511 AC Amplifier\textsuperscript{3}), and digitized at two KHz with an analog-to-digital converter (CED model 1401\textsuperscript{4}). Data was stored using a digital acquisition program (Signal Data Acquisition Software\textsuperscript{5}) and analyzed off-line.

Two examiners were present during the mapping process and consistently performed the same tasks. The first examiner performed the stimulating procedures and monitored the participant, while the second examiner recorded the frame number, stimulus intensity, and stimulated map coordinate. The TMS coil was placed directly on the cap over the hemisphere contralateral to the test limb with the handle pointing 45 degree posteriorly and laterally, as this position has been shown to most directly activate the corticospinal tract\textsuperscript{100}. The UE region was estimated to be approximately five cm lateral to midline, along the interaural line. In individuals with SCI, stimulation intensity was initially set at approximately 90\% maximal stimulator output (MSO), whereas in ND individuals the stimulation intensity was initially set at approximately 60\% MSO. Using an intensity which evoked an motor evoked potential (MEP), the coil was moved in small increments until the “hot spot” (site at which the amplitude is greatest and latency is shortest) was identified\textsuperscript{101}. Stimulus intensity was reduced to a level that did not evoke a motor response (approximately 30\% MSO) and systematically increased in five percent increments to determine motor threshold (MT) at the hot spot. MT was defined as minimum stimulus intensity at which five out of ten responses of at least 50 microvolts could be evoked\textsuperscript{101}. To create the motor map, the stimulator intensity was increased to

\textsuperscript{3} Grass-Telefactor, 600 E Greenwich Ave, West Warwick, RI 02893.
\textsuperscript{4} Cambridge Electronic Design Ltd, Science Park, Milton Rd, Cambridge, UK, CB4 OFE.
\textsuperscript{5} Cambridge Instrument Division, UK.
120% of MT. Starting at the hot spot and moving medially toward midline, each site on the grid of the cap was stimulated three times\textsuperscript{101}. The coil was then shifted laterally in one cm increments until encountering a site at which no MEP on the three trials could be evoked at the test intensity.

The map area\textsuperscript{102} (in cm\textsuperscript{2}) was defined as the region encompassing sites from which an MEP of at least 50 microvolts could be evoked when averaged on three subsequent trials, and calculated as follows:

Equation 1: if $a_i \geq 0.05 \text{ mV}$ then $b_i = 1$; else $b_i = 0$;

\[
\text{Area} = \sum b_i
\]

The variable $a_i$ represents the mean amplitude of three subsequent stimuli at the same site. The variable $b_i$ represents the presence or absence of an MEP at a particular site. The cortical volume was defined\textsuperscript{102} as the sum of all active sites, and calculated as follows:

Equation 2: Volume $= \sum a_i$

The normalized cortical volume\textsuperscript{102} was defined as the sum of all active sites normalized to the maximum MEP, and calculated as follows:

Equation 3: Normalized Volume $= \sum a_i / m_i$

The variable $m_i$ represents the mean maximum MEP. The COG was determined by creating a map representing the amplitude-weighted sites of the excitable area, according to the distance from Cz (x=0, y=0). Each site was weighted for both its longitudinal and latitudinal position relative to Cz. Using this convention, sites anterior to Cz had positive values, whereas sites posterior to Cz had negative values. The formula\textsuperscript{102} for the longitudinal value of the $Y_{COG}$ calculation is as follows:

Equation 4: $Y_{COG} = \sum (a_i / m_i)y_i / \sum a_i$
Where $a_i$ is the mean amplitude at an individual scalp site whose coordinate is $y_i$ cm from Cz. Following the same convention, the latitude value of the COG is calculated in a similar manner:

Equation 5: $X_{COG} = \sum (a_i / m_i)x_i / \sum a_i$

The mean MT, cortical map volume, normalized cortical map volume, and cortical map area were determined for each muscle. The mean values for the MT for both thenar muscles and biceps brachii of individuals with SCI and ND individuals were compared using a two sample t-test. The level of significance was accepted at an $\alpha \leq 0.05$.

**Results**

The MT of the thenar muscles was significantly greater in individuals with SCI (mean MT = 76%, standard deviation = 21.0%) compared to ND individuals (mean MT = 44%, standard deviation = 19%) ($t= 0.004; p=0.01$) (Figure 2.4). The MT of the biceps muscle in individuals with SCI (mean MT = 59%, standard deviation = 10%) was similar to that of ND individuals (mean MT = 56%, standard deviation = 20%) ($t=0.58; p=0.57$).

The mean cortical map area, cortical volume, and normalized cortical volume for both all groups of participants are found in Table 2.2. These values were similar between the groups.
Discussion

*Less Cortical Motor Excitability in Muscles Affected by Injury.* The MT for the thenar muscles was significantly greater in individuals with SCI which may reflect a decrease in cortical excitability of muscles affected by the injury. This has been observed by numerous authors\(^{10,14,103}\). Davey *et al.*\(^{10}\) found MT to be significantly higher in muscles affected by the injury (specifically thenar muscles) than the MT in ND individuals. Not only was the MT found to be greater in individuals with SCI compared to ND individuals, but the MEPs in the thenar muscles in response to higher stimulus intensities were smaller in amplitude in individuals with SCI\(^{10}\); we found similar findings (Figure 2.2 and Figure 2.6).

*Similar Cortical Motor Excitability in Muscles Spared by the Injury.* The cortical excitability of muscles spared by the injury is similar to those of ND individuals as demonstrated by the similar values in MT (Figure 2.4 and 2.6). Lotze *et al.*\(^{104}\) also found the MT of muscles spared by the injury (both the biceps brachii and thenar muscles) in individuals with complete paraplegia to be similar to that of ND individuals.

*Location of Center of Gravity in Muscles Affected by the Injury.* It appears that some individuals with SCI may have a COG in a location that is more posterior to that of ND individuals (Figure 2.3), however there is evidence that the location of the COG is variable both between individuals and between hemispheres within individuals\(^{105,106}\). In ND individuals the COG can move as much as 1.70 cm between testing sessions\(^{106}\), and the average movement of COG in individuals with stroke in their affected hemisphere is 1.13 cm\(^{105}\). Given the small sample size of this study, it is difficult to draw definitive conclusions regarding the location of the COG in individuals with SCI.
Conclusion

Cortical representations of muscles affected by spinal cord injury have significantly less cortical excitability than cortical representation of muscles in ND individuals. There is evidence to suggest that the difference maybe associated with impaired function, and that training can alter this impaired cortical excitability\textsuperscript{63}.

Limitations of study. The limitations to this study include the small sample size. All groups had very small sample sizes, which may limit the application of this study to larger groups. Another limitation is that both muscles were not measured in the individuals with SCI. This was done to reduce the discomfort for these participants as the stimulation intensities were much higher for these participants. Future studies should evaluate both muscles within the same individual.
Figure 2.1: Experimental set-up. The examiner is holding the coil for the TMS unit over the right scalp. The participant is wearing a cap with a grid marked with stimulation points and has EMG electrodes on her thenar muscles and olecranon. She is in a long sitting position with hips at approximately 120 degrees flexion and knee extended.
Figure 2.2: Cortical Maps of Thenar Muscles in a ND individual (Top) and an individual with SCI (Bottom). Note the amplitude of the mean responses in individuals with injury compared to those who are ND, even though the intensity at which the maps were created were normalized to the individual’s motor threshold (120% MT).
Figure 2.3: Location of COG of cortical representation of thenar muscles in ND individuals and individuals with SCI. It appears that the location of the COG in individuals with SCI is more posteriorly located in some participants, however in individuals with movement disorders (stroke) the amount of movement of the COG in absence of intervention is 1.13 cm$^{105}$. 
Figure 2.4: Cortical Maps of Biceps Muscles in a ND individual (Top) and an individual with SCI (Bottom). The amplitude of the responses in ND individuals are smaller than that of the individuals with SCI, even though the intensity at which the maps were created were normalized to the individual’s motor threshold (120% MT).
Figure 2.5: Location of COG of cortical maps of biceps in ND individuals (red squares) and individuals with SCI (blue diamonds). It appears that the location of the COG in individuals with SCI is more posteriorly located in some participants, however in individuals with movement disorders (stroke) the amount of movement of the COG in absence of intervention is 1.13 cm.$^{105}$
Figure 2.6: Motor threshold for the biceps muscle is represented in blue, whereas the thenar muscles are represented in pink. Darker colors represent individuals with SCI, while lighter colors represent ND individuals. Note the greater intensity at which to achieve a minimum motor response in the thenar muscles in individuals with SCI.
Figure 2.7: MEP of thenar muscles in individual with SCI (Top) and ND individual (Bottom). Note the MEP in the individual with SCI has multiple peaks, whereas that in the ND individual only has one peak. Also note that the MEP in the individual with SCI has longer latency. The amplitude of the first peak (with the shortest latency) has the greatest reliability\textsuperscript{107}, and therefore should be used in analysis.
Figure 2.8: MEP of biceps muscles in individual with SCI (Top) and ND individual (Bottom). Note these evoked potentials are similar in latency and shape, whereas those of the thenar muscles appear very different.
Table 2.1: Group Equivalence.

<table>
<thead>
<tr>
<th>Intervention Group</th>
<th>SCI: Biceps</th>
<th>SCI: Thenar</th>
<th>Non-Disabled</th>
<th>Test-Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Mean = 24.60 ± 6.54; Range = 16 - 32 years</td>
<td>Mean = 36.00 ± 13.00; Range = 20 - 49 years</td>
<td>Mean = 36.8 ± 12.42; Range = 25 - 55 years</td>
<td>F = 1.91, p = 0.19</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>80% Male, 20% Female</td>
<td>80% Male; 20% Female</td>
<td>20% Male; 80% Female</td>
<td>x² = 5.00, p = 0.08</td>
</tr>
<tr>
<td><strong>ASIA Classification</strong></td>
<td>60% B, 40% C</td>
<td>40% B, 60% C</td>
<td></td>
<td>p = 1.00</td>
</tr>
<tr>
<td><strong>Level of Injury</strong></td>
<td>20% C5, 80% C6</td>
<td>80% C6, 20% C7</td>
<td></td>
<td>p = 0.56</td>
</tr>
<tr>
<td><strong>Duration of Injury</strong></td>
<td>Mean = 4.00 ± 2.92; Range = 3.00 - 9.00 years</td>
<td>Mean = 3.40 ± 1.52; Range = 2.00 - 5.00 years</td>
<td></td>
<td>t = 0.41; p = 0.69</td>
</tr>
<tr>
<td><strong>Cause of Injury</strong></td>
<td>100% Traumatic</td>
<td>80% Traumatic, 20% Non-Traumatic</td>
<td></td>
<td>x² = 1.11, p = 0.29</td>
</tr>
<tr>
<td><strong>Thenar MMT</strong></td>
<td>Median = 3; Range = 1 - 4</td>
<td>Median = 3; Range = 1 - 4</td>
<td></td>
<td>p = 0.714</td>
</tr>
<tr>
<td><strong>Biceps MMT</strong></td>
<td>Median = 5; Range = 5 - 5</td>
<td>Median = 5; Range = 5 - 5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2.2: Mean values and ± associated standard deviations of TMS results for individuals with SCI and ND individuals (ND). Blue represents biceps muscle and pink represents thenar muscles. Darker color represents ND individuals and lighter color represents individuals with SCI. Note the motor threshold of the thenar muscles in individuals with SCI is different from that of ND individuals. The cortical map area, volume, and normalized volume are similar between the groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Motor Threshold (% MSO)</th>
<th>Cortical Area (cm²)</th>
<th>Cortical Volume (cm³)</th>
<th>Normalized Cortical Volume (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ND: Biceps</td>
<td>56% ± 5%</td>
<td>18 ± 4</td>
<td>3.59 ± 1.74</td>
<td>10.52 ± 3.56</td>
</tr>
<tr>
<td>SCI: Biceps</td>
<td>59% ± 16%</td>
<td>23 ± 10</td>
<td>6.67 ± 4.46</td>
<td>12.49 ± 5.92</td>
</tr>
<tr>
<td>ND: Thenar</td>
<td>44% ± 6%</td>
<td>19 ± 7</td>
<td>8.50 ± 8.07</td>
<td>8.04 ± 3.80</td>
</tr>
<tr>
<td>SCI: Thenar</td>
<td>76% ± 17%</td>
<td>11 ± 6</td>
<td>3.48 ± 1.76</td>
<td>10.19 ± 5.68</td>
</tr>
</tbody>
</table>
CHAPTER 3: FUNCTIONAL AND CORTICAL CHANGES IN INDIVIDUALS WITH CERVICAL SPINAL CORD INJURY FOLLOWING EITHER UNIMANUAL OR BIMANUAL MASSED PRACTICE TRAINING: A PILOT STUDY

There are 11,000 occurrences of spinal cord injury each year in the United States, according to the National Spinal Cord Injury Database\(^1\). Of these individuals, 34% have cervical incomplete injuries which result in tetraplegia\(^1\). According to two different surveys of individuals with tetraplegia due to spinal cord injury (SCI), the single factor that would most improve quality of life is recovery of hand function\(^2,3\). Anderson et al.\(^2\) found that 48% of individuals with tetraplegia prioritized hand function to be more important than six other dysfunctions associated with SCI (bowel and bladder function, trunk stability, sexual function, walking, sensation, and chronic pain). Similarly, Snoek et al.\(^3\) surveyed individuals with SCI and found 77% of individuals with tetraplegia expected a significant change in their quality of life with the recovery of hand function. There are few therapeutic interventions that describe associated improvements in hand function in individuals with chronic SCI in the literature. Therefore, determining the optimal training paradigm for recovery of hand function for individuals with tetraplegia is important.

Deficits in arm and hand function in individuals with cervical SCI are due to different combinations of damage to upper motor neurons, lower motor neurons, and support cells of the nervous system which are vital for fine motor control. The injury then leads to impairments in strength, precision, modulation of muscle tone, and sensory perception. In addition to impairments, secondary plastic reorganization in the central nervous system is associated with loss of function\(^6,16\). Deleterious reorganization may include decreased area of sensorimotor cortical representation\(^108\), location of cortical
representation that is more posterior than in non-disabled individuals\textsuperscript{17,18}, decreased intracortical inhibition\textsuperscript{9}, decreased cortical motor excitability\textsuperscript{10}, and impaired cortical drive\textsuperscript{10}. In order to maximize recovery, interventions designed to improve arm and hand function must address activity limitations and sensorimotor impairments.

The changes in cortical organization that occur after SCI are similar to those that occur following stroke. Therefore, interventions that are effective in improving arm and hand function in individuals with stroke might be effective in individuals with SCI. Two interventions shown to be effective in improving cortical control of movement in individuals with stroke are constraint-induced movement therapy\textsuperscript{58,59} and somatosensory stimulation\textsuperscript{92,109}.

\textit{Massed Practice.} Constraint-induced movement therapy is a combination of repetitive task practice and shaping. The goal of repetitive task practice or massed practice is to improve performance of functional tasks related to those tasks practiced during the intervention. Constraint-induced movement therapy has been shown to be effective in improving performance of functional skills in individuals with stroke and has been associated with cortical reorganization\textsuperscript{58,59,110}. Likewise, in individuals with SCI, there is evidence that massed practice can induce functional and cortical changes\textsuperscript{62,63}. Beekhuizen and Field-Fote\textsuperscript{62,63} have recently shown that participants with incomplete, cervical SCI who were given a combination intervention of unimanual massed practice and somatosensory stimulation demonstrate greater improvements in functional skills, when compared to each intervention applied in isolation. In addition, there was significantly greater cortical excitability (measured by a decrease in transcranial magnetic stimulation motor threshold) following the combination intervention\textsuperscript{62,63}. 
**Bimanual Massed Practice.** Given the evidence that unimanual training (in the form of constraint-induced movement therapy) can induce practice-dependent plasticity in individuals with stroke\textsuperscript{58,59} and individuals with SCI\textsuperscript{62,63}, then training using a bimanual paradigm may induce similar or even greater plastic changes. In bimanual tasks, the central nervous system must control a greater number of degrees of freedom than in unimanual tasks, resulting in greater cortical activation\textsuperscript{71-73}. In addition, bimanual training provides the opportunity to address functional deficits in both limbs simultaneously.

Evidence suggests bilateral movements may increase cortical excitability and thereby facilitate movement, both in non-disabled individuals\textsuperscript{74,75} and individuals with impaired movement\textsuperscript{76}. In non-disabled individuals, the output from the muscle is greater when the contralateral homologous muscle is contracted\textsuperscript{74,75}. This facilitation is thought to occur at the level of the cortex as there were no changes in spinal motoneuron excitability (measured through F-waves)\textsuperscript{75}. In individuals post-stroke, muscle contractions on the non-affected side create a facilitory effect in the cortically-evoked response in the affected hand\textsuperscript{76}. Further, there are more cortical motor areas active during bimanual tasks than during unimanual tasks, even when the tasks are similar\textsuperscript{71}. De Weerd *et al.*\textsuperscript{71} compared brain activation levels using functional magnetic stimulation imaging (fMRI) in non-disabled individuals while learning either a unimanual or bimanual, asymmetrical finger tapping sequence. The investigators found greater activation of supplementary motor area and premotor area during the bimanual training activity.
Alternatively, perhaps the number of degrees of freedom required to perform the task (rather than the coordination of both limbs) is responsible for the increases in brain activation levels\textsuperscript{111}. Koeneke \textit{et al.}\textsuperscript{111} compared brain activation levels (using fMRI) during a visual-motor task involving pushing two buttons in either a unimanual condition (index finger and middle finger) or a bimanual condition (two index fingers). The researchers found \textit{no} difference in the level of cortical activity for the different conditions, concluding that the number of degrees of freedom accounts for the greater activity identified during bimanual tasks. If bimanual tasks increase cortical activity due to the greater number degrees of freedom necessary to control, then bimanual training is a simple way to increase the cortical activity in the central nervous system.

In addition to the evidence of neural facilitation between the limbs, there is behavioral evidence which suggests that the use of one limb increases the speed of the contralateral limb during symmetrical movements. Rose and Winstein\textsuperscript{77} compared the difference in velocity of the paretic limb during unilateral reaching and bilateral reaching. The paretic limb had greater peak velocity during reaching in the bimanual condition. However, the increase in velocity may be limited to tasks with symmetry. Daily activities are primarily asymmetrical, where the dominant hand frequently performs the manipulation and the non-dominant hand functions as an assistive hand. By training with both symmetrical and asymmetrical tasks, the nervous system must learn to couple and decouple the upper extremities as required by the task.

\textit{Somatosensory Stimulation}. The sensory cortex is one of the primary sources of excitation for the motor cortex through direct connections\textsuperscript{112}. Furthermore, the reduction of sensory input through local anesthesia\textsuperscript{94} or a blood pressure cuff\textsuperscript{22} in non-disabled
individuals is associated with decreased excitability of the corresponding area in the
motor cortex\textsuperscript{22,94,95}. While the primary motor cortex makes the largest contribution to the
corticospinal tract, it is important to note that the sensory cortex also contributes to the
corticospinal tract and synapses at the dorsal horn (Figure 3.1)\textsuperscript{27,29,98}. Therefore, it seems
plausible that increasing sensory input would both increase the excitability of M1
(thereby increasing voluntary drive) as well as increasing the efficacy of the corticospinal
tract output. Alternatively, providing SS continuously throughout the intervention may
confuse the system and inhibit motor learning.

Somatosensory stimulation with a long pulse duration (one millisecond) is
thought to preferentially activate the large type I sensory nerve fibers\textsuperscript{93}. This type of
electrical stimulation is above sensory threshold, and may play a critical component in
inducing cortical reorganization\textsuperscript{94,95}. Cortical excitability is not reduced when cutaneous
and joint afferents alone are transiently disrupted\textsuperscript{94}; however the transient disruption of
muscle, joint, and cutaneous afferents does result in decreased cortical excitability\textsuperscript{95}. Therefore increasing sensory information related to muscle afferents with both electrical
stimulation and movement may increase cortical excitability (Figure 3.1) and thereby
induce reorganization (changes in cortical map area, volume, or COG) that supports
improved function.

In both non-disabled individuals\textsuperscript{91} and individuals with impaired movement\textsuperscript{63}, somatosensory stimulation is associated with increased cortical motor excitability
(measured through a decrease in motor threshold associated with transcranial magnetic
stimulation (TMS)). There is evidence to suggest that increases in cortical excitability
are not due to increases in spinal motoneuron excitability\textsuperscript{70,91}. In both non-disabled
individuals\textsuperscript{91} and individuals with SCI\textsuperscript{70}, there was not an increase in spinal motoneuron excitability (measured through F-waves) after somatosensory stimulation. However, in individuals with weakness due to SCI\textsuperscript{62,63} or stroke\textsuperscript{92,109}, prolonged application of somatosensory stimulation alone increases pinch grip force\textsuperscript{63,92}.

The purpose of this study was to investigate the functional and cortical changes following either unimanual or bimanual massed practice training, combined with somatosensory stimulation. We hypothesized that following the intervention, all participants would improve in both clinical and neurophysiological outcome measures. We further hypothesized that following the intervention, those in the bimanual massed practice training group would demonstrate greater increases in cortical area and volume compared to the unimanual group.

**Methods**

*Design.* The study followed a pre/post intervention design (Figure 3.2) where participants were randomly assigned to one of two groups: unimanual or bimanual training, both combined with somatosensory stimulation. The group assignment was chosen by drawing papers with intervention assignments written on them out of an envelope. After the removal of the group assignment from the envelope, the group assignment was replaced for the subsequent assignment of groups. Participants in both groups were instructed to maintain their usual exercise routine and were asked not to participate in any new therapies or exercises during the course of the four week study.

*Participants.* Thirteen participants agreed to participate and met the following inclusion criteria: cervical SCI rostral to C8, at least one year post injury, and a visible
muscle twitch in at least one of their thenar muscles. These inclusion criteria were chosen to ensure all participants had deficits in hand function, were stable in their neurological recovery\textsuperscript{31}, and had good potential for improvement. Our pilot studies indicate that individuals who do not have voluntary activity in at least some intrinsic hand muscles do not derive functional benefits from participation in this form of intervention. Participants were excluded from this study if they had a history of head injury, stroke, or metal implants in their cranium. These criteria were chosen to reduce the likelihood of seizure when performing the TMS procedures\textsuperscript{113}. The experimental procedures were approved by the internal review board at the University of Miami, Miller School of Medicine.

Of the thirteen individuals with cervical SCI who were enrolled in the study, two participants were unable to complete the study (one in the unimanual group and one in the bimanual group). One of these participants developed a urinary tract infection (unrelated to the study) severe enough to be hospitalized, and thus had to stop the intervention. Another participant had difficulties with transportation to the research facility. The groups were similar in terms of ASIA classification, neurological level of injury, duration of injury, upper extremity motor and sensory score, cause of injury, gender, and age (Table 3.2). The pre-intervention scores on the Jebsen Taylor Hand Function test, Chedoke Arm and Hand Activity Inventory, Semmes Weinstein Monofilament test, and pinch grip strength were also similar between the groups (Table 3.2).

\textit{Testing Procedures.} Participants performed two different types of testing: clinical and neurophysiological. The clinical tests included American Spinal Injury Association
(ASIA) impairment scale, Jebsen Taylor Hand Function test, Chedoke Arm and Hand Activity Inventory, Semmes-Weinstein Monofilament test, and pinch grip strength. These measures were chosen to include both measures of activity limitations (Jebsen Taylor Hand Function test and Chedoke Arm and Hand Activity Inventory) and impairments (Semmes Weinstein Monofilament test and pinch grip strength). The Jebsen Taylor Hand Function test was chosen as it is a measure of unimanual hand function and is designed to measure change in hand function after therapeutic intervention. The Chedoke Arm and Hand Activity Inventory was chosen as it is a measure of bimanual hand function, and we hypothesized would be sensitive to change following a bimanual training intervention. Both the Semmes Weinstein Monofilament test and pinch grip strength measures were chosen as these measures have detected change in the combination intervention of massed practice with somatosensory stimulation in previous studies. The neurophysiological outcome measures included: TMS motor threshold, cortical motor area, normalized cortical motor volume, and COG of the cortical map. TMS motor threshold was chosen as previous studies indicate this measure is sensitive to change following a combination intervention of massed practice and somatosensory stimulation. Cortical map area was chosen as evidence suggests these measures are sensitive to change following somatosensory stimulation in non-disabled individuals. Finally, the COG was chosen as evidence suggests movement potentials (measured by EEG) change locations following recovery of function.

**Outcome Measures.** The ASIA sensory and motor testing were performed according to the ASIA guidelines. Inter-rater reliability of the pinprick, light touch,
and motor evaluation in individuals with SCI, as measured by the intra-class correlation coefficient (ICC), is between 0.96 to 0.99\textsuperscript{118,119}.

For the clinical tests, participants were positioned in their wheelchair with the shoulder in neutral, elbow positioned to 90 degrees of flexion, and the forearm resting on a table. Upper-extremity motor function was measured using both a test of unimanual hand function (Jebsen Taylor Hand Function test) and a test of bimanual hand function (Chedoke Arm and Hand Activity Inventory). The Jebsen Taylor Hand Function test assesses the capacity of unilateral hand function and improvement in hand function associated with therapeutic interventions\textsuperscript{114}. This test has been validated for use in individuals with C6 and C7 tetraplegia. The test-retest reliability is 0.89 to 0.99 in individuals with neurological disorders with movement impairment\textsuperscript{114}. It is a seven item, timed test which incorporates writing, turning pages, picking up small objects, feeding, stacking, picking up large objects, and picking up heavy objects. The total test score is the sum of the time (in seconds) for all of the items. This measure of unimanual hand function was investigated in both hands individually and scored separately.

The Chedoke Arm and Hand Activity Inventory\textsuperscript{115} was designed to measure the performance of bimanual hand tasks as they relate to functional ability in individuals post stroke. The inter-rater reliability of the Chedoke Arm and Hand Activity Inventory in individuals with stroke has an ICC of 0.98\textsuperscript{115}. To establish the validity of this test in individuals with SCI we assessed the relationship between the pre-intervention values of the Jebsen Taylor Hand Function test and the Chedoke Arm and Hand Activity Inventory. The test consists of 13 items and each item is given a score from one to seven, with one meaning the individual is unable to perform the task; and seven meaning the individual is
able to perform the task independently. Items number 12 and 13 were excluded. These items correspond with placing a large container on the table from the floor and carrying a bag up stairs. We did not feel these items would change with this type of training, further it would be unsafe for some participants to perform these activities.

Semmes Weinstein Monofilament testing was used to measure the degree of sensitivity in the median nerve region\textsuperscript{116,120}. The inter-rater reliability of the Semmes Weinstein Monofilament test in individuals with peripheral nerve injury, as well as non-disabled individuals, as measured by the ICC is 0.97\textsuperscript{121}. In addition, the responsiveness to change has an effect size of 1.5 in individuals recovering from peripheral nerve damage\textsuperscript{121}. This test includes five monofilaments ranging in diameter from 2.83 mm to 6.65 mm. The region of the hand innervated by the median nerve was tested at the tip of the thumb, tip of the index finger, and base of the index finger. With the participant’s eyes closed, the smallest monofilament was used first. The monofilament was depressed until it bent and was removed after 1.5 seconds. The participant was instructed to respond verbally when a touch was perceived. If the individual did not respond, the next larger monofilament was used. Increasingly larger monofilaments were used until the participant responded to at least five out of ten stimuli with the same monofilament. The monofilament diameter was coded on a six point scale where zero means unable to perceive the largest diameter monofilament (6.65 mm) on at least 50\% of the trials and five means able to perceive the smallest diameter monofilament (2.83 mm) on at least 50\% of the trials (Figure 3.3). The scores for the three sites were combined for a total maximum score of 15 for the median nerve region. A lower score indicates poorer sensory perception, whereas a higher score indicates better sensory perception.
Pinch grip strength was measured with a handheld dynamometer (Microfet4). Participants were instructed to squeeze the dynamometer using a key pinch grip with the instruction “squeeze as hard as you can” for at least three seconds. The average force produced on three trials was recorded and the mean force was calculated. This method of measuring pinch grip force has been shown to be a reliable measure in individuals with SCI.

Cortical motor maps of the thenar muscles were created in response to a stimulus evoked by TMS. The test-retest reliability of ICC of resting motor threshold (MT) of four different upper extremity muscles in non-disabled individuals is 0.90-0.97. The area of the cortical map of upper limb muscles is a stable measure having an ICC of 0.63-0.86 with greater reliability in the medial to lateral coordinate than in the anterior to posterior coordinate. In individuals with impaired movement due to stroke, Butler et al. found no between session variability over three sessions for resting MT, cortical map area, normalized cortical map volume and shift in center of gravity (COG).

Monophasic TMS was delivered by a Magstim 200 stimulator (maximum magnetic field strength = two Tesla) using a figure-eight coil. The weaker limb (determined by the ASIA motor score) was tested. However, if the individual had no voluntary control of the thenar muscles in the weaker hand, then the stronger limb was tested. This limb was also chosen for the somatosensory stimulation and focus of the massed practice intervention.

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6 Hoggan Health Industries, 8020 South 1300 West, West Jordan, UT 84088
7 The Magstim Co Ltd, Spring Gardens, Whitland, Carmarthenshire, Wales, United Kingdom SA34 OHR
Participants sat reclined on a treatment table with hips extended to approximately 120 degrees and with knees extended (over a pillow for comfort). The head rested on a headrest with a roll behind the neck to minimize head movement. A pillow supported their upper extremity in a position of slight shoulder and elbow flexion. Participants wore a tight-fitting cap\textsuperscript{8} with an imprinted grid demarking one cm squares. To ensure reliable placement of the cap, marks were placed on the cap indicating the location of the nasion, inion, ears, and Cz (the point at which the interaural line and the line connecting nasion and inion intersect). The participant used the same marked cap for all testing sessions. The thenar muscles were palpated and the overlying skin was abraded with an alcohol swab. Two surface Ag Ag/Cl electrodes (3.2 cm by 2.2 cm) were placed two cm apart in a muscle tendon montage with a ground electrode over the olecranon. To ensure the muscle was at rest, 200 milliseconds were recorded before and 300 milliseconds were recorded after the stimulus was applied. The electromyography (EMG) signals were amplified by 1000 and band pass filtered (10-2KHz) with a Grass P511 AC Amplifier\textsuperscript{9}. The signals were digitized with an analog-to-digital converter (CED model 1401\textsuperscript{10}) at a sampling rate of 2 KHz. Data was stored using a digital acquisition program (Signal 2.15\textsuperscript{11}) and analyzed off-line.

The stimulation was applied with the TMS coil placed directly on the cap over the contralateral hemisphere with the handle pointing 45 degree posteriorly and laterally (this

\textsuperscript{8} The Bobby Co, 4807, Mercury St, San Diego, CA 92111

\textsuperscript{9} Grass-Telefactor, 600 E Greenwich Ave, West Warwick, RI 02893

\textsuperscript{10} Cambridge Electronic Design Ltd, Science Park, Milton Rd, Cambridge, UK CB4 OFE

\textsuperscript{11} Cambridge Electronic Design, Cambridge, UK
handle position is known to most directly activate the corticospinal tract\textsuperscript{100}. The upper extremity region was estimated to be approximately five cm lateral to the interaural line. The stimulator was initially set to approximately 70-90\% maximal stimulator output (MSO). Using this intensity range, the coil was moved in small increments until the “hot spot” (site at which the amplitude is greatest and latency is shortest) was found. To determine MT at the hotspot, stimulus intensity was reduced to a level which did not evoke a motor response (approximately 30\% MSO) and systematically increased by increments of five percent. MT was defined as minimum stimulus intensity at which five out of ten responses of at least 50 microvolts in amplitude were achieved. To create the motor map, the stimulator intensity was increased to 120\% of MT. Starting at the site at which the hotspot was found and moving to midline, each site on the cap’s grid was stimulated three times. The coil was moved laterally by one cm increments until reaching a site at which no motor evoked potential (MEP) could be evoked at the test intensity.

The map area\textsuperscript{102} (in cm\textsuperscript{2}) was defined as the region encompassing sites from which an MEP of at least 50 microvolts could be evoked when averaged on three subsequent trials, and calculated as follows:

Equation 1: if \( a_i \geq 0.05 \text{ mV} \) then \( b_i = 1 \); else \( b_i = 0 \);

\[
\text{Area} = \sum b_i
\]

The variable \( a_i \) represents the mean amplitude of three subsequent stimuli at the same site. The cortical volume was defined\textsuperscript{102} as the sum of all active sites, and calculated as follows:

Equation 2: \( \text{Volume} = \sum a_i \)
The normalized cortical volume\textsuperscript{102} was defined as the sum of all active sites normalized to the maximum MEP, and calculated as follows:

\textbf{Equation 3:} \textit{Normalized Volume} = \sum a_i / m_i

The variable $m_i$ represents the mean maximum MEP. The COG was determined by creating a map representing the amplitude-weighted sites of the excitable area, according to the distance from Cz ($x=0$, $y=0$). Each site was weighted for both its longitudinal and latitudinal position relative to Cz. Using this convention, sites anterior to Cz had positive values, whereas sites posterior to Cz had negative values. The formula\textsuperscript{102} for the longitudinal value of the $Y_{COG}$ calculation is as follows:

\textbf{Equation 4:} \textit{Y}_{COG} = \sum (a_i / m_i)y_i / \sum a_i

Where $a_i$ is the mean amplitude at an individual scalp site whose coordinate is $y_i$ cm from Cz. Following the same convention, the latitude value of the COG is calculated\textsuperscript{102} in a similar manner:

\textbf{Equation 5:} \textit{X}_{COG} = \sum (a_i / m_i)x_i / \sum a_i

\textit{Intervention.} The intervention protocol consisted of either unimanual or bimanual massed practice training in conjunction with somatosensory stimulation, for two hours a day, five days a week, for three weeks. The somatosensory stimulation was applied only to the weaker hand or the hand chosen for TMS testing.

\textit{Massed Practice Training Protocol.} For both the unimanual and bimanual training, the activities were divided into five movement categories focused on the distal extremity (Table 3.1 provides a few examples and descriptions of the tasks). The movement categories included finger isolation, pinch, pinch with rotation, grasp, and
grasp with rotation. The activities for both the unimanual and bimanual training were designed to be as similar as possible.

The massed practice protocol was modeled after the unimanual massed practice training described in previously published reports from our lab. The participant performed the manipulation portion of the task with their weaker limb (or limb chosen for testing), and when necessary, to allow tasks to be accomplished with one hand, the object was stabilized by glue, putty, or a clamp. For example, in the container opening task, jars were glued onto a large board and participants practiced removing the lids. Likewise, in the nuts and bolts tasks, participants practiced removing nuts from a bolt while the bolt was stabilized in a block of wood.

The bimanual tasks were as similar as possible to the unimanual tasks with slight modifications so the tasks were performed bimanually. Using the previous example, participants in the bimanual group opened containers using one hand to stabilize the container and the other hand to remove the lid. Similarly, in the nuts and bolts task, one hand stabilized the bolt while the other hand removed the nut. For half of the training, the weaker hand performed the manipulative portion of the task (while the stronger hand stabilized), and the other half of the training time the weaker hand performed the stabilization portion of the task (while the stronger hand performed the manipulation).

For those in the bimanual massed practice group, tasks were both symmetrical and asymmetrical, meaning some tasks required that both hands perform a similar movement pattern, whereas other tasks required that each hand perform a different movement pattern. In tasks that were symmetrical, the participants were encouraged to perform similar movement patterns with both hands simultaneously. For example, in the
piano keyboard task, the participants were instructed to press the keys using the same digit on both hands concurrently. In asymmetrical movement tasks, one hand functioned as an assistive or stabilizing hand and the other hand performed the manipulative portions of the task (such as stabilizing the calculator to press the buttons). In these types of tasks the participant practiced the task using their weaker hand to stabilize the object and also practiced the tasks using their weaker hand to manipulate the object.

Each training session was two hours in duration, divided into 20 to 25 minute movement categories. Each of the five movement categories had five to ten associated activities in which the participant selected two tasks from each category during a single training session (Table 1). Participants chose the tasks to practice to ensure the task had relevance to the individual. The intent was to practice a variety of tasks to engage the hand or hands in as many degrees of freedom as possible.

The focus of both the unimanual and bimanual interventions was to restore movement patterns typical of individuals who are not disabled. To accomplish this, the trainer first demonstrated the appropriate performance of the task. The participant then practiced the task. If the participant used a strategy that greatly differed from the typical way, the trainer encouraged the participant to modify their strategy. Compensatory strategies were discouraged. For example, if the individual utilized excessive shoulder and elbow motion to maintain a tenodesis grip, encouragement was given to reduce the shoulder motion and rely more heavily on their extrinsic and intrinsic hand muscles. Likewise, if a participant used shoulder abduction to hyperextend their finger (and thereby use the passive forces of the joint capsule and ligaments) to depress a button, the
participant was instructed to reduce the shoulder and elbow motion and be forced to utilize their finger flexors and extensor indices (Figure 3.4).

Some tasks were more challenging than others for each individual participant. This was determined if individuals were unable to complete the task as demonstrated by the trainer. If the individual was unable to complete a task independently using a typical movement pattern, then hand over hand assistance was provided to ensure they could complete the task successfully. While providing hand over hand assistance provides additional sensory information, we felt it was more important for the participant to practice the task without compensatory strategies. Hand over hand assistance was provided over the individual’s hands (not the object) so the individual was able to complete the task. The assistance was gradually reduced until the individual could perform the task independently.

Alternatively, it is possible that the task chosen was insufficiently challenging for the participant. The task was determined to be insufficiently challenging if the participant performed the task as demonstrated by the trainer, and rated the task less than three on a ten point scale, where ten represented great effort to complete the task and one represented minimal effort to complete the task. If the task was not challenging, the demands of the task were increased by altering the setup. For example, to increase the difficulty for the writing task, the writing utensil was progressed from a felt tip pen to a pencil, and finally to a crayon. Using this progression, the subject was required to progressively produce greater force on the writing utensil to mark on the paper. This was done to ensure the tasks were sufficiently challenging, because evidence suggests tasks must be challenging to induce cortical reorganization\textsuperscript{123}. 

Somatosensory Stimulation Protocol. Surface Ag / Ag-Cl electrodes were placed on the volar surface of the wrist in the region of the median nerve. The somatosensory stimulation was delivered using a constant current stimulator (Digitimer model DS7A\textsuperscript{12}) according to a previously published protocol\textsuperscript{62}. The trains were delivered at a frequency of ten Hz. Each train consisted of five pulses of one millisecond in duration. Stimulus intensity was set to a level just below that which evoked an observable twitch in any of the muscles innervated by the median nerve. The stimulation was applied concurrently with the massed practice.

Statistical Analysis. Repeated measures ANOVA was used to compare the pre- and post-intervention changes on the clinical data between the unimanual and bimanual massed practice groups. For the TMS data, a two tailed, paired T-test was used to compare the pre- and post-intervention changes on the entire group. This was done as there were only six participants to complete this portion of the study. To determine the concurrent validity of the Chedoke Arm and Hand Activity Inventory, a Pearson Correlation coefficient was used. The level of significance was accepted at an \( \alpha \leq 0.05 \).

Results

Change in Clinical Outcome Measures. The mean and median pre- and post-intervention scores and the associated standard deviations in the clinical outcome measures are summarized in Table 3.3. For the Jebsen Taylor Hand Function test there was a significant effect of time (\( F=10.00, p=0.01 \)), indicating that the entire group of participants improved in score on the test of unimanual hand function (Table 3.3). The

\textsuperscript{12} Digitimer Ltd, 37 Hydeway, Welwyn Garden City, Hertfordshire, United Kingdom, AL7 3BE.
interaction between time and group was not significant (F=1.02, p=0.34); indicating there was no difference in the amount of change between the groups. The mean change in the unimanual group was a decrease in time (91.67 ± 15.51 seconds) whereas there was a smaller mean decrease in the bimanual group (47.27 ± 36.65 seconds) (Figure 3.5).

On the Chedoke Arm and Hand Activity Inventory, there was also a significant difference between pre- and post-intervention scores (F=6.63, p=0.02) (Table 3.3). The interaction between time and group was not significant (F=0.34, p=0.34) (Figure 3.6) indicating there was no difference in the amount of change between the groups. The mean change for the bimanual group (3.50 ± 1.84) was similar to that of the unimanual group (2.17 ± 0.79).

For the Semmes Weinstein monofilament test, there was a significant difference between pre- and post-intervention values for all the participants (F=14.44, p=0.004) (Table 3.3), but no difference between those individuals who participated in unimanual and bimanual training groups (F=0.07, p=0.80). Both intervention groups showed improvement in sensation by 1-2 monofilaments (Figure 3.7).

For pinch grip strength, there was a trend towards improvement, however there was no difference between pre- and post-intervention values (F=1.94, p=0.20) (Table 3.3). The bimanual group had a greater mean change (1.24 ± 1.02 pounds) in pinch grip force than the unimanual group (0.24 ± 0.17 pounds), however the interaction between time and group was not significant (F=0.62, p=0.45) (Figure 3.8).

*Validity of the Chedoke Arm and Hand Activity Inventory.* Sixteen participants were included in this portion of the study, both individuals with intrinsic hand muscles and those who use tenodesis to grasp objects. There was a significant inverse linear
relationship between the score on the Jebsen Taylor Hand Function test and the Chedoke Arm and Hand Activity Inventory ($r = -0.59, p=0.02$) (Figure 3.9).

**Change in TMS Outcome Measures.** TMS outcome measures included resting motor threshold, cortical map area, normalized cortical map volume, and COG of the cortical map before and after intervention. Resting MEPs (Figure 3.10) could be evoked in nine of the fourteen participants. Of those who had resting MEPs, seven had stable baseline responses of consistent latency and amplitude, and therefore could be distinguished from spontaneous potentials. Two participants had spontaneous potentials, which occurred independent of the stimulation, and when the latency was similar to the expected latency for the MEPs (between 20-30 msec) the two potentials could be easily confused (Figure 3.11). Thus, cortical mapping could not be performed in these two individuals. An example of the cortical map before and after intervention in one participant can be seen in Figure 3.12. The TMS-related outcome measures comparing pre- and post-intervention values are summarized in Table 3.5.

**Cortical Map Area.** There was a significantly larger cortical map area following intervention ($T=2.56, p=0.05$) for the entire group of participants who completed the cortical mapping sessions before and after the intervention ($n=6$). For those in the unimanual group, the change in cortical map area was $3.16 \text{ cm}^2$ and for those in the bimanual group the change in cortical map area was $4.51 \text{ cm}^2$ (Figure 3.13).

**Cortical Motor Threshold.** There was no difference between pre- and post-intervention values for motor threshold ($T=1.10, p=0.30$) (Table 3.5) for the entire group of participants who completed the TMS testing before and after the intervention ($n=6$). For the unimanual group, the motor threshold decreased by 11% MSO whereas the
bimanual group increased by 2% MSO. The mean change in motor threshold following unimanual massed practice training decreased by 13% MSO more than the bimanual group (Figure 3.14).

**Cortical Map Volume.** There was no difference in the normalized cortical map volume found before and after the intervention for the entire group of participants who completed the cortical mapping sessions before and after the interventions (Table 3.5). For the unimanual group, the mean change in normalized cortical map volume was 3.54 cm³ and in the bimanual group the mean change in normalized cortical map volume was 3.20 cm³ (Figure 3.15).

**Location of Center of Gravity.** There was no difference in location of the COG of the cortical map before and after intervention. The mean COG of the cortical map was 0.94 cm anterior to Cz at the pre-intervention testing session, whereas it was 1.70 cm anterior to Cz following the intervention. The shift of the COG for the individual participants can be found in Figure 3.16.

**Discussion**

**Clinical Outcome Measures for all Participants.** The purpose of this study was to evaluate the effectiveness of a combination physical therapy intervention (massed practice training combined with somatosensory stimulation) for individuals with tetraplegia. The results suggest regardless of whether training is done with one hand or both hands, the combined intervention improves unimanual hand function, bimanual hand function, and sensory function. Beekhuizen *et al.* also found the combined intervention significantly improved unimanual hand function and sensory function. These
investigators found the combination intervention also improved pinch grip strength. Although there was a trend toward greater strength, we did not see a difference before and after the intervention. It’s plausible this is due to a floor effect. Out of the eleven individuals, only six were able to create enough force to register a force on the dynamometer. No change was observed in individuals who were unable to create an initial force on the dynamometer.

The relative contribution from the sensory stimulation and the massed practice training can not be determined by our research design. Sensory stimulation alone can improve sensory function, pinch grip strength, and unimanual hand function\textsuperscript{63}. However, in previous studies, the combination of the two interventions demonstrated greater mean changes than either intervention in isolation\textsuperscript{63}. Similar findings are evident in individuals with hand impairment due to stroke. Conforto \textit{et al.}\textsuperscript{109} investigated the effects of training following a single session of either sensory stimulation or sham stimulation in individuals post-stroke. The investigators found significant improvements in unimanual hand function following the sensory stimulation intervention compared to the sham intervention\textsuperscript{109}. When the stimulation was followed by training there were significantly greater functional test scores in the group that received sensory stimulation plus training compared to the group that received sham stimulation plus training. Further, the functional changes were retained for 30 days in the sensory stimulation and training group.

\textit{Comparison of Unimanual vs. Bimanual MP in Terms of Clinical Outcome Measures}. No significant differences were found when the two interventions were compared to each other, however the trends suggest the outcomes may depend on the
type of practice. The functional outcome measures demonstrate the importance of task specificity. Those participants in the unimanual training group performed better on the test of single hand function (i.e., the Jebsen Taylor Hand Function test) whereas participants assigned to the bimanual training group performed better on the test of bimanual hand function (i.e., the Chedoke McMaster Hand Activity Inventory). None of the testing items on the Jebsen Taylor Hand Function test measure the ability to stabilize an object, whereas all of the items on the Chedoke Activity Inventory involve both stabilization and manipulation. Thus, training under a unimanual paradigm may set the stage for changes in unimanual hand function, whereas bimanual training improves bimanual hand function. However, the amount of change on the Chedoke Arm and Hand Activity Inventory was small (mean change = 2-3 points). The minimal clinical difference associated with this test is a change of 6 points\textsuperscript{115}.

Alternatively, participants in the bimanual group may have demonstrated less change on the Jebsen Taylor Hand Function test because their practice was divided between the manipulation portion of the task with one hand for part of the training session and they then switched to practice the stabilization portion of the task with that hand. This training protocol thereby reduced the intensity of the training for a single hand compared to the unimanual group. If this hypothesis is correct, then by changing the training protocol such that the weaker limb practiced the manipulation portion of the task during the entire training session, the bimanual group should make similar changes on the Jebsen Taylor Hand Function test.

On some items of the Jebsen Taylor Hand Function test, no improvement in task performance time was observed. This may be because the participant modified the
strategy used to perform the task, a factor not measured by this time-based test. For example, prior to intervention, a participant turned cards over by sliding each card to the edge of the table (Figure 3.17) allowing her to place her thumb underneath to obtain a grasp on the card. This strategy was efficient in that it required little effort and time, because it had been well learned. However, this motor strategy was not flexible because it does not work in a variety of situations. If presented with a stack of cards or pages to turn in a book, she would be unable to slide a single card or page to the edge, thus the strategy would fail. Following intervention, the same participant was again presented with the cards, and she approached the task with a new movement pattern in which she grasped and lifted the cards directly from the table without sliding them to the edge. While this new pattern may have required more energy and time because it was a new skill (at the time), it is functional for a variety of circumstances. Given adequate practice with the new strategy, it’s possible the individual will be just as efficient and demonstrate more flexibility with this skill.

The change in sensory function, as measured by monofilament threshold, was similar for both training interventions, and reflected a change of 1 or 2 monofilaments. This change is equal to the effect size (1.5) reported in the literature\textsuperscript{121}.

There was no difference in pinch grip strength between interventions. The bimanual group had more than a one pound change in force production, whereas the unimanual group only increased by 0.24 pounds. For individuals with very small pinching force, a one pound change can not only improve the performance of tasks, but can also provide new opportunities of independence. Baker \textit{et al.}\textsuperscript{124} found many everyday tasks such as zipping a zipper, plugging in an electrical cord, cutting food with
a knife, and removing a key from a lock require two Newtons (approximately 0.5 pound) of force to perform.

Validity of the Chedoke Arm and Hand Activity Inventory. The Chedoke Arm and Hand Activity Inventory was inversely and moderately correlated with the Jebsen Taylor Hand Function test. A low score on the Jebsen Taylor Hand Function Test implies that an individual can perform the test items quickly, whereas a high score on the Chedoke Arm and Hand Activity Inventory suggests that the individual can perform the items with greater independence. Thus, an inverse correlation would be expected. The correlation was only moderate which can be explained by the differences between the tests. Individuals with very asymmetrical injuries may score very low on the Jebsen Taylor Hand Function test (meaning it takes a long time to complete the one handed tasks), but they are able to compensate when both hands are used concurrently on the Chedoke Arm and Hand Activity Inventory.

Neurophysiological Outcome Measures. There was a significant difference between the size of the cortical map before and after intervention. Other investigators have also found an increase in size of the cortical map following interventions focusing on a single limb. Liepert et al. investigated the size of the cortical map following constraint-induced therapy in individuals post-stroke. The investigators found an increase in size of the cortical map of the abductor pollicis brevis following this intervention.

While there was a significant increase in cortical map area, there was not a significant increase in the measures of cortical excitability (resting motor threshold and normalized cortical map volume). This was not expected, as the somatosensory
stimulation increases cortical excitability in non-disabled individuals. Further, Beekhuizen and Field-Fote identified a small but statistically significant decrease in motor threshold in individuals who received unimanual massed practice with somatosensory stimulation. It is possible that this study was underpowered for these outcome measures, as we only had six individuals who completed the TMS testing and training. This is unlikely, though, as the effect size was only 0.26 and the associated power was 11.5%. Alternatively, it is possible that improvements in hand function in individuals with SCI are more related to increases in cortical representation, rather than changes in cortical excitability. The somatosensory stimulation may induce a short-term increase in cortical excitability which provides an opportunity for cortical reorganization.

While the mean resting motor threshold was not different following intervention, the mean change in motor threshold was greater for those in the unimanual training intervention than the bimanual training intervention. Perhaps those individuals who focused on training a single upper extremity have greater changes in cortical excitability. In the unimanual group, individuals practiced the manipulative portion of the task with their weaker limb during an entire training session, whereas in the bimanual group, individuals practiced half the training session with their weaker limb performing the manipulative portion of the task and half the session, the weaker limb was performing the stabilizing portion of the task. As a result, individuals in the unimanual group spent a greater amount of time performing the manipulative portion of the task with their weaker limb, which is also the test hand for the cortical stimulation.

There are conflicting results regarding the cortical reorganization after bimanual training in stroke. Luft et al. used functional magnetic resonance imaging to investigate
the size of the cortical map following a bimanual training program and found an increase in size of the map following the intervention. Other investigators have not identified an enlargement of the cortical map, but rather more symmetrical levels of cortical excitability. Lewis and Byblow\textsuperscript{81} investigated the cortical map changes in both hemispheres following a rhythmic bilateral movement training program in individuals post-stroke. The investigators did not find a change in the cortical map outcome measured in the affected hemisphere, but found a reduction in the cortical volume on the non-affected side. The authors suggested the balancing of interhemispheric inhibition and excitation could be an explanation for their findings\textsuperscript{81}.

Finally, the COG appeared to shift to a more anterior position in four individuals (Figure 3.16). However, the magnitude of this shift (one cm) is not greater than that which can be expected to change in the absence of intervention\textsuperscript{105,106}. While the stability of the COG in individuals with SCI is not known, it can be hypothesized based on the stability of the map in individuals with other movement disorders. The average movement of the COG in the affected hemisphere in individuals with chronic stroke in the absence of intervention was found to be 1.13 cm\textsuperscript{105}.

**Conclusion**

Individuals with chronic tetraplegia due to SCI can improve in hand function with a simple, intensive hand training program. Greater numbers of participants are needed to confirm this conclusion. The type of training (unimanual or bimanual) may influence the degree of change in specific clinical outcome measures, wherein unimanual training improves unimanual hand function and bimanual training improves bimanual hand
function. Further, to improve both unimanual and bimanual hand function, future studies should investigate a bimanual training program in which the participants focus on using the weaker limb for the manipulative portion of the task.

**Limitations of this study.** There are very few numbers of participants included in the TMS data primarily due to two factors: the lack of an MEP in response to 100% MSO of the TMS, and the presence of spontaneous potentials which could not be distinguished from MEPs (Figure 3.11). To increase the sample size for this outcome measure, future investigations should evaluate changes in TMS outcomes under muscle contraction. Muscle contraction will lower the motor threshold, thus allowing potentials to be recorded from individuals with very high resting motor thresholds. In addition, spontaneous potentials will be integrated into the contractions and thus individuals with spontaneous potentials may also be included in the data collection. Finally, investigating MEPs under conditions of low level muscle contraction may prove to be more responsive to change following an intervention due to the relevance of these neurons to movement.
Figure 3.1: Diagram of hypothesized mechanism for increased cortical excitability for somatosensory stimulation. Black solid arrows indicate known connections between structures and dashed blue arrows indicate hypothesized connections. Bold arrows indicate possible pathway activated during somatosensory stimulation. Somatosensory stimulation activates large sensory afferents which travel to the spinal cord and into the sensory cortex. The sensory cortex increases excitability of motor cortex, which increases motor drive to the anterior horn cell. It is possible that descending connections from the sensory cortex also increase the motor drive to anterior horn cell.
Figure 3.2: Study Design

Participants Recruited for Study (n=13)

Participants Randomized to Group (n=13)

Randomized to Unimanual MP and SS Group (n=6)

Pre-Intervention Testing (n=6)

Dropout (n=1)

Intervention (n=6)

Post-Intervention Testing (n=5)

Randomized to Bimanual MP and SS Group (n=7)

Pre-Intervention Testing (n=7)

Intervention (n=7)

Dropout (n=1)

Post-Intervention Testing (n=6)
Figure 3.3: Six point scale for Semmes Weinstein Monofilament test. Monofilament threshold was defined as being able to identify the location of a monofilament of a specific diameter on five out of ten trials. The associated score was then assigned for the site tested.

<table>
<thead>
<tr>
<th>Score</th>
<th>Filament Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Unable to detect the largest monofilament.</td>
</tr>
<tr>
<td>1</td>
<td>6.65 mm</td>
</tr>
<tr>
<td>2</td>
<td>4.56 mm</td>
</tr>
<tr>
<td>3</td>
<td>4.31 mm</td>
</tr>
<tr>
<td>4</td>
<td>3.61 mm</td>
</tr>
<tr>
<td>5</td>
<td>2.83 mm</td>
</tr>
</tbody>
</table>
Figure 3.4: Participant using compensatory strategies is redirected during training. He is using excess shoulder and elbow movement, as well as, passively hyperextending the index finger to depress the button (Top). Upon redirection, the participant reduces the shoulder and elbow movement and utilizes the finger flexors and extensor indices to complete the task (Bottom).
Figure 3.5: Test for unimanual hand function at pre- and post-intervention testing for participants in the unimanual and bimanual massed practice training group. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Decrease in time represents improvement in score. Note that both groups improved in time to complete the seven testing items.

Figure 3.6: Test for bimanual hand function at pre- and post-intervention testing for participants in the unimanual and bimanual massed practice training group. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Increase in score represents improvement. Note that both groups improved in score.
Figure 3.7: Test for sensation in median nerve region at pre- and post-intervention testing for participants in the unimanual and the bimanual massed practice training group. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Increase in score represents improvement. Note that both groups improved by similarly in score.

Figure 3.8: Pinch grip force at pre- and post-intervention testing for participants in the unimanual and bimanual massed practice training group. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Increase in force represents improvement. Note that neither group improves in pinching force.
Figure 3.9: Correlation between Chedoke Arm and Hand Activity Inventory with Jebsen Taylor Hand Function test. X axis represent score on the Jebsen Taylor Hand Function test, Y axis represents score on the Chedoke Arm and Hand Activity Inventory. Concurrent validity of the Chedoke Arm and Hand Activity Inventory was established with $r = -0.59$. 
Figure 3.10: MEP in participant with C4 SCI at hotspot at 100% MSO prior to intervention (Top). MEP in the same participant at the hotspot at 88% MSO following intervention. (Bottom). X-axis represents time and Y-axis represents amplitude of the response. At time 0 the stimulus artifact is seen. The MEP is seen at 23 milliseconds.
Figure 3.11: Example of participant spontaneous potentials. X-axis represents time and Y-axis represents amplitude of the response. At time 0 the stimulus artifact is seen. Note the first potential appears to be an MEP, as the amplitude and latency are similar to what would be expected for a thenar muscle MEP (Top), however a potential that has the same shape is then seen prior to the stimulus and therefore must not be an evoked potential from the TMS (Bottom).
Figure 3.12: Cortical map of the thenar muscles, where each bar represents an average of three MEPs, prior to intervention (Top) and following intervention (Bottom). The letters and numbers represent the coordinate system on the cap. Note the greater number of sites and greater amplitude of responses in the second figure.
Figure 3.13: Cortical map area of thenar muscles at pre- and post-intervention testing for participants in unimanual and bimanual massed practice training groups. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Note increase in cortical map area for both groups.

Figure 3.14: Cortical motor threshold of thenar muscles at pre- and post-intervention testing for participants in unimanual and bimanual massed practice training groups. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Note decrease in cortical motor threshold for unimanual massed practice group.
Figure 3.15: Normalized cortical map volume of thenar muscles at pre- and post-intervention testing for participants in unimanual and bimanual massed practice training groups. Blue diamond represents unimanual group, red square represents bimanual group, and black bars indicate standard deviation. Note increase in cortical map area for both groups.
Figure 3.16: Distance between COG and Cz in the longitudinal direction of the cortical map at pre and post-intervention testing for all participants. Arrows indicate direction of change following intervention. Note only one participant’s COG is more anterior by a distance greater than that which can be expected in the absence of intervention (1.13 cm).
Figure 3.17: Change in grasping strategy before intervention (top) and following intervention (bottom) for the card turning task on the Jebsen Taylor Hand Function test. Note before intervention the participant must slide the card to the edge to position her thumb on the other side of the card. Following intervention, she is able to turn the card on the table without sliding. This strategy may be more useful in a variety of circumstances.
Table 3.1: Sample list of items and movement categories in massed practice training.

<table>
<thead>
<tr>
<th>Finger Isolation</th>
<th>Pinch</th>
<th>Pinch with Rotation</th>
<th>Grasp</th>
<th>Grasp with Rotation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typing on a Keyboard:</strong></td>
<td>Picking up Small Objects:</td>
<td>Turning Twist Ties:</td>
<td>Plugging in Cords:</td>
<td>Scooping Sugar:</td>
</tr>
<tr>
<td>Unimanual - Participant uses one hand to type typing sequence.</td>
<td>Unimanual - Participant picks up washers and nails to place in container on table.</td>
<td>Unimanual - Remove and replace twist ties on a stabilized card.</td>
<td>Unimanual - Participant plugs extension cords into power strip.</td>
<td>Unimanual - Participant scoops sugar and into container on table.</td>
</tr>
<tr>
<td>Bimanual - participant uses both hands to type typing sequence.</td>
<td>Bimanual - Participant picks up washers and nails to place in container in hand.</td>
<td>Bimanual - Remove and replace twist ties on a card that is stabilized in hand.</td>
<td>Bimanual - Participant plugs extension cords into each other.</td>
<td>Bimanual - Participant stabilizes container with hand and scoops sugar.</td>
</tr>
</tbody>
</table>

| Dialing a Cell Phone:        | Threading Needle:                    | Screwing Nuts and Bolts:            | Cutting with Scissors:               | Pouring Liquid:                 |
| Unimanual - Participant uses one hand to dial phone list on stabilized cell phone. | Unimanual - Thread fishing line into stabilized needle. | Unimanual - Unscrew nuts from a bolt that is stabilized. | Unimanual - Participant cuts stabilized paper with scissors. | Unimanual - Participant measures liquid into measuring cup on table. |
| Bimanual - participant uses both hands to dial phone list on cell phone in hand. | Bimanual - Thread fishing line into needle in hand. | Bimanual - Unscrew nuts from a bolt that is stabilized by the participant | Bimanual - Participant cuts paper stabilized with hand. | Bimanual - Participant measures liquid in measuring cup in hand. |

| Calculating Math:           | Writing on Paper:                    | Turning a Key in a Lock:            | Playing Cards:                       | Opening Containers:             |
| Unimanual - Participant calculates answers to problems on stabilized calculator. | Unimanual - Participant copies shapes with a pen, pencil, or crayon on stabilized paper. | Unimanual - Place key in doorknob to unlock door. | Unimanual - Participant plays card game with one hand alone. | Unimanual - Participant opens screw top containers stabilized on table. |
| Bimanual - Participant calculates answers to problems on calculator stabilized by their hand. | Bimanual - Participant copies shapes with a pen, pencil, or crayon on paper stabilized with their hand. | Bimanual - Place key in padlock to unlock lock. | Bimanual - Participant holds deck of cards and plays card game with other hand. | Bimanual - Participant opens screw top containers in hand. |

| Pushing Buttons:            | Popping Bubble Wrap:                 | Turning Knobs:                       | Squeezing a Spray Bottle:           | Scooping with Measuring Cups:   |
| Unimanual - Participant uses one hand to push buttons on a videogame that is stabilized. | Unimanual - Squeezing bubble wrap with one hand. | Unimanual - Participants turn knobs with one hand. | Unimanual - Participant sprays water into cup stabilized on table. | Unimanual - Participant measures beans in measuring cups with cup stabilized on table. |
| Bimanual - participant uses both hands to squeeze bubble wrap. | Bimanual - Participants turn knobs with both hands. | Bimanual - Participants turn knobs with both hands. | Bimanual - Participant sprays water into cup stabilized with hand. | Bimanual - Participant measures beans in measuring cups with cup stabilized in hand. |
Table 3.2: Baseline Equivalence Table comparing intervention groups. Nominal data was compared using a $\chi^2$ statistic, ordinal data was compared using a wilcoxon rank sum test, and ratio data was compared using a student t-test.

<table>
<thead>
<tr>
<th>Intervention Group</th>
<th>Unimanual Massed Practice</th>
<th>Bimanual Massed Practice</th>
<th>Test-Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASIA Classification</td>
<td>Mode = C; 14% B, 57% C, 14% D</td>
<td>Mode = C; 42% B, 57% C</td>
<td>$p = 0.12$</td>
</tr>
<tr>
<td>Level of Injury</td>
<td>Mode = C5; 17% C3, 17% C4, 50% C5,</td>
<td>Mode = C6; 42% C5, 57% C6</td>
<td>$p = 0.07$</td>
</tr>
<tr>
<td>Duration of Injury</td>
<td>Mean = 2.83 ± 1.17 years; Range = 2 - 5 years</td>
<td>Mean = 4.33 ± 4.05 years; Range = 1 - 13 years</td>
<td>$t = 0.82$, $p = 0.44$</td>
</tr>
<tr>
<td>UE Motor Score (max = 50)</td>
<td>Median = 32; Range = 22 - 46</td>
<td>Median = 32; Range = 19 - 43</td>
<td>$p = 0.71$</td>
</tr>
<tr>
<td>UE Sensory Score (max = 40)</td>
<td>Median = 40; Range = 28 - 40</td>
<td>Median = 34; Range = 18 - 40</td>
<td>$p = 0.11$</td>
</tr>
<tr>
<td>Cause of Injury</td>
<td>Mode = Traumatic; 100% Traumatic</td>
<td>Mode = Traumatic; 86% Traumatic, 14% Non-Traumatic</td>
<td>$\chi^2 = 0.93$, $p = 0.34$</td>
</tr>
<tr>
<td>Gender</td>
<td>Mode = Male; 83% Male, 17% Female</td>
<td>Mode = Male; 71% Male; 29% Female</td>
<td>$\chi^2 = 0.26$, $p = 0.61$</td>
</tr>
<tr>
<td>Age</td>
<td>Mean = 42.0 ± 16.93 years; Range = 20 - 67 years</td>
<td>Mean = 34.71 ± 15.71 years; Range = 16 - 55 years</td>
<td>$t = 0.80$, $p = 0.44$</td>
</tr>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>Mean = 292.25 ± 95.35 sec; Range = 140.33 - 386.96 sec</td>
<td>Mean = 222.14 ± 147.22 sec; Range = 87.91 - 483.33 sec</td>
<td>$t = 0.91$, $p = 0.39$</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory (max = 77)</td>
<td>Mean = 57.40 ± 20.67; Range = 21 - 71</td>
<td>Mean = 53.67 ± 14.47; Range = 35 - 64</td>
<td>$t = 0.35$, $p = 0.73$</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Score (max = 15)</td>
<td>Median = 11; Range = 5 - 15</td>
<td>Median = 12; Range = 4 - 15</td>
<td>$p = 0.97$</td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>Mean = 2.49 ± 3.74 pounds; Range = 0 - 8.50 pounds</td>
<td>Mean = 3.43 ± 4.14 pounds; Range = 0 - 10.10 pounds</td>
<td>$t = 0.39$, $p = 0.70$</td>
</tr>
</tbody>
</table>
Table 3.3: Mean pre- and post-intervention values and (standard deviation) for clinical outcome measure for all participants. Asterisks values indicate significant difference between pre and post-intervention test.

<table>
<thead>
<tr>
<th>Clinical Outcome Measure</th>
<th>Pre-Intervention (N=11)</th>
<th>Post-Intervention (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Jebsen Taylor Hand Function Test (Seconds)</td>
<td>254.00 (125.76)</td>
<td>* 186.55 (68.52)</td>
</tr>
<tr>
<td>Mean Chedoke McMaster Hand Activity Inventory (Score)</td>
<td>55.36 (16.64)</td>
<td>* 58.27 (15.92)</td>
</tr>
<tr>
<td>Mean Semmes Weinstein Monofilament Score</td>
<td>11 (3.56)</td>
<td>* 13 (3.28)</td>
</tr>
<tr>
<td>Mean Pinch Grip Strength (Pounds)</td>
<td>3.00 (3.80)</td>
<td>3.83 (4.48)</td>
</tr>
</tbody>
</table>

Table 3.4: Mean pre- and post-intervention values and (standard deviation) for clinical outcome measures for participants in different intervention groups.

<table>
<thead>
<tr>
<th>Clinical Outcome Measure</th>
<th>Unimanual Massed Practice (N=5)</th>
<th>Bimanual Massed Practice (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Intervention</td>
<td>Post-Intervention</td>
</tr>
<tr>
<td>Mean Jebsen Taylor Hand Function Test (Seconds)</td>
<td>292.25 (95.35)</td>
<td>200.59 (63.82)</td>
</tr>
<tr>
<td>Mean Chedoke McMaster Hand Activity Inventory (Score)</td>
<td>57.40 (20.67)</td>
<td>59.60 (21.73)</td>
</tr>
<tr>
<td>Mean Semmes Weinstein Monofilament Score</td>
<td>11.00 (3.83)</td>
<td>14.00 (4.09)</td>
</tr>
<tr>
<td>Mean Pinch Grip Strength (Pounds)</td>
<td>2.49 (3.74)</td>
<td>2.83 (3.87)</td>
</tr>
</tbody>
</table>
Table 3.5: Mean pre and post-intervention values and (standard deviation) for TMS related outcome measures, for all participants. Asterisks values indicate significant difference between pre and post-intervention values.

<table>
<thead>
<tr>
<th>TMS Related Outcome Measure</th>
<th>Pre-Intervention (N=6)</th>
<th>Post-Intervention (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical Map Area (Square Centimeters)</td>
<td>8 (7.0) cm²</td>
<td>* 11 (10.2) cm²</td>
</tr>
<tr>
<td>Resting Motor Threshold (Percent Maximum Stimulator Output)</td>
<td>81% (17.8)</td>
<td>76% (22.1)</td>
</tr>
<tr>
<td>Normalized Cortical Map Volume (Cubic Centimeters)</td>
<td>3.27 (2.63) cm³</td>
<td>4.96 (4.25) cm³</td>
</tr>
</tbody>
</table>

Table 3.6: Mean change in TMS related outcome measures and (standard deviation) for participants in unimanual and bimanual massed practice groups.

<table>
<thead>
<tr>
<th>TMS Related Outcome Measure</th>
<th>Unimanual Massed Practice (N=3)</th>
<th>Bimanual Massed Practice (N=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in Cortical Map Area (Square Centimeters)</td>
<td>3.16 (3.55) cm²</td>
<td>3.52 (3.11) cm²</td>
</tr>
<tr>
<td>Change in Resting Motor Threshold (Percent Maximum Stimulator Output)</td>
<td>-11% (11.0)</td>
<td>1.67% (2.1)</td>
</tr>
<tr>
<td>Change in Normalized Map Volume (Cubic Centimeters)</td>
<td>0.48 (0.35) cm³</td>
<td>2.90 (2.50) cm³</td>
</tr>
</tbody>
</table>
CHAPTER 4: PRACTICE-RELATED PLASTICITY: FUNCTIONAL AND CORTICAL CHANGES IN INDIVIDUALS WITH CERVICAL SPINAL CORD INJURY FOLLOWING FOUR DIFFERENT HAND TRAINING INTERVENTIONS

There are approximately 253,000 individuals living with chronic tetraplegia due to cervical spinal cord injury (SCI) in the United States\(^1\). Of these individuals 34% have incomplete injuries\(^1\), suggesting that some may have potential for recovery of arm and hand function. In a survey of individuals with tetraplegia, 48.7% prioritized recovery of arm and hand function as the factor that would most change their quality of life\(^2\). In a survey of 565 individuals with tetraplegia, 75-80% reported that improvement in hand function would be important\(^3\). These surveys demonstrate a compelling need for rehabilitation specialists to identify rehabilitation interventions to improve hand function and determine which intervention can induce the greatest changes in function for individuals with chronic tetraplegia.

While there is much evidence that individuals with *acute* tetraplegia improve in upper extremity function, strength, and sensation\(^6,31,125\), there is limited evidence of recovery of upper limb function in individuals with *chronic* tetraplegia. Individuals with incomplete injury tend to plateau in recovery of upper limb function after nine to twelve months of rehabilitation\(^31\). It is plausible that individuals participating in these studies were not been given sufficient intervention dosage and/or the most appropriate intervention. Studies from our laboratory have suggested given intensive, task-oriented training program, individuals with chronic tetraplegia can improve in hand function\(^62,63,78\). Further, this change in function is associated with changes in cortical neurophysiology\(^62,63,78\).
Following a cervical spinal cord injury (SCI), many maladaptive plastic changes occur in the central nervous system which may contribute to deficits in upper extremity function. Cortical reorganization occurs wherein the areas of the body affected by the injury have less cortical representation\textsuperscript{13,16,108}, there is less cortical excitability to muscles that are paretic as a result of the injury\textsuperscript{9,10,97}, and the cortical drive to these muscles is reduced\textsuperscript{10}. Finally, the cortical motor potential of upper limb musculature in individuals with cervical SCI is more posterior than non-disabled individuals\textsuperscript{17,18}. Interventions designed to improve upper extremity function in individuals with tetraplegia should consider not only activity limitations, but also cortical reorganization as reversing these neurophysiological impairments may contribute to recovery of function.

There are multiple approaches described in the literature that are thought to induce recovery of upper limb function including task-oriented training\textsuperscript{58-60,126}, electrical stimulation\textsuperscript{85,86,92,109,127}, strengthening\textsuperscript{128}, and motor imagery\textsuperscript{129}. When selecting the type of intervention, an intervention should ideally address both activity limitations and the maladaptive cortical reorganization that occurs following injury.

\textit{Massed Practice Training}. Massed practice (MP), a form of task-oriented training, has been shown to induce both cortical reorganization, as well as functional changes in individuals with tetraplegia\textsuperscript{62,63}. Much of the evidence regarding the effectiveness of MP training comes from the constraint-induced movement therapy trials in individuals with stroke where MP is one component of constraint-induced movement therapy\textsuperscript{58,59}. In constraint-induced movement therapy, individuals with chronic hemiparesis practice hand activities with their weaker limb alone and receiving shaping of motor behaviors, using an intensive training schedule over a two week period\textsuperscript{60}. In our
studies we have chosen not to incorporate shaping as part of the intervention, which allows the therapist to provide progressively less feedback during the intervention. We feel that if the participant receives less feedback from the therapist, he or she learns a reference of correctness for the new movement pattern, and thereby become more independent. Constraint-induced movement therapy is based on the theory of learned non-use, wherein individuals with asymmetrical injuries learn to perform activities with compensatory strategies such as using primarily their less affected limb. Later when more function is possible, individuals continue to use these well-learned compensatory strategies. In an effort to reverse the effects of learned non-use, many studies have investigated unimanual training of the weaker limb combined with shaping.

Unimanual training has the unique benefit of focusing on improving function in the weaker limb, and providing more opportunity for practice with this limb. Previous studies have investigated this form of massed practice training in individuals with SCI and found improvements in function and cortical changes associated with the improvements. Further our pilot study suggests that unimanual training may induce greater changes in cortical excitability compared to bimanual MP training. However, it is plausible that it is the concentrated practice with the manipulative portion of the task that is associated with the extent of the functional and cortical changes and not the use of a single hand alone. In our pilot study, participants in the bimanual group practiced the manipulative portion of the task only half of the time with their weaker limb and practiced the stabilization portion of the task half of the time with their weaker limb. By altering the intervention such that the participants practice the manipulative portion of the task with their weaker limb during the entire training session while the stronger limb
practices the stabilization; we may be able to induce greater changes in both function and transcranial magnetic stimulation (TMS) related outcome measures under the bimanual paradigm.

There is conflicting evidence from the stroke literature regarding the effectiveness of bimanual training approaches. Mudie and Matays\textsuperscript{79} found training both limbs simultaneously (practicing symmetrical unimanual tasks) resulted in greater changes on functional outcome measures compared to training the weaker limb alone. Conversely, Lewis and Byblow\textsuperscript{81} used a similar paradigm (practicing symmetrical unimanual tasks) and found limited effectiveness of the intervention on both functional and neurophysiological outcome measures. Neither of these interventions focused on coupling the limbs together to perform a common goal, which maybe an important aspect to improving bimanual limb function.

Theorin and Johansson\textsuperscript{131} used functional magnetic resonance imaging (fMRI) to investigate the differences in brain activation in non-disabled individuals during a unimanual and a bimanual activity. In this study cortical activation patterns during the performance of a task when the tool was stabilized by external means (the contralateral limb was not used) were compared to those of the same task under a bimanual condition in which the tool is stabilized by the contralateral limb. The investigators found that the greatest predictor of increased brain activation was the use of the non-dominant limb to perform the manipulative aspects of the task. This was true regardless of whether the activity was performed under the unimanual or bimanual condition. Further, the areas within the sensorimotor cortex activated under the unimanual condition were different from the bimanual condition. These findings suggest that when the weaker limb
performs the manipulative portion of the task, there is increased cortical activation. Therefore, during a unimanual or bimanual training intervention, the weaker limb should always perform the manipulative portion of the task, regardless of whether the individual is assigned to the unimanual or bimanual condition. In addition, to utilize the sensorimotor cortex dedicated to bimanual hand use, the individuals assigned to the bimanual group should practice tasks in which the hands are coupled to perform a common goal.

**Electrical Stimulation.** In individuals with cervical SCI, more functional and cortical changes are found when the MP training is augmented by somatosensory stimulation (SS) than MP training alone\(^{62,63}\). The parameters of electrical stimulation which provide the optimal environment to induce change are not known. SS is a form of electrical stimulation where the intensity is below motor threshold, the pulse duration is long (one millisecond), and the trains of stimulation are continuous\(^{91}\). This type of stimulation (specifically the long pulse width) is thought to preferentially target the large sensory fibers associated with the type I muscle afferents\(^{93}\). SS has also been associated with improvements in function and cortical plasticity. In individuals with weakness due to SCI\(^{63}\) or stroke\(^{92}\), prolonged application of SS alone increased pinch grip force\(^{63,92}\) and unimanual hand function\(^{63,109}\). Further, SS is associated with increased cortical motor excitability\(^{63}\), and is hypothesized to prepare the system for reorganization\(^{132}\).

Functional electrical stimulation (FES) is a form of electrical stimulation, wherein the stimulation is used as a neural prosthesis to improve hand grasping function in individuals with SCI\(^{87}\), however the use of an FES system as a training intervention may result in improved hand function even when the device is not in use\(^{86,88}\). Practice with an
FES system has been shown to be effective in improving arm and hand function without the assistance of the device in individuals with SCI\textsuperscript{86,88} and stroke\textsuperscript{86,89,133}. The mechanism for functional recovery following FES is hypothesized to be neural plasticity associated with motor learning\textsuperscript{88}. As the degree of neural reorganization is dependent on the task demands and motor learning in which the individual engages\textsuperscript{123}, providing more opportunities for practice of challenging tasks may result in greater improvement in function and cortical reorganization.

The mechanism behind improvements in function induced by SS and FES are thought to be similar. SS has been shown to increase cortical excitability in both non-disabled individuals\textsuperscript{91} and individuals with sensorimotor impairment due to stroke\textsuperscript{92} and SCI\textsuperscript{63}. In non-disabled individuals\textsuperscript{91} and individuals with SCI\textsuperscript{70}, SS does not increase spinal motoneuron excitability which suggests the increase in excitability is at the cortical level. Cortical neurophysiology associated with improvements in grasping function induced by FES have not been investigated, however changes in cortical excitability following FES in the lower limb have been investigated. Kido \textit{et al.}\textsuperscript{90} investigated the changes in cortical excitability following 30 minutes of FES assisted walking. The investigators found increased cortical motor excitability of the tibialis anterior after the intervention\textsuperscript{90}. In a similar study, Thompson \textit{et al.}\textsuperscript{134} investigated the impact of FES assisted walking on spinal neurophysiology. The investigators found no change in H-reflex amplitude, recipricocal inhibition, and presynaptic inhibition. From these results, it was concluded that the changes in cortical excitability must be at the cortical level. It is possible that training the upper limb through an intervention that utilizes FES will also increase cortical excitability.
The primary purpose of this study was to evaluate the effectiveness of MP training combined with electrical stimulation over a control condition by assessing both clinical and neurophysiological outcome measures using a delayed intervention design. We hypothesized that the immediate intervention group would demonstrate greater changes in both the clinical outcome measures and neurophysiological outcome measures. The secondary purpose of this study was to evaluate the effectiveness of two different MP interventions: unimanual or bimanual MP, when combined with a single electrical simulation paradigm: SS or FES. Based on results from pilot data, we hypothesized that those assigned to the unimanual group would demonstrate greater changes on the test of unimanual hand function and the bimanual group would demonstrate greater changes on the test of bimanual hand function. We further hypothesized that those assigned to the SS group would demonstrate greater changes in sensory score, pinch grip strength, and performance of functional outcome measures.

**Methods**

*Study Design.* This study utilized a delayed intervention design (Figure 4.1). Participants were stratified according to whether they had voluntary control over their intrinsic hand muscles (specifically the thenar muscles). This method of randomization was chosen as pilot data suggested a trend toward a moderate correlation between initial pinch strength and change on the Jebsen Taylor Hand Function test \((r=0.75, p = 0.086)\). In addition, upper extremity motor scores were not correlated with change on the Jebsen Taylor Hand Function Test \((r=0.17, p=0.74)\) or change on the Chedoke Arm and Hand Activity Inventory \((r=-0.13, p=0.81)\). Further, voluntary control of intrinsic hand
muscles has been shown to be a good predictor of recovery of hand function. If participants had voluntary control in intrinsic hand muscles bilaterally, they were considered high functioning, and if participants had voluntary control in intrinsic hand muscles unilaterally, they were considered low functioning. Participants without voluntary control in their intrinsic hand muscles were excluded from the study. Using this stratification, participants were randomly assigned by a research assistant to one of two groups: control / delayed intervention group or immediate intervention group. Simultaneously, individuals were also randomly assigned to one of four intervention conditions consisting of the following combinations: unimanual MP with SS, bimanual MP with SS, unimanual MP with FES, or bimanual MP with FES.

Following randomization, all participants received an evaluation by a physical therapist, and a neurophysiological evaluation. Those individuals assigned to the control / delayed intervention group underwent a three week waiting period before completing a second session of testing, whereas those assigned to the immediate intervention group started the intervention phase immediately. Further, the changes in the TMS outcome measures over a three week time period in individuals with SCI are not known, and this design allowed us to evaluate the stability of these outcome measures. During the waiting period, participants in the control / delayed intervention group were instructed to continue their therapy and exercise programs, but asked not to start any new therapy or exercise program. After a second session of testing, those assigned to the control / delayed intervention group received their intervention. Following the intervention all participants received a final session of testing. By comparing individuals who received immediate intervention, to those who were assigned to the control group / delayed intervention, we
addressed the following question: do individuals with chronic SCI improve in hand function after a combined intervention of MP training and electrical stimulation compared to a control condition. Further, by comparing the pre- and post-intervention data of all participants, we were able to compare the four different interventions designed to improve hand function in individuals with cervical SCI (Figure 4.2 and Table 4.1).

Participants: Twenty-four participants were recruited from the database at the Miami Project to Cure Paralysis. Half of the participants were from the Miami area, 17% were from the state of Florida (outside of Miami), and 33% were from out of state. The data was collected in Miami, Florida. We included individuals with incomplete SCI that fit the following inclusion criteria: diagnosis of cervical spinal cord injury at the level of C7 or above, chronic injury (one year post-injury), the ability to voluntarily activate at least one of their thenar muscle groups, and the ability to perform at least two items on the Jebsen Taylor Hand Function Test. We excluded individuals with seizure disorder, epilepsy, head injury, stroke, upper extremity contracture (inability to fully extend or flex the fingers), or a score equal to or greater than 73 on the Chedoke McMaster Hand Activity Inventory. The exclusion criteria was chosen to leave out participants who had increased risk of seizure with the use of TMS, individuals who may have been unable to activate the FES, and individuals who may have reached a ceiling effect on the Chedoke Arm and Hand Activity Inventory. A score of 73 was chosen based on the mean change in the bimanual group on this outcome measure in the pilot study. The mean change in this outcome measure in the pilot study was 3.5, and the maximum score on this outcome measure is 77, therefore individuals who score 73 or higher may not change due to a ceiling effect, and were not included in this study.
During data collection, the following descriptive data was compared to ensure baseline equivalency between groups: American Spinal Injury Association (ASIA) classification, duration of injury, ASIA upper extremity motor score, strength in three hand muscles (finger flexors, thenar, and hypothenar), and ASIA upper extremity sensory score (Tables 4.3, 4.4, and 4.5).

**Outcome Measures:** The clinical testing protocols were completed by a second physical therapist. Although this evaluator was not blinded to assignment of the control / delayed intervention group and immediate intervention group, she was blinded to intervention assignment. We do not think this impacted the results of the study as the primary outcome measure, the Jebsen Taylor Hand Function test, is scored by timing the completion of seven tasks and not through clinical judgment. Clinical tests included measures of unimanual hand function, bimanual hand function, pinch grip strength, sensory function and a disability questionnaire. These measures were chosen to include both measures of impairments, activity limitation, and participation level data. The Jebsen Taylor Hand Function test was chosen as it is a measure of unimanual hand function and is designed to measure change in hand function after therapeutic intervention. The Chedoke Arm and Hand Activity Inventory was chosen as it is a measure of bimanual hand function. Both the Semmes Weinstein Monofilament test and pinch grip strength measures were chosen as these measures have detected change in the combination intervention of massed practice with somatosensory stimulation in previous studies.\textsuperscript{62,63}

During the clinical test (with exception of the ASIA), participants were seated in their wheelchair at a table adjusted to their elbow height. The ASIA sensory and motor
testing were performed according to published guidelines\textsuperscript{117}. Inter-rater reliability of the pinprick, light touch, and motor evaluation in individuals with SCI, as measured by the intra-class correlation coefficient (ICC), is between 0.96 to 0.99\textsuperscript{118,119}. Participants were positioned in supine with a pillow under their head for comfort. In addition to the ASIA motor test, a manual muscle test of the thenar muscles was also done. The manual muscle test of the finger flexors, thenar muscles, and hypothenar muscles was combined to create a distal hand motor score.

Upper extremity motor function was measured using both a test of unimanual hand function (the Jebsen Taylor Hand Function Test) and a test of bimanual hand function (Chedoke Arm and Hand Activity Inventory). All functional testing was videotaped. The Jebsen Taylor Hand Function test assesses the capacity for unilateral hand function and is sensitive to improvement in hand function associated with therapeutic interventions. This test has been validated for individuals with C6 and C7 tetraplegia. The test-retest reliability is 0.89 to 0.99 in individuals with neurological disorders with movement impairment\textsuperscript{114}. It is a timed test based on the following seven items: writing, turning cards, picking up small objects, feeding, stacking, picking up large objects, and picking up heavy objects. Both hands were tested individually, with the more affected limb tested first. For each item, the evaluator explained the directions for the task to the participant and demonstrated the item. The time to perform each of the individual testing items was recorded, and the sum of all seven tasks was used as the final score.

The Chedoke Arm and Hand Activity Inventory was used to evaluate the use of both hands together\textsuperscript{115}. The inter-rater reliability of the Chedoke Arm and Hand Activity
Inventory in individuals with stroke has an ICC of 0.98. Concurrent validity has been established in individuals with tetraplegia through correlation between the Jebsen Taylor Hand Function Test and the Chedoke Arm and Hand Inventory ($r = -0.59$). The minimal detectable change score associated with this measure is 6.4. This outcome measure is an ability test designed to measure the performance of bilateral hand tasks as they relate to function in individuals with stroke. There are 13 items and each item is given a score from one through seven, with one being dependent or unable to perform the item and seven being independent in performance of the task. Items number 12 and 13 were omitted. These items correspond with placing a large container on the table from the floor and carrying a bag up stairs. It was felt that these items would be unlikely to change with in response to the type of training utilized in this study, and further it would be unsafe for some participants to perform these activities. Participants were instructed to use both hands to complete the tasks. Each task was then demonstrated by the examiner, and was attempted twice by the participant. The higher score was documented.

Pinch grip strength was measured with a handheld dynamometer (Microfet). The participant was instructed to squeeze using a key pinch grip, with the instruction to “squeeze as hard as you can”, for three seconds. The average force produced on three trials was recorded and the mean force calculated. This method of measuring grip strength has been shown to be reliable in individuals with SCI.

Sensory function was evaluated using the Semmes Weinstein Monofilament Test. The inter-rater reliability of the Semmes Weinstein Monofilament test in

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13 Hoggan Health Industries, 8020 South 1300 West, West Jordan, UT 84088
individuals with peripheral nerve injury, as well as non-disabled individuals, as measured by the ICC is 0.97\textsuperscript{121}. In addition, the responsiveness to change has an effect size of 1.5 in individuals recovering from peripheral nerve damage\textsuperscript{121}. Five monofilaments ranging in diameter from 2.83 mm to 6.65 mm were used. With the participant’s eyes closed, the smallest monofilament was presented first. The monofilament was depressed until it was bent and was removed after 1.5 seconds. The participant was instructed to respond when and where a touch was perceived. If the participant did not respond, subsequent monofilaments were used until the participant perceived five out of ten stimuli. The region of the hand innervated by the median nerve (tip of the thumb, tip of index finger and base of index finger) was evaluated\textsuperscript{135}. Each monofilament was assigned a score based on an ordinal scale from zero to five, where zero means unable to feel the monofilament with a diameter of 6.65 mm and five means able to feel the monofilament with a diameter of 2.83 mm on at least five out of ten trials. The three scores (representing the three regions) were summed to determine a total sensory function for the median nerve region (maximum score is 15). Higher scores indicated smaller diameter of the monofilaments and increased sensitivity.

A health assessment questionnaire\textsuperscript{136} was completed by each participant. The questionnaire was designed for individuals with rheumatoid arthritis, and has eight categories (in its original form): dressing and grooming, arising, eating, walking, hygiene, reaching, griping, and performing daily activities\textsuperscript{136,137}. We limited the questionnaire to items that we felt would be responsive to this type of intervention, and therefore we used only items in the following four categories: dressing and grooming, eating, reaching, and griping. The participant was instructed to classify each activity on a difficulty rating
scale where a rating of one indicates no difficulty with the task and a rating of four indicates unable to perform the task. The items included activities such as dressing using buttons, zippers, and tying shoes; opening a new container of milk; and turning on water facet in a sink. The individual items were summated for a final disability score, where a low score indicates low disability and a high score indicates great disability.

Cortical motor maps and recruitment curves of the thenar muscles were constructed by recording motor evoked potentials (MEPs) in response to a stimulus evoked by transcranial magnetic stimulation (TMS). Monophasic single pulse TMS was delivered by a Magstim 200 stimulator\textsuperscript{14} (maximum magnetic field strength of two Tesla) using a figure eight magnetic coil. The limb chosen for testing was the weaker limb (based on the ASIA motor scores). However, if the individual had no voluntary control over the thenar muscles in their weaker hand, or the individual was not able to perform any items on the Jebsen Taylor Hand Function test with this limb, then the stronger limb was tested.

Participants were seated in their wheelchairs, such that they could see the computer monitor for the purposes of biofeedback. Participants were fit with a tight fitting cap with a grid measuring one cm squares (Magicap Elite\textsuperscript{15}). To ensure reliable cap placement, the nasion, inion, and ears were drawn on the cap, and the distance between the cap and the nasion was measured. The thenar muscles were palpated, swabbed and abraded with Lemon Prep and alcohol. Recording and reference Ag / Ag-Cl surface electrodes were placed in a muscle-tendon montage, with a ground over the

\textsuperscript{14} The Magstim Co Ltd, Spring Gardens, Whitland, Carmarthenshire, Wales, United Kingdom SA34 OHR.

\textsuperscript{15} The Bobby Co, 4807 Mercury St, San Diego, CA 92111.
styloid process. To ensure reliable electrode placement, distance between the electrodes was measured, and the hand, fingers, and electrodes were traced onto a transparent plastic sheet for comparison at subsequent testing sessions. The electromyography (EMG) signals were amplified x1000 and band pass filtered (10-2KHz) using a Grass S88 amplifier\textsuperscript{16}. The EMG responses were digitized using an analog to digital converter (model 1401\textsuperscript{17}) and stored on a computer using Signal 2 software\textsuperscript{18}.

Two examiners were present during the mapping process and consistently performed the same tasks. The first examiner performed the stimulating procedures and monitored the participant, while the second examiner evaluated the signal and recorded the frame number, as well as the intensity of the stimulus or site of the map. The coil was placed directly on the cap over the test hemisphere with the handle pointing 45 degrees posteriorly and laterally, as this position is known to most directly activate the corticospinal tract\textsuperscript{100}. The region representing the thenar muscles was identified on each participant individually (approximately five cm lateral to midline). The hypothesized thenar region was stimulated and the coil moved around until the “hot spot” (where the amplitude is greatest and latency is shortest) was found.

MEPs were evoked while the participant performed a minimal voluntary contraction (10% maximum voluntary force). The individual’s maximum voluntary contraction of thenar muscles was measured on three subsequent trials using a force

\textsuperscript{16} Grass-Telefactor, 600 E Greenwich Ave, West Warwick, RI 02893.

\textsuperscript{17} Cambridge Electronic Design Ltd, Science Park, Milton Rd, Cambridge, UK, CB4 0FE.

\textsuperscript{18} Cambridge Instrument Division, UK
transducer (Flexiforce Economical Load and Force System\textsuperscript{19}) which displayed force on a computer screen. The largest of these three values was noted as the individual’s maximal voluntary force\textsuperscript{10}. Using the Flexiforce computer software as biofeedback, participants were instructed to maintain a target muscle contraction of 10% of their maximum voluntary contraction\textsuperscript{138} during groups of either five stimuli (for the recruitment curves) or three stimuli (for the cortical maps). Ten percent of the maximum voluntary contraction force was chosen to reduce variability in the electromyography. Participants were provided with rest periods between groups of stimuli to reduce the influence of fatigue on the testing procedures.

A MEP was defined as a response having a root mean square (RMS) amplitude of at least 50 microvolts above the baseline EMG level at 10% maximum voluntary contraction prior to the stimulus with a subsequent silent period following the evoked potential\textsuperscript{139}. This definition was used to ensure that any increase in amplitude was related to the stimulation and not variability in the muscle contraction. Other investigators have found MEP amplitude to be correlated with the duration of the silent period\textsuperscript{140} therefore requiring both an increase in amplitude as well as the presence of the silent period ensured that the potential was related to the stimulus. To find active motor threshold (AMT), the stimulus intensity was decreased to an intensity that did not evoke a motor response, typically 65% maximum stimulator output (MSO) for individuals with SCI and systematically increased in five percent increments. The AMT was defined as stimulus intensity which evoked five out of ten MEPs\textsuperscript{65,66}.

\textsuperscript{19} Tekscan Inc. 307 West First Street, South Boston, MA 02127
Recruitment curves were created by measuring the MEPs in response to increasing intensities of stimuli. The intensity was normalized to the participant’s AMT. The first value was 80% of AMT and subsequent stimuli increased by 20% of AMT (i.e., 80% AMT, 100% AMT, 120% AMT, 140% AMT, etc.). The final stimulating intensity was 100% MSO. At each stimulator intensity, five MEPs were recorded.

For the mapping procedure, we used a stimulus intensity of 120% of the AMT. Starting at the hot spot, each site on the grid of the cap was stimulated three times. The coil was moved laterally by one cm increments until there was no MEP response.

To control for individual variation in motoneuron excitability, the MEP values were normalized to the maximum response of the median nerve to direct stimulation (M-wave). To find the maximum M-wave for the median nerve, Ag / Ag - Cl stimulating electrodes were placed in the cubital fossa with the cathode more distal than the anode. Single pulses of 500 µsec duration were applied in increasing intensities until no further increases in amplitude of the response were observed.

**EMG Processing.** The EMG data was analyzed using Signal 2 software. To determine the difference between the amplitude of the signal associated with the MEP and the baseline contraction amplitude, the difference between the RMS amplitude at 20-40 milliseconds following the stimulus and the RMS amplitude of a 20 millisecond time interval prior to the stimulus was calculated. For the recruitment curves, RMS amplitude (at each normalized intensity) was averaged across five MEPs. For cortical maps, the RMS amplitude (at each site) was averaged across the three MEPs. The MEPs were normalized to the maximum amplitude of the m-wave.
The outcome measures from the recruitment curves included AMT, mean normalized maximum MEP, and maximum slope of the recruitment curve. Other investigators have used maximum slope to investigate the effect of an upper extremity training intervention on recruitment curves\textsuperscript{67}. The Boltzman equation\textsuperscript{141} was not used, as this equation did not accurately describe the recruitment curves of our participants, as many of the recruitment curves were more linear than sigmoidal in shape. Most of the recruitment curves measured did not reach a plateau in response to the TMS.

The outcome measures for the cortical maps included cortical map area, normalized cortical map volume, and the location of the center of gravity (COG). The cortical map area was defined as the number of sites that elicited an MEP\textsuperscript{102}. The normalized cortical map volume was defined as the sum of the normalized MEPs\textsuperscript{102}. To determine if there was a shift in the excitable region, the COG was determined and the MEP amplitudes were weighted according to the distance from Cz. Each site was weighted for both a longitudinal (anterior / posterior) and a latitudinal (medial / lateral) direction\textsuperscript{102}. As the COG moved more anteriorly to Cz, the weightings became larger and as the COG moved more posteriorly they became smaller. A negative value indicated a site posterior to Cz. Likewise, as the COG shifts more laterally, the value becomes larger and as the COG shifts more medially, the values become smaller. Therefore, a shift in the anterior and lateral direction would be reflected by an increase in both the longitudinal and latitude values. The formula for the latitudinal COG calculation\textsuperscript{102} is as follows:

\[ X_{COG} = \frac{\sum a_i x_i}{\sum a_i} \]
Where $a_i$ is the mean amplitude at an individual scalp site whose coordinate is $x_i$ centimeters from Cz. Following the same lines, the longitude COG is calculated in a similar manner:

$$Y_{COG} = \frac{\sum a_i y_i}{\sum a_i}$$

**Intervention Protocol:** The intervention schedule was five days per week, two hours per day, for three weeks. This schedule was chosen as prior studies from this laboratory have shown that this training schedule is adequate to demonstrate changes in hand function and cortical excitability. In addition, other investigators have used a similar dosage when investigating the impact of FES, and found it to be adequate for improvements in hand function.

**Massed Practice Training Protocol.** The MP protocol was modeled after the unimanual MP training described in previously published reports from our lab. When necessary, the task-related object was stabilized by glue, putty, or a clamp to allow tasks to be accomplished with one hand. The participants then practiced the manipulation portion of the task with their weaker limb (or limb chosen for testing). For example, in the container opening task, jars were glued onto a large board and participants were instructed to remove the lid (Figure 4.3). Likewise, in the pick-up sticks task, participants practiced a tripod grasp with their weaker limb to move objects on the table (Figure 4.4).
The bimanual tasks were as similar as possible to the unimanual tasks with slight modifications so that the tasks were practiced bimanually. Using the previous example, participants in the bimanual group practiced opening containers using the stronger hand to stabilize the container and the weaker hand to remove the lid (Figure 4.3). During the entire training session, the weaker hand practiced the manipulative portion of the task, and the stronger limb practiced the stabilization portion of the task. Likewise, in the pick-up sticks task participants practiced a tripod grasp with both hands (Figure 4.4).

For those in the bimanual MP group, tasks were both symmetrical and asymmetrical, symmetrical tasks required that both hands perform a similar movement pattern, whereas asymmetrical tasks required that each hand perform a different movement pattern. In tasks that were symmetrical, the participants were encouraged to perform similar movement patterns with both hands simultaneously. For example, in the pick-up sticks task, the participants utilized a tripod grasp on both sticks concurrently (Figure 4.4). In asymmetrical movement tasks, one hand functioned as an assistive or stabilizing hand and the other hand performed the manipulative portion of the task (such as picking up magnetic discs from the table to place in a container) (Figure 4.5). In these types of tasks the participant practiced the task using their weaker hand to manipulate the object and the stronger hand to stabilize the object.

Each training session was two hours in duration, divided into 20 to 25 minute increments of practice in each of the movement categories. Each of the five movement categories had five to ten associated activities in which the participant selected one to two tasks from each category during a single training session (Table 4.2). Participants chose the tasks practiced in order to ensure the task had relevance for them. The intent was to
practice a variety of tasks in order to engage the hand or hands in as many degrees of freedom of movement as possible.

The focus of both the unimanual and bimanual interventions was to restore movement patterns typical of individuals who are not disabled. To accomplish this, the physical therapist first demonstrated the appropriate performance of the task. The participant then performed the task. If the participant performed the task in a way that differed greatly from the typical way, the therapist encouraged the participant to modify their strategy. Compensatory strategies were discouraged. For example, if the individual utilized excessive shoulder and elbow motion to maintain a tenodesis grip, encouragement was given to reduce the shoulder motion and rely more heavily on their extrinsic and intrinsic hand muscles (Figure 4.5).

Some tasks were more challenging than others for each individual participant. If the individual was unable to complete a task independently using a typical movement pattern, then hand-over-hand assistance was provided to ensure they could complete the task successfully. Hand-over-hand assistance was provided over the individual’s hands (not the object) so the individual was able to complete the task as independently as possible (Figure 4.6). The assistance was gradually removed until the individual could perform the task independently.

Alternatively, if the task was not sufficiently challenging, the demands of the task were increased by altering the setup. The task was determined to be insufficiently challenging if the participant performed the task as demonstrated by the trainer, and rated the task greater than eight of ten scale, where one represented great effort to complete the task and ten represented minimal effort to complete the task. For example, to increase
the difficulty for the bean sorting task, the participant first picked up individual beans from a bowl filled with beans, progressing to pick up the beans from the table, then progressing to shooting beans (by pinching between thumb and index finger) into a container lying on its side, and finally shooting beans into an upright container. This was done to ensure the tasks were sufficiently challenging, because evidence suggests tasks must be sufficiently challenging to induce cortical reorganization. Activities were practiced until the participant was fatigued, with emphasis on movement accuracy and fluency. When the participant was fatigued, the therapist either reduced the demands of the task such that the participant was able to complete the task successfully or a rest break was provided.

**Electrical Stimulation Protocol.** During each training session, participants received electrical stimulation applied to their weaker limb (or the limb chosen for testing) in conjunction with the MP training. Ag/Ag-Cl surface electrodes were placed over the volar surface of wrist just lateral to midline, in the region of the median nerve.

The somatosensory stimulation was delivered using a constant current stimulator (Digitimer model DS7A) according to a previously published protocol. The trains were delivered at a frequency of ten Hz. Each train consisted of five pulses of one millisecond duration. Stimulus intensity was set to a level just below that which evoked an observable twitch in any of the muscles innervated by the median nerve. The stimulation was applied throughout the intervention session concurrently with the MP.

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20 Digitimer Ltd, 37 Hydeway, Welwyn Garden City, Hertfordshire, United Kingdom, AL7 3BE.
The FES was delivered only when triggered by the participant. The stimulating electrodes were placed in the same location as the somatosensory stimulation, and recording electrodes were placed on the thenar muscles with a ground electrode over the styloid process. The EMG was amplified and digitized using an analog-to-digital converter (Model #1401\textsuperscript{21}) and visualized in computerized software (Spike\textsuperscript{22}). The software triggered the constant current stimulator when the participant activated their thenar muscles. When threshold was reached, trains of electrical stimuli were delivered at 40 pulses per second, 200 microseconds duration, and at 120% of the intensity required to elicit a twitch in the thenar muscles. The stimulation was designed to assist the participant with grasp at the point in the movement when the stimulation would be most useful.

Statistical Analysis: Statistical analysis was performed using SAS version 9.1.3 and NCSS software. As the data was collected, summary statistics were generated and data was graphed in the form of histograms to ensure equality of groups in terms of voluntary control over intrinsic hand muscles, upper extremity motor score, severity of injury (ASIA classification scale), and duration of injury (Tables 4.3, 4.5, and 4.7). The effects of the control condition or intervention on the clinical and neurophysiological outcome measures were examined using repeated measure ANOVA. The level of significance was accepted at an $\alpha \leq 0.05$. A repeated measures ANOVA was used to compare the effects of the interventions (Unimanual, Bimanual, FES, and SS).

\textsuperscript{21} Cambridge Electronic Design Ltd, Science Park, Milton Rd, Cambridge, UK CB4 OFE

\textsuperscript{22} Cambridge Electronic Design Ltd, Science Park, Milton Rd, Cambridge, UK CV4OFE
Correlations between clinical outcome measures, TMS outcome measures, and the combination were determined using a Pearson Correlation Coefficient.

Results

Participants. Twenty-four participants were recruited for this study. Twelve participants were randomly assigned to the control / delayed intervention group and twelve were randomly assigned to the immediate intervention group (Figure 4.2). Three participants were excluded, as they scored 73 or higher on the Chedoke Arm and Hand Activity inventory. Two participants did not complete the intervention phase of the study (Figure 4.2) and therefore there were four or five participants in each combination intervention group (Table 4.1). For the purposes of the statistical analysis, the participants who received similar massed practice training were grouped together and the participants who received similar electrical stimulation protocols were also grouped together (Table 4.1).

For clarity, we well refer to the participants in the control / delayed intervention group as the control group (although, these participants did participate in the intervention), and participants who were not in the control group will be referred to as the immediate intervention group. For this comparison the testing sessions will be referred to as testing sessions one and two. When the four different interventions were compared, all participants are included. These groups will be referred to by their specific type of training: unimanual, bimanual, SS, or FES groups, although each participant received a single type of massed practice training and a single type of electrical stimulation. For this comparison, testing sessions will be referred to as pre- and post-intervention testing.
In this study, we compared a physical therapy intervention (which consisted of a combination intervention of massed practice and electrical stimulation) to a delayed intervention control condition. Repeated measures ANOVAs were used to compare the changes between testing sessions one and two of the control group with that of the immediate intervention group. The effect of time indicates there was a change between the two testing sessions, when the groups (control or immediate intervention) are combined. The effect of group suggests that the groups were different when the testing sessions were combined. Finally, the interaction between time and group would suggest that the amount of change in one group is greater than the amount of change in the other group. Thus, it is the interaction of time and group which provides the most information.

Hypothesis 1: Immediate intervention group will demonstrate greater changes in both the clinical and neurophysiological outcome measures. The control group and immediate intervention group were similar in their demographic information (Table 4.3) and their baseline testing scores, except for one outcome measure (Table 4.4). At the first testing session, participants in the control group performed significantly better on the Jebsen Taylor Hand Function test, than participants in the immediate intervention group (Table 4.3). It is possible this is because there were six individuals who had moderate spasticity in their test limb, four of which were assigned to the immediate intervention group and only two which were assigned to the control group. The mean baseline score for these six participants was 662.42 seconds with a standard deviation of 209.40 seconds. When these six participants were omitted from the analysis, the immediate intervention group (mean = 293.95, standard deviation = 224.70) and control group (mean = 221.43, standard deviation = 160.48) become equal (t = 1.40, p = 0.21). When
analyzed separately, these six participants do significantly improve from pre- to post-intervention testing ($t = 2.70, p = 0.04$) (Figure 4.9) with a change similar (mean change $= -63.87$ seconds) to that of the immediate intervention group (mean change $= -71.63$).

**Unimanual Hand Function.** For the Jebsen Taylor Hand Function test, the effect size (the difference between the change in the control group and the immediate intervention group) is $-81.14$ seconds. We are 95% confident that the true mean difference lies between $-5.12$ and $-157.18$ seconds. As this confidence interval does not include zero, we can be 95% confident that the intervention alone group improves more than those in the control group. Using a repeated measures ANOVA, there was a significant time and group interaction ($F=5.31, p=0.03$) between the control group and immediate intervention group at testing session one and two (Figure 4.7). The control group did not improve after the control period, demonstrated by a slight increase in total time score (mean change $= 9.52$, SD $= 45.55$ seconds), whereas the immediate intervention group improved, demonstrated by a decrease in total time score (mean change $= -71.63$, SD $= 100.16$ seconds).

However, the groups were not similar at baseline on this outcome measure (Table 4.4) so it’s possible that the control group reached a floor effect or the immediate intervention group had a greater change because they had more range on the test to improve. We do not feel this is the case. The mean value of participants in the control group was 225.72 seconds, which is still much greater than the normative data published by Agnew et al.$^{142}$ Men between the ages of 36-45 years without disability, score a total mean value of 37.68 seconds, whereas the lower end of the range in the control group was 96.27 seconds$^{142}$. Further, participants who were initially assigned to the control
group did complete the intervention after the control period and improved by a similar amount (mean change = -51.63, SD = 17.08 seconds) (Figure 4.8) to those in the immediate intervention group (mean change = -71.63, SD = 100.16) after the training. The change from pre- to post-intervention testing in participants in the control group is significant \((t=3.04, p = 0.01)\), indicating that they did improve in unimanual hand function following the intervention. Finally, there is no correlation between initial test score and the amount of change seen in this outcome measure \((r=-0.31, p = 0.19)\), indicating that the initial score does not relate to the amount of change on this test.

**Bimanual Hand Function.** For the Chedoke Arm and Hand Activity inventory, there was not a significant time and group interaction \((F=2.25, p=0.15)\) between those in the control group and immediate intervention group at testing session one and two (Figure 4.10). The control group did not change in total score (mean change = 0.90, SD = 4.15) whereas the immediate intervention group increased slightly in total score (mean change = 2.10, SD = 4.77).

**Pinch Grip Strength.** For pinch grip strength, there was not a significant time and group interaction \((F=0.61, p = 0.44)\) between the control group and immediate intervention group between testing session one and two (Figure 4.11) indicating that there was no difference in change in pinch grip strength between the control group and the immediate intervention group. The control group did not change (mean change = 0.0001, SD = 1.62 pounds) whereas the immediate intervention group increased slightly in mean strength (mean change = 0.50, SD = 1.12 pounds).

**Sensory Function.** On the Semmes Weinstein Monofilament test, there was not a significant time and group interaction \((F=0.28, p=0.60)\) between those in the control
group and immediate intervention group between testing session one and two (12). This suggests that neither the control group (mean change = 0.30, SD = 1.42), nor the immediate intervention group (mean change = 0.60, SD = 1.08) changed in sensory score, as the effect size associated with change on this test is a score change of 1.5\textsuperscript{121}.

**Disability Questionnaire.** On the Health Assessment Questionnaire, there was not a significant time and group interaction (F=0.56, p=0.46) between the control group and immediate intervention group at testing session one and two (Figure 4.13). This indicates that neither the change in the control group (mean change = -0.5, SD = 2.17) was similar to that of the intervention group (mean change = -1.22, SD = 1.99).

The TMS data is summarized in Table 4.10. Out of the 19 participants who completed the study, five were unable to complete the TMS testing session: one did not tolerate the TMS, three had excessive stimulation artifact associated with the recording, and we were not confident that one participant satisfied the exclusion criteria (specifically the history of head injury). An example of an MEP, a cortical map and a recruitment curve before and after intervention is found in Figures 4.14, 4.15, and 4.16.

**Cortical Map Area.** For cortical map area, there was a significant time and group interaction (F=5.69, p=0.03) between the control group and immediate intervention group at testing session one and two (Figure 4.17). The control group did not change (mean change = -1.33, SD = 3.93 cm\(^2\)) whereas the intervention group increased in cortical map area (mean change = 6.33, SD = 7.12 cm\(^2\)). The effect size was 7.67 cm\(^2\). We are 95% confident that the difference between the control group and intervention group is between 0.72 and 14.61 cm\(^2\).
Cortical Map Volume. For the normalized cortical map volume, there was not a significant time and group interaction between the control group and immediate intervention group between testing session one and two (F=3.46, p=0.08) (Figure 4.18) indicating there was no difference between the change in the control group and the change in immediate intervention group. There was a trend for an increase in normalized cortical map volume for the intervention group (mean change = 1.30, SD = 1.98 cm$^3$), whereas the control group stayed relatively stable (mean change = -0.25, SD = 0.53 cm$^3$).

Center of Gravity. For the shift in the longitudinal direction (anterior/posterior direction) of the COG, there was not a significant time and group interaction (F=0.39, p=0.54). Neither the control group (mean change = 0.12, SD = 0.56 cm) nor the immediate intervention group shifted in COG in the longitudinal direction (mean change = 0.14, SD = 0.91 cm).

Active Motor Threshold. For AMT, there was not a significant time and group interaction (F=2.77, p = 0.12) between the control group and immediate intervention group at testing session one and two (Table 4.10). Neither the control group (mean change = -3.60, SD = 6.56 % MSO) nor the immediate intervention group changed in AMT (mean change = 2.00, SD = 9.70 % MSO).

Maximum Motor Evoked Potential. For the maximum MEP amplitude, there was not a significant time and group interaction (F=0.01, p=0.93) between the control group and immediate intervention group comparing testing session one and two (Table 4.10). Neither the control group (mean change = 3.35%, SD = 4.49 % Mmax) nor the intervention group increased in mean maximum MEP amplitude (mean change = 2.63%, SD = 10.70% Mmax).
**Maximum Slope of Recruitment Curve.** The largest change in slope was typically at the same intensity (normalized to the participant’s AMT) before and following the intervention and this intensity was usually the increase in amplitude between (120% AMT and 140% AMT). For the maximum slope of recruitment curve, there was not a significant time and group interaction (F=2.76, p=0.13) between the control group and immediate intervention group (Figure 4.19, Table 4.10). Neither the control group (mean change = -0.56, SD = 1.14) nor the intervention group changed in maximum slope of the curve (mean change = 0.97, SD = 1.96).

*Hypothesis II: The Unimanual Group will demonstrate greater changes on the test of unimanual hand function and the bimanual group will demonstrate greater changes on the test of bimanual hand function.*

The participants assigned to the unimanual and bimanual massed practice groups were similar in demographic (Table 4.5) and baseline measures (Table 4.6), except for the age of the participants. The participants in the bimanual massed practice group were significantly older than the unimanual massed practice group (Table 4.5). The range for the bimanual group was 21-62 years, whereas the range in the unimanual group was 19–54 years. This difference did not appear to influence the results as the older participants (participants 55 and older) improved to a similar extent as those in the immediate intervention group. On the Jebsen Taylor Hand Function test the mean change for participants 55 and older was an improvement by - 46.31 seconds. This is similar to the change from those in the immediate intervention group (mean change = -71.63). On the Chedoke Arm and Hand Activity Inventory, participants 55 and over improved by a mean of 6 points. This improvement is greater than the change in the immediate intervention
group (mean change = 2.10). On the pinch grip outcome measure, participants 55 and over improved by a mean of 0.08 pounds, which is less than the mean change in the immediate intervention group (mean change = 0.50 pounds). On the Semmes Weinstein Monofilament test, participants in the 55 and older group (like the intervention group) did not change (median score = 0). Finally, on the disability questionnaire, participants 55 and over decreased in disability perception by a mean of -1.50. This change is similar to the change in the immediate intervention group (mean change = -1.20).

**Unimanual Hand Function.** For the pre- and post-intervention scores on the Jebsen Taylor Hand Function test, there was not a significant difference in the pre- and post-intervention change between unimanual and bimanual groups (F=0.33, p=0.57) (Figure 4.20). There was a significant effect of time for all the groups combined (F=9.87, p = 0.0006) indicating that participants improved compared to their baseline measures, regardless of group assignment. The mean change in time score decreased for both the unimanual group (mean change = -69.67, SD = 103.77 seconds) and the bimanual group (mean change = -44.91, SD = 46.93 seconds).

**Bimanual Hand Function.** For the pre- and post-intervention score on the Chedoke Arm and Hand Activity Inventory, there was a significant interaction between the type of MP intervention (F=5.57, p=0.03) (Figure 4.21). This indicates that the change in the bimanual group is significantly greater than the change in the unimanual group. The mean change in total score did not change for the unimanual group (mean change = 0.00, SD = 5.39) whereas the total score did increase for those in the bimanual group (mean change = 4.70, SD = 3.27). The effect size for the difference in the change scores between the groups is 4.70. We are 95% confident that the difference between the
change scores is between 0.44 and 8.96. However, this amount of change is not greater than the minimally detectable change of 6.3 points\textsuperscript{115}.

**Pinch Grip Strength.** For the pre- and post-intervention pinch grip strength, there was not a significant interaction between the type of MP training (F=1.54, p = 0.23) (Figure 4.22) meaning there was no difference between the interventions on the changes in pinch grip strength. There was a trend toward an effect of time (F= 3.98, p = 0.06), indicating that when all participants are combined (n=19), there may be an effect of the intervention on pinch grip strength. The mean change in pinching force increased for both the unimanual (mean change = 1.00, SD = 2.46 pounds) and bimanual (mean change = 0.77, SD = 1.37 pounds) groups. While this change is small, a one pound change can not only improve the performance of tasks, but can also provide new opportunities of independence. Baker *et al.*\textsuperscript{124} found many everyday tasks such as zipping a zipper, plugging in an electrical cord, cutting food with a knife, and removing a key from a lock require two Newtons (approximately 0.5 pound) of force to perform.

**Sensory Function.** For the pre- and post-intervention sensory score, there was not a significant interaction between the type of MP training (F=1.98, p = 0.18) (Figure 4.23). The sensory score did not change for either the unimanual (mean change = 0.22, SD = 0.97) and bimanual (mean change = 0.70, SD = 1.34) groups.

**Cortical Map Area.** For the cortical map area, there was not a significant interaction between the type of massed practice intervention at the pre- and post-intervention testing sessions (F=0.79, p = 0.40) (Figure 4.25), but there was an effect of time indicating that map area increased for all intervention groups (F=5.63, p = 0.04). This indicates that the cortical map area increases with intervention, regardless of the
type of intervention. The cortical map area increased for both the unimanual group (mean change = 10.60, SD = 9.13 cm²) and the bimanual group (mean change = 7.00, SD = 3.89 cm²).

**Cortical Map Volume.** For the pre- and post-intervention normalized cortical map volume, there was not a significant interaction between the type of massed practice intervention (F=0.15, p=0.71) (Figure 4.26), indicating there was no difference between the interventions at pre- and post-intervention testing sessions. The mean change in normalized cortical map volume increased for both the unimanual group (mean change = 2.11, SD = 2.42 cm³) and the bimanual group (mean change = 1.00, SD = 1.61 cm³).

**Center of Gravity.** For the longitudinal shift between the pre- and post-intervention testing session, there was not a significant interaction between the type of massed practice intervention (F=0.65, p=0.44). The changes in COG in the anterior / posterior direction were small for all the intervention groups (mean change in the unimanual group = -0.39, SD = 0.70 cm) and (mean change in the bimanual group = 0.48, SD = 0.99 cm).

**Active Motor Threshold.** For the pre- and post-intervention AMT, there was not a significant interaction between the type of massed practice intervention (F=0.85, p=0.38). The mean change in AMT did not change for either the unimanual group (mean change = 2.80, SD = 4.38 % MSO) or the bimanual group (mean change = -2.75, SD = 16.8% MSO).

**Maximum MEP.** For the pre- and post-intervention maximum MEP, there was not a significant interaction between the type of massed practice intervention (F=0.00, p=1.00) indicating that the type of intervention did not influence the change found in the
participants. The mean change in maximum MEP did not change for either the unimanual group (mean change = 10.48%, SD = 19.61% Mmax) or the bimanual group (mean change = 5.45%, SD = 10.99% Mmax).

**Maximum Slope of Recruitment Curve.** For the pre- and post-intervention recruitment curves, there was not a significant interaction between the type of massed practice intervention (F=0.27, p=0.62). The mean change in the maximum slope of the recruitment curve did not change for either the unimanual group (mean change = 1.04, SD = 2.56) or the bimanual group (mean change = 0.303, SD = 1.87).

**Hypothesis III: The SS group will demonstrate greater changes in sensory score, pinch grip strength, and performance of functional outcome measures over the FES group.**

The participants assigned to the SS and FES groups were similar in demographics and baseline scores (Tables 4.7 and 4.8).

**Unimanual Hand Function.** For the pre- and post-intervention scores on the Jebsen Taylor Hand Function test, there was not a significant difference in the pre- and post-intervention change between SS and FES groups (F=0.55, p=0.46) (Figure 4.27). The mean change in time score decreased to a similar extent for both SS (mean change = -66.15, SD = 98.20 seconds) and FES (mean change = -48.07, SD = 57.90 seconds) groups. Thus, both groups improved on the Jebsen Taylor Hand Function test to a similar extent.

**Bimanual Hand Function.** There was no time group interaction between the electrical stimulation protocols on the Chedoke Arm and Hand Activity Inventory (F=0.18, p = 0.68). The mean change in score increased for both SS (mean change =
2.22, SD = 5.40) and FES (mean change = 2.70, SD = 4.69) groups. Thus, the type of electrical stimulation does not influence the change on this outcome measure (Figure 4.28). Further, the magnitude of change on this outcome measure is small, and thus it’s possible that this outcome measure is not sensitive to changes in bimanual hand function in individuals with SCI.

**Pinch Grip Strength.** For the pre- and post-intervention pinch grip strength, there was not a significant interaction between the type of electrical stimulation (F=0.04, p = 0.85) (Figure 4.29) meaning there was no difference between the interventions on the changes in pinch grip strength. The mean change in pinching force increased for both SS group (mean change = 0.75, SD = 2.45 pounds) and FES group (mean change = 1.00, SD = 1.40 pounds).

**Sensory Function.** For the pre- and post-intervention sensory score, there was not a significant interaction between the type of electrical stimulation (F=1.72, p = 0.21) (Figure 4.30). The sensory score did not change for participants in the SS group (mean change = 0.11, SD = 1.27) or the FES group (mean change = 0.80, SD = 1.03).

**Cortical Map Area.** For the cortical map area, there was not a significant interaction between the type of stimulation at the pre- and post-intervention testing sessions (F=4.40, p = 0.07) (Figure 4.32). The cortical map area increased for both the SS group (mean change = 2.80, SD = 3.83) and FES group (mean change = 11.88, SD = 4.88).

**Cortical Map Volume.** For the pre- and post-intervention normalized cortical map volume, there was not a significant interaction between the type of electrical stimulation (F=3.19, p=0.12) (Figure 4.33), indicating there was no difference between
the stimulation at pre- and post-intervention testing sessions. The normalized cortical map volume increased for both SS (mean change = 0.12, SD = 0.14 cm³) and FES (mean change = 2.24, SD = 2.12 cm³) groups.

**Center of Gravity.** For the longitudinal shift between the pre- and post-intervention testing session, there was not a significant interaction between the type of electrical stimulation (F=0.69, p=0.43). The changes in COG in the anterior / posterior direction were small for both electrical stimulation groups (mean change in the SS group = 0.13, SD = 1.17 cm) and (mean change in the FES group = 0.15, SD = 0.90 cm).

**Active Motor Threshold.** For the pre- and post-intervention AMT, there was not a significant interaction between the type of electrical stimulation (F=1.84, p=0.21). The AMT did not change for the SS (mean change = -9.60, SD = 15.27% MSO) and FES (mean change = 5.00, SD = 8.90 % MSO) groups.

**Maximum MEP.** For the pre- and post-intervention maximum MEP, there was not a significant interaction between the type of electrical stimulation (F=3.38, p=0.10) indicating that the type of intervention did not influence the change found in the participants. The maximum MEP amplitude also did not change for the SS group (mean = 2.37%, SD = 4.57% Mmax) or the FES group (mean = 8.53%, SD = 12.64% Mmax).

**Maximum Slope of Recruitment Curve.** For the pre- and post-intervention recruitment curves, there was not a significant interaction between the type of electrical stimulation (F=0.51, p=0.50). The maximum slope of the recruitment curve also did not change for the SS group (mean change = 0.43, SD = 0.57) or FES group (mean change = 0.15, SD = 2.60).
Correlation of Clinical Outcome Measures and Transcranial Magnetic Stimulation Outcome Measures. The Jebsen Taylor Hand Function test was inversely correlated with the cortical map area, but the relationship was not significant (r=-0.39, p=0.16) (Figure 4.36). The Jebsen Taylor Hand Function test was significantly and inversely correlated with the Chedoke Arm and Hand Activity Inventory (r=-0.74, p=0.0004) (Figure 4.37). The cortical map area was positively correlated with the normalized cortical map volume and the relationship was significant (r=0.59, p=0.03). The maximum MEP was also positively correlated with the normalized cortical map volume and the relationship was significant (r=0.69, p=0.01). For individuals without upper limb spasticity, the distal hand motor score was significantly and inversely correlated with the Jebsen Taylor Hand Function test (r=-0.61, p=0.035) (Figure 4.38) and positively correlated with the Chedoke Arm and Hand Activity Inventory (r=0.80, p=0.002) (Figure 4.39). For all participants the weaker limb’s ASIA motor score was significantly correlated with both the Jebsen Taylor Hand Function test (r=-0.64, p = 0.0008) (Figure 4.40) and the Chedoke Arm and Hand Activity Inventory (r=0.70, p=0.0001) (Figure 4.41).

Discussion

Hypothesis 1: Immediate intervention group will demonstrate greater changes in both the clinical and neurophysiological outcome measures. This study demonstrates that individuals with chronic SCI can improve in arm and hand function following a combined intervention of task-oriented training with electrical stimulation compared to no intervention (Figure 4.8). The effect size of the intervention group was 81.14 seconds
faster compared to the control group. Further, when the participants in the delayed intervention / control group completed the intervention, they performed significantly better at the post-intervention testing session than at the pre-intervention testing session, and the amount of change was similar (51.63 seconds) to that of participants in the immediate intervention group (71.63 seconds).

The control group and immediate intervention group were similar in their demographic information and their baseline testing scores, except for one outcome measure. At baseline, participants in the control group performed significantly better on the Jebsen Taylor Hand Function test than participants in the immediate intervention group (Table 4.4). This is likely due to the fact that randomization of small numbers does not always produce equivalent groups, and stratification was not based on result of Jebsen Taylor Hand Function test score. It’s possible that the unanticipated influence of spasticity on the performance of some participants resulted in unequal groups. There were six participants who had moderate spasticity in their upper extremities that were included this study. Four of which were randomly assigned to the immediate intervention group. The Jebsen Taylor Hand Function test is a time-based outcome measure and is dependent on the speed of a participant’s performance. Individuals with increased muscle tone frequently have difficulty turning muscles on and off quickly, and therefore the time to complete the items on the Jebsen Taylor Hand Function test is greater than that of individuals without increased muscle tone. Despite the difference in their baseline scores, participants with increased muscle tone improved to a similar extent as the other participants in the immediate intervention group.
The results from the Jebsen Taylor Hand Function test are similar to those of other studies from our laboratory\textsuperscript{62,63}, where a combination intervention of unimanual MP and SS was found to significantly improve unimanual hand function over a no-treatment control condition. However, it was not known if the combination intervention would induce changes on a measure of bimanual hand function. On the bimanual hand function outcome measure, no difference was found between the immediate intervention group and the control group (Figure 4.9). This may be because the immediate intervention group consisted of both unimanual and bimanual training (Figure 4.3). It is possible that the changes in the immediate intervention group were diluted by the inclusion of both individuals who received unimanual and bimanual training, as those who received bimanual training improved more than those who received unimanual training.

Alternatively, it’s also possible that the Chedoke Arm and Hand Activity Inventory is not sensitive to change in individuals with SCI, as the instrument was designed for individuals post-stroke.

There was no difference in pinch grip strength between participants in the control and immediate intervention group between testing session one and two (Figure 4.10). This may be due to the variability in the response. Two participants in the immediate intervention group did worse on this outcome measure. Both these participants had difficulty with spasticity, which can cause daily fluctuations in motor output and result in variability on measures of strength. Other investigators have found a combination of massed practice with SS improves pinch grip strength in individuals with SCI\textsuperscript{62,63}. It maybe, that there were more participants with spasticity included in this study than previous studies. Individuals with spasticity perform much slower on timed performance
tests (such as the Jebsen Taylor Hand Function test), and participants in our study were much slower than those of previous reports. While the amount of pinch grip strength is similar between participants in this study and those of prior published reports, it is possible that individuals with spasticity have greater variability in their response on this outcome measure.

Alternatively, the difference in demographics may explain the difference in results. We included participants with both complete and incomplete injuries, as long as the inclusion criteria were all met, whereas prior studies included only participants with an ASIA classification of C and D. The ASIA classification of incomplete injury is dependent on the integrity of the last sacral segment, as well as sensorimotor scores in the lower limb. We did not believe that these factors would influence arm and hand function, however it’s possible that including individuals classified as A and B may include individuals with less potential for improvements. Individuals with motor complete injury (ASIA A and B) may have smaller improvements in strength than individuals with ASIA classification of C and D. This is unlikely though, as omitting individuals with motor complete injury (ASIA A and B) produces a similar mean change and slightly increases the variability (mean = 0.85, SD = 2.03 pounds).

Two possible mechanisms which could explain the improvements in hand function are changes in the size and location of the cortical map, or changes in cortical excitability. The size of the cortical map was significantly greater in the immediate intervention group compared to the control condition (Figure 4.17). Other investigators have also found increases in size of the cortical map following unimanual training in the form of constraint-induced therapy. Liepert et al. found an increase size of the
cortical map of the abductor pollicis brevis following one session of constraint-induced therapy. The same researchers also investigated the effect of a two week intervention and found an increase in cortical representation of the abductor pollicis brevis, however there was no correlation between the clinical measure (motor activity log) and the extent of the increase in cortical map area\textsuperscript{110}. Ro \textit{et al.}\textsuperscript{143} investigated the size of the cortical map in patients with subacute stroke and found a correlation between increase in cortical motor map size and improvements in function.

There is less evidence in the literature describing the effects of bimanual training on TMS evoked cortical maps. Lewis and Byblow\textsuperscript{81} found an increase in cortical map area in the first dorsal interossei following bimanual training in one participant with hemiparesis due to stroke. However, another participant, following the same intervention, had a decrease in cortical map area. Other studies investigating the effects of bimanual training have found trends of increased cortical map volume, but no statistical significant difference between pre- and post-intervention values\textsuperscript{84}.

A change in location of the COG was not apparent in the intervention group (Figure 4.34) or the control group (Figure 4.35). Other investigators have found a shift in the COG to a more anterior position in participants who recover upper extremity function\textsuperscript{18}. It is possible shifts in COG are variable\textsuperscript{105,106}. In the absence of intervention, Butler \textit{et al.}\textsuperscript{105} found the mean COG shifts 1.13 cm in the more affected hemisphere in individuals post stroke. Only three participants had an anterior shift in their COG which was greater than 1.13 cm. The participants whose COG shifted forward all received bimanual training and all demonstrated improvements in hand function. However, the
bimanual training cannot be used to explain this difference as we have found in previous studies an anterior shift in COG after unimanual training.

We did not find a significant increase in measures of cortical excitability including AMT, maximum MEP amplitude, or maximum slope of the recruitment curve (Table 4.10, Figure 4.15). This was surprising as other studies from our laboratory have found a decrease in resting motor threshold and an increase in maximum MEP amplitude\textsuperscript{63}. However, analysis of the participant demographics may explain these differences. There were six participants who had moderate spasticity in their upper limbs, four of which were assigned to the intervention group. It’s possible that improvements in these participants would be better correlated with the inhibitory cortical circuitry, which would be measured by intracortical inhibition or interhemispheric inhibition. In a recent study by Liepert et al.\textsuperscript{32}, the investigators found no change in motor threshold following a constraint-induced therapy intervention; however, there were changes in intracortical inhibition. Alternatively, it is possible that the somatosensory stimulation had an immediate, but short-term effect of increasing cortical excitability which allowed for the increased cortical map size. Thus, the end result was increased cortical map size, with no long term change in cortical excitability.

\textit{Hypothesis II: The unimanual group will demonstrate greater changes on the test of unimanual hand function and the bimanual group will demonstrate greater changes on the test of bimanual hand function.} On the bimanual hand function outcome measure, participants who received bimanual training performed significantly better than those who received unimanual training (Figure 4.9). It is likely this is due to the effect of task-specificity. Those in the unimanual group did not practice with their stronger hand, nor
did they practice coupling the limbs together. All of the items on the Chedoke Arm and Hand Activity Inventory involve coupling the limbs such that one limb functions to manipulate the objects while the other limb performs stabilization. However, the mean change for participants in the bimanual group did not exceed the published minimally detectable difference for the Chedoke Arm and Hand Activity Inventory (change of score of 6 points). Thus, it’s also possible this instrument is not as sensitive to change for individuals with SCI, as the Chedoke Arm and Hand Activity Inventory was created for individuals post-stroke.

The massed practice groups were different in one demographic area, which may have influenced this outcome measure. The bimanual group was older than the unimanual group. We would have expected age to negatively impact the outcome of the intervention, but the participants 55 years and older performed similarly (if not better on this outcome measure) to those in the intervention group.

*Hypothesis III: The SS group will demonstrate greater changes in sensory score, pinch grip strength, and performance of functional outcome measures over the FES group.* Participants in the SS group received continuous electrical stimulation, while those in the FES group only received stimulation when appropriate for the task. It appears that the timing of the stimulation to the movement may not important for improvements in function. It also appears that the long pulse width, an essential component of SS, is not critical to induce changes in hand function. It’s possible that simply providing electrical stimulation to increase both the sensory and motor components of movement is sufficient to induce changes in function. Evidence suggests
that when MP is augmented by SS, both changes in functional and TMS related outcome measures are significantly greater than either intervention in isolation\textsuperscript{62,63}.

The threshold at which the FES system would trigger the electrical stimulation was set for each individual. However, in two individuals, spontaneous muscle spasms in the thenar muscles triggered the electrical stimulation inappropriately. The triggered stimulus was usually at a time when the stimulation would not be useful for the individuals, and result in a movement error. The error forced the individuals to intentionally reduce muscle spasms. Both participants reported a reduction in muscle spasms during effortful performance.

\textit{Future Studies.} This study illustrates the importance of stratifying groups according to the factor that best predicts hand function. We chose to stratify on the voluntary control of one intrinsic hand muscle (the thenar muscles) which we hypothesized would be most predictive of hand function. However, because other factors influence upper limb function, it maybe better to stratify based on a combination of muscles, such as the upper extremity motor score of the weaker limb. We found that the motor score of the weaker limb (max score = 25) is correlated inversely with the total time score on the Jebsen Taylor Hand Function test and is directly correlated with the score on the Chedoke Arm and Hand Activity Inventory. This may be because the strength of the weaker limb is the factor which limits the speed of performance using one hand alone (on the Jebsen Taylor Hand Function test) and the ability to use the hands together performing separate aspects of the same task (on the Chedoke Arm and Hand Activity Inventory). Future studies should stratify groups according to the motor score in
the weaker limb to ensure baseline equivalence in the two functional outcome measures (Jebsen Taylor Hand Function test and Chedoke Arm and Hand Activity Inventory).

Conclusion

Individuals with chronic SCI can improve in unimanual hand function with a combined intervention of massed practice training and electrical stimulation. Those who practice bimanual massed practice training can improve in bimanual hand function. The type of electrical stimulation is not a critical component, but providing electrical stimulation is necessary to induce both functional and cortical changes\textsuperscript{62,63}. These changes in function are moderately correlated with an increase cortical map area. No changes in cortical excitability were found.
Figure 4.1: Flow chart of study design.

1. Initial Contact of Participant
2. Participant Randomized to Intervention Only Group
3. Participant Randomized to Delayed Intervention Control Group
5. Intervention
6. Three Week Waiting Period
7. Final Testing Session

Study Coordinator Reviews Inclusion and Exclusion Criteria and Performs Consenting Process

Blinded Study Assistant Randomizes Participants to either Intervention Only or Delayed Intervention Control Group. Assistant also Randomizes to Intervention Assignment.


Intervention Physical Therapist provides Intervention: Unimanual MP & SS, Bimanual MP & SS, Unimanual MP & FES, Bimanual MP & FES

Evaluator Physical Therapist performs Final Evaluation. TMS Examiner performs Neurophysiological Testing.
Figure 4.2: Flow Chart of Participant Group Assignment.
Figure 4.3: Example of container opening task in the unimanual MP training (Top) and bimanual MP training (Bottom). Note the containers are stabilized in the above photograph whereas the participant is stabilizing the container in the photograph below.

Figure 4.4: Example of pick up stix task in the unimanual MP training paradigm (Top) and the bimanual MP training paradigm (Bottom).
Figure 4.5: Example of how the unimanual task was modified for bimanual training: unimanual task found in the top photograph, whereas the bimanual training task is in the bottom two photographs. In addition, many participants rely on tenodesis to grasp objects and use excessive abduction and medial rotation of the shoulder, as seen in the above photograph. Participants were redirected to reduce excessive shoulder motion and wrist extension; thereby practice the tasks utilizing their finger flexors (actively), as well as, intrinsic hand muscles.
Figure 4.6: Example of hand-over-hand assistance is applied.
Figure 4.7: Mean time score on Jebsen Taylor Hand Function test at testing session 1 and 2 for participants in the control group and those in the immediate intervention group. Red squares indicate participants in the immediate intervention group, whereas blue diamonds indicate participants in the delayed intervention control group. Black bars indicate standard deviation. A decrease in time represents improved score. Note the difference in slope between the groups.

Figure 4.8: Mean pre- and post-intervention testing for participants in the delayed intervention group. Black bars represent standard deviation. Asterisks indicate significant difference between pre- and post-intervention. A decrease in time represents improved score. Note that following the intervention this group does improve in function.
Figure 4.9: Mean pre- and post-intervention testing for six participants with increased muscle tone. Black bars represent standard deviation. Asterisks indicate significant difference between pre- and post-intervention. A decrease in time represents improved score. Note that following the intervention this group does improve in function.

![Jebsen Taylor Hand Function test](image)

Figure 4.10: Mean score on the Chedoke Arm and Hand Activity Inventory at testing session 1 and 2 for participants in the control group and those in the immediate intervention group. Red square represents immediate intervention group. Blue diamonds represent delayed intervention group. Black bars indicate standard deviation. An increase in score represents improvement.

![Chedoke Arm and Hand Activity Inventory](image)
Figure 4.11: Mean Pinch Grip Strength at testing session 1 and testing session 2 for participants in the control group and in those in the immediate intervention group. Red square represents immediate intervention group. Blue diamonds represent delayed intervention group. Black bars are standard deviation. An increase in force indicates improvement in pinch strength.

Figure 4.12: Median Semmes Weinstein Monofilament test scores at testing session 1 and testing session 2 for participants in the control group and in those in the immediate intervention group. Red square represents immediate intervention group. Blue diamonds represent delayed intervention group. An increase in sensory score indicates improvement.
Figure 4.13: Mean Disability Score at testing session 1 and 2 for participants in the control group and those in the immediate intervention group. Red square represents immediate intervention group. Blue diamonds represent delayed intervention group. Black bars are standard deviation. A decrease in score represents improvement.
Figure 4.14: Example of MEP at pre- (Top) and post-intervention testing (Bottom). The x-axis is time, the y-axis is amplitude. The stimulus artifact is seen between 0 and 20 milliseconds (cursor 2 and 3). The MEP is at 23 milliseconds. The silent period is seen at 45 milliseconds. The blue box contains amplitude value between the cursors. The MEP is between cursor 3 and 4. Note the larger MEP following intervention.
Figure 4.15: Example of Recruitment Curve at pre- (Top) and post-intervention testing (Bottom). Note, following the intervention the slope of the recruitment curve is greater, especially between the 120% and 160% motor threshold. Also note the larger maximum mean amplitude following the intervention.
Figure 4.16: Example of cortical map at pre- (Top) and post-intervention testing (Bottom). The numbers and letters are a coordinate system correlating to the grid on the cap. The bars indicate mean amplitude of three MEPs. Note increase in size of MEP following intervention, even though both cortical maps were constructed at 120% MT.
Figure 4.17: Mean cortical map area at testing session 1 and testing session 2 for participants in the control group and in those in the immediate intervention group. Red square represents immediate intervention group. Blue diamonds represent delayed intervention group. Black bars are standard deviation. Note the different slope in the participants in the immediate intervention group compared to the control group.

Figure 4.18: Mean Normalized Cortical Map Volume at testing session 1 and testing session 2 for participants in the control group and in those in the immediate intervention group. Red square represents immediate intervention group. Blue diamonds represent delayed intervention group. Black bars are standard deviation. Note the trend for a difference in slope.
Figure 4.19: Recruitment curves before and after intervention for all participants. Solid lines represent individuals before and after intervention and dashed lines represent individuals in the control group. Red lines indicate first testing session, whereas blue lines indicate seconds testing session. Note the curve has shifted slightly to the left indicating, greater cortical excitability following the intervention, however both immediate intervention and control group increase in MEP amplitude at 140% MT.
Figure 4.20: Mean Score on Jebsen Taylor Hand Function test at pre- and post-intervention testing sessions for participants in the unimanual massed practice group and those in the bimanual massed practice group. Red square represents unimanual massed practice group. Blue diamonds represents bimanual massed practice group. Black bars are standard deviation. Decrease in time represents improved score. Note the similar slopes between the two groups.

![Jebsen Taylor Hand Function Test](image)

Figure 4.21: Mean score on the Chedoke Arm and Hand Activity Inventory at pre- and post-intervention testing session for participants in the unimanual and those in the bimanual group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars represent standard deviation. Increase in score represents improvement. Note the greater slope in those in the bimanual massed practice group. However, it is possible the effect is due to the lower baseline measure in those in the bimanual group (though these baseline values are not significantly different).

![Chedoke Arm and Hand Activity Inventory](image)
Figure 4.22: Mean pinch grip strength at pre- and post-intervention testing for participants in the unimanual group and in those in the bimanual group. Red squares indicate unimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Increase in force represents improvement.

Figure 4.23: Median Semmes Weinstein Monofilament test scores at pre- and post-intervention testing for participants in the unimanual group and in those in the bimanual group. Red squares indicate unimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Increase in score represents improvement.
Figure 4.24: Mean Disability Score at pre- and post-intervention testing for participants in the unimanual group and those in the bimanual group. Red squares indicate unimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Decrease in score represents improvement.

Figure 4.25: Mean cortical map area at pre- and post-intervention testing for participants in the unimanual group and those in the bimanual group. Red squares indicate unimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Note the similar increase in slope.
Figure 4.26: Mean normalized cortical map volume at pre- and post-intervention testing for participants in the unimanual group and those in the bimanual group. Red squares indicate unimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Note the similar increase in slope.
Figure 4.27: Mean time scores on the Jebsen Taylor Hand Function test at pre- and post-intervention testing session for participants in the SS group and those in the FES group. Red square represents FES group. Blue diamonds represents SS group. Black bars are standard deviation. Decrease in time represents an improvement in score. Note the similar slopes between the two groups.

Figure 4.28: Mean score on the Chedoke Arm and Hand Activity Inventory at pre- and post-intervention testing session for participants in the SS group and those in the FES group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Increase in score represents improvement. Black bars indicate standard deviation.
Figure 4.29: Mean Pinch Grip Strength at pre- and post-intervention testing for participants in the SS group and those in the FES group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Increase in force represents improvement.

![Pinch Grip Strength](image)

Figure 4.30: Median Semmes Weinstein Monofilament test scores at pre- and post-intervention testing for participants in the SS group and in those in the FES group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Increase in score represents improvement.

![Semmes Weinstein Monofilament Test](image)
Figure 4.31: Mean Disability Score at pre- and post-intervention testing for participants in the SS group and those in the FES group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Decrease in score represents improvement.

Figure 4.32: Mean cortical map area at pre- and post-intervention testing for participants in the SS group and those in the FES group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation. Note the similar change in slope between the groups.
Figure 4.33: Mean normalized cortical map volume at pre- and post-intervention testing for participants in the SS group and those in the FES group. Red squares represent bimanual massed practice group. Blue diamonds represent unimanual massed practice group. Black bars indicate standard deviation.
Figure 4.34: Location of COG at pre- and post-intervention testing for all participants.
Figure 4.35: Location of COG at testing session one and two for participants in control group.
Figure 4.36: Correlation between change on Jebsen Taylor Hand Function test and change in Cortical Map Area (cm$^2$): ($r=-0.39$, $p=0.16$).

Figure 4.37: Correlation between Jebsen Taylor Hand Function test and Chedoke Arm and Hand Activity Inventory ($r = -0.74$, $p = 0.0004$).
Figure 4.38: Correlation of a distal hand score (sum of MMT from finger flexors, thenar muscles, and hypothenar muscles) with score on Jebsen Taylor Hand Function test: $r=-0.61$, $p = 0.03$. (Note participants with upper limb spasticity were ommitted from this analysis).

![Graph showing correlation between distal hand score and Jebsen Taylor Hand Function test score.](image)

Figure 4.39: Correlation of a distal hand score (sum of MMT from finger flexors, thenar muscles and hypothenar muscles) with score on Chedoke Arm and Hand Activity Inventory: $r=0.80$, $p=0.0017$. (Note participants with upper limb spasticity were ommitted from this analysis).

![Graph showing correlation between distal hand score and Chedoke Arm and Hand Activity Inventory score.](image)
Figure 4.40: Correlation of the weaker limb’s upper extremity motor score with the Jebsen Taylor Hand Function test: $r=-64$, $p = 0.0008$.

Figure 4.41: Correlation between weaker limb’s ASIA motor score and the Chedoke Arm and Hand Activity Inventory: $(r=0.70$, $p=0.0001)$. 
Table 4.1: Matrix used for analysis of the different interventions. There were nine or ten participants in each group for comparison. The nine participants in the unimanual MP group were compared to the ten participants in the bimanual MP group. The nine participants in the SS group were compared to the ten participants in the FES group.

<table>
<thead>
<tr>
<th>Group Assignment</th>
<th>Somatosensory Stimulation</th>
<th>Functional Electrical Stimulation</th>
<th>Total for Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unimanual MP</td>
<td>4 Participants in Unimanual MP &amp; SS</td>
<td>5 Participants in Unimanual MP &amp; FES</td>
<td>9 Participants in Unimanual MP</td>
</tr>
<tr>
<td>Bimanual MP</td>
<td>5 Participants in Bimanual MP &amp; SS</td>
<td>5 Participants in Bimanual MP &amp; FES</td>
<td>10 Participants in Bimanual MP</td>
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<tr>
<td>Total for Analysis</td>
<td>9 Participants in Somatosensory Stimulation</td>
<td>10 Participants in Functional Electrical Stimulation</td>
<td>19 Participants</td>
</tr>
<tr>
<td>Finger Isolation</td>
<td>Pinch</td>
<td>Pinch with Rotation</td>
<td>Grasp</td>
</tr>
<tr>
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<tr>
<td><strong>Typing on a Keyboard:</strong>&lt;br&gt;Unimanual - Participant uses one hand to type typing sequence.&lt;br&gt;Bimanual - Participant uses both hands to type typing sequence.</td>
<td><strong>Picking up Small Objects:</strong>&lt;br&gt;Unimanual - Participant picks up washers and nails to place in container on table.&lt;br&gt;Bimanual - Participant picks up washers and nails to place in container in hand.</td>
<td><strong>Turning Twist Ties:</strong>&lt;br&gt;Unimanual - Remove and replace twist ties on a stabilized card.&lt;br&gt;Bimanual - Remove and replace twist ties on a card that is stabilized in hand.</td>
<td><strong>Plugging in Cords:</strong>&lt;br&gt;Unimanual - Participant plugs extension cords into power strip.&lt;br&gt;Bimanual - Participant plugs extension cords into each other.</td>
</tr>
<tr>
<td><strong>Dialing a Cell Phone:</strong>&lt;br&gt;Unimanual - Participant dials phone list on stabilized cell phone.&lt;br&gt;Bimanual - Participant dials phone list on cell phone in hand.</td>
<td><strong>Threading Needle:</strong>&lt;br&gt;Unimanual - Thread fishing line into stabilized needle.&lt;br&gt;Bimanual - Thread fishing line into needle in hand.</td>
<td><strong>Screwing Nuts and Bolts:</strong>&lt;br&gt;Unimanual - Unscrew nuts from a bolt that is stabilized.&lt;br&gt;Bimanual - Unscrew nuts from a bolt that is stabilized by the participant</td>
<td><strong>Cutting with Scissors:</strong>&lt;br&gt;Unimanual - Participant cuts stabilized paper with scissors.&lt;br&gt;Bimanual - Participant cuts paper stabilized with hand.</td>
</tr>
<tr>
<td><strong>Calculating Math:</strong>&lt;br&gt;Unimanual - Participant calculates answers to problems on stabilized calculator.&lt;br&gt;Bimanual - Participant calculates answers to problems on calculator stabilized by their hand.</td>
<td><strong>Writing on Paper:</strong>&lt;br&gt;Unimanual - Participant copies shapes with a pen, pencil, or crayon on stabilized paper.&lt;br&gt;Bimanual - Participant copies shapes with a pen, pencil, or crayon on paper stabilized with their hand.</td>
<td><strong>Turning a Key in a Lock:</strong>&lt;br&gt;Unimanual - Place key in doorknob to unlock door.&lt;br&gt;Bimanual - Place key in padlock to unlock lock.</td>
<td><strong>Playing Cards:</strong>&lt;br&gt;Unimanual - Participant plays card game with one hand alone.&lt;br&gt;Bimanual - Participant holds deck of cards and plays card game with other hand.</td>
</tr>
<tr>
<td><strong>Pushing Buttons:</strong>&lt;br&gt;Unimanual - Participant pushes buttons on a videogame that is stabilized.&lt;br&gt;Bimanual - Participant pushes buttons on a videogame that is in their hand.</td>
<td><strong>Popping Bubble Wrap:</strong>&lt;br&gt;Unimanual - Squeezing bubble wrap with one hand.&lt;br&gt;Bimanual - Use both hands to squeeze bubble wrap.</td>
<td><strong>Turning Knobs:</strong>&lt;br&gt;Unimanual - Participants turn knobs with one hand.&lt;br&gt;Bimanual - Participants turn knobs with both hands.</td>
<td><strong>Squeezing a Spray Bottle:</strong>&lt;br&gt;Unimanual - Participant sprays water into cup stabilized on table.&lt;br&gt;Bimanual - Participant sprays water into cup stabilized with hand.</td>
</tr>
</tbody>
</table>
Table 4.3: Baseline Equivalence Tables for Demographic Characteristics for the Comparison of Control Group and Immediate Intervention Group. *Astrisks indicates significant difference between control or immediate intervention group.*

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Control / Delayed Intervention Group (n=10)</th>
<th>Immediate Intervention Group (n=10)</th>
<th>Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASIA</strong></td>
<td>10% A&lt;br&gt;20% B&lt;br&gt;50% C&lt;br&gt;20% D</td>
<td>0% A&lt;br&gt;10% B&lt;br&gt;40% C&lt;br&gt;55% D</td>
<td><em>p = 0.10</em></td>
</tr>
<tr>
<td><strong>Level of Injury</strong></td>
<td>0% C3&lt;br&gt;20% C4&lt;br&gt;10% C5&lt;br&gt;40% C6&lt;br&gt;30% C7</td>
<td>10% C3&lt;br&gt;30% C4&lt;br&gt;10% C5&lt;br&gt;30% C6&lt;br&gt;20% C7</td>
<td><em>p = 0.13</em></td>
</tr>
<tr>
<td><strong>Duration of Injury</strong></td>
<td>Mean = 6.40 (7.60) years&lt;br&gt;Range = 1-23 years</td>
<td>Mean = 4.70 (6.38) years&lt;br&gt;Range =1-22 years</td>
<td><em>t=0.54&lt;br&gt;p=0.59</em></td>
</tr>
<tr>
<td><strong>Upper Extremity Motor Score (Max = 50)</strong></td>
<td>Mean = 30.20 (5.98)&lt;br&gt;Range = 23-39</td>
<td>Mean = 28.80 (7.54)&lt;br&gt;Range = 19-44</td>
<td><em>t=0.46&lt;br&gt;p=0.65</em></td>
</tr>
<tr>
<td><strong>Upper Extremity Sensory Score (Max = 40)</strong></td>
<td>Mean = 31.00 (6.32)&lt;br&gt;Range = 18-40</td>
<td>Mean = 27.70 (7.72)&lt;br&gt;Range = 17-40</td>
<td><em>t=1.05&lt;br&gt;p=0.31</em></td>
</tr>
<tr>
<td><strong>Cause of Injury</strong></td>
<td>100% Traumatic</td>
<td>100% Traumatic</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>70% Male&lt;br&gt;30% Female</td>
<td>70% Male&lt;br&gt;30% Female</td>
<td><em>x²=0.00&lt;br&gt;p=1.00</em></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Mean = 39.80 (16.13) years&lt;br&gt;Range = 19-62 years</td>
<td>Mean = 42.20 (14.03) years&lt;br&gt;Range = 20-61 years</td>
<td><em>t=0.36&lt;br&gt;p=0.73</em></td>
</tr>
</tbody>
</table>
Table 4.4: Baseline Equivalence Tables for Outcome Measures for Comparison of Control Group and Immediate Intervention Group. Astrisks indicates significant difference between Control or Immediate intervention group.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Control / Delayed Intervention Group (n=10)</th>
<th>Immediate Intervention Group (n=10)</th>
<th>Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>Mean = 225.72 ± 172.88 sec; Range = 96.27 - 678.40 sec</td>
<td>Mean = 482.76 ± 296.53 sec; Range = 70.69 - 809.00 sec</td>
<td>t = 2.37, p = 0.03 *</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory</td>
<td>Mean = 40.07 ± 13.23; Range = 18.00 - 62.00</td>
<td>Mean = 40.18 ± 17.03; Range = 19.00 -70.00</td>
<td>t = 0.63, p = 0.54</td>
</tr>
<tr>
<td>(max = 77)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>Mean = 4.64 ± 6.33 pounds; Range = 0 - 18.7 pounds</td>
<td>Mean = 4.43 ± 4.08 pounds; Range = 0 - 13.7 pounds</td>
<td>t = 0.09, p = 0.93</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Score</td>
<td>Mean = 10.90 ± 3.90; Range = 4 - 15</td>
<td>Mean = 9.7 ± 4.08; Range = 3 - 15</td>
<td>t = 0.67, p = 0.51</td>
</tr>
<tr>
<td>Health Assessment Questionnaire</td>
<td>Mean = 27.50 ± 8.86; Range = 18 - 44</td>
<td>Mean = 31.20 ± 9.01; Range = 19.00 - 44.00</td>
<td>t = 0.93, p = 0.37</td>
</tr>
<tr>
<td>Active Motor Threshold</td>
<td>Mean = 80.67% ± 21.8% MSO; Range = 50 - 100% MSO</td>
<td>Mean = 70% ± 21% MSO; Range = 42 - 100% MSO</td>
<td>t = 0.98, p = 0.35</td>
</tr>
<tr>
<td>Maximum MEP</td>
<td>Mean = 0.13 ± 0.14 mV; Range = 0.01 - 0.37 mV</td>
<td>Mean = 0.22 ± 0.15 mV; Range = 0.08 - 0.47 mV</td>
<td>t = 1.04, p = 0.32</td>
</tr>
<tr>
<td>Maximum Slope of Recruitment Curve</td>
<td>Mean = 2.22 ± 1.56; Range = 0.10 - 4.53</td>
<td>Mean = 1.20 ± 0.54; Range = 0.56 - 2.01</td>
<td>t = 1.50, p = 0.18</td>
</tr>
<tr>
<td>Cortical Map Area</td>
<td>Mean = 14.67 ± 15.45 cm²; Range = 1.00 - 37.00 cm²</td>
<td>Mean = 11.78 ± 6.53 cm²; Range = 1.00 - 24.00 cm²</td>
<td>t = 0.50, p = 0.62</td>
</tr>
<tr>
<td>Cortical Map Volume</td>
<td>Mean = 1.23 ± 1.71 cm³; Range = 0.02 - 4.34 cm³</td>
<td>Mean = 0.68 ± 0.53 cm³; Range = 0.05 - 1.74 cm³</td>
<td>t = 0.93, p = 0.37</td>
</tr>
<tr>
<td>COG of Cortical Map (Longitudinal</td>
<td>Mean = 2.14 ± 1.77 cm; Range = -0.09 - 5.14 cm</td>
<td>Mean = 1.69 ± 1.91 cm; Range = -0.75 - 5.96 cm</td>
<td>t = 0.48, p = 0.63</td>
</tr>
</tbody>
</table>
Table 4.5: Baseline Equivalence Table for Demographic Characteristics for the Comparison of Massed Practice Groups. 
Astrisks indicates significant difference between Unimanual or Bimanual Massed Practice Groups.

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Unimanual Massed Practice Group (n=9)</th>
<th>Bimanual Massed Practice Group (n=10)</th>
<th>Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASIA</td>
<td>0% A 12% B 56% C 33% D</td>
<td>10% A 20% B 30% C 40% D</td>
<td>$x^2=1.93$ p=0.59</td>
</tr>
<tr>
<td>Level of Injury</td>
<td>11% C3 22% C4 22% C5 22% C6 22% C7</td>
<td>0% C3 30% C4 0% C5 40% C6 30% C7</td>
<td>$x^2=4.03$ p=0.40</td>
</tr>
<tr>
<td>Duration of Injury</td>
<td>Mean = 3.44 (3.97) years Range = 1 - 13 years</td>
<td>Mean = 6.60 (8.51) years Range = 1 - 23 years</td>
<td>t=1.01 p=0.32</td>
</tr>
<tr>
<td>Upper Extremity Motor Score (Max = 50)</td>
<td>Mean = 30.22 (7.50) Range = 23-44</td>
<td>Mean = 28.91 (6.20) Range = 19-39</td>
<td>t=0.65 p=0.52</td>
</tr>
<tr>
<td>Upper Extremity Sensory Score (Max = 40)</td>
<td>Mean = 29.44 (6.80) Range = 20-40</td>
<td>Mean = 29.00 (7.97) Range = 17-40</td>
<td>t=0.13 p=0.90</td>
</tr>
<tr>
<td>Cause of Injury</td>
<td>100% Traumatic</td>
<td>100% Traumatic</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>78% Male 22% Female</td>
<td>60% Male 40% Female</td>
<td>$x^2=0.69$ p=0.41</td>
</tr>
<tr>
<td>Age</td>
<td>Mean = 31.78 (12.37) years Range = 19-54 years</td>
<td>Mean = 48.20 (12.97) years Range = 21-62 years</td>
<td>t=2.92 p=0.01</td>
</tr>
</tbody>
</table>
Table 4.6: Baseline Equivalence Table for Outcome Measures for Comparison of Massed Practice Groups. Asterisks indicates significant difference between Unimanual or Bimanual Massed Practice Groups.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Unimanual Massed Practice Group (n=9)</th>
<th>Bimanual Massed Practice Group (n=10)</th>
<th>Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>Mean = 303.7 ± 246.02 sec;</td>
<td>Mean = 426.45 ± 281.66 sec;</td>
<td><em>t</em> = 1.03,</td>
</tr>
<tr>
<td></td>
<td>Range = 70.69 - 777.94 sec</td>
<td>Range = 95.44 - 809.00 sec</td>
<td><em>p</em> = 0.32</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory</td>
<td>Mean = 44.56 ± 13.94;</td>
<td>Mean = 34.64 ± 13.60;</td>
<td><em>t</em> = 1.61,</td>
</tr>
<tr>
<td>(max = 77)</td>
<td>Range = 32 - 70</td>
<td>Range = 14 - 55</td>
<td><em>p</em> = 0.13</td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>Mean = 3.79 ± 4.30 pounds;</td>
<td>Mean = 5.65 ± 6.78 pounds;</td>
<td><em>t</em> = 0.71,</td>
</tr>
<tr>
<td></td>
<td>Range = 0.00 - 13.70 pounds</td>
<td>Range = 0 - 24.03 pounds</td>
<td><em>p</em> = 0.49</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Score</td>
<td>Mean = 11.0 ± 4.06;</td>
<td>Mean = 9.45 ± 4.34;</td>
<td><em>t</em> = 0.81</td>
</tr>
<tr>
<td>(max = 15)</td>
<td>Range = 4 - 15</td>
<td>Range = 3 - 15</td>
<td><em>p</em> = 0.43</td>
</tr>
<tr>
<td>Health Assessment Questionnaire</td>
<td>Mean = 26.00 ± 4.78;</td>
<td>Mean = 30.91 ± 11.79;</td>
<td><em>t</em> = 1.23,</td>
</tr>
<tr>
<td></td>
<td>Range = 19 - 34</td>
<td>Range = 15 - 46;</td>
<td><em>p</em> = 0.23</td>
</tr>
<tr>
<td>Active Motor Threshold</td>
<td>Mean = 68.60 ± 24.37% MSO;</td>
<td>Mean = 69.11 ± 18.63 % MSO;</td>
<td><em>t</em> = 0.04,</td>
</tr>
<tr>
<td></td>
<td>Range = 42 - 100% MSO</td>
<td>Range = 48 - 100% MSO</td>
<td><em>p</em> = 0.97</td>
</tr>
<tr>
<td>Maximum MEP</td>
<td>Mean = 0.26 ± 0.17% Mmax;</td>
<td>Mean = 0.14 ± 0.13% Mmax;</td>
<td><em>t</em> = 1.39,</td>
</tr>
<tr>
<td></td>
<td>Range = 0.08 - 0.47% Mmax</td>
<td>Range = 0.00 - 0.37% Mmax</td>
<td><em>p</em> = 0.19</td>
</tr>
<tr>
<td>Maximum Slope of Recruitment Curve</td>
<td>Mean = 1.50 ± 0.69;</td>
<td>Mean = 1.24 ± 0.80;</td>
<td><em>t</em> = 0.55,</td>
</tr>
<tr>
<td></td>
<td>Range = 0.56 - 2.03</td>
<td>Range = 0.04 - 2.62</td>
<td><em>p</em> = 0.60</td>
</tr>
<tr>
<td>Cortical Map Area</td>
<td>Mean = 11.80 ± 7.19 cm²;</td>
<td>Mean = 14.67 ± 10.21 cm²;</td>
<td><em>t</em> = 0.55,</td>
</tr>
<tr>
<td></td>
<td>Range = 1 - 24.00 cm²</td>
<td>Range = 1 - 29 cm²</td>
<td><em>p</em> = 0.59</td>
</tr>
<tr>
<td>Cortical Map Volume</td>
<td>Mean = 0.82 ± 0.61 cm³;</td>
<td>Mean = 0.84 ± 0.79 cm³;</td>
<td><em>t</em> = 0.04,</td>
</tr>
<tr>
<td></td>
<td>Range = 0.20 - 1.74 cm³</td>
<td>Range = 0.02 - 2.55 cm³</td>
<td><em>p</em> = 0.97</td>
</tr>
<tr>
<td>COG of Cortical Map</td>
<td>Mean = 2.47 ± 2.10 cm;</td>
<td>Mean = 1.13 ± 1.12 cm;</td>
<td><em>t</em> = 1.58,</td>
</tr>
<tr>
<td>(Longitudinal Direction)</td>
<td>Range = 0.48 - 5.96 cm</td>
<td>Range = -0.75 - 2.91 cm</td>
<td><em>p</em> = 0.14</td>
</tr>
</tbody>
</table>
Table 4.7: Baseline Equivalence Table for Demographic Characteristics for the Comparison of Electrical Stimulation Groups. Astrisks indicates significant difference between SS or FES Groups.

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Somatosensory Stimulation Group (n=9)</th>
<th>Functional Group (n=10)</th>
<th>Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASIA</td>
<td>0% A</td>
<td>10% A</td>
<td>p=0.29</td>
</tr>
<tr>
<td></td>
<td>11% B</td>
<td>20% B</td>
<td></td>
</tr>
<tr>
<td></td>
<td>78% C</td>
<td>10% C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11% D</td>
<td>60% D</td>
<td></td>
</tr>
<tr>
<td>Level of Injury</td>
<td>11% C3</td>
<td>0% C3</td>
<td>p=0.36</td>
</tr>
<tr>
<td></td>
<td>22% C4</td>
<td>30% C4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11% C5</td>
<td>10% C5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>44% C6</td>
<td>20% C6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11% C7</td>
<td>40% C7</td>
<td></td>
</tr>
<tr>
<td>Duration of Injury</td>
<td>Mean = 8.30 (8.92) years</td>
<td>Mean = 2.80 (1.93) years</td>
<td>t=1.82</td>
</tr>
<tr>
<td></td>
<td>Range = 1 - 23 years</td>
<td>Range = 1 - 7 years</td>
<td>p=0.09</td>
</tr>
<tr>
<td>Upper Extremity Motor Score (Max = 50)</td>
<td>Mean = 26.70 (5.33)</td>
<td>Mean = 32.30 (7.51)</td>
<td>t=2.03</td>
</tr>
<tr>
<td></td>
<td>Range = 19-44</td>
<td>Range = 23 - 44</td>
<td>p=0.07</td>
</tr>
<tr>
<td>Upper Extremity Sensory Score (Max = 40)</td>
<td>Mean = 29.00 (6.70)</td>
<td>Mean = 28.80 (7.51)</td>
<td>t=0.34</td>
</tr>
<tr>
<td></td>
<td>Range = 17-40</td>
<td>Range = 18-40</td>
<td>p=0.74</td>
</tr>
<tr>
<td>Cause of Injury</td>
<td>100% Traumatic</td>
<td>100% Traumatic</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>67% Male</td>
<td>70% Male</td>
<td>$\chi^2=0.02$</td>
</tr>
<tr>
<td></td>
<td>33% Female</td>
<td>30% Female</td>
<td>p=0.88</td>
</tr>
<tr>
<td>Age</td>
<td>Mean = 43.9 (13.14) years</td>
<td>Mean = 38.10 (16.40) years</td>
<td>t=0.87</td>
</tr>
<tr>
<td></td>
<td>Range = 19-62 years</td>
<td>Range = 20-61 years</td>
<td>p=0.39</td>
</tr>
</tbody>
</table>
Table 4.8: Baseline Equivalence Table for Outcome Measures for Comparison of Electrical Stimulation Groups. Asterisks indicate significant difference between SS or FES Groups.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Somatosensory Stimulation Group (n=9)</th>
<th>Functional Electrical Stimulation Group (n=10)</th>
<th>Test Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>Mean = 432.42 ± 254.24 sec; Range = 113.43 - 809.00 sec</td>
<td>Mean = 341.50 ± 284.42 sec; Range = 70.69 - 777.94 sec</td>
<td>t = 0.73, p = 0.47</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory (max = 77)</td>
<td>Mean = 34.56 ± 10.14; Range = 19 - 54</td>
<td>Mean = 42.3 ± 17.32; Range = 14 - 70</td>
<td>t = 1.17, p = 0.26</td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>Mean = 2.38 ± 1.90 pounds; Range = 0 - 9.2 pounds</td>
<td>Mean = 6.57 ± 7.40 pounds; Range = 0 - 24.03 pounds</td>
<td>t = 1.64, p = 0.11</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Score (max = 15)</td>
<td>Mean = 8.33 ± 4.12; Range = 3 - 15</td>
<td>Mean = 11.6 ± 3.98; Range = 3 - 15</td>
<td>t = 1.76, p = 0.10</td>
</tr>
<tr>
<td>Health Assessment Questionnaire</td>
<td>Mean = 30.78 ± 9.95; Range = 15 - 44</td>
<td>Mean = 28.2 ± 9.16; Range = 15 - 46</td>
<td>t = 0.59, p = 0.56</td>
</tr>
<tr>
<td>Active Motor Threshold</td>
<td>Mean = 78% ± 23.37% MSO; Range = 50% - 100% MSO</td>
<td>Mean = 62.13% ± 14.92% MSO; Range = 42 - 80% MSO</td>
<td>t = 1.55, p = 0.15</td>
</tr>
<tr>
<td>Maximum MEP</td>
<td>Mean = 0.13 ± 0.13 %Mmax; Range = 0.00 - 0.32 %Mmax</td>
<td>Mean = 0.20 ± 0.16 %Mmax; Range = 0.03 - 0.47 %Mmax</td>
<td>t = 0.85, p = 0.42</td>
</tr>
<tr>
<td>Maximum Slope of Recruitment Curve</td>
<td>Mean = 1.24 ± 0.04; Range = 0.04 - 2.62</td>
<td>Mean = 1.38 ± 0.53; Range = 0.56 - 2.03</td>
<td>t = 0.30, p = 0.77</td>
</tr>
<tr>
<td>Cortical Map Area</td>
<td>Mean = 11.67 ± 9.91 cm²; Range = 1.00 - 27.00 cm²</td>
<td>Mean = 15.13 ± 8.74 cm²; Range = 5 - 29 cm²</td>
<td>t = 0.69, p = 0.50</td>
</tr>
<tr>
<td>Cortical Map Volume</td>
<td>Mean = 0.58 ± 0.59 cm³; Range = 0.02 - 1.48 cm³</td>
<td>Mean = 1.01 ± 0.77 cm³; Range = 0.33 - 2.55 cm³</td>
<td>t = 1.14, p = 0.28</td>
</tr>
<tr>
<td>COG of Cortical Map (Longitudinal Direction)</td>
<td>Mean = 1.34 ± 1.04 cm; Range = -0.75 - 1.99 cm</td>
<td>Mean = 1.8 ± 1.97 cm; Range = -0.03 - 5.96 cm</td>
<td>t = 0.55, p = 0.59</td>
</tr>
</tbody>
</table>
Table 4.9: Pre- and Post-Intervention Data for Participants assigned to the Delayed Intervention Control Group and Immediate Intervention Group. Astrisks indicates time / group interaction.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Delayed Intervention Control (n=10)</th>
<th>Immediate Intervention (n=10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Testing Session One: Mean (SD)</td>
<td>Testing Session Two: Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>225.72 (177.88)</td>
<td>235.23 (174.20)</td>
<td>482.76 (296.53)</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory</td>
<td>40.70 (13.23)</td>
<td>39.80 (14.41)</td>
<td>36.9 (13.81)</td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>4.64 (6.33)</td>
<td>4.65 (5.75)</td>
<td>4.44 (4.08)</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Test</td>
<td>12.50 (3.90)</td>
<td>13.0 (4.61)</td>
<td>9.50 (4.08)</td>
</tr>
<tr>
<td>Health Disability Questionnaire</td>
<td>27.50 (8.86)</td>
<td>27.00 (9.24)</td>
<td>31.20 (9.02)</td>
</tr>
</tbody>
</table>
Table 4.10. Mean values and (standard deviation) of TMS related outcome measures for participants in the delayed intervention control group and the immediate intervention group. Asterisks indicate value is significantly different. Note the increase in cortical map area following intervention. Also note trend for increased cortical volume.

<table>
<thead>
<tr>
<th>TMS Outcome Measure</th>
<th>Control / Delayed Intervention</th>
<th>Immediate Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Testing Session 1</td>
<td>Testing Session 2</td>
</tr>
<tr>
<td>Cortical Map Area (cm²)</td>
<td>14 (15.45)</td>
<td>13 (11.33)</td>
</tr>
<tr>
<td>Cortical Map Volume (cm³)</td>
<td>1.24 (1.71)</td>
<td>0.96 (1.30)</td>
</tr>
<tr>
<td>COG in Longitudinal Direction (cm)</td>
<td>1.64 (1.29)</td>
<td>1.76 (1.07)</td>
</tr>
<tr>
<td>Active Motor Threshold (% MSO)</td>
<td>81% (22)</td>
<td>74% (21)</td>
</tr>
<tr>
<td>Maximum MEP Amplitude (% M-wave)</td>
<td>13.22% (13.90)</td>
<td>16.57% (15.70)</td>
</tr>
<tr>
<td>Maximum Slope of Recruitment Curve</td>
<td>3.86 (1.67)</td>
<td>3.29 (1.04)</td>
</tr>
</tbody>
</table>
Table 4.11: Pre- and post-intervention test for participants in the unimanual and bimanual massed practice groups. Astrisks indicates time / group interaction.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Unimanual Massed Practice (n=9)</th>
<th>Bimanual Massed Practice (n=10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Intervention Test: Mean (SD)</td>
<td>Post-Intervention Test: Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>291.49 (259.21)</td>
<td>225.48 (188.67)</td>
<td>p=0.57</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory</td>
<td>44.55 (13.93)</td>
<td>44.56 (17.16)</td>
<td>p=0.03 *</td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>3.79 (4.30)</td>
<td>4.79 (4.24)</td>
<td>p=0.23</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Test</td>
<td>10.0 (5.15)</td>
<td>12.0 (5.32)</td>
<td>p=0.18</td>
</tr>
<tr>
<td>Health Disability Questionnaire</td>
<td>23.56 (10.01)</td>
<td>21.78 (8.81)</td>
<td>p=0.74</td>
</tr>
</tbody>
</table>
Table 4.12: Pre- and post-intervention test for participants in the SS and FES Groups. Astrisks indicates time / group interaction.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Somatosensory Stimulation (n=9)</th>
<th>Functional Electrical Stimulation (n=10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Intervention Test: Mean (SD)</td>
<td>Post-Intervention Test: Mean (SD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jebsen Taylor Hand Function Test</td>
<td>432.42 (254.34)</td>
<td>365.96 (242.84)</td>
<td>329.50 (285.84)</td>
</tr>
<tr>
<td>Chedoke Arm and Hand Activity Inventory</td>
<td>34.56 (10.14)</td>
<td>36.89 (9.52)</td>
<td>42.30 (17.32)</td>
</tr>
<tr>
<td>Pinch Grip Strength</td>
<td>2.38 (1.90)</td>
<td>3.05 (1.86)</td>
<td>6.57 (7.40)</td>
</tr>
<tr>
<td>Semmes Weinstein Monofilament Test</td>
<td>7.00 (4.12)</td>
<td>8.00 (3.84)</td>
<td>12.50 (3.98)</td>
</tr>
<tr>
<td>Health Disability Questionnaire</td>
<td>30.78 (9.95)</td>
<td>28.56 (9.29)</td>
<td>28.20 (9.16)</td>
</tr>
</tbody>
</table>
CHAPTER 5: IMPLICATIONS FOR THE NEUROREHABILITATION SPECIALIST

Evidence suggests that cortical reorganization occurs after SCI and appears to be related to both the loss of sensory and motor pathways. However, it’s possible that lack of use is also associated with cortical reorganization. In chapter two, we addressed the following research question: are cortical maps different for muscles affected by the injury and muscles not affected by the injury? We investigated the changes that occur in the cortical map of the thenar muscles (the muscle affected by the injury) with the cortical map of biceps (the muscle unaffected by the injury). The cortically evoked potentials of the thenar muscles were much smaller in amplitude and the intensity at which they could be evoked was much greater than those of non-disabled individuals. The cortically evoked potentials of the biceps muscle were of similar amplitudes and the intensity at which they could be evoked was similar to that of non-disabled individuals.

Based on the results from this study we reject the hypothesis that muscles spared by the injury are different from non-disabled individuals. We further conclude that muscles affected by the injury have less cortical excitability than those of non-disabled individuals. Cortical excitability is an outcome measure which could be investigated in intervention studies.

Individuals with chronic SCI begin to plateau in functional improvements nine months after their injury. However, recent studies suggest intensive, task-oriented training focused on a single upper extremity can induce both improvements in function and cortical organization. Yet, individuals with SCI frequently have deficits in both limbs, and therefore may benefit from a bimanual training intervention. The question remained: Do individuals with SCI who participate in a bimanual massed practice
training program receive similar benefits to those who participate in a unimanual massed practice training program? Chapter three and four addressed this question. The results from chapter three suggested that a bimanual massed practice intervention in which individuals trained both hands to stabilize the object and manipulate the object (switching during the intervention) induced less change in unimanual hand function and cortical reorganization. Individuals in the bimanual group demonstrated similar changes on the test measuring bimanual hand function.

Based on these results, the intervention was modified such that those in the bimanual group practiced only the manipulative portion of the task with their weaker hand and the stabilization portion of the task with their stronger hand (chapter four). Using this intervention, individuals in the bimanual group demonstrated similar changes in the outcome measure investigating unimanual hand function and cortical map area. Further, individuals in the bimanual group demonstrated greater changes on the outcome measure investigating bimanual hand function. Therefore, we conclude that improvements in bimanual hand function are dependent on task-specific practice.

Finally, electrical stimulation augments functional changes associated with task-oriented training. However, it was not known if the type of nerve fiber targeted (sensory or motor) provides a more optimal environment than the other. Further, it was not known if the timing of the electrical stimulation was a critical factor in improving hand function. In chapter four we also compared two different electrical stimulation paradigms: somatosensory stimulation and functional electrical stimulation. It appears that both electrical stimulation paradigms (when paired with massed practice training) induce similar changes in function and cortical reorganization. The long pulse width of the
somatosensory stimulation, nor the timing of the stimulation from the functional electrical stimulation is a critical component of the electrical stimulation.

Conclusions. Individuals with chronic cervical SCI can improve in arm and hand function over a no treatment control condition. Those in bimanual massed practice intervention group demonstrate greater changes on an outcome measure of bimanual hand function. These changes are associated with increased cortical map area. Changes in cortical excitability were not evident in all participants following the intervention. It’s possible that these deficits may be dependent on an individual’s unique neurophysiology such as amount of intracortical inhibition and the initial location of the center of gravity of the cortical map.
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Ref Type: Abstract

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Ref Type: Conference Proceeding


Ref Type: Abstract


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