The Impact of Manual-assisted Locomotor Training on Walking Ability and Sensory and Motor Scores in Chronic Motor Incomplete Spinal Cord Injury

Thesis

Presented in Partial Fulfillment of the Requirements for the Degree Master’s of Science in Allied Health Management in the Graduate School of Allied Medical Professions of The Ohio State University

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Spinal Cord Injury (SCI) is a devastating disability that negatively impacts quality of life and the inability to ambulate or ambulate well is considered by many to be the greatest functional limitation. Therefore, development of rehabilitation interventions that maximize locomotor abilities for those with SCI are vital. Manual-assisted Locomotor Training is an activity-based therapy developed to induce locomotor and functional gains in those with neurologic impairment. However, the impact of Locomotor Training on locomotor ability, balance, strength and sensation in chronic motor incomplete SCI is currently unknown.

This study determined the magnitude and rate of locomotor improvement following Locomotor Training and the amount of Locomotor Training needed to elicit these changes for persons with chronic motor incomplete SCI treated in the multi-site NeuroRecovery Network (NRN). Locomotor performance was measured by gait speed, distance and attainment of functional speeds reported for in-home (<0.44 m/s) or community ambulation (≥0.44 m/s). In addition, we determined the impact of Locomotor Training on American Spinal Injury Association (ASIA) exam sensory and motor scores for lower extremity strength and sensation. The relationship between sensory and motor scores and recovery of locomotion and balance after Locomotor Training was examined. Lastly, we determined the degree of agreement in final gait speeds obtained for short bout locomotion during the 10 meter walk test (10MWT) and for long bout locomotion during the 6 minute walk test (6MWT).

Using a prospective, cohort design, we compared sensory and motor scores and functional outcomes pre and post-intervention for individuals that had completed Locomotor Training in the NRN from March 2005 to July 2010. Participants included
225 individuals with chronic motor incomplete SCI with ASIA Impairment Scale of C or D (mean 2.45±3.79 years post-injury). The NRN Locomotor Training intervention consisted of manual-assisted body-weight supported treadmill step training, over ground assessment and community reintegration for about 1.5 hrs per session. Training occurred 3-5 times a week for an average of 60 sessions over an average of 5 months.

Outcome measures collected before and after the intervention included: AIS classification; lower extremity and upper extremity motor scores (LEMS, UEMS); lower extremity pin prick scores; lower extremity light touch scores; gait speeds for the 10MWT and the 6MWT; gait distances for the 6MWT; and, balance using the Berg Balance Scale (BBS). Comparisons were made for the overall sample, AIS C and D subsets, paraplegia/tetraplegia subsets and functional gait speed stratifications.

No significant changes in sensory or motor scores were found following Locomotor Training except LEMS (pre: 31.85±13.98; post: 38.61±12.29; p<0.05) and UEMS (pre: 38.36±10.83; post: 41.44±8.27; p<0.05). Significant gains in gait speed (pre: 0.32±0.40 m/s; post: 0.55±0.55 m/s; p<0.05), gait distance (pre: 94.4±115.09 m; post: 164.42±159.82 m; p<0.05), and balance (BBS pre: 20.48±17.70; post: 29.24±20.60; p<0.05) were found. While significant correlations occurred, no relationship was found for AIS C and D subsets between sensory and motor scores and gait speed ($r^2 = 0.026$-$0.070$; $r^2 = 0.051$-$0.241$ respectively), distance ($r^2 = 0.011$-$0.097$; $r^2 = 0.037$-$0.251$ respectively) or balance ($r^2 = 0.109$-$0.177$; $r^2 = 0.072$-$0.333$ respectively) following Locomotor Training. A significant (p<0.05) moderate positive relationship between initial LEMS and final Berg Balance Scores occurred for paraplegia and tetraplegia subsets ($r^2 = 0.497$ and 0.478 respectively). Conversion between functional gait speed stratifications occurred following Locomotor Training with 47% of the sample ambulating at community gait speeds at discharge ($\geq 0.44$ m/s). Sixty-four percent of the sample achieved peak gait speed at discharge. Final speeds obtained from the 10MWT
for the overall sample were 17% higher than speeds obtained from the 6MWT. However, 20% produced higher gait speeds during long bout 6MWT ambulation compared with short bout 10MWT ambulation at discharge.

Manual-assisted Locomotor Training improves gait speed, distance, balance and functional ambulation ability in individuals with chronic motor incomplete SCI. The ASIA exam sensory and motor scores and AIS classification appear to be poor indicators of recovery of walking and care should be taken when using them to determine treatment efficacy or functional improvement. Functional classification based on gait speed during short bout ambulation may be a more sensitive indicator of meaningful locomotor recovery. That 16% of subjects at enrollment produced faster speeds during long bout locomotion suggests that even these classifications may underreport recovery. Whether speeds derived from the 6MWT align more closely with community ambulation ability than the 10MWT should be examined. It seems likely that each test describes different domains of walking ability in those with chronic incomplete SCI following Locomotor Training. Finally, different functional severities may require different doses of Locomotor Training to maximize locomotor abilities. These results will help determine allocation of resources to maximize locomotor outcomes as efficiently and effectively as possible in people with chronic SCI.
Dedication

To Jackie, Ella, Jackson and Emilia
Acknowledgements

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Lastly, thanks to the School of Allied Medical Professions Graduate Program for allowing me this opportunity to attain my Master’s Degree in Allied Health Management.
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Field of Study

Physical Therapy: Master’s of Science in Allied Health Management
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CHAPTER 1: INTRODUCTION

Spinal cord injury (SCI) is a devastating and potentially fatal disability that can have a large negative impact on individuals’ lives. Spinal cord injury affects approximately 12,000 individuals in the United States annually. The prevalence of SCI is actually lower than that of other major disabilities but the direct and indirect health care costs and negative impact on quality of life exceeds that of other disorders. Also, the average age of onset is quite young compared to other common and devastating conditions such as heart disease (age of first heart attack in men is age 66) or stroke (75% of all strokes occur over the age of 65). Furthermore, most people with SCI are unemployed or underemployed and face high lifetime medical costs due to their injury thereby creating greater economic burden for them and their families. Thus, the impact on overall quality of life for an individual sustaining a SCI and their families is tremendous.

Many individuals with SCI describe their most devastating and apparent disability as the inability to ambulate or an inability to ambulate without significant deviations. These physical limitations may account in part for higher health care costs and the lower rate of employment and warrant further attention. Taking into account the relatively young age of onset and an increasingly aging population, the impact of improving functional independence (ie ambulation ability) on quality of life and financial burden could be substantial. According to the National Spinal Cord Injury Statistical Center (NSCISC), up to $400 billion could possibly be saved on future overall lifetime costs with the development of new interventions and the prevention of new injuries within the United States.

Current SCI rehabilitation models are based on the assumption that the central nervous system (CNS) is hard-wired or incapable of changing or repairing itself when injured.
Rehabilitation potential and functional prognosis is currently based on initial sensory and motor assessments (ASIA exam scores), psychosocial and cognitive assessments, and clinical judgment. For example, it has been discussed in the literature that those individuals with more severe injuries (AISA A and B) appear less likely to achieve functional ambulation than those with less severe injuries (ASIA C and D). Those with chronic injuries are expected to achieve less improvement than those with acute injuries. However, actual locomotor gains are often inconsistent with these prognoses. Research using animal models of SCI the last several decades challenges notion of a hard-wired nervous system and shows that the CNS has the potential for activity-based plasticity as well as the ability to perform complex, rhythmic behaviors in the absence of supraspinal input, like ambulation. This research has recently been translated to rehabilitation for humans with SCI. As these new concepts are being applied to persons with SCI, we continue to see inconsistencies in functional gains, specifically locomotion.

Locomotor Training is a novel rehabilitation approach with guidelines developed from basic science research on central pattern generation (CPG) in adult mammals. Locomotor Training attempts to retrain locomotor ability in neurologically injured individuals by utilizing the intrinsic mechanisms of the spinal cord itself. Locomotor Training can be delivered manually or through the use of robotic assistance. Manual Locomotor Training is advantageous because it can be tailored to fit the specific needs and limitations of the individual on-the-fly, providing only the forces that are specifically needed to generate a proper stepping pattern. Locomotor Training is highly resource intensive, requiring manpower and financial resources beyond that of conventional rehabilitation. It is important to consider the intensity, amount and duration of Locomotor Training delivered to elicit changes in locomotor outcomes given that it requires more repetition and longer treatment durations than conventional therapy. Therefore, a realistic estimation of functional outcomes expected
and the magnitude, rate and duration of treatment needed to see these changes is clinically and economically relevant.

Several recent studies have attempted to identify factors that predict walking ability as well as establish minimal criteria required for independent community ambulation for individuals with incomplete SCI. Dobkin et al suggests that gait speed and lower extremity motor scores (LEMS) are predictive of ambulation ability. They concluded that ASIA C individuals were likely to achieve functional community ambulation if they reached a FIM-L score of ≥3 (able to ambulate ≥50 ft with moderate assistance) after starting rehabilitation by 8-14 weeks post injury. Dobkin suggests that ASIA C individuals still requiring significant physical assistance by approximately 20 weeks post-injury are less likely to achieve functional community ambulation. Winchester et al suggests that voluntary bowel and bladder voiding, spasticity, initial walking speed, and time since injury are good predictors of walking ability in persons with incomplete SCI utilizing robotic Locomotor Training for 36 sessions. Van Hedel et al found that a minimum gait speed of 0.44 m/s is required for a person with an incomplete SCI to ambulate in the community with aid or assistive device and a minimum change in gait speed of 0.3 m/s is needed to achieve independent ambulation within this population. In contrast, Musselman determined that the minimally important difference (MID) in gait speed after Locomotor Training with BWS for incomplete SCI receiving Locomotor Training with BWS was 0.05-0.06 m/s. The MID is defined as the minimal amount of change in an outcome measure that is considered to be due to the intervention rather than variability of the sample or by chance. This is often referred to as clinical meaningfulness. However, it is not specifically stated what clinical meaningfulness is and whether or not it signifies the ability to ambulate independently. No studies to date have attempted to analyze these predictive factors and ambulation criteria in the subacute and chronic incomplete SCI population following manual Locomotor Training of a prolonged duration. Therefore, we are asking the following research questions:
Research Questions and Research Approaches

Using a functional classification of ambulation determined by van Hedel et al ¹, we stratified each subject into one of three groups based on gait speed at enrollment. We used a gait speed of 0.44 m/s, the minimum speed for people with incomplete SCI to ambulate independently in the community with or without an assistive device. These stratifications formed 3 groups: 1) Non ambulatory subjects had initial gait speeds of 0 m/s; 2) Subjects with initial gait speeds greater than 0 but less than 0.44 m/s align with in-home ambulation with or without assistance; and, 3) Subjects with initial gait speeds greater than or equal to 0.44 m/s aligned with community ambulation with or without assistive devices.

Since the proposal, the overall scope of this thesis was significantly increased with the addition of several other questions involving the relationship and impact of Locomotor Training on AISA examination parameters. The analyses were compiled into a publication quality manuscript presented in its entirety in chapter 3 and an addendum which reports results not captured in the manuscript. Chapter 3 explored the following questions:

1) **What is the impact of Locomotor Training on conversion of AIS classification for those with chronic motor incomplete SCI?**

Initial AIS classification was determined for all subjects at enrollment using the ASIA examination and these classifications were compared with AIS classification at Discharge. Conversion rates between AIS classes C and D were calculated.
2) **What is the impact of Locomotor Training on functional gait speed categories as described by van Hedel** [1] **and are these gains sufficient for community ambulation?**

We used van Hedel’s gait speed categories as our criteria for determining *independent community ambulation ability* [1]. We analyzed initial evaluation gait speeds for all subjects. We then looked at gait speeds at discharge evaluation to see what percent of those individuals achieved gait speeds of 0.44 m/s or higher. We then analyzed these results by stratification as described above.

3) **What is the impact of Locomotor Training on sensation (LE pin prick and light touch scores) and how is it related to locomotor and balance performance?**

We assessed and compared LE pin prick and light touch scores at enrollment and at discharge. We then correlated sensation scores with gait speeds and distances derived from the 10MWT and the 6MWT to determine association. Comparisons were made between AIS C and D subsets, paraplegia and tetraplegia subsets and functional gait speed stratifications.

4) **What is the impact of Locomotor Training on strength (Lower Extremity Motor Score- LEMS) and how is it related to locomotor and balance performance?**

We assessed and compared LEMS at enrollment and at discharge. We then correlated LEMS with gait speeds and distances derived from the 10MWT and the 6MWT to determine association. Comparisons were made between AIS C and D subsets, paraplegia and tetraplegia subsets and functional gait speed stratifications. **Within the Addendum, these 2 questions from the original Thesis proposal were addressed:**
1. What is the largest rate and magnitude of locomotor improvement (increase in gait speed) obtained and what amount of Locomotor Training is necessary to elicit these changes for persons with incomplete spinal cord injury (SCI) who have completed LT in the NRN?

**Magnitude and Rate**
We analyzed initial gait speeds collected at initial evaluation for all subjects from the 10MWT and the 6MWT as well as distance calculated from the 6MWT. We then looked at subsequent reevaluations (obtained every 20 Locomotor Training sessions) and found the fastest obtained gait speed for each measure (10MWT, 6MWT). We also did the same calculation with distance ambulated during the 6MWT. This gave us largest magnitude of locomotor improvement. We also determined the amount of Locomotor Training necessary to elicit the peak magnitude where amount of Locomotor Training is defined operationally as Locomotor Training sessions needed to obtain that fastest gait speed. (ie 20, 40, 60, etc)

2. What is the degree of agreement in final gait speed between the 10MWT and the 6MWT for persons with incomplete spinal cord injury following Locomotor Training?

   We calculated initial gait speeds for all subjects using the 10MWT and the 6MWT. We subtracted the initial gait speed from the final gait speed. We then compared final gait speeds for the 10MWT and the 6MWT. We then compared absolute differences in speeds between the two tests.

   The following question from the original Thesis proposal will be addressed in a subsequent study with permission of the Thesis Committee:
What factors predict locomotor outcomes (gait speed) for persons with incomplete spinal cord injury (SCI) enrolled in the NRN?

All changes in scope and suspension of the prediction question were approved by the thesis committee via email.

Operational Definitions

1. **Locomotor improvement:**
   a. This was defined as increases in gait speed in meters per second (m/s) as suggested by the literature [1, 6, 9, 21, 22, 29, 31, 35-37].
   b. This was calculated from the 10MWT by taking 10 meters and dividing it by the seconds needed to complete the test. \(\frac{10 \text{ m}}{\text{ s}} = \text{ m/s}\)
   c. This was also calculated from the 6MWT by overall distance ambulated in 6 minutes or by converting the distance to speed (m/s) by taking the total distance and dividing it by 360.

2. **Amount or dose of Locomotor Training:** The number of Locomotor Training sessions provided. (20, 40, 60, etc)

3. **Locomotor training session:** A treatment session that obtains at least 20 minutes of “step retraining time” and 55 minutes of “total weight-bearing time.” If these goals were not obtained during one particular session, two consecutive sessions were combined to equate to one Locomotor Training session.
   a. **Total weight bearing time (TWB):** Total time a person with SCI spends weight bearing within the body weight supported treadmill training (BWSTT) environment.
   b. **Step retraining time (SRT):** Total time a person with SCI spends weight bearing within the BWSTT environment ambulating or stepping at greater than 2.0 MPH while therapists manually manipulate and appropriately cue the patient’s body for optimal pre-injury kinematics.
4. **Independent community ambulation**: The ability to ambulate independently at or above 0.44 m/s with or without aide.

5. **Spasticity**: Assessed in bilateral lower extremities using the Modified Ashworth Scale (MAS).

6. **Time post-injury**: Number of days converted to years post-injury.

7. **LEMS**: manual muscle score of key muscle groups in both legs during the ASIA scale. The maximum score is 50 with higher scores indicating better performance.

8. **UEMS**: manual muscle score of key muscle groups in both arms during the ASIA scale. The maximum score is 50 with higher scores indicating better performance.

9. **Berg Balance Scale (BBS)**: A 14-item performance measure that looks at functional sitting and standing balance during multiple functional tasks. Maximum score is 56 with higher scores indicating better performance.

10. **Body Mass Index**: A statistical measure that looks at healthy body weight based on height. It is not a measure of percent body fat. \[ \text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2} \]

11. **Lower extremity pin prick scores**: Scores obtained by assessing dermatomes from T11-S4/S5 using a 2 point scale bilaterally. Maximum lower extremity scores for pin prick is 44 with higher scores indicating more normal sensation.

12. **Lower extremity light touch scores**: Scores obtained by assessing dermatomes from T11-S4/S5 using a 2 point scale bilaterally. Maximum lower extremity scores for light touch are 44 with higher scores indicating more normal sensation.
Spinal cord injury (SCI) is a devastating and potentially fatal trauma that can have a large negative impact on individuals’ lives. Spinal cord injury can affect individuals physically, psychologically, emotionally and functionally, all of which can greatly diminish the quality of life (QOL) of the injured as well as the QOL of those around them or caring for them. Recently, increasing awareness as well as new advances in treatment and management of SCI complications have allowed individuals sustaining SCI to live longer and have more satisfying lives.

**Epidemiology**

The societal impact of spinal cord injury in the United States and the world has changed due to a recent shift in epidemiological trends. Approximately 6 million people in the U.S. (1.9% of U.S. population) live with paralysis which is 33% higher than previously estimated. Approximately 1,275,000 people report paralysis due to SCI (0.4% of U.S. population) which is five times higher than previous estimates according to recent data provided by the Christopher and Dana Reeve Foundation. Spinal cord injury is the second leading cause of paralysis in the U.S. (23% of all paralysis) following stroke (29% of all paralysis). Thirty-five percent of people with SCI report that they have “a lot of difficulty moving” and 29% report having “some difficulty moving”. Men are four times more likely to sustain an injury than woman but recently there has been an increase in women with SCI (18.2% in 1970’s to 21.8% in the 2000’s). Caucasians compromise the largest proportion of SCI (67.4%), followed by African Americans (19.4%) and Hispanic-Latino (10.1%). Currently, the most frequent neurologic category of injury is incomplete tetraplegia (incomplete loss of motor or sensory function below the level of injury in all four limbs) (34.1%), followed by complete paraplegia (complete loss of
motor and sensory function below the level of injury in both legs) (23.0%), complete tetraplegia (complete loss of motor and sensory function below the level of injury in all four limbs) (18.3%) and incomplete paraplegia (incomplete loss of motor or sensory function below the level of injury in both legs (18.5%) \(^3\). In the late 1970’s, the average age of injury was quite young, 28.7 years, with most injuries occurring between 16 and 30 years of age. However, recently, average age of onset has increased to an average of 37.6 years between 2000 and 2003, believed to be caused by the increasing age of the general population \(^38\). This average age of onset remains quite young compared to other common and devastating conditions such as heart disease (age of first heart attack in men is age 66) or stroke (75% of all strokes occur over the age of 65) \(^7\). Also, due to recent advances in medical technology, overall life expectancies have increased, so individuals with SCI are living longer than in the past \(^39\). Current life expectancy ranges for a 20 year old sustaining a severe SCI (complete or severe incomplete tetraplegia) are from 37-44 years \(^39\) and the life expectancy of a paraplegic person beyond the time of injury is normal \(^40\). These shifting trends have important implications for management of SCI as well as health related costs of SCI given the early age of onset and longer life expectancies after injury.

**Costs of Spinal Cord Injury**

Significant costs accrue throughout the life of an individual with SCI with higher costs seen as injury severity increases. These costs include initial hospitalizations and readmissions, rehabilitation, modifications to homes and vehicles and recurrent costs of durable medical equipment (DME), medications, supplies and homecare assistance \(^41\). It has been estimated that $8 billion is spent annually in the U.S. caring for and managing SCI \(^42\). Since individuals with SCI are living longer after injury, they are also incurring higher costs than in the past \(^43\). Total costs for the first year of care are almost 3 times higher for a person with high tetraplegia (C1-C4) compared to a person with paraplegia.
The lifetime costs of a 25 year old with high tetraplegia (C1-C4) are also almost three times higher than the lifetime costs of a 25 year old with paraplegia (see table 2). Within the United States, up to $400 billion could possibly be saved on future overall lifetime costs with the development of new interventions and the prevention of new injuries according to the National Spinal Cord Injury Statistical Center (NSCISC). Injury level and severity of injury are important factors to consider, since those individuals with high tetraplegia incur greater than 3 times the costs than people with incomplete or lower levels of injury.

### Average Yearly Expenses (Table 1)

<table>
<thead>
<tr>
<th>Severity of Injury</th>
<th>First Year</th>
<th>Each Subsequent Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>High quadriplegia (C1-C4)</td>
<td>$775,567</td>
<td>$138,923</td>
</tr>
<tr>
<td>Low quadriplegia (C5-C8)</td>
<td>$500,829</td>
<td>$56,905</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>$283,388</td>
<td>$28,837</td>
</tr>
<tr>
<td>Incomplete motor function at any level</td>
<td>$228,566</td>
<td>$16,018</td>
</tr>
</tbody>
</table>

### Estimated Lifetime Costs by Age of Injury (Table 2)

<table>
<thead>
<tr>
<th>Severity of Injury</th>
<th>25 Years Old</th>
<th>50 Years Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>High quadriplegia (C1-C4)</td>
<td>$3,059,184</td>
<td>$1,800,958</td>
</tr>
<tr>
<td>Low quadriplegia (C5-C8)</td>
<td>$1,729,754</td>
<td>$1,095,411</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>$1,022,138</td>
<td>$697,163</td>
</tr>
<tr>
<td>Incomplete motor function at any level</td>
<td>$681,843</td>
<td>$494,145</td>
</tr>
</tbody>
</table>
Community Reintegration and Impact on Quality of Life (QOL)

Community reintegration following SCI can be quite challenging and often does not fully occur. Community reintegration is a primary goal of rehabilitation in that it attempts “to promote the assumption or resumption of culturally and developmentally appropriate societal roles after injury or illness”\(^4\). Many individuals with SCI are able to resume many of their pre-injury roles; however, it is debated if these individuals are truly able to participate in their communities at their highest potential level of function and independence\(^4\). Factors such as family support, emotional adjustment and coping style most positively influence successful community reintegration. One of the biggest barriers to full community participation is limited community resources\(^4\). Also, psychological issues can have an impact on community reintegration after SCI. Those newly injured frequently express distress concerning the demand their injury inflicts on those caring for them. Spouses who serve as primary caregivers subjectively demonstrate increased stress, fatigue, resentment and depression compared with spouses who are not caregivers\(^4\). Furthermore, those with SCI have a lower probability of returning to work after injury. For example, 57.4% of those with SCI were employed at the time of injury. However, only 32.4% of those with paraplegia and 24.2% of those with tetraplegia were employed 10 years after injury\(^8\). The problem is that most current SCI rehabilitation focuses on minimizing functional limitations, not maximizing community participation. Also, household income for those with SCI is much lower than that of the country as a whole. For example, 24.0% of persons with SCI report annual household incomes < $10,000 (census reports 7.0%) and 15.4% of persons with SCI report annual household incomes $10,000 - $15,000 (census reports 5.8%)\(^2\). Therefore, this population of individuals is experiencing extremely high costs of living with extremely low incomes compared with the country as a whole. Current and conventional approaches to SCI rehabilitation need to be modified and advanced in order to better address these issues.
concerning community reintegration and to optimize the likelihood of success of these individuals as they regain their independence following their injury.

**Functional and Clinical Anatomy - Ascending and Descending Pathways within the CNS**

The spinal cord relays motor information from the brain to the rest of the body and receives sensory information from the body and periphery and transfers it to the brain. The spinal cord and the brain make up the central nervous system (CNS). On cross-section, the spinal cord is made up of gray matter centrally which is surrounded by white matter. The central gray matter is divided into three horns: 1) the dorsal (posterior) horn where projections of cell bodies of sensory fibers from the dorsal root ganglia are found; 2) the lateral or intermediate horn where sympathetic neurons are found and; 3) the anterior or ventral horn where motor neurons are found. The surrounding white matter forms three main columns or tracks: 1) the dorsal column system (fasciculus gracilis and fasciculus cuneatus) which relays sensory information like proprioception, vibration and light touch to the brain; 2) the lateral column (anterolateral system) which carries sensory and motor information including pain, temperature, pressure and touch, and 3) the anterior (ventral) column (corticospinal tract) which primarily carries motor information (see Figure 1). The dorsal column system is called an *ascending pathway* because it carries sensory information from the periphery to lower levels of the brain like the brain stem and then to higher levels like the thalamus and cerebral cortex. On the other hand, *descending pathways* originating from higher centers in the cerebral cortex and brainstem carry motor signals to motor neurons in the spinal cord. The brainstem controls less voluntary aspects of motor control such as muscle tone and posture, whereas the cerebral cortex controls more voluntary aspects of motor control. These descending motor pathways are responsible for initiating coordinated voluntary movements and postural control. The majority of these pathways synapse on spinal cord *interneurons*, although
some synapse directly on motor neurons\textsuperscript{45}. There are six main motor pathways (see figure 1) whose axons travel through the white matter of the spinal cord and synapse on interneurons (found dorsal to the ventral horn) or motor neurons (found in the ventral horn). The corticospinal tract, for example, carries motor information from the cerebral cortex (primary motor cortex on the precentral gyrus of the frontal lobe) to these interneurons and motor neurons found in the gray matter of spinal cord\textsuperscript{46}. The spinal cord, on a very simplistic level, is a vital pathway that allows a two-way flow of information between the brain and the rest of the body.

**Figure 1 – Spinal cord cross-section showing ascending and descending tracts\textsuperscript{5}**

![Spinal cord cross-section showing ascending and descending tracts](image)

**Interneurons and Motor Neurons**

The spinal motor network within the cord is made up of motor neurons (α motor neurons and γ motor neurons) which innervates muscles in the periphery and are part of networks
of interneurons within the gray matter of the spinal cord. The cell bodies of motor
neurons (motor nuclei) that control the trunk and proximal muscle groups are found in the
medial portion of the ventral horn and the motor nuclei that control the distal extremity
muscles are found in the lateral portion of the ventral horn. These motor nuclei that
control the distal extremity muscle groups (arms and legs) are found primarily within the
cervical (C3-T1) and lumbar (L1-S2) enlargements of the spinal cord. The majority of
the inputs to these motor nuclei come from networks of excitatory and inhibitory
interneurons which are located in the intermediate zone of the gray matter. The
interneurons receive and integrate information from sensory afferents coming from the
periphery, as well as from supraspinal motor centers in the brain. These interneuronal
networks are responsible for the final formation of motor activity by integrating
ascending sensory input from the environment with descending motor input from the
brain. Hence, these interneuronal networks demonstrate some degree of extrinsic and
intrinsic control over motor nuclei activity. This allows some level of spinal control over
more complex types of motor coordination without complete supraspinal control. For
example, interneurons convey information between motor nuclei within the ventral horn
to coordinate movement within a limb; and across the cord to coordinate movement of
pairs of limbs with minimal supraspinal input. Complex movement patterns such as
walking may be organized, initiated and regulated within the cord by these interneuronal
networks, organized into a group called Central Pattern Generators (CPG). By
integrating sensory input with supraspinal control, these networks can adapt to changes in
the environment such as uneven surfaces during ambulation without full voluntary,
supraspinal activation of all motor output.

**Upper and Lower Motor Neurons**

The physical manifestation of symptoms derived from injury to upper motor neurons
(UMN) and lower motor neurons (LMN) is crucial in determining whether or not intact,
functional interneuronal networks are present below the level of the lesion. Upper motor neurons do not leave the CNS. Lower motor neurons (LMN) originate in the ventral horn of the gray matter with axons that leave the CNS and innervate peripheral muscles. UMN injury is indicated by spasticity, muscle weakness or lack of motor control, hyperreflexia and a positive Babinski sign. Lower motor neuron injury is indicated by abnormal EMG potentials, fasciculations, hyporeflexia or flaccidity, muscle weakness and muscle atrophy. In most individuals the spinal cord ends at about the L2 vertebral body and continues distally as the cauda equina or peripheral nerves. Therefore, most injuries occurring to the spinal cord above L2 will usually present clinically as an UMN injury indicating injury to descending UMN axons within the spinal cord. Those injuries occurring below L2 typically present clinically as an LMN injury with frank muscle atrophy and hyporeflexia due to damage to motor nerves of the cauda equina. With an LMN injury there is no actual injury to the spinal cord and hence no spinal cord or intact interneuronal networks below the lesion. With an UMN injury, there is still some spinal cord as well as intact interneuronal networks below the lesion.

FIGURE 2. Dermatome distribution for the entire body.
Spinal Cord Injury Classification and Examination

Spinal cord injuries are classified based on guidelines created by the Neurological Standards Committee of the American Spinal Injury Association (ASIA) referred to as the International Standards for Neurological Classification of Spinal cord Injury. The neurologic examination consists of testing 10 key muscle groups (5 upper extremity, 5 lower extremity) (see table 3), light touch and pin prick sensation in 28 dermatomes (see fig. 2) and a rectal exam testing sensation and voluntary sphincter contraction. The motor examination consists of manual muscle testing (0-5 on a 5 point scale) of these key muscle groups on both sides of the body. Grades 1 and 2 indicate trace muscle contraction or partial movement of the joint. Grades 3 and higher indicate muscle contractions and joint movement though the entire range of motion against gravity. Grades 4 and 5 indicate full, against-gravity motion with partial or normal resistance respectively. The motor level of injury is defined by the lowest key muscle group that has a grade of at least 3/5 while all key muscle groups above that level are graded 5/5. The sensory level of injury is defined as the most distal (caudal) segment of the spinal cord with normal sensory function on both sides of the body. A “neurologic” level of injury is defined as the most distal (caudal) spinal segment with normal muscle testing and sensation. The rectal examination is used to determine the presence or absence of intact voluntary sphincter control and deep anal sensation. The presence of deep anal sensation may be the only
Table 3: 10 Key Muscles Tested to Determine an ASIA SCI Classification

<table>
<thead>
<tr>
<th>Muscle Group</th>
<th>Root Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper limb</strong></td>
<td></td>
</tr>
<tr>
<td>Elbow flexors</td>
<td>C5</td>
</tr>
<tr>
<td>Wrist extensors</td>
<td>C6</td>
</tr>
<tr>
<td>Elbow extensors</td>
<td>C7</td>
</tr>
<tr>
<td>Long finger flexors</td>
<td>C8</td>
</tr>
<tr>
<td>Small finger abductors</td>
<td>T1</td>
</tr>
<tr>
<td><strong>Lower limb</strong></td>
<td></td>
</tr>
<tr>
<td>Hip flexors</td>
<td>L2</td>
</tr>
<tr>
<td>Knee extensors</td>
<td>L3</td>
</tr>
<tr>
<td>Ankle dorsiflexors</td>
<td>L4</td>
</tr>
<tr>
<td>Long toe extensor</td>
<td>L5</td>
</tr>
<tr>
<td>Ankle plantarflexors</td>
<td>S1</td>
</tr>
</tbody>
</table>

indicator of an incomplete SCI and appears to predict recovery of ambulation if present within 3 days of injury. A clinically “complete” injury is defined as the absence of sensory and motor function in the lowest sacral segment. A clinically “incomplete” injury has partial preservation of sensory or motor function in the lowest sacral segments. The ASIA Impairment Scale (AIS) is used to classify the injury based on severity of impairment (see table 4). Examining and classifying SCI in this way provides objectivity and consistency as well as allowing us to more easily study and generalize findings within or across different classifications.
Table 4

ASIA IMPAIRMENT SCALE

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A = Complete:</strong></td>
<td>No motor or sensory function found in the sacral segments S4-S5.</td>
</tr>
<tr>
<td><strong>B = Incomplete:</strong></td>
<td>Sensory function but no motor function found below the neurological level including the sacral segments S4-S5.</td>
</tr>
<tr>
<td><strong>C = Incomplete:</strong></td>
<td>Motor function found below the neurological level, and greater than half of key muscles below the neurological level graded less than 3.</td>
</tr>
<tr>
<td><strong>D = Incomplete:</strong></td>
<td>Motor function found below the neurological level, and greater than or equal to half of key muscles below the neurological level graded of 3 or more.</td>
</tr>
<tr>
<td><strong>E = Normal:</strong></td>
<td>Normal motor and sensory function.</td>
</tr>
</tbody>
</table>

Clinically Complete vs Anatomically Complete

Just because a patient may present clinically as “complete” based on the ASIA Impairment Scale Classification (ie ASIA A) doesn’t necessarily indicate an anatomically complete SCI. In fact, one study showed that only 7% of clinically complete SCI’s studied had true cord transection under magnetic resonance imaging (MRI)\(^{48}\). The sensitivity of MRI in showing soft tissue structure and injury is good for studying anatomical extent of injury and mechanisms of spinal cord damage\(^{49}\). MRI differentiates between spinal cord edema, contusion or hemorrhage, each of which has different prognostic implications\(^{49}\). Mahmood et al\(^{49}\) found that those patients with acute cervical SCI with spinal cord edema on MRI had a “favorable neurological outcome” indicated by overall higher motor scores (UEMS and LEMS) upon admission and improved scores at follow-up. Those individuals with MRI’s showing spinal cord contusions showed “less favorable outcomes” indicated by lower initial motor scores upon admission with
improved scores at follow-up. Those individuals with MRI’s showing spinal cord hemorrhage showed “poor neurological recovery” and were mostly associated with clinically complete injuries with no improvement in motor scores at follow-up. Several studies of human SCI using MRI and functional magnetic imaging (fMRI) have shown that the majority of patients diagnosed with clinically complete SCI had either spinal cord contusion or hemorrhage and few (7%) showed true transected cords. From a rehabilitation perspective, it is important to note that even individuals with clinically severe or “complete” injuries likely have intact neural substrates (ascending or descending) across the lesion which may promote some functional recovery.

In mammals such as cats with a completely transected spinal cord, purposeful neural activity occurs below the level of the lesion without supraspinal input. Many studies showed that the adult mammalian spinal cord can regain the ability to generate stepping in the absence of descending drive. It remains inconclusive whether the human spinal cord is sufficient to produce locomotion due to difficulty confirming anatomically complete lesions. However, Stroman et al. looked at acute and chronic SCI using fMRI to assess spinal cord damage and activity in segmental regions well below the level of injury. They found that spinal fMRI results of 27 cervical and thoracic SCI individuals consistently demonstrated activity in the lumbar spinal cord in response to thermal stimulation of the skin along the L4 dermatome (inner calf) in all subjects regardless of clinical classification. Even those individuals with clinically complete SCI consistently demonstrated diminished, but not absent, activity in the ipsilateral dorsal gray matter as well as increased activity in the ipsilateral and contralateral ventral regions of the spinal cord. They also showed that there is still a considerable amount of activity remaining in the injured spinal cord below the lesion level even decades after injury. Basso et al. compared the effects of Locomotor Training on rats with completely transected cords to rats with minimally and moderately contused cords with less than 10% of descending axonal sparing. After 7 weeks the rats with some amount of sparing
demonstrated marked improvement in locomotion compared with those rats with completely transected cords. At 7 weeks the rats with spared descending axons were then completely transected as well. There was an initial dramatic drop in locomotor ability in this group but surprisingly over the next several weeks they showed an increase in locomotor ability with training, although not as large as what was initially seen before complete transection. This suggests that the spared descending axons could influence and increase the capacity of the spinal cord to produce movement. This also suggests that the isolated mammalian spinal cord can retain some degree of locomotor capacity without supraspinal control which explains the ability of the rats to improve in locomotor ability even once the cord was completely transected.

Current or Conventional Model of SCI Rehabilitation

The current model of SCI rehabilitation has guided clinical decision-making, goals and duration of treatment to date. The conventional and prevailing assumption regarding SCI emanates from the elegant work of neuroscientist Santiago Ramón y Cajal in 1928 which holds that the CNS is “hard-wired, non-malleable and incapable of repairing itself” \(^\text{10}\). In other words, significant motor recovery is not expected beyond that seen at initial clinical assessment \(^\text{55}\). Therefore, until recently, the focus of rehabilitation for SCI has been toward compensating for functional impairments and little attention to facilitating recovery of these deficits. Furthermore, limitations and guidelines instituted by health care providers and payor sources have significantly limited the number and duration of therapy sessions allowed, requiring therapists to only address immediate patient needs \(^\text{55}\). *Compensation*, the primary rehabilitation strategy until the early 2000s, expects no improvement in strength, motor control, sensation and balance. This treatment methodology encourages the patient to use other functional abilities to complete a task or to modify the task or environment to allow successful completion. Goals of conventional SCI rehabilitation are tempered by level and severity of injury and include: strengthen the
available muscles, use leverage, momentum and/or substitution, and apply braces or assistive devices to *compensate* for weakness and paralysis. \(^{10,55}\)

Ultimately, this conventional approach limits the type and amount of rehabilitation that is being provided to those with SCI resulting in inconsistent and often inaccurate physical therapy prognoses. The conventional approach described above does not take advantage of the inherent capacity or ability of the nervous system and more specifically the spinal cord. These compensatory strategies fail to take advantage of the neuroplasticity of the CNS as well as likely spared substrates and inherent, longstanding functional capacity of segmental systems below the level of injury. New approaches to SCI rehabilitation have challenged this current way of thinking. Since the mid-1970’s the human spinal cord has been studied in order to determine its role in controlling movement and locomotion. \(^{10}\) Recent findings and research from both basic and applied science provides a new perspective on the role of rehabilitation for recovering motor function following SCI. \(^{55}\)

**New Approaches and Bases for SCI Rehabilitation: Animal SCI Research**

**Movement Control Capacity of the Mammalian Spinal Cord**

Mammalian spinal cord injury and the ability to ambulate have been studied since the early 1900’s. Sherrington \(^{52}\) was the first to describe the “flexion-reflex” of the hind-limb of cats with complete spinal cord transections where reflexive flexion of the cats’ hind-limb was evoked by stimulation of the skin of the limb. Sherrington also proved that the spinal cord, independent of supraspinal drive, had the capacity to produce reciprocal, coordinated hind-limb movements. Brown found that after removing afferent sensory input and supraspinal control animals could still demonstrate complex motor activity which has been further elucidated as walking, swimming and scratching. \(^{56,57}\) Barbeau and Rossignol \(^{17}\) found that pinching on the perineal or abdominal area only 1-2 days after spinalization in adult cats induces bilateral hind-limb extension with periods of
coordinated stepping. Several studies also showed that appropriate sensory input can help normalize the spinal reflex output in spinal cord-injured mammals. Thus, the mammalian spinal cord is capable of generating movement patterns, including locomotion, in the absence of supraspinal input with appropriate sensory input.

The Role of Afferent Sensory Input in Locomotion in Adult Mammals in the Absence of Supraspinal Input

Many studies since the 1970’s have shown the ability of the transected adult cat spinal cord to interpret afferent sensory information and generate and adapt complex motor patterns without supraspinal input. These studies showed that all types of sensory input received from the environment can impact and modulate motor output and the motor output generated was related to the type of sensory information received. For example, Sherrington was the first to suggest that the proprioceptors responding to hip extension in spinalized adult cats are vital to initiating swing. Grillner and Rossignol demonstrated the importance of kinematics for motor output by showing that the hip position (hip extension) and the contralateral step cycle are important for initiating swing in spinal adult cats. The stretch of the hip flexors and the weight shift onto the contralateral limb trigger initiation of swing without supraspinal input. They also showed that the transected adult cat spinal cord can adapt to changes in sensory input without supraspinal control. For example, they showed a decrease in stance phases and extensor EMG activity when the treadmill speed was increased. This was further demonstrated by Rossignol who showed that the same stimulus (touching the dorsum of the foot) provided to adult spinalized cats induced different responses depending on if the stimulus was applied during stance or swing. When applied during stance the extensors are activated and when applied during swing the flexors were activated. This also shows the phase-dependent nature of the motor responses to the same stimulus. Pearson and Duysens showed that by increasing the load of the hind-limbs of adult spinal cats
increased extensor activity and inhibited swing. Furthermore, Edgerton describes how loading the hind-limbs beyond normal weight during stepping in adult spinal cats greatly improved stepping which was evident by lengthened stance phases, increased activation of extensors and improved coordination of agonists and antagonists seen via EMG. These studies support the theory that the lumbar mammalian spinal cord can generate complex locomotor outputs by interpreting afferent sensory input (like kinematics, joint position, load, light touch, treadmill speed) from the environment without supraspinal control.

**Training Effects on the Locomotor Capacity of Spinal Cats.**

Many studies suggest that the mammalian lumbar spinal cord can show improved locomotor capacity and output when exposed to repetitive and appropriate sensory input through locomotor training. These studies showed that those cats with completely transected lower thoracic cords that received locomotor training on a treadmill were able to regain the ability to reciprocally step with full weight bearing even 1-3 weeks after spinalization. Lovely et al was the first to compare locomotor ability in trained and untrained spinal cats in order to compare training effect with spontaneous recovery. They found that the cats receiving regular locomotor training showed significant improvements in gait speed compared with untrained cats. De Leon et al conducted a similar study and showed that the EMG patterns of the cats with complete spinal cord transections trained were closer to those of normal cats during locomotion than the untrained group. Barbeau and Rossignol showed that adult spinal cats exposed to regular treadmill training demonstrated increased step quality (ability to place foot flat during stance), increased step length and increased ability to support weight as early as 4 weeks after spinalization. They also showed increased coordination between limbs and increased stability of the walking pattern at higher speeds when trained at these speeds. Also, during periods of less training, walking performance decreased, but when
training intensity was increased again, walking ability increased. Hodgson et al further illustrated this training effect by showing the importance of specificity of training. They compared adult spinal cats that were trained to step with those that were trained to stand. They found that each group was able to perform that specific skill well but the training would not carry over to the other skill. Also, these effects were shown to be reversible when the other skill was trained for an extended period of time. These studies provide evidence that suggests that the transected adult cat spinal cord, when provided with appropriate training and task specific sensory input can see significant improvement in locomotor ability and quality without supraspinal input.

**Effective Training Parameters for Improving Locomotor Capacity in Adult Spinal Cats**

These studies helped to determine optimal training parameters to maximize locomotor outcomes in adult spinal cats. For example, most of these studies trained the cats for 30 minutes a day, 5 times a week with variable treatment durations (up to 1 year). Improvement in locomotor ability was seen in most studies when trained up to 3 months and then locomotor ability or standing ability plateaus. De Leon showed that the rate of locomotor recovery and as well as the plateau level reached was significantly improved with step training. Hodgson et al showed that more successful locomotor outcomes were achieved the earlier the training was initiated (even 1 week after spinalization). Lastly, all of these studies emphasized the necessity of appropriate load, speed and kinematics to fully maximize locomotor outcomes. Most importantly these parameters provide the basis and scientific justification for translation of locomotor training to humans with SCI.
Central Pattern Generation and the Relationship with Afferent Sensory Input

The ability of the spinal cord in adult spinal cats to integrate and adapt to sensory information suggests an organizational phenomenon where a network of spinal interneurons in the spinal cord itself form a basic motor pattern of ambulation without supraspinal control. These spinal interneuronal networks have been found to generate rhythmic, cyclical patterns in some mammals needed for many vital functions (like ambulation, breathing and chewing) and they are referred to as central pattern generators (CPGs)\(^\text{63}\). In fact, these self-sustained patterns of neural activity can be generated without supraspinal or afferent input\(^\text{64}\). In this way, fairly complex, yet repetitive-type tasks can be simplified and generated within the spinal cord itself\(^\text{63}\). This takes some of the responsibility to form complex, coordinated movement patterns away from the higher centers, somewhat simplifying their role. Therefore, the supraspinal role in locomotion is to activate or inhibit the CPGs themselves and to modify their output in some way\(^\text{57}\).

Also, as discussed in the previous section it has been shown in multiple studies in adult mammals that motor output can be generated and modified by afferent sensory input by the spinal cord without supraspinal input\(^\text{13-18}\). This suggests that the CPGs within the adult mammal spinal cord can integrate specific sensory input to adapt the type of motor output required by the environment without supraspinal control. In other words the functional output is highly responsive to environmental demands. The existence of CPGs and their role in locomotion has been well studied in animal models but since it is unethical to intentionally and completely transect a human spinal cord, the existence of CPGs in humans can not be directly proven.

Evidence of CPGs in humans

Many studies have shown that the human spinal cord does respond similarly to that of other mammals in response to sensory input from the environment as though locomotor
CPGs do exist within them\(^{20-29}\). If the injured human spinal cord receives specific sensory input like that received during locomotion before injury (light touch, joint positions, load, kinematics, speed, muscle tendon stretch), appropriate locomotor outputs are observed regardless of the level of supraspinal control. Wernig et al\(^{22}\) refers to this application of specific sensory cues during locomotion as “rules of spinal locomotion”. Also, this locomotor output has been shown to be more complex than the simplistic muscle-tendon stretch reflex as previously thought\(^{25, 26, 28}\). For example, Harkema et al\(^{28}\) looked at the role of sensory information (load, muscle-tendon lengths and kinematics) during manual-assisted Locomotor Training for incomplete SCI subjects. They found modulated EMG activity of the soleus and gastrocnemius that was more closely associated with limb peak load than muscle tendon stretch. Muscle tendon stretch is considered a surrogate for spasticity. Therefore, these findings suggest that the EMG changes are occurring independent of spasticity and are actually more dependent on afferent sensory input. Wernig et al\(^{21}\) and Beres-Jones/Harkema\(^{65}\) made similar observations in similar types of subjects provided with BWSTT. They found that initiation and maintenance of stepping with a highly involved limb was usually only possible when the knee was fully extended during stance and the hip was extended past neutral with appropriate unloading. Also, many studies describe the modulation of lower extremity EMG activity when provided with BWSTT including appropriate locomotor sensory input where appropriate increases and decreases in EMG activity are seen in a phase appropriate manner\(^{20, 21, 24, 26, 28}\). This phase dependent EMG activity was further described by Harkema et al\(^{28}\) who showed that appropriate EMG activity was highly dependent upon the phase of the step cycle regardless of load. This suggests that the spinal networks within the human spinal cord must be able to integrate sensory input to coordinate movements between limbs. Also, several studies with incomplete SCI subjects exposed to BWSTT showed minimal or no active lower extremity movement when tested at rest. However, during locomotion, appropriate, phasic flexion and extension of the lower extremities was observed and recorded through EMG\(^{21, 22}\).
Harkema \(^{66}\) studied 29 subjects with clinically complete SCI (ASIA A) and found 4 distinct EMG patterns of locomotor activity. This varied response to similar sensory input suggests “state-dependence” of the spinal networks within the human spinal cord. Also, in a series of kinematically similar steps, the level of EMG activity can vary even without bursts in muscles for several steps. When the bursts of muscle activity return, the timing and pattern is the same \(^{66}\). This feature has been identified as an important characteristic of CPGs. Harkema \(^{66}\) also showed that although individuals with clinically complete SCI can demonstrate improved locomotor ability within the BWS environment, they can not ambulate over ground. This suggests that although the pattern for locomotion may be generated at the cord level, it can not sustain enough excitability without supraspinal influence to achieve full weight-bearing ambulation in subjects with clinically complete injuries. Lastly, several studies indicate that some level of reflex hyperactivity (increased spasticity) was beneficial to motor pattern generation during locomotion and those subjects with hyporeflexia showed less pattern generation \(^{21,24}\). This suggests that some amount of spinal cord activity is needed below the lesion level in order to activate these pattern generators in humans further supporting the existence of CPGs in humans. Therefore, although it can not be proven, there is ample evidence to support the existence of central pattern generation for locomotion in humans.

**Training Effects of Locomotor Training in Humans with SCI**

The training effects of locomotor training in animals has been well studied as discussed previously and more recent research has shown similar training effects in human subjects \(^{20-26,28}\). All studies utilized body weight supported locomotor training with similar parameters that were used on animal models as discussed previously. Also, most studies utilized the “rules of spinal locomotion” as described by Wernig \(^{22}\) where appropriate sensory input for locomotion was provided through appropriate load, joint positions, kinematics and speed. Visintin and Barbeau \(^{20}\) trained 7 incomplete, spastic SCI subjects
at 0% and 40% body weight support (BWS). They found that with repetitive training, EMG activity of the lower extremity muscles was appropriately modulated in relation to the gait cycle. They also observed an increase in single limb stance phase, decrease in double limb support, increase in stride lengths and increase in gait speed. Wernig et al \textsuperscript{21} trained 8 subjects with incomplete SCI (5-20 months post injury) for 30-60 minutes per day, 5 times per week for up to 7 months. They observed an increase in ability to tolerate load, increase in distance with ambulation and increase in speed. Wernig et al \textsuperscript{22} compared 89 chronic and acute incomplete SCI subjects trained with Locomotor Training with 64 similar subjects trained with conventional rehabilitation. They found that 76\% of those with chronic SCI learned to ambulate independently with Locomotor Training. Of the 18 wheelchair dependent subjects receiving Locomotor Training, 14 became independent ambulators whereas only 1 out of 14 subjects receiving conventional therapy became an independent ambulator. Also, 92\% of those with acute SCI who were initially wheelchair dependent learned to ambulate independently compared to only 50\% (12/24) of wheelchair dependent subjects in the conventional group. Deitz et al \textsuperscript{25} studied 14 subjects with different severities of incomplete SCI and showed that the training effect of Locomotor Training is separate from gains achieved simply from spontaneous neurological recovery. Furthermore, several studies have shown that these locomotor abilities gained with Locomotor Training can be effectively transferred to overground ambulation outside of the treadmill environment \textsuperscript{21, 24, 29}. Lastly, Wernig \textsuperscript{23} showed that the gains achieved in locomotion following Locomotor Training for incomplete SCI can be maintained with normal everyday activity 6 months to 6 ½ years after discontinuing training. These studies provide strong evidence that Locomotor Training for humans with SCI can be effective in improving ambulation ability that is transferable to over ground and maintainable after cessation of training.
Locomotor Training as an Activity-based Therapy

Activity-based therapies (ABT) are therapeutic activities used in clinical rehabilitation that attempt to restore function based on accepted principles of psychology, exercise physiology and neuroscience. Activity-based therapies have more recently been utilized at more prominent rehabilitation facilities with the goal of restoring lost function for SCI as opposed to learning compensatory strategies. Principles of ABT stem from the research and findings previously discussed specifically activity-dependent plasticity, task specificity, afferent sensory input and repetitive practice. Dromerick defines ABT as an intervention that attempts to restore neurologically-lost function. Behrman and Harkema state that ABT specifically refers to activities or interventions that “provide activation of the neuromuscular system below the level of lesion with the goal of retraining the nervous system to recover a specific motor task.” This approach utilizes repetitive practice of a specific task with the goal of achieving functional reorganization of the CNS and restoring lost function. Examples of ABT for SCI include muscle strengthening below the lesion, functional electrical stimulation (FES) cycling and manual and robotic locomotor training. One of the most developed and accepted ABT at this time especially for SCI is locomotor training.

Principles of Locomotor Training

Locomotor training is a rehabilitation approach to retraining walking after neurologic injury that uses the intrinsic mechanisms of the spinal cord and specific afferent sensory input generated by the task of walking to generate stepping. Originally studied through animal models and more recently translated to humans, several principles have been developed and accepted. Wernig et al refers to these principles as “rules of spinal locomotion” while Behrman and Harkema describe “locomotor principles” as being necessary for activity-based locomotor training. These principles have been developed.
based on current literature and are based on the premise of using repetitive practice to provide the body with the “sensorimotor experience of walking” \(^{55}\).

1. **Maximize loading of the lower extremities** and minimize weight-bearing through the upper extremities. Research shows that increases in lower extremity weight bearing in both animals and humans following SCI and even individuals without SCI, increased lower extremity electromyographic (EMG) amplitudes. Also, increased load during locomotion helped to modulate EMG activity in relation to the gait cycle \(^{20, 21, 24, 26, 28}\). This contributes to an increase in appropriate activation of muscles below the level of lesion that are too weak to contract voluntarily \(^{55}\). Therefore, loading of the lower extremities is encouraged and loading through the upper extremities is discouraged.

2. **Optimize the sensory cues for walking.** Normal adult walking speed (0.8-1.2 m/s) provides the body with sensory input that is characteristic of and specific to the activity of walking, including the unique sequence of sensory input provided. Several studies have observed a velocity-dependent modulation of EMG activity in individuals with and without SCI \(^{65, 68}\). In theory, if we can provide the injured CNS with the exact same sensory cues that it would receive prior to injury, including gait speed, we should see a stronger motor response in the form of locomotion.

3. **Optimize kinematics.** Kinematics and posture also provide the CNS with afferent input similar to sensory cues and load as discussed previously. The position, movement and loading of each joint in the body provides the CNS with very specific sensory input in the form of proprioception and kinesthesia. This sensory input is specific to the task performed and must be as close to pre-injury as possible to elicit a proper motor response. For example, during transition from stance to swing, we see an unloading of one limb with appropriate hip extension (assuming a proper upright trunk) and a loading of the other limb. During this transition there is appropriate limb loading and associated appropriate muscle and tendon stretching, proprioception and cutaneous sensory input, followed by unloading of the other limb, hip flexor stretching and the proprioception and cutaneous sensory input associated with it. Therefore, proper kinematics of the entire
body, including trunk and upper extremities (ie arm swing) is vital and may contribute to task-specific, activity-dependent plasticity 55.

4. Maximize recovery, minimize compensation. “Recovery” refers to the ability of the body and the CNS to perform the task properly and appropriately as it would before injury 55. This includes proper pre-injury kinematics and motor activity without use of leverage, momentum or substitution of stronger yet improper muscle groups to make up for lack of specific function (ie compensation). “Maximizing recovery” would necessitate the individual maintain proper upright trunk, no use of upper extremities, and proper hip and knee flexion that mirrors pre-injury locomotion. Any assistance that may be needed to perform this task properly can be provided as long as compensatory movements from the individual are avoided and the proper sensory input to the body and the CNS are maximized 55. These principles are summarized nicely by Barbeau 69 who states that appropriate sensory input, like maximizing load, proper trunk posture, hip extension and appropriate lower extremity loading and unloading, are crucial for maximizing functional recovery.

Body Weight Supported Treadmill Training- An Ideal Locomotor Training Environment

It has been suggested in the literature that the body weight supported treadmill environment may provide an individual with a safe yet liberal environment for walking that most closely imitates the sensorimotor experience of locomotion 17, 55. This training environment has been studied since the 1970s 13-18, 60, 62 with animal models and then applied clinically to humans with SCI in 1987. Barbeau et al 51 in 1987 developed a treadmill and harness system where an individual could be safely suspended and all sensorimotor parameters of locomotion could be controlled. Barbeau suggested that conventional locomotor rehabilitation strategies were limited in their ability to train the three “required components of locomotion” (posture, balance and stepping)
simultaneously. This type of a system allows the possibility of training these three locomotor components simultaneously and easily. It also allows for more control and quantification of the specific parameters associated with locomotion. For example, loading of the lower extremities and speed of the treadmill can be controlled and progressively increased as appropriate. Also, specific aspects of gait can be focused on and the trainer can directly intercede during locomotion as appropriate. In this way, trainers can use manual assistance to appropriately control and facilitate upright trunk posture and support, limb flexion and extension patterns, pelvic rotation and weight shifting necessary for recovered human locomotion. Also, this environment allows for the necessary intensity, repetition and practice that have been shown to be needed for functional reorganization of spinal and supraspinal locomotor networks especially when compared with locomotor training over ground. Therefore, the body weight supported treadmill environment is an ideal environment for Locomotor Training training which provides safety, control, appropriate sensory cues, flexibility and repetition, all of which can maximize locomotor recovery in individuals with SCI.

**Step Training on a Treadmill using Manual vs Robotic Assistance**

Body weight supported treadmill training can be provided to an individual manually through the use of skilled trainers or mechanically through the use of robotic assistance. Locomotor training in this environment requires the coordination of various tasks simultaneously or in appropriate sequencing (ie knee extension during stance, knee and hip flexion during swing, the timing and location of foot placements, weight shifting and pelvic rotations, etc). Each type of assistance has its own advantages and disadvantages and currently research has aimed at studying these differences in more detail. Manual assistance can require up to four trainers and is considered to be highly labor intensive and strenuous. Also, it is almost impossible to provide manually-assisted BWSTT with appropriate trainer ergonomics making the risk of injury quite high.
Since manually-assisted BWSTT requires up to four trainers for one subject, the cost of treatment delivery can be quite high as well. However, manual assistance has one very important benefit: Manual assistance can be tailored to fit the specific needs and limitations of the individual on-the-fly, providing only the forces that are specifically needed to generate a proper stepping pattern. The trainer can adapt immediately to changes in subject performance and therefore maximize proper kinematics and sensory cues needed. Robotic assistance, most often provided by a first generation gait-training robot the Lokomat, consists of an exoskeleton with motors that provide forces at the hips and knees and can be integrated with BWSTT to provide the pattern of lower extremity flexion and extension necessary for locomotion. Robotic assistance requires less manpower, offers less risk of injury, is less labor intensive and may be more cost effective. It also may provide a more consistent pattern of limb movements and eliminates trainer fatigue. However, robotic assistance cannot immediately adapt to changes in subject performance and therefore, may not be as clinically effective as manually-assisted Locomotor Training. Several studies have looked at the effectiveness of robotic locomotor training and found significant improvements in walking speed but these outcomes have not been shown to be better than manual Locomotor Training or Locomotor Training with FES. Ultimately, more studies need to be conducted in order to determine effects and outcomes of manual versus robotic BWSTT as they apply to Locomotor Training for individuals with SCI.

Locomotor Training for Spinal Cord Injury- Randomized Clinical Trials

Only four randomized clinical trails and 1 Cochrane review have studied the effects of locomotor training after spinal cord injury on locomotion ability. Postans et al looked at the effects of partial weight-bearing supported treadmill training with FES augmentation on 12 acute incomplete SCI subjects and found improvements in gait speed and gait endurance with the intervention. Field-Fote et al compared manual Locomotor
Training, robotic Locomotor Training, Locomotor Training with FES and overground training with FES on 27 subjects with chronic incomplete SCI. They found a significant training effect across all groups demonstrating improvements in gait speed and gait quality (increased stride lengths and improved step symmetry), however there was no statistical difference between groups. Dobkin et al 74 conducted a single-blinded, parallel group, multicenter, randomized clinical trail (The Spinal Cord Injury Locomotor Trial or SCILT) comparing the effects of manual Locomotor Training (BWSTT) with a control program of overground mobility training of similar intensity and duration for 146 acute and subacute incomplete SCI subjects. Although both groups improved in walking-related outcomes, there was no significant difference between groups. Hornsby 72 looked at robotic-assisted Locomotor Training in subacute incomplete SCI subjects but data from this study is not yet published. Mehrholz et al 73 reviewed these studies and determined that the results were inconclusive. There was no statistically significant effect of manual Locomotor Training, robotic Locomotor Training or Locomotor Training with FES on walking function compared with conventional interventions. This suggests that there is a strong need for more randomized clinical trials in the future comparing the effects of Locomotor Training for incomplete SCI with conventional interventions.

Treatment Parameters for Locomotor Training within the BWSTT Environment

It is evident from the literature that Locomotor Training and BWSTT may provide an effective avenue for incomplete SCI rehabilitation, however, there is little research describing treatment parameters for this population of individuals. Several studies 19-26, 28, 37 suggest initial training parameters for BWSTT including training intensity, frequency and duration of treatment that has been derived from animal models as discussed previously. Typically described sessions include a portion of time (30-60 minutes) within the BWSTT environment, followed by a portion of time (10-30 minutes)
focusing on overground activities (activities practiced outside of the BWSTT environment). Parameters that can be controlled within the BWSTT environment are body-weight support (BWS), treadmill speed, treatment time, frequency, total treatment duration and assistance provided. Also, treatment can be further controlled by type of activity (standing or walking) and type of training principle (retraining or adaptability) (see table 5).

Table 5. Type of training principle

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<tr>
<th>Training principle</th>
<th>Description</th>
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| Retraining         | - An intervention or activity that closely resembles pre-injury form and kinematics  
                     - *Retrains* the CNS via the principles previously described  
                     - Activation of locomotor CPG networks at the level of the spinal cord  
                     - Requires minimal voluntary effort on the part of the individual (minimal supraspinal input)  
                     - Effort provided mostly by manual trainers to obtain ideal pre-injury form |
| Adaptability       | - An intervention or activity that requires the active and voluntary effort of the individual  
                     - Less focus on ideal kinematics or posture  
                     - More focus on voluntary supraspinal control and recovery  
                     - Effort provided mostly by the individual not the manual trainers |
In those studies described \(^{19-26, 28, 37}\), BWS was initially set from 32\% to 80\% and was often adjusted based on ability of the individual to tolerate the maximal load possible without knee buckling during stance. Initial training speeds were usually set at speeds found to be “most comfortable” for the individual (usually within the range of 0.04 m/s to 0.67 m/s) or at speeds close to the individual’s normal walking speed (0.88-1.32 m/s). Frequencies were usually set at 3 or 5 days a week and total treatment durations were from 3 weeks to 7 months. The SCILT\(^{74}\) was the only multi-centered randomized clinical trial of its kind comparing BWSTT to over ground mobility training without Locomotor Training. This study used parameters based on the available research and provided the BWSTT group with up to 1 hour of BWSTT followed by 10 to 20 minutes of overground activities, 5 days a week for up to 60 sessions (12 week treatment duration). It is quite evident that there is tremendous variability in the treatment parameters used for Locomotor Training in the BWSTT environment for incomplete SCI and more research is needed to help determine parameter guidelines to increase effectiveness and efficiency of treatment.

Although initial treatment parameters for Locomotor Training in the BWSTT environment have been described, clinical decision-making regarding treatment progression and evaluation of progression has been given little attention in recent literature. None of the studies described above discussed the clinical decision-making process or evaluation process for progressing individuals by manipulating the parameters described above. The most prevalent way to progress individuals within this environment was to try to decrease BWS and increase treadmill speed in order to maximizing quality of stepping. However, specific protocols or criteria for this type of progression have not yet been established. Also, the incorporation of over ground training in adjunct with BWSTT has been studied but inconsistency in application (when and how much) from study to study is still evident\(^{37}\). Behrman et al\(^{37}\) presents a case report where progression of Locomotor Training to improve walking ability in an
individual with an incomplete SCI was successfully performed and described. In this study, progression was achieved by: “1) using a decision-making algorithm; 2) resetting identified training parameters of body-weight load, speed, posture and kinematics, endurance, independence, and adaptability; 3) daily examination of the patient’s stepping ability on the treadmill and overground; 4) establishing new goals based on the examination results; and 5) daily transfer of skills from the treadmill to community ambulation. It is suggested that this progression process may be applicable to other incomplete SCI individuals with UMN injuries, including different severities of injury and levels of functional ability. However, it has yet to be determined which individuals will benefit from Locomotor Training as well as when post-injury the benefit will be maximized. Therefore, further research is needed to help answer these questions.

The NeuroRecovery Network

The NeuroRecovery Network (NRN) is a recently established organization whose main purpose is to help answer these questions discussed above. The NRN was originally formed through the Christopher and Dana Reeve Foundation (CDRF) and funded through a cooperative agreement with the Center for Disease Control and Prevention. Its mission is to provide supervisory and financial resources to specialized clinical centers across the country for provision and study of activity-based therapies, including Locomotor Training for incomplete SCI individuals. Furthermore, the NRN attempts to apply recent scientific and clinical evidence to the formulation and standardization of Locomotor Training treatment interventions for this patient population as well as evaluate the effectiveness of such interventions on these individuals’ function and quality of life. Locomotor and functional gains of these individuals are closely documented and assessed regularly through the utilization of various quantitative assessment tools and reevaluations. There are currently seven centers that are a part of the NRN in the United States. This highly unique organization has the capacity to contribute to the advancement
of SCI rehabilitation and recovery of locomotion in a challenging and prevalent population of individuals.

**Phases of Recovery- A Functional Approach to SCI Classification**

One important accomplishment of the NRN to date is the establishment of a new way to functionally classify individuals with SCI. This is referred to as “phasing” and it assesses many aspects of the individual’s functional abilities both within the BWST environment and over ground. In this way, the “severity” of injury can be functionally defined based on the actual functional abilities of the individual. This is the primary limitation of the currently utilized and globally accepted ASIA SCI classification system which primarily uses only motor and sensory assessments to classify and determine severity of injury. Also, phasing is a way to capture functional recovery when it is measured at multiple times during rehabilitation. This new approach assesses many aspects of the individual’s functional abilities both within the BWST environment and over ground. Functional tasks of interest include standing, walking, sitting balance, transfers and bed mobility. Specific criteria have been established within each of these functional categories that define certain levels of ability. Each functional category is then assessed and graded by a skilled therapist based on these established criteria. Once all categories have been graded the individual can be assigned a “phase” based on their performance. The phasing system uses numbers 1 through 4 to describe overall locomotor and functional recovery where 1 is equivalent to poorest functional ability and 4 is equivalent to best functional ability. Each phasing number is broken down further to more accurately describe the individual’s abilities through the use of letters A through C. Each phasing number represents gross locomotor and functional abilities. (See Table 6) This scale allows very accurate descriptions of individuals’ locomotor ability while providing a visible framework in which to progress the individual towards independent, deviation-free ambulation.
<table>
<thead>
<tr>
<th></th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4</th>
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<tbody>
<tr>
<td><strong>Home wheelchair dependence</strong></td>
<td>Wheelchair dependent</td>
<td>Primarily wheelchair dependent</td>
<td>Little or no wheelchair use</td>
<td>No wheelchair use</td>
</tr>
<tr>
<td><strong>Home ambulation</strong></td>
<td>Unable to ambulate without gross compensatory mechanisms, assistive device or maximal physical assistance</td>
<td>Beginning to ambulate in the home using moderate compensatory mechanisms, with assistive device, with no physical assistance</td>
<td>Ambulating independently in home with minimal compensatory mechanisms, may use assistive device, but no physical assistance</td>
<td>Ambulating independently in home without compensatory mechanisms, no assistive device and no physical assistance</td>
</tr>
<tr>
<td><strong>Community mobility</strong></td>
<td>Wheelchair dependent in community</td>
<td>Wheelchair dependent in community</td>
<td>Ambulating independently in community with or without assistive device</td>
<td>Ambulating independently in community without compensatory mechanisms, no assistive device and no physical assistance</td>
</tr>
<tr>
<td><strong>Sit to stand transfers</strong></td>
<td>Unable to transfer sit to stand without gross compensatory mechanisms, assistive device or maximal physical assistance</td>
<td>Able to transfer sit to stand with moderate compensatory mechanisms, with or without assistive device, with no physical assistance</td>
<td>Able to transfer sit to stand with minimal compensatory mechanisms, may use assistive device, with no physical assistance</td>
<td>Able to transfer independently without compensatory mechanisms or physical assistance</td>
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Functional Outcome Measures for SCI

Outcome measures for individuals with SCI are needed in order to quantitatively describe functional and locomotor gains from specific interventions; however, there is tremendous variability in the literature as to which outcome measures should be used. Some tools such as the Functional Independence Measure (FIM), the Spinal Cord Independence Measure (SCIM), the Modified Barthel Index (MBI), and the Quadriplegia Index of Function (QIF) assess activities of daily living (ADLs), global function and assistance needed but may not be the best descriptors of ambulation ability or recovery.\(^1\),\(^5\),\(^7\) Also, these tools look at gross ability to perform a functional task, but do not separate compensatory mechanisms from true recovery.\(^5\) Therefore, they may not be the best tools to measure recovery of ambulation from the intervention Locomotor Training.

There are actually few tools that have been validated to date for assessing walking ability in individuals with SCI.\(^7\) The Spinal Cord Injury- Functional Ambulation Inventory (SCI-FAI) and the Walking Index for Spinal Cord Injury (WISCI) are two tools that have been validated for assessing walking in this population.\(^7\) Other measures such as the 10 meter walk test (10MWT) and the 6 minute walk test (6MWT) have been studied and used to measure increases in gait speed and ambulation endurance and have been validated for the SCI population.\(^7\) Also, Holden et al.\(^7\) found good interrater reliability (r=0.99) and test-retest reliability (r=0.90) for the 10MWT in individuals with neurologic involvement. Behrman and Harkema\(^5\) suggest that in order to truly measure and describe walking ability or recovery in individuals with SCI, we should look at ability to perform a reciprocal gait pattern, balance and adaptation to the environment. Other experts feel that a combination of outcome measures should be used to accurately describe locomotor recovery in individuals with SCI where gait speed, gait quality, functional independence in the community and the home are fully addressed.\(^5\),\(^7\),\(^8\) In other words, one measure is probably not sufficient to reflect recovery of ambulation.
However, performing multiple tests and measures may be too time consuming and impractical in our current rehabilitation environment. Locomotor or functional outcome measures need to be determined that may quickly and accurately describe locomotor ability in this population of individuals.

Gait speed in particular has been an outcome measure widely used to assess ambulation ability in the SCI population and it is by far the most common locomotor outcome assessed. The 10MWT, which ultimately measures un-aided walking speed, is considered to measure overall walking ability and may be predictive of ability to ambulate in the home and the community for this population. However, Behrman and Harkema state that although gait speed may be a meaningful outcome measure showing speed required for safe community ambulation, it should be interpreted carefully since a certain percent change in gait speed may not show a functional increase in ambulation ability. This is especially true for individuals with incomplete SCI that are highly impaired since a 100% increase in a gait speed of 0.05 m/s is only 0.10 m/s which is far from functional. The 10MWT is also highly volatile for those individuals who are low functioning as well as those individuals that are high functioning. A small increase or decrease in time needed to complete the 10MWT respectively can show a significant percentage change in gait speed, which can be easily caused by measurement error and may not represent a clinically meaningful change.

There is some debate among experts as to whether the 6MWT or the 10MWT is most suitable for measuring gait speed for individuals with SCI. The primary purpose of the 6MWT is to measure walking endurance and fatigability. The 6MWT may be a better measure of community ambulation since it tests walking for a longer time period, requires changes in direction, and challenges dynamic balance more than the 10MWT. Van Hedel et al found that there was no difference between 10MWT walking speed and 6MWT walking speed in subjects with stroke or SCI, even when tested at maximum
walking speed. Van Hedel suggests that this may indicate that in persons with neurological deficits, distance walked during 6 minutes may not be limited by cardiovascular limits but by other deficits, like sensorimotor\textsuperscript{82}. Barbeau compared the sensitivity of the 10MWT and 6 MWT for recovery of SCI and found that they may not represent distinctly different areas of ambulation ability in this population of individuals\textsuperscript{81}. One benefit of the 10MWT and the 6MWT is their ease of administration and low cost. However, although both tests can be used to determine gait speed, the 10MWT has been established in the literature to be the standard for determining gait speed for individuals with SCI. The 10MWT is therefore more valid and most easily comparable to other studies that have analyzed gait speed for this population.

Several studies have attempted to use gait speed to determine and analyze changes in walking ability for those with SCI. For example, van Hedel et al\textsuperscript{1} sought a practical, valid and reliable test that could give an accurate estimation of functional walking ability after SCI. They were able to define several functional ambulation categories characterized by minimal gait speeds for SCI individuals with good sensitivity (>0.98) and specificity (>0.94). Also, gait speed correlated well with these functional ambulation categories (>0.84)\textsuperscript{1}. Specifically, subjects that walked without aid or assist produced a minimum speed of $0.70 \pm 0.13$ m/s and an increase in gait speed of 0.3 m/s was needed to change from a community ambulator with use of an aid to a community ambulator without aid\textsuperscript{1}. Furthermore, Musselman\textsuperscript{34} determined that the minimally important difference (MID) in gait speed for incomplete SCI receiving Locomotor Training with BWS is 0.05-0.06 m/s. The MID is defined as the minimal amount of change in an outcome measure that is considered to be due to the intervention and not the variability of the sample or by chance. This is often referred to as \textit{clinical meaningfulness}. However, it is not specifically stated what \textit{clinical meaningfulness} is and whether or not it signifies the ability to ambulate independently. There are several other descriptors of clinical significance in the literature all of which have unique mathematical derivations: \textit{smallest}
real difference (SRD), minimal detectable change (MDC), smallest detectable change (SDC), smallest detectable difference (SDD) and minimal clinical difference (MCD). However, there is lack of consensus in the literature regarding how these descriptors for SCI are interpreted and used. Therefore, although gait speed may not be the best descriptor of overall gait quality and ability in the SCI population, it appears to be a practical and inexpensive estimation of independent functional walking ability as well as a measure of clinically significant change in locomotion.

Predictors of Ambulation for SCI

Many recent studies have attempted to determine specific factors that may predict the ability for individuals with incomplete SCI to ambulate after injury. The most often described and studied predictors of ambulation in this population are: severity of injury, time since injury, level of injury, initial gait speed, preservation of pin prick sensation, initial lower extremity motor score (or strength), spasticity, and voluntary bowel and bladder voiding\textsuperscript{6, 9, 11, 47}. Several of these predictors may be better measures than others in terms of ease, cost and efficiency of administration as well as overall predictive value.

Neurologic level of injury and severity of injury have been commonly used to provide a gross prognosis of ambulation ability in this population. Neurologic level of injury below T11 is associated with an increased potential for ambulation\textsuperscript{11}. Gittler\textsuperscript{11} discussed that those individuals graded ASIA A (complete tetraplegia) will not regain LE movement and will not become community ambulators. Gittler\textsuperscript{11} also states that motor incomplete individuals have a better prognosis for ambulation than sensory incomplete individuals. Maynard et al\textsuperscript{83} showed that 87% of motor incomplete individuals were eventually able to ambulate. Dobkin et al\textsuperscript{9} found that following Locomotor Training rehabilitation, ASIA D individuals showed larger functional gains than ASIA C or B individuals. Also, they found that individuals graded ASIA C are more likely to achieve functional walking
speeds if they score at least a 3 on the FIM-L, (able to ambulate 50 ft with moderate assistance), 8-14 weeks after injury. Dobkin suggests that future studies should look at the relatively few ASIA C individuals that still required substantial physical assistance by 20 weeks post injury since their likelihood of achieving functional ambulation is thought to be small. In the SCILT trials, the amount of functional gain was greatest in less severe injuries. Dobkin et al also found that starting Locomotor Training sooner after injury resulted in greater improvements in functional outcomes but cautions that this may be due to the fact that this allows some subject to start rehabilitation at a lower functional level than they would have if they started Locomotor Training later. Level and severity of injury are also readily available information and usually assessed on all SCI individuals making it an easy and accessible measure.

Strength or initial LEMS was also shown in several studies to be predictive of ambulation ability. Crozier et al found that those individuals with at least 2/5 quadriceps strength that improved to 3/5 by 2 months post-injury were more likely to ambulate at 1 year post-injury. Dobkin et al found a strong correlation between initial LEMS and initial walking speed and as LEMS approaches 40, walking speeds approach functionality. This correlation of LEMS and gait speed make both measures extremely attractive for study and for possibly predicting ambulation ability in this population. Strength or LEMS is also a readily accessible and easy measure and can usually be found for all SCI individuals as well.

The amount of sensory sparing below the level of injury has also been associated with potential for ambulation. Individuals with sensory incomplete and motor complete injuries with preserved pinprick sensation below the level of injury were likely to regain functional ambulation. These predictors make physiologic and neurophysiologic sense for predicting ambulation ability in those with severe injuries or those with minor injuries. However, there is lack of evidence in the literature to suggest reliable predictive
factors for those individuals with incomplete injuries graded ASIA C and D including when the recovery occurs, how quickly it occurs and how much of it occurs. Instead high variability in functional outcomes within this population occurs \(^6,^9\).

One study to date looked at several of these measures to try to determine which may be the best at predicting ambulation ability in this population. Winchester et al.\(^6\) attempted to study predictive factors of gait following 36 sessions of robotic and manual Locomotor Training. In 30 motor incomplete ASIA C and D individuals \(\leq 60\) months post-injury, over ground walking speed was predicted in 8 test participants within \(4.15 \pm 2.22\) cm/s. The predictive factors included time post-injury, the presence or absence of voluntary bowel and bladder voiding, spasticity, and walking speed before Locomotor Training to be highly predictive of gait speed following Locomotor Training for this population of individuals. \([\text{Final overground walking speed} = 21.48 + (\text{voluntary bowel and bladder voiding} \times 18.78) + (\text{functional spasticity score} \times 14.3) + (\text{initial walking speed} \times 0.87) - (\text{square root time from injury onset} \times 6.06)]\). More specifically, time since injury is negatively correlated with final gait speed, so those with chronic injuries should be less likely to improve final gait speeds. Initial gait speed and ability to voluntarily void bowel and bladder are positively correlated with final gait speed. Lastly, higher levels of spasticity were associated with slower final gait speeds. These finding support the notion that those with acute or subacute injuries will be more likely to show greater recovery than chronic injuries. Also, this suggests that those with chronic injuries (but still \(\leq 60\) months) who can ambulate before Locomotor Training will show greater recovery than those with chronic injuries who cannot ambulate before Locomotor Training. No studies to date have attempted to analyze these predictive factors and ambulation criteria in the subacute and chronic incomplete SCI population following manual Locomotor Training of a prolonged duration. Also, no study to date has attempted to analyze where we see the largest rate and magnitude of improved ambulation ability within this population during manual Locomotor Training of a prolonged duration. Lastly, no study to date has
attempted to analyze the impact of Locomotor Training on ASIA parameters for chronic incomplete SCI.
CHAPTER 3: ASIA MANUSCRIPT

Abstract

Objective: Individuals with spinal cord injury (SCI) frequently describe loss or difficulty of ambulation as their most devastating functional limitation. Manual-facilitated Locomotor Training is an activity-based therapy developed to induce locomotor and functional gains after incomplete SCI. However, the impact of Locomotor Training as well as its relationship to locomotor ability, balance, strength and sensation for those with chronic motor incomplete SCI is unknown. The purpose of this analysis is to determine the impact of and association between Locomotor Training and: 1) American Spinal Injury Association (ASIA) exam; 2) locomotion (gait speed, distance); 3) balance; and 4) functional gait speed stratifications after chronic incomplete SCI.

Design: A prospective, cohort design with pre and post-intervention comparisons of sensory and motor scores and functional outcomes.

Setting: Outpatient rehabilitation for chronic SCI in the NeuroRecovery Network (NRN).

Participants: Two hundred and twenty-five individuals with chronic motor incomplete SCI (AIS C and D; mean 2.45±3.79 years post-injury) completed Locomotor Training in the NRN from March 2005 to July 2010.

Intervention: The NRN Locomotor Training Program consisted of manual-facilitated body-weight supported standing and stepping on a treadmill and over ground for
approximately 1.5 hrs per session. Training was provided 3-5 times a week for an average of 60 sessions over an average of 5 months.

**Outcome Measures:** The American Spinal Injury Association (ASIA) Impairment scale (AIS) classification, lower extremity and upper extremity motor scores (LEMS, UEMS), lower extremity pin prick and light touch scores (T11-S4/5 dermatomes), gait speed derived from the 10 meter walk test and 6 minute walk test; gait distance derived from the 6 minute walk test; and, Berg Balance scores. Comparisons for the overall sample, AIS C and D subsets, paraplegia/tetraplegia subsets and functional gait speed stratifications occurred.

**Results:** No significant changes in sensory and motor scores occurred after manual-facilitated Locomotor Training except LEMS (pre: 31.85±13.98; post: 38.61±12.29; p<0.05) and UEMS (pre: 38.36±10.83; post: 41.44±8.27; p<0.05). For AIS C and D subsets, no relationship occurred between initial sensory and motor scores and gait speed or distance following Locomotor Training. A significant (p<0.05) moderate positive relationship between final Berg Balance Scores and initial LEMS was found for paraplegia and tetraplegia subsets (r²=0.497 and 0.478 respectively). Significant gains in gait speed (pre: 0.32±0.40 m/s; post: 0.55±0.55 m/s; p<0.05), gait distance (pre: 94.4±115.09 m; post: 164.42±159.82 m; p<0.05), and balance (BBS pre: 20.48±17.70; post: 29.24±20.60; p<0.05) resulted. Considerable conversion between functional gait speed stratifications occurred following Locomotor Training with 47% of the overall sample ambulating at community gait speeds at discharge (≥0.44 m/s). Minimal AIS conversion occurred with 92% of the overall sample remaining unchanged (n=23 AIS C; n= 109 AIS D). Only 28.1% of AIS C subjects (9/32) converted to AIS D following Locomotor Training.
**Conclusions:** Locomotor Training improves gait speed, distance, balance and functional ambulation after chronic motor incomplete SCI. The ASIA variables and AIS classification may be poor indicators of walking recovery after Locomotor Training. Functional classification based on gait speed may provide an effective measure of treatment efficacy or functional improvement after incomplete SCI.

**Introduction**

Spinal cord injury (SCI) is a devastating and potentially fatal disability that can have a large negative impact on individuals’ lives. Spinal cord injury affects approximately 12,000 individuals in the United States annually yielding about 262,000 people living with SCI in 2009. The average age of onset is quite young (40.2 years) compared to heart disease (age of first heart attack in men is age 66) or stroke (75% of all strokes occur over the age of 65). Typically prevalence is higher in males although recently the number of women with SCI has increased to about 25%. The most frequent neurologic category at discharge from inpatient rehabilitation is incomplete tetraplegia (38.3%). Incomplete tetra- and paraplegia account for 60% of all SCI. The majority of those living with SCI are chronic in nature and average time since injury is 14 ± 12.37 years. Many individuals with SCI describe among their most devastating and apparent disabilities as the inability to ambulate or an inability to ambulate without significant deviations. Taking into account the relatively young age of onset and an increasingly aging population, the impact of improving functional independence, specifically ambulation ability, on quality of life could be substantial. Therefore, it is crucial that rehabilitation strives to maximize the locomotor abilities and subsequent functional recovery of these individuals.
Previously, many SCI rehabilitation models considered the central nervous system (CNS) to be essentially hard-wired and largely incapable of change or repair after injury \(^8^5\). Experimental evidence of improvement in stepping and motor control after activity-based training in animal SCI models and human research has been translated into clinical neurorehabilitation \(^1^3, 1^5, 1^6, 1^8, 1^9, 2^1-2^3, 2^8, 5^1, 8^5\). Manually-assisted Locomotor Training is an activity-based therapeutic intervention with the goal of reproducing kinematics of locomotion and providing sufficient afferent input to the nervous system to promote motor “re-learning” after SCI. The multi-site NeuroRecovery Network (NRN) applies Locomotor Training for chronic, motor incomplete SCI (hereafter designated iSCI). One focus of the NRN is to induce functional gains, including locomotion, during and beyond traditional treatment periods after injury. Whether functional changes reflect some resolution of neuropathology with chronic SCI remains unknown.

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) developed by the American Spinal Cord Injury Association (ASIA) and endorsed by the International Spinal Cord Society is a well-accepted measurement tool which classifies neurologic deficit after SCI \(^8^6, 8^7, 8^8\). The ISNCSCI exam is also known as the “ASIA examination”. It scores several components: 1) Light touch; 2) pinprick; and 3) motor strength of the upper and lower extremities which are used to determine the last neurologic level with normal sensory and motor function as well as zones of partial preservation. The ASIA Impairment Scale (AIS) classifies severity of SCI according to motor complete (AIS A and B) and motor incomplete injury (AIS C and D). The AIS C and D classes are determined by calculating the proportion of key muscle groups below the level of injury that have muscle grades of 3 or higher (\(\geq 50\%\) of muscle groups 3 or more= AIS D; \(>50\%\) of muscle groups \(<3 = AIS C\) \(^8^7\). The primary focus of this study is AIS C and D (motor incomplete). Although the ASIA exam sensory and motor scores
and AIS components were developed to measure neurologic impairment and injury severity, recent clinical trials have used them to measure therapeutic efficacy\textsuperscript{89, 90}.

Conversion of AIS classification and components of the ASIA exam are widely-used indicators of recovery during clinical trials of pharmaceutical treatments\textsuperscript{89, 90}. Recent studies report spontaneous AIS conversion rates for those with acute (< 1 year) and chronic SCI (1 to 5 years)\textsuperscript{91-94}. Typically, the greatest rate of conversion between AIS categories, 70-90\%, occurs within the first year of injury\textsuperscript{91-93}. However, in chronic SCI (1 to 5 years post-injury) these rates are much lower at about 21\%\textsuperscript{94}.

Certain ASIA scores collected acutely appear to discriminate the potential for future ambulation. Early lower extremity or sacral pin prick sensation (72 hrs or 4 weeks post-injury) or early LEMS correlate with walking at 1 year after SCI\textsuperscript{11, 12, 47, 95-100}. While the predictive ability of the ASIA exam appears most accurate and reliable 72 hours after acute SCI, its ability to capture changes in impairment or function at chronic time points is unknown\textsuperscript{91}. It remains unclear how an intervention such as Locomotor Training administered in chronic SCI effects ASIA exam scores and whether functional improvements are related to changes in some or all ASIA variables. It is also unknown if patients with different ASIA exam scoring will respond equally to locomotor training.

Currently gait speed is perhaps the most widely used measure of walking ability after SCI and it appears to be a good indicator of community ambulation\textsuperscript{1, 6, 21, 22, 29, 35, 74}. Gains in ambulation do not often report levels of independence or reliance on braces or assistive devices. To our knowledge, van Hedel et al\textsuperscript{1} is the only group to establish a relationship between gait speed and independent community ambulation after SCI. For 886 European individuals with SCI (AIS A – D), attaining a minimum gait speed of 0.44 m/s after SCI.
resulted in independent community ambulation with aid or assistive device. Thus, 0.44 m/s may serve as a functionally relevant threshold by which to stratify individuals with SCI in order to gauge changes in other outcome measures and ASIA exam sensory and motor scores.

The purpose of this paper is to determine the association between ASIA exam sensory and motor scores and locomotor performance changes induced by NRN Locomotor Training applied in chronic iSCI. This paper will examine the impact of Locomotor Training on: a) conversion of AIS classification; b) improvement in gait speed stratifications; c) sensation (LE pin prick and light touch scores) and its association with locomotor and balance performance; and, d) strength (lower extremity motor score-LEMS) and its association with locomotor and balance performance.

**Methods**

**Research Design**

In a prospective cohort design, we analyzed SCI data collected from March 2005 to July 2010 within the NeuroRecovery Network (NRN). Analysis focused on functional outcome and ASIA examination data from enrolled individuals who completed Locomotor Training. Subjects with iSCI treated in the NRN no longer participated in acute inpatient rehabilitation and did not have lumbar lower motor neuron signs. Patients with pacemakers, ventilators or open wounds were ineligible to participate in the NRN.

**Inclusion criteria:** Subjects were included in the NRN Locomotor Training Program if they met the following criteria:
1. Currently not participating in acute inpatient rehabilitation.

2. Medically stable. If subjects had any recent surgeries (tendon lengthening, spinal fusion, etc), they must have approval from their surgeon to participate.

3. Spinal cord lesion at the level T10 or above; T11 and T12 lesions may be considered if they do not present with lower motor neuron signs.

4. The following diagnoses are included:
   a. Traumatic SCI
   b. Transverse myelitis
   c. Spinal cord infarction
   d. Primary tumors that have been surgically decompressed (excluding radiation and chemotherapy)
   e. Stable treated infections (excluding HIV)

5. Able to voluntarily extend the head.

6. Able to follow verbal commands.

7. Must have some lower extremity movement and be classified AIS C or D with upper motor neuron signs in the absence of anti-spasticity medication.

8. Must have the capacity to generate a reciprocal alternating flexion/extension pattern in the body-weight supported treadmill training environment.

9. Normal or increased tone (hypertonicity) in the absence of anti-spasticity medication.

10. Compliance to wean or eliminate anti-spasticity medications delivered orally or via intrathecal pump (baclofen, morphine or clonidine).

11. Compliance to eliminate or minimize lower extremity orthotics.

12. Motivated and compliant to participate.

Exclusion criteria\(^{101}\): Subjects were excluded from the NRN Locomotor Training Program if they met any of the following criteria:
1. Subjects were under the age of 14 years at the time of enrollment.
2. Subjects with pacemakers.
3. Subjects with open or non-healing wounds.
4. Subjects with lower motor neuron signs.
5. The following diagnoses will be excluded:
   a. Multiple sclerosis
   b. Amyotrophic lateral sclerosis (ALS)
   c. Lower motor neuron disorders
6. Subjects that are ventilator dependent.
7. Subjects with painful musculoskeletal dysfunction or unhealed fractures that would contraindicate locomotor training.
8. Subjects who used botox within the last 3 months.
9. Subjects currently using illegal drugs

Guidelines for the Use of Medications for Neuropathic Pain and Spasticity

Subjects were weaned from any neuropathic or anti-spasticity medications using a standardized weaning protocol established by the NRN. Once weaned subjects could take the smallest dose needed to control their symptoms at night only. Maximum doses were not to exceed those listed below:

Neuropathic Pain Medications
- Neurontin 300 mg
- Lyrica 50 mg
Anti-spasticity Medications
- Zanaflex 4 mg
- Dantirum 25 mg
- Oral Baclofen 20 mg

Discharge Criteria from the NRN

Subjects were discharged from the program if they exhibited any of the following criteria established by the NRN:
1. Subject met all rehabilitation goals.
2. Subject’s function plateaued, and in the best clinical judgment of the therapist in consultation with the physician, the subject would not make any more functional gains or improvements with continued intervention.
3. In the best clinical judgment of the therapist in consultation with the physician, the subject was noncompliant with attendance, home program or medication recommendations. Three no-shows/no call appointments without an acceptable excuse constituted noncompliance with attendance.
4. Physician discharges the patient from rehabilitation services.
5. Subject and/or family decided to discontinue rehabilitation services.
6. Subject is not able to meet 80% of their scheduled appointments. If a subject misses 5 or more consecutive treatment sessions, he/she may be discharged from the program and readmitted once consecutive sessions can be maintained. If a subject does not have
sufficient means for payment (insurance coverage or out of pocket expenses) he/she may be discharged from the program.

**Subjects**

The final study population consisted of 225 subjects with chronic iSCI with full, complete data sets for functional outcomes and ASIA exam records at enrollment. See Table 7 for demographic profile. A total of 416 records were initially analyzed, and 307 subjects had full functional outcome records. Subjects that completed fewer than 15 training sessions, were under 17 years old (n=27), had motor-complete SCI (n=3), or an injury level at T11 or below (n=15) were excluded. Of the remaining subjects, 225 had initial ASIA evaluation records and 146 had discharge ASIA evaluations with 144 having discharge AIS classification. The initial ASIA evaluation records (n= 225) had individual components missing: 4 lower extremity motor scores (LEMS), 18 pin prick and 27 light touch scores. The discharge ASIA evaluation records (n= 146) had the following individual components missing: 16 LEMS, 22 pin prick and 28 light touch scores. Subjects were categorized based on AIS classification, tetra- and paraplegia, and ambulation ability (initial gait speed) at enrollment. A check for data integrity and errors within AIS classifications included verification of neurological level and appropriate AIS assignment. Of the 416 original records, a 2.18% error rate occurred. All subjects gave informed consent in advance of being enrolled in the program and affirmed their understanding of the risks, contraindications, implications of treatment and use of data collected for analysis.
Table 7: Demographics. Means ± SD with range in Brackets and group size for each variable.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total</th>
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<tr>
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<tr>
<td>Age at enrollment (yr)</td>
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<td></td>
<td>[17.4;85.7 ] n=225</td>
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<tr>
<td>Time since injury (yr)</td>
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<tr>
<td></td>
<td>[.09;25.8 ] n=219</td>
</tr>
<tr>
<td>Gender M:F (225)</td>
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<tr>
<td># of Sessions</td>
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<tr>
<td></td>
<td>[15;312] n=225</td>
</tr>
<tr>
<td>Paraplegia/Tetraplegia (225)</td>
<td>59/166</td>
</tr>
<tr>
<td>ASIA Level at Enrollment C/D (224)</td>
<td>57/167</td>
</tr>
<tr>
<td>C Paraplegia/Tetraplegia (57)</td>
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</tr>
<tr>
<td>C mean # sessions</td>
<td>81.7±76.5</td>
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<tr>
<td></td>
<td>[15;312] n=57</td>
</tr>
<tr>
<td>C time from injury (yrs)</td>
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</tr>
<tr>
<td></td>
<td>[0.20;25.8] n=54</td>
</tr>
<tr>
<td>C age at enrollment (yrs)</td>
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</tr>
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<td></td>
<td>[18.3;69.4] n=54</td>
</tr>
<tr>
<td>D Paraplegia/Tetraplegia (167)</td>
<td>41/126</td>
</tr>
<tr>
<td>D mean # sessions</td>
<td>52.1±38.6</td>
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</tr>
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<td>D time from injury (yrs)</td>
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<td></td>
<td>[0.09;22.0] n=164</td>
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<tr>
<td>D age at enrollment (yrs)</td>
<td>45.1±16.3</td>
</tr>
<tr>
<td></td>
<td>[17.4;85.7] n=167</td>
</tr>
</tbody>
</table>
**Outcome Measures**

Gait speed calculated from the 10 Meter Walk Test and the 6 Minute Walk Test, distance calculated from the 6 Minute Walk Test and balance calculated from the Berg Balance Scale (BBS) were collected at initial evaluation, all re-evaluations and discharge evaluation. Locomotor data were collected using an “initial device” which was the device used for the first walking assessment. Subjects that progressed from one device to another less restrictive device were tested twice using the initial device followed by the current device for both gait speed and endurance. Gait speeds reported here reflect the highest speed attained regardless of device during the 10 Meter Walk Test and the 6 Minute Walk Test. In general, the current device produced the highest gait speeds and greatest endurance for the 10 Meter Walk Test and 6 Minute Walk Test. Gait speed was the primary dependent variable. No bracing or assistance was provided during any gait or balance testing.

The full ASIA examination and AIS classification were performed at enrollment and at discharge by trained physicians or physical therapists. Impairment measures such as the AIS classification, LEMS, UEMS, lower extremity pin prick sensation and lower extremity light touch sensation scores were collected and analyzed. The AIS classification was determined using the criteria established by the ISNCSCI. Lower extremity motor scores (LEMS) represent the sum of individual strength scores across 5 key myotomes bilaterally- hip flexors, knee extensors, ankle plantar flexors, ankle dorsiflexors, and great toe extensors. Using a 5 point scale, maximum LEMS score is 50. Likewise, UEMS yield a total score of 50 and represent the sum of 5 key muscle groups in the upper extremity bilaterally – biceps, triceps, wrist extensors, finger flexors and abductors. Lower extremity pin prick (PP) scores and light touch (LT) scores were obtained by assessing dermatomes from T11-S4/S5 using a 2 point scale bilaterally. Maximum lower extremity scores for pin prick and light touch were 44 each. The Berg
Balance score was derived from 14 sitting and standing balance tasks with a maximum score of 56. In all tests, higher scores represent better performance.

**Locomotor Training**

Locomotor Training is an activity-based therapy that stimulates neuromuscular activation below and across the level of the lesion by modulating walking speed, manual assistance and weight bearing through the legs. The subject was supported in a harness over a treadmill to generate kinematically-appropriate stepping with the least amount of manual facilitation. Sensory cues were optimized through light touch, joint proprioception, and tendon stretch. Locomotor Training applied within the NRN consists of 3 components: 1) Manual-facilitated, body-weight supported step training within the treadmill environment; 2) Overground assessment, and; 3) Community reintegration. For a full description of Locomotor Training see The Locomotor Training Manual.

**Treatment Intervention (NRN- Locomotor Training Program)**

All subjects received manual assisted Locomotor Training 3-5 days a week for 1 hour followed by 15-30 minutes of overground training or community reintegration training. Treatment frequency was 5 times per week for nonambulatory subjects, 4 days a week when subjects required marked assistance and 3 days a week when subjects walked independently but with moderate impairments. Re-evaluations occurred after every 20 Locomotor Training sessions. Progression of Locomotor Training sessions was based on a standardized functional approach across all sites. All sessions were provided by physical therapists, physical therapist assistants and rehabilitation technicians who underwent yearly hands-on training and education to deliver standardized treatment across centers.
Statistical Analyses

All statistical analysis was performed using SAS Version 9.2. Basic descriptive statistics were calculated for all variables using mean ± standard deviation (SD). Functional outcome variables and ASIA sensory and motor scores at enrollment and discharge were compared using Wilcoxon Signed Rank Tests. The level of significance was adjusted for multiple comparisons via a Bonferonni adjustment.

For correlational analyses, linear regression was used to describe the relationship between ASIA exam scores and functional measures of gait speed on 10 Meter Walk, distance during 6 minute walk test and Berg Balance Scores. The independent variables included initial lower extremity motor, pin prick and light touch scores at enrollment. Separate regression models were formulated for paraplegia and tetraplegia. Pearson correlation coefficients (r) and coefficient of determination (r²) were determined for all comparisons.

Indicator variables were constructed for each of the lower extremity motor component scores (L2, L3, L4, L5 and S1) to specify if a subject exhibited fair to normal function (4 or 5) or trace function to paralysis (0 or 1). McNemar’s test was used to compare the initial and discharge frequency of subjects in each of the function categories (gait speed = 0, 0 to 0.44 m/s, ≥ 0.44 m/s) and chi-square test was used to determine statistical significance.
Results

Rate of AIS Conversion After Locomotor Training

Little AIS conversion occurred following Locomotor Training regardless of AIS class or level of injury. Of the 144 subjects with AIS classifications pre and post Locomotor Training, 28.1% of AIS C subjects improved to AIS D (9/32), while 92% of the overall sample remained unchanged (n=23 AIS C; n=109 AIS D). Three subjects (2%) classified AIS D regressed to AIS C at discharge. No regression to AIS B occurred for AIS C. Mean overall treatment duration was 4.97±4.96 months with an average of 60±53.2 sessions provided (Table 7). Longer durations were found for AIS C subjects (6.5±6.03 months; 82±76.5 sessions) and shorter durations were found for AIS D subjects (4.2±3.63 months; 52±38.6 sessions; Table 7). Tetreplegic and Paraplegic subjects had durations similar to the overall mean (4.8±4.3 months and 5.4±6.5 months respectively; 57±49.5 and 70±62.1 sessions).

Overall changes in functional outcomes following Locomotor Training

Gains in gait speed, ambulation distance and balance occurred following Locomotor Training regardless of initial AIS classification (n=225) (Table 8). In general, functional outcomes were highly variable, reflecting the diversity of the sample (Table 8). For the overall sample, mean gait speeds derived from the 10 Meter Walk Test improved by 72% from 0.32 ± 0.40 m/s to 0.55 ± 0.55 m/s following Locomotor Training. Ambulation distance during the 6 Minute Walk Test which is considered a measure of functional endurance improved by 74% from 94.4 ± 115.09 to 164.42 ± 159.82 meters. Berg Balance Scores improved by 43% from a mean score of 20.48 ± 17.70 to 29.24 ± 20.60. Also, improvements in balance, locomotor speed and endurance occurred for both AIS C and D groups. Less variability is noted in these outcome measures when looking at
subsets of AIS C vs AIS D subjects. Overall values and extent of relative change for AIS D subjects was similar to the overall sample, likely due to the high proportion of AIS D in the overall sample (Table 8). For AIS C, overall values and extent of change were generally 10-30% of the overall sample although relative gains were much higher (200-300%)(Table 8).

Table 8: Functional Outcome measures Pre- and Post- Intervention for the overall sample, AIS C and AIS D. Means ± SD with range in brackets and sample size per variable; note that sample size is expressed as a range for each cohort due to missing cases or missing subsets of data primarily within the ASIA exam; Nonparametric Wilcoxon Sign Rank Test (p< 0.05)
Conversion Rates between Functionally Stratified Groups

Using van Hedel’s gait speed thresholds validated for functional ambulation\(^1\), subjects were stratified by initial ambulation status into three functionally unique groups: 1) Unable to ambulate; 2) Slow or household ambulators (0 to \(< 0.44\) m/s); 3) Community ambulators (\(\geq 0.44\) m/s). Gait speeds for these groups are less variable than those for the entire sample. Conversion rates between functionally stratified groups following Locomotor Training are shown in Figure 3.
FIGURE 3: Functional stratifications based on van Hedel cut-offs of Non-ambulatory, slow in-home ambulators (>0 to <0.44m/s) and community ambulators (≥0.44 m/s) before and after manual Locomotor Training. Of the overall sample, 70% improved in gait speed with almost half the sample walking at community speeds after Locomotor Training. Twenty-two percent of the sample remained nonambulatory after training.

Two hundred and thirteen subjects had both initial and discharge functional stratification designations. Of those 213 subjects, 31% of subjects were non ambulatory, 41% were slow ambulators and 28% walked at speeds sufficient for community ambulation at enrollment (Figure 3). Locomotor Training reduced the non-ambulators and slow ambulators by 9% and 10% respectively and significantly increased ambulators with community sufficient gait speeds by 19% (Figure 3). Of the 66 subjects entering the program unable to ambulate, 44 remained non-ambulatory (66.7%), 18 (27.3%) became slow ambulators and 4 (6.1%) attained speeds at or above 0.44 m/s following Locomotor Training. Two subjects that were slow ambulators at enrollment were non-ambulatory at discharge (2.27%) and two subjects that were faster ambulators became slow walkers (3.39%). Of the subjects who never ambulated 32 (73%) enrolled as AIS C and 12 (27%)
enrolled as AIS D. In general, more AIS D subjects converted from nonambulatory status to higher stratifications than AIS C subjects. A modest number of AIS C and D subjects converted to slow walking speeds (AIS C=7; AIS D=11) while 4 AIS D and no AIS C subjects converted to fast ambulators (Table 9).

Eighty-eight subjects were categorized as slow ambulators (<0.44 m/s) at enrollment and nearly half (n = 41; 47%) improved to fast ambulators (≥0.44 m/s) following Locomotor Training. Subjects classified as AIS D made up the majority of slow ambulators at enrollment (87% for AIS D vs 13% for AIS C) but there was no significant difference in rates of functional conversion between AIS classes (Table 9).

Fifty-nine subjects entered the program as fast ambulators (≥0.44 m/s). All 59 were classified as AIS D upon admission. Fifty-seven subjects (96.6%) stayed in the fast ambulation category (≥0.44 m/s) with mean final gait speed 1.18 ± 0.42 m/s. Two subjects converted to slow ambulators with mean final gait speed 0.32 ± 0.03 m/s (Table 9).
Table 9: Maximum gait speed (10MWT) at discharge for the overall group, AIS class (C and D), and para/tetraplegia and conversion between functional stratifications per van Hedel’s cut-off (0.44 m/s) \(^1\).

<table>
<thead>
<tr>
<th>Initial Status</th>
<th>Discharge Status</th>
<th>Overall Gt speed (m/s)</th>
<th>AIS C m/s</th>
<th>AIS D m/s</th>
<th>Para m/s</th>
<th>Tetra m/s</th>
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<tr>
<td>Nonamb (n=66)</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td>0.18±0.13</td>
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<td>0.14±0.09</td>
<td>0.10±0.04</td>
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<tr>
<td>&lt;.44 m/s</td>
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<tr>
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<td>&lt;.44 m/s</td>
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<td>n=57</td>
<td>N=13</td>
<td>N=44</td>
<td></td>
</tr>
</tbody>
</table>

* 1 subject lacking pre- or post- AIS classification
Sensation and Locomotor Training

For the majority of initial pin prick or light touch scores there was a wide distribution of gait speeds, distances and Berg Balance Scores achieved following Locomotor Training (Figure 4). In people that never ambulated, marked variability occurred in both light touch scores (3-44) and pin prick scores (0-44). As expected, those classified as AIS C had mean pin prick and light touch scores 5 to 6 points lower than AIS D. A small group of subjects (n= 6) with pin prick scores of zero became ambulators after Locomotor Training and 3 of these subjects had gait speeds greater than 0.44 m/s (Figure 4A). In contrast, only 1 subject with a light touch score of zero ambulated after Locomotor Training (~0.3 m/s; Figure 4B). The results were quite similar for Berg Balance Scores where several subjects (n= 13) had lower extremity pin prick scores of zero and 2 of these subjects demonstrated Berg scores greater than 50 (Figure 4C). Interestingly, there appears to be two fairly distinct and equal groupings (42%) of Berg scores for both pin prick and light touch; one group with Berg Scores of 40 and above and another group with Berg scores of 20 and below (Figure 4C, D). Our sample rarely had lower extremity light touch scores < 10 (n=10; 4%) whereas many more subjects (n=42; 19%) had lower extremity pin prick scores < 10 (Figure 4). Pin prick scores of 0-30 which included ~75% of the sample failed to distinguish differences in Berg (Figure 4C), 6 Minute Walk and 10 Meter Walk (Figure 4A) following training, suggesting that it may not be a sensitive indicator of function in chronic iSCI.

Pin prick and light touch scores at enrollment do not correlate with gait speed, endurance or balance following locomotor training regardless of AIS class or level of injury (Figure 4). Also, locomotor training did not induce changes in either pin prick or light touch scores (Table 8).
Locomotor Training and UEMS

Interestingly, upper extremity motor scores (UEMS) for the overall sample were significantly higher following Locomotor Training (pre training = 38.36 ± 10.83; post training = 41.44 ± 8.27; p<0.05). This reflects an 8% increase in UEMS with Locomotor Training. Similar gains in UEMS (~3 points) occurred for both AIS C and AIS D classifications following training (Table 8).
FIGURE 4: Lower extremity pin prick (A, C) and light touch (B, D) scores at enrollment compared to the maximum 10 Meter Walk gait speed (A, B) and Berg Balance scores at discharge (C, D) for AIS C and D subsets. No relationship exists for either AIS classification. Note the prevalence of high gait speeds and high Berg scores despite low pin prick scores.
Overall LEMS vs Gait speed, distance and balance

Lower extremity motor scores (LEMS) at enrollment did not correlate well with gait speed, endurance or balance following locomotor training (Figure 5). However, locomotor training induced significant changes in LEMS (pre training= 31.85 ± 13.98; post training= 38.61 ± 12.29; p<0.05) which is a 21% improvement (Table 8). In general, subjects with fast gait speeds, good gait distances and high Berg scores at discharge had modest but not low LEMS at enrollment; however wide variability existed. It was common to find people with high initial LEMS scores who had very low gait speeds, gait distances and balance scores (Figure 5). Likewise, post-training walking speeds ≥ 0.44 m/s occurred with LEMS 0-50. Although rare, fast gait speeds and moderate Berg Balance Scores (15-29) occurred with LEMS of 0 (n=2) after Locomotor Training.

When AIS C subjects are distinguished from AIS D subjects, there is less overlap of LEMS and the relationships between initial LEMS and final gait speed, distance and Berg scores are different between the two groups (Figure 5). Subjects classified as AIS D show a weak but positive correlation between initial LEMS and post-training gait speed and distance (r²= 0.241 and 0.251 respectively; p<0.05) whereas AIS C subjects do not show any correlation. Also, there was a significant positive, yet weak (r²=0.333; p<0.05) relationship between initial LEMS and post-training Berg Scores for those classified as AIS D.

Moderately strong correlations occurred between initial LEMS and balance variables for both para and tetraplegia (Figure 6). The highest correlation occurred between LEMS and final Berg scores for paraplegia (r²= 0.497; p<0.05) and tetraplegia (r²= 0.478; p<0.05). Weaker correlations occurred for LEMS and 6 minute walk distance (paraplegia: r²=0.385, p<0.05; tetraplegia r²= 0.359, p<0.05) and gait speed (paraplegia
$r^2 = 0.303, \ p<0.05$; tetraplegia $r^2 = 0.373; \ p<0.05$) (All $p$ values represent Bonferroni adjusted $p$-values for 18 comparisons: $0.05/18=0.003$ for significance). While several other significant correlations occurred for tetraplegia, their strength was extremely poor with $r^2$ values ranging from 0.065 to 0.179 and did not warrant further consideration.
FIGURE 5: Lower extremity motor score (LEMS) at enrollment compared to maximum 10 Meter Walk gait speed (A), maximum 6 Minute Walk gait distance (B) and Berg Balance scores (C) at discharge for AIS C and D subsets. Note no significant relationship occurred for LEMS and gait speed or distance in AIS C subjects. Significant yet weak relationships occurred for AIS D subjects.
FIGURE 6: Lower extremity motor scores (LEMS) at enrollment compared to maximum 10 Meter Walk gait speed (A), maximum 6 Minute Walk gait distance (B) and Berg Balance scores (C) at discharge for tetraplegic and paraplegic subsets. Note moderately strong significant correlations between LEMS and Berg scores.
Most subjects (70%) showed an improvement in their gait speed over the course of training (Figure 7). For those showing improvement, LEMS ranged from 0-50 with the greatest change in gait speed (≥1.0 m/s) in subjects with an initial LEMS of 20-50 (Figure 7). Twenty-one percent enrolled in the program non-ambulatory and remained non-ambulatory at discharge. For these non-responders, 50% had initial LEMS below 15 (LEMS range 2-39). A handful of subjects (9%) showed declines in gait speed over the course of training and had initial LEMS ranging from 14-50 (Figure 7). Of the AIS C subjects that increased gait speed with training, gains were typically below 0.5 m/s while those classified as AIS D demonstrated gains from 0.05 m/s to over 1.6 m/s (Figure 7).
FIGURE 7: Lower extremity motor scores (LEMS) at enrollment compared to change in maximum 10 Meter Walk gait speeds from pre to post training. Note that the highest gains in speed were associated with initial LEMS in mid- to high range (20 or higher). Note that declines in speed also occurred over about this same LEMS range.

Influence of Strong vs Weak Lower Extremity Muscles on Recovery

To determine whether the effect of Locomotor Training was dependent on the proportion of muscles with good strength, we examined the number of lower extremity muscle groups within AIS C and D groups for each gait speed classification (Table 10). Interestingly, those non-ambulatory subjects classified as AIS D that convert to ambulators after Locomotor Training typically have 60-80% (6.4-8.2/10) of the lower
extremity muscle groups with at least 4 or 5 strength. Those non-ambulatory subjects classified as AIS C that convert to ambulators typically have about 8% of the lower extremity muscle groups with at least 4 or 5 strength and have significantly more paralyzed muscle groups (53%) compared to AIS D (0-12%). However, they demonstrated significantly less paralysis than those classified as AIS C that never ambulated (72% 0 or 1’s).

Table 10: Overall initial LEMS and number of lower extremity muscle groups with good strength (4 or 5 muscle score) or paralysis (0-1 muscle score) for functional stratifications as determined by van Hedel’s cut off (0.44 m/s) \(^1\).

<table>
<thead>
<tr>
<th>Speed Category</th>
<th>Observations</th>
<th>LEMS Score</th>
<th>Number of 4 or 5 LEMS Scores</th>
<th>Number of 0 or 1 LEMS Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial 10 MW</td>
<td>Final 10 MW</td>
<td>AIS C</td>
<td>AIS D</td>
<td>AIS C</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>32</td>
<td>12</td>
<td>10.7±7.8</td>
</tr>
<tr>
<td>&lt;.44</td>
<td>7</td>
<td>11</td>
<td>14.6±7.3</td>
<td>35.1±6.7</td>
</tr>
<tr>
<td>≥.44</td>
<td>0</td>
<td>4</td>
<td>N/A</td>
<td>41.0±2.7</td>
</tr>
<tr>
<td>&lt;.44</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>25.0</td>
</tr>
<tr>
<td>&lt;.44</td>
<td>6</td>
<td>38</td>
<td>22.2±7.0</td>
<td>35.7±7.5</td>
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<tr>
<td>≥.44</td>
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<td>37</td>
<td>17.0±11.5</td>
<td>39.4±6.4</td>
</tr>
<tr>
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<td>&lt;.44</td>
<td>0</td>
<td>2</td>
<td>N/A</td>
</tr>
<tr>
<td>≥.44</td>
<td>≥.44</td>
<td>0</td>
<td>57</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Individual muscle groups and recovery

For the overall sample, strength of individual lower extremity muscles changed with Locomotor Training (Table 11). The knee extensors (L3) were the most common muscle group with fair to normal strength at enrollment (83.8%) but it was not typically combined with good strength in the hip flexors (L2) (65.4%)(Table 11). Before
Locomotor Training, paralysis or trace movement occurred in ankle dorsiflexors (L4) more often than any other muscle (40%). The greatest return to near normal strength following Locomotor Training occurred in the knee extensors (L3) and the greatest return from paralysis (ie decrease in number of muscles scoring 0 or 1) occurred in the hip flexors and ankle dorsiflexors (13.1% and 11.5% respectively). When looking across the lower extremity, the greatest strength recovery occurred proximally with hip flexors and quadriceps (~14% increase in 4s and 5s) compared to ankle dorsiflexors and plantarflexors (8.5% increase in 4s and 5s). Completion of Locomotor Training increased the prevalence of proximal and distal muscle groups with good strength and reduced the occurrence of paralysis or trace movement (Table 10). Despite improvements in strength for individual muscles, more than a quarter of the overall sample (28.5%) continued to have paralysis/trace movement of the ankle dorsiflexors (L4) at discharge (Table 11).

Table 11: Number and percentage of the overall sample with good or poor motor response in at least 1 lower extremity during LEMS testing (n=130)

<table>
<thead>
<tr>
<th></th>
<th>Initial Eval</th>
<th>Discharge Eval</th>
<th>Initial Eval</th>
<th>Discharge Eval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fair to normal resistance 4 or 5 MMT</td>
<td>Trace Mvt or paralysis 0 or 1 MMT</td>
<td>Trace Mvt or paralysis 0 or 1 MMT</td>
<td></td>
</tr>
<tr>
<td>Hip flexors L2</td>
<td>86 (66.2%)</td>
<td>36 (27.7%)</td>
<td>103 (79.2%)***</td>
<td>19 (14.6%)***</td>
</tr>
<tr>
<td>Quads L3</td>
<td>109 (83.8%)</td>
<td>16 (12.3%)</td>
<td>117 (90%)</td>
<td>12 (9.2%)</td>
</tr>
<tr>
<td>Ankle DF L4</td>
<td>92 (70.8%)</td>
<td>52 (40%)</td>
<td>101 (77.7%)</td>
<td>37 (28.5%)***</td>
</tr>
<tr>
<td>Ankle Pf S1</td>
<td>97 (74.6%)</td>
<td>25 (19.2%)</td>
<td>106 (81.5%)</td>
<td>15 (11.5%)***</td>
</tr>
<tr>
<td>Hip flexors and Quads</td>
<td>85 (65.4%)</td>
<td>15 (11.5%)</td>
<td>103 (79.3%)***</td>
<td>11 (8.5%)</td>
</tr>
<tr>
<td>Ankle DF and PF</td>
<td>84 (64.6%)</td>
<td>22 (16.9%)</td>
<td>95 (73.1%)</td>
<td>14 (10.8%)</td>
</tr>
</tbody>
</table>

***McNemar Test : Bonferroni adjusted p-values <= 0.05 vs proportion at Initial Evaluation
Discussion

To our knowledge, this cohort study of 225 subjects is the largest to date looking at the relationship between sensory and motor scores and functional outcomes after standardized activity-based therapy (Locomotor Training) in chronic iSCI. Overall, 70% of the subjects improved with Locomotor Training while 30% did not respond or worsened. For those that improved (n=148) average improvement in gait speed was 0.35±0.34 m/s and average improvement in distance ambulated in 6 minutes was 99.36±101.05 m. Significant gains in gait speed, endurance and balance occurred with Locomotor Training which likely support conversion to home or community ambulation based on gait speed categories validated by van Hedel. The improvements in ambulation were accompanied by increased strength and some resolution of paralysis in certain LE muscle groups; however, these gains were accompanied by a modest rate of AIS conversion and no improvement in sensation of the LEs. Thus, improvements in locomotion and balance induced by Locomotor Training may not be detected using broad classification measures of AIS but muscle-specific measures may hold promise.

Conversion of AIS Classification

Locomotor Training did not significantly impact conversion of AIS classification in chronic SCI. For AIS C, 70-90% conversion to AIS D is expected while a regression rate of less than 5% occurs for motor incomplete injuries during the first year. By comparison, a 21% conversion rate from AIS C to D is expected between 1 and 5 years post SCI while regression is higher at 17-21%. Applying NRN Locomotor Training in chronic SCI resulted in a slightly higher than expected conversion rate of 28% from AIS C to D. Interestingly, AIS conversion from C to D (n=9) occurred with an average of 82 sessions of Locomotor Training over approximately 6.5 months rather than a 4 year timeframe. This rate of conversion is especially noteworthy given that 50% of the
NRN sample was greater than one year post injury and 13% was greater than 5 yrs post SCI. Furthermore, Locomotor Training appeared to lessen regression for chronic SCI (3% vs 17-21%)\(^\text{94}\). However, these lower regression rates may reflect the shorter time period (5 months vs 4 years) and selection bias of those patients that were eligible for and interested in pursuing NRN Locomotor Training. While causes of spontaneous regression in chronic iSCI remain unknown, contributing factors may include onset of illness or infection, heightened spasticity, complications from other medical co-morbidities, depression and/or loss of interest in pursuing ongoing therapy. Many of these factors can be modulated by regular exercise of moderate intensity in non-disabled individuals\(^\text{107}\). Perhaps Locomotor Training reduces spontaneous regression in AIS classification by producing beneficial effects of exercise similar to that observed in nondisabled individuals such as a stronger immune system and improved cardiovascular function\(^\text{108}\). Of considerable interest is whether Locomotor Training reduces spasticity as has been anecdotally reported by some individuals treated in the NRN. Future studies may examine the relationship between exercise-induced functional recovery and resolution of co-morbidities in people with chronic iSCI.

Recently, Middendorp\(^\text{92}\) studied 273 acute (<1 year post-injury) SCI AIS A through D and found that return to walking as measured by the Timed Up and Go and the 10 Minute Walk Test did not mirror conversion rates. Approximately 25-50% of those that converted from AIS A, B or C to AIS D remained non-ambulatory at 1 year. Likewise, in chronic SCI, AIS conversion is not particularly sensitive to functional improvements produced by activity-based therapy. Indeed, 33% of nonambulators became walkers and 47% of slow walkers improved to faster walkers whereas AIS conversion from C to D was only 28% and no one classified as AIS D converted to E. Therefore, in acute SCI AIS conversion outpaces gains in walking ability, yet in chronic iSCI following Locomotor Training gains in walking ability outpace AIS conversion. Our data supports the proposition that AIS conversion may be a poor indicator for recovery of walking
ability in both acute and chronic SCI and suggests that care must be taken when relying on AIS category conversion to determine treatment efficacy.

**Conversion between Functional Stratifications**

We used gait speed of 0.44 m/s to stratify patients into presumptive functional categories. In 886 subjects with SCI undergoing inpatient rehabilitation from the European Multicenter Study for Human Spinal Cord Injury, minimum gait speeds were defined for functional ambulation categories based on the Spinal Cord Independence Measure (SCIM). Although this study looked at individuals classified as AIS A through D and community ambulation was typically assessed as part of day passes from inpatient rehabilitation, there is no other study to date analyzing such a large sample size to validate gait speed as a measure of functional independence after SCI. The minimum gait speed for community ambulators with an assistive device was 0.44 ± 0.14 m/s and without a device was 0.70 ± 0.13 m/s. Independent, in-home ambulators had a minimum gait speed of 0.15 ± 0.08 m/s. These speeds are remarkably similar to case studies and a clinical trial for treadmill training in the U.S. Field-Fote (2010 in press) reported post-training gait speeds of 0.14 m/s for subjects that were not ambulating in the community but were walking short distances in their homes. Likewise, Behrman reported a gait speed of 0.19 m/s for an iSCI independent in-home ambulator. The conversion from non-ambulatory status to community walking was reported at gait speeds of 0.33 - 0.53 m/s in 2 cases. Many studies report significant gains in gait speed but it is unclear if such changes supported in-home or community ambulation. Other studies report functional improvements without gait speeds. Although gait speed used to estimate level of functional ambulation has not been previously studied in SCI, Perry et al divided stroke subjects into 3 functional ambulation categories based on walking speeds: household ambulators (<0.4 m/s), limited community ambulators (0.4-0.8 m/s), and full community ambulators (>0.8 m/s). They found that those subjects who progressed
from one ambulation group to the next showed improvement in quality of life and participation. Certainly further study of gait speed criteria is warranted especially in chronic SCI with and without activity-based training; however, there appears to be at least some face validity for these speeds after SCI in the U.S.

Locomotor Training significantly increased conversion between functionally stratified groups based on validated gait speed thresholds for our chronic iSCI population. Those subjects entering the program able to ambulate regardless of speed, were more likely to show functionally significant gains in gait speed following Locomotor Training with 47% of the slow ambulators (< 0.44 m/s) converting to fast ambulators (≥ 0.44 m/s). This occurred independent of AIS classification with equal proportions of AIS Cs and Ds converting to fast ambulators. Also, although a large proportion of initial non-ambulatory AIS D subjects (56%; 15/27) converted to ambulators after Locomotor Training, 18% (7/39) of initial non-ambulatory AIS C subjects converted to ambulators as well. These findings suggest that classifying those with chronic iSCI based on functional ambulation criteria may be more valuable in indicating appropriateness of and responsiveness to Locomotor Training than AIS classification. Future studies may need to validate functional ambulation categories based on gait speed for chronic iSCI for U.S. populations to determine alignment and agreement with those determined by van Hedel.

**Gains in Strength Following Locomotor Training**

Interestingly, robust gains in LEMS occurred following Locomotor Training (pre-31.85±13.98; post- 38.61±12.29). Not surprisingly the rate of spontaneous recovery of strength following SCI is highest during the first year after SCI. Although recently motor scores have been separated into UEMS and LEMS, most research on recovery of strength after SCI has been done on motor index scores (MIS) which is the sum of the UEMS and the LEMS (total of 100 pts). Marino showed spontaneous gains in motor scores
for AIS C (tetra- 43 ; para- 21.0 ) and D (tetra-25.7 ; para- 13.9) during the first year. Steeves showed similar gains in MIS for AIS C and D subjects (12.9) during the first year for several large clinical trials. From 1 to 5 years however, the rate of strength recovery slows. According to Kirshblum, typical spontaneous recovery of strength from 1 to 5 years post-injury regardless of injury severity was minimal (mean change in MIS 1.38±6.22). Only 58.1% of incomplete injuries gained strength between 1 and 5 years and only 27.9% gained more than 6 points. On average, our subjects gained almost 7 points in LEMS (not including UEMS) after Locomotor Training with average treatment durations of about 5 months. Although direct comparisons are difficult to draw, it appears likely that the gains in LEMS were due at least in part to Locomotor Training. However, whether gains in strength occurred due to neuroplastic changes in the CNS, increased motor unit recruitment or changes in the muscle fibers (Type I, IIa, IIb) remains unknown based on the current data. Future studies may look closer at the specific physiologic changes that occur in relation to gains in LEMS and how these changes are impacted or influenced by Locomotor Training for those with chronic motor iSCI.

**Gains in Balance Following Locomotor Training**

Berg Balance scores significantly improved with Locomotor Training (43%; p<0.001) for the overall sample as well as for AIS C and D subjects. These improvements in balance in response to Locomotor Training are not novel and have been reported elsewhere. Also, the similar increase in LEMS across classification and moderate relationship between Berg scores and initial LEMS support the theory that standing balance improves as lower extremity strength improves. One thing that is not evident from this study was the impact of Locomotor Training on trunk control and strength given that UEMS and LEMS do not assess core strength. It seems logical that if Locomotor Training improves LEMS, UEMS and balance that improvement in trunk strength would also occur. Careful examination of the factors related to gains in balance performance and the effect of those
gains on locomotion is critical. With new trunk assessments, future studies may be able to determine the role of trunk strength and motor control in recovery of ambulation in chronic iSCI and whether Locomotor Training further improves these outcomes.

**Pin prick and light touch**

An early harbinger of recovery of motor function following SCI is the presence of sacral or LE sensation. Pin prick sensation at 72 hours to 4 weeks over sacral or lower extremity regions predicts recovery of walking by 1 year post SCI. Acute pin prick sensation may be a surrogate marker for lesion extent given the close approximation of the lateral spinothalamic tract to the lateral corticospinal tract in humans. Indeed, poor prognosis for ambulation occurs when light touch without pin prick sensation is preserved below the level of injury. In contrast, light touch scores reflect modalities such as proprioception which play a direct role in locomotor function. Therefore, both pin prick and light touch scores have been shown to be sensitive predictors of motor recovery after acute and chronic SCI. Surprisingly, our study found that below-level sensation had no relationship to locomotor recovery (both gait speed and endurance) following Locomotor Training in chronic iSCI. This is in agreement with Winchester et al who identified predictive factors of gait speed after manual and robotic training in iSCI and found that lower extremity pin prick did not contribute significantly to the model. It may be that locomotor ability following Locomotor Training is less dependent on conscious perception of sensation and more dependent upon the interaction of sensation with interneuronal networks at the cord level or at subcortical levels such as the cerebellum or basal ganglia. Also, although those that ambulated after Locomotor Training showed a wide range of light touch and pin prick scores, it may be that particular dermatomal segments in the lower extremities such as the plantar surface of the foot are more related to locomotor ability than the overall lower extremity score. Future exploration of the relationship between specific lower
extremity dermatomes or dermatomal patterns and ambulation ability following Locomotor Training in chronic iSCI is most certainly indicated.

Similarly, neither lower extremity light touch nor pin prick were correlated with final Berg scores for balance following Locomotor Training. Subjects demonstrated a wide range of Berg scores across pin prick and light touch scores (Figure 4) with an almost equal distribution showing marked impairments (<20) or high balance function (>40). It appears that two distinct subsets of balance function exist which are independent of AIS classification, level of injury and sensory function (Figure 4C,D).

**Overall LEMS vs Gait speed, distance and balance**

Overall LEMS at enrollment does not indicate responsiveness to Locomotor Training or final outcomes in gait speed or endurance regardless of type or severity of injury (AIS C, D; tetra- vs paraplegia). This is in agreement with Winchester et al ⁶ who did not find LEMS to be predictive of gait speed following robotic or manual Locomotor Training. In our study, there was surprisingly high variability in LEMS before and after Locomotor Training for groups functionally stratified according to gait speed which may account for the poor correlations with locomotor outcomes. Whether this variability reflects Locomotor Training or chronicity of the injury is unknown. It is also noteworthy that the LEMS values collected from our subjects that were ambulating at community speeds (≥0.44 m/s) are much more variable than the cut-off of 40 suggested by Dobkin et al ⁷⁴ for locomotor training in acute iSCI. With chronic iSCI, gains in gait speed and endurance occurred in about a third of patients with LEMS ≤ 20. Of all those classified as AIS C who could ambulate after Locomotor Training, 50% had LEMS scores < 20.

Our findings clearly differ from expectations early after iSCI. Waters et al showed a relationship between early LEMS (>10 at 1 month) and ability to ambulate at 1 year for
both incomplete para- and tetraplegia\textsuperscript{95, 96}. In a subsequent study, Waters found LEMS ≤ 20 to be associated with limited ambulators and LEMS ≥ 30 to be associated with community ambulators for 26 subjects with SCI\textsuperscript{97}. According to van Hedel, during the first year after SCI, LEMS is moderately correlated to ambulation distance during the 6 minute walk test but weakly correlated to gait speed\textsuperscript{120}. The differences could also be explained by the fact that van Hedel’s subjects were all high functioning, demonstrated a ceiling effect for LEMS and attained normal walking speeds (1.39 m/s) within 6 months of SCI. By comparison, our subjects were more impaired, had lower LEMS and a significant number were unable to walk at enrollment.

The high variability in LEMS and ambulation ability following Locomotor Training suggests that there are probably other components of motor control besides strength that contribute to the recovery of locomotor function. In fact, higher voluntary strength may be linked with higher spasticity or tone, either at rest or during locomotion that could negatively impact the gait outcome measures of speed or distance. For example, some subjects with high tone may be able to voluntarily use or work through their tone to resist a manual muscle test but their tone becomes a barrier to initiating and coordinating complex movement patterns associated with walking.

Higher initial LEMS is associated with greater recovery of balance as measured by the Berg Balance Scale following Locomotor Training in chronic iSCI. A weak relationship between initial LEMS and final performance on the Berg for AIS C (12\% of variance) occurred and may be partly related to the modest number of subjects in this classification. It may also result from the high variability in Berg Scores for AIS C subgroup where scores ranged from 0 to 56 when LEMS ≤ 20. Although those classified as AIS D typically had higher Berg Balance Scores and LEMS (r\textsuperscript{2}=0.333), about 13\% had Berg Balance Scores under 10 while LEMS ranged from 10 to 44. Also, there was a significant ceiling effect for LEMS and Berg scores for AIS D which could possibly
inflate the r and r² values. Overall, lower extremity strength at enrollment accounts for only 33% of the variance in final Berg scores for AIS D. Balance performance may also depend on other variables like trunk control or the ability to initiate movements quickly as is typical during normal balance reactions. Normal balance and righting reactions take place through several different mechanisms such as ankle dorsiflexion or plantarflexion for minor perturbations in the sagittal plane; trunk and hip flexion or extension for moderate perturbations; and a stepping reaction for larger perturbations \(^\text{121}\). High LEMS does not necessarily mean the individual can react with sufficient speed and control of the lower extremities to restore balance using these typical mechanisms. Additionally, balance synergies may be markedly impaired or absent when requisite individual muscle groups are paralyzed like ankle dorsiflexors or hip extensors. Furthermore, high LEMS does not indicate high trunk strength which is vital for standing and walking balance as well. Interestingly, both paraplegic and tetraplegic subjects showed significant positive correlations (r²=0.497 and r²=0.478 respectively) between initial LEMS and post-intervention Berg Balance Scores. It should be pointed out that within both paraplegics and tetraplegics, there could be a wide range of trunk motor control which could explain the similarity in this relationship. Future studies may look closer at the relationship between balance and trunk control as well as how they relate to ambulation ability following Locomotor Training. Also, this may warrant an investigation into the relationship of individual lower extremity or trunk muscle groups and balance following Locomotor Training.

There was no difference in relationship between LEMS and gait speeds for subjects with tetra- vs paraplegia. The importance of trunk control and UE function to recovery of locomotion following iSCI is unclear. Perhaps sub-groups of tetraplegia exist (central cord syndrome, Brown-Sequard syndrome, different patterns of UE function) within our sample that present differently and our analysis is not sensitive enough to discriminate between these differences. A surprising outcome of locomotor training was the
significant increase in upper extremity (UE) strength for the overall sample and AIS C and D classifications. It should be noted however, that we did not control for specific types of SCI like central cord syndrome or Brown-Sequard injuries which may introduce ceiling and floor effects for UEMS. Steeves$^{122}$ found that in the first year after sensorimotor complete SCI, the average spontaneous gain in UEMS was 10-11 points. In our study, the UEMS increased by an average of 3.22 points which likely underrepresents the strength gains given that a ceiling effect occurred for a number of subjects who had normal UE muscle strength initially. Even the weakest individuals demonstrated improvements in UEMS of 9 points for the overall sample, AIS C and tetraplegia, 6 points for AIS D and 4 points for paraplegia before and after training. Future studies may look to identify which factors of UEMS are most related to locomotor gains following Locomotor Training for those with chronic iSCI and whether these factors vary among sub-groups of tetraplegia and individuals that never ambulate. An important study will be to determine whether gains in UEMS are related to gains in LEMS and improvement in walking speed, endurance and balance.

**Influence of Strong vs Weak Lower Extremity Muscles on Recovery**

The ability to respond to Locomotor Training may depend on the degree of strength and paralysis of lower extremity muscle groups rather than the overall LEMS. For subjects with AIS D classification, the number of muscle groups with good strength (scoring 4 or 5; ≥ 64%) appears to distinguish non-ambulators from slow (<0.44 m/s) or faster walkers (≥0.44 m/s). In contrast, the degree of paralysis or severe paresis (scoring 0 or 1; ≤ 53%) delineated walking ability for people with AIS C classification. Regardless of these trends, there is no particular number of muscle groups which separates walkers from non-walkers across all subjects. Future studies will need to determine if muscle strength, paralysis or the ratio of the two criteria can be used to predict the extent of locomotor and balance recovery for people with AIS C and D classifications.
Individual muscle groups and distribution patterns of strength recovery

Locomotor training induced improvements in muscle strength as evidenced by more muscle groups scoring in the near normal range (4 or 5) and fewer muscle groups with paralysis or severe paresis (0 or 1). The greatest return of near normal strength occurred in the knee extensors while the greatest persistence of weakness or paralysis occurred in ankle dorsiflexors. Overall, Locomotor Training appeared to induce the greatest strength gains in proximal more than distal muscle groups. Importantly, Kim et al.\textsuperscript{123} showed that proximal muscle strength was more highly correlated than distal muscles with ambulation distance and speed after chronic iSCI. Thus, the significant gains in distance and speed after Locomotor Training may, in part, be explained by improved hip and knee strength. Whether strength of specific muscles predicts the responsiveness to Locomotor Training and final locomotor outcome is currently underway.

The ramifications of persistent impairments such as paralysis or severe paresis of the ankle dorsiflexors, can have a large impact on overall disability and community participation. While the inability to dorsiflex the ankle may sound trivial in terms of impact on functional independence, its actual effect can be devastating. Lack of dorsiflexion can lead to “toe drag” which could lead to a subsequent decrease in gait speed and safety, increased fatigue and decreased overall community participation. Within the NRN we have the ability to track these interrelationships between these seemingly small impairments and disability. We can hypothesize that those with weak ankle dorsiflexors may ambulate at slower speeds and walk shorter distances. Future studies may look closer at the relationship between specific impairments and functional limitations or disability for those with chronic iSCI following Locomotor Training.
The number of training sessions needed to improve locomotion seems to depend on the extent of paralysis at enrollment. More training sessions were needed to attain faster walking speeds ($\geq 0.44 \text{ m/s}$) for AIS C with higher rates of paralysis than for AIS D with less paralysis. Perhaps a combination of number of treatment sessions and change in LEMS paralysis could be used to determine responsiveness to Locomotor Training in people who are initially non-ambulatory. Delivery of an average of 50 sessions was associated with a 20% reduction in paralysis for AIS C and 20% increase in strength for AIS D. Hence, a check of LEMS at or before 50 sessions for non-ambulatory patients may indicate whether further training will be effective. Overall, recovering gait speed sufficient for community ambulation occurs faster for AIS D with greater muscle strength but may also be attainable for a subset of people with AIS C that train longer.

**Relationships between patient categories, AIS measures and gait measures in the NRN Locomotor Training program.**

With clinical experience, we have come to expect certain relationships between functional recovery induced by a therapeutic intervention and the SCI phenotype that is being treated. In this study, patients classified as AIS C and AIS D appear to be largely distinct populations in chronic iSCI as many clinicians would predict. However, the extensive overlap between subjects with paraplegia and tetraplegia was unexpected. Clinically, we predict greater locomotor and balance recovery with paraplegia than tetraplegia because more of the neurological axis is spared and more motor function in the upper extremities and trunk may be preserved. These assumptions are not supported by the current study.

Trunk motor control may differ greatly within the same SCI classification and level of injury. Types of injury like central cord syndrome or Brown-Sequard may produce greater trunk function than other iSCI lesions at the same neurological level (para- or
tetraplegia) or AIS classification (C or D). This may in part explain why the response of paraplegics and tetraplegics to NRN training was indistinguishable. Alternatively, a highly unlikely explanation is that trunk control plays little role in recovery of balance and locomotion. The fact that arm strength improved with Locomotor Training regardless of AIS classification strongly suggests that dynamic upright training produces remarkable changes throughout the neuroaxis and musculoskeletal system. Perhaps gains in trunk control and strength with training enable greater upper extremity use at home and in the community which induces greater upper extremity strength. Further research is necessary to identify the contribution of trunk motor control and arm function to recovery of gait and balance. While new trunk assessments are available for iSCI (phase paper in press), tools to quantify recovery of arm and hand function in response to Locomotor Training are needed. Furthermore, future analyses of the data in the current study will distinguish central cord patients from non-central cord patients using an algorithm that makes use of motor (and perhaps sensory) scores from the upper extremities and lower extremities in comparison to each other. These studies will help determine whether certain sensorimotor phenotypes in iSCI are more responsive to the NRN intervention than others and whether interventions for the arms should be conducted concomitantly with Locomotor Training.
CHAPTER 4: ADDENDUM

Research Questions:

1. What is the largest rate and magnitude of locomotor improvement as measured by increase in gait speed and what amount of Locomotor Training is necessary to elicit these changes for persons with incomplete spinal cord injury (iSCI)?

2. What is the degree of agreement in final gait speed between the 10 Meter Walk Test (10MWT) and the 6 Meter Walk Test (6MWT) for persons with incomplete spinal cord injury following Locomotor Training?

Methods

Research Design

Using the data set described in chapter 3, we analyzed gait speeds calculated from the 10 Meter Walk Test and the 6 Minute Walk Test pre- and post-intervention from enrolled individuals who completed Locomotor Training.

Subjects

The final study population consisted of 219 subjects with chronic motor iSCI (average time since injury= 2.45±3.79 years) that had complete data sets for 10 Meter Walk Test
while 6 subjects were missing 6 Minute Walk Test data leaving 213 subjects for comparison of 10 Meter Walk Test and 6 Minute Walk Test gait speed comparison. Subjects were included if they attained at least 15 sessions of Locomotor Training, were 17 or older, had an Initial and Discharge Evaluation and met the inclusion criteria (see chapter 3). All subjects were AIS C or D as defined in Chapter 3. Treatment durations ranged from 15 to 305 sessions. Using van Hedel’s gait speed thresholds validated for functional ambulation \(^1\), subjects were stratified by initial gait speed on the 10 Meter Walk Test into three functionally unique groups: 1) Unable to ambulate; 2) Slow or household ambulators (<0.44 m/s); 3) Community ambulators (≥0.44 m/s).

**Outcome Measures**

Locomotor function was measured using 10 Meter Walk Test for gait speed over short distances \(^{31,78}\) and 6 Minute Walk Test for longer distances \(^{78,81}\). Gait speeds calculated from the 10 Meter Walk Test were collected at initial and discharge evaluations and after every 20 sessions. Gait speeds derived from the 6 Minute Walk Test were calculated from the discharge evaluation or last re-evaluation collected. Gait speeds were collected with subjects using an appropriate assistive device for their needs at that particular time without outside assistance provided by the clinician. As subjects improved during their treatment duration, 107 subjects progressed from their “initial device” to a different less restrictive or “current device”. Therefore, the maximal speed obtained regardless of device was calculated and used as peak gait speed. Gait speed was the primary dependent variable. No bracing or assistance was provided during any gait or balance testing.

Gait speed means and standard deviations were calculated. Peak gait speed obtained for short distance ambulation was determined as well as where within the treatment duration this speed occurred. The re-evaluation and concurrent session number where peak gait
speed occurred was divided by the total number of sessions delivered to yield the percentage of total treatment duration. For comparison of final gait speed during 10 Meter Walk Test and 6 Minute Walk Test, the total distance walked in 6 minutes was converted to gait speeds.

Statistical Analyses

All statistical analysis was performed using SAS Version 9.2. Basic descriptive statistics were calculated for all variables using mean ± standard deviation (SD). Functional outcome variables at enrollment and discharge were compared using Wilcoxon Signed Rank Tests.

Results

Gait speed

We determined the peak gait speed for each subject who ambulated by discharge (n=176) (Figure 8). Speeds were calculated for the overall sample as well as each functional ambulation category (Figure 8). All groups improved and gains were statistically significant for each group and the overall sample (p<0.05). Those initial non-ambulators who were ambulating by discharge improved from 0 m/s to 0.30 ± 0.36 m/s. Those enrolled as “slow ambulators” (< 0.44 m/s) improved from 0.21 ± 0.12 to 0.52 ± 0.40 m/s (150.7% improvement). Those enrolled as “fast ambulators” (≥ 0.44 m/s) improved from 0.86 ± 0.39 m/s to 1.21 ± 0.43 m/s (40.3% improvement). The overall sample improved from 0.39 ± 0.42 m/s to 0.72 ± 0.54 m/s (81.7% improvement). Not surprisingly, those subjects categorized initially as “fast ambulators” obtained the highest peak speeds at discharge and those categorized as non-ambulatory obtained the smallest peak speeds at discharge. However, relative gains were highest for the non-ambulator and slow
ambulator groups. The minimal important difference (MID)\(^{34}\) using the standard error of measurement (SEM) method was 0.067 m/s for the overall sample. Although this number may not indicate clinical meaningfulness, our gains in gait speed were on average much higher than the MID.

![Peak Gait Speed- Ambulators - Max Device - 10 M](image)

Figure 8. Mean gait speed (m/s) at enrollment and mean peak gait speed (m/s) achieved during treatment on the 10 Meter Walk Test per functional category as described by van Hedel \(^1\): 1) Non-ambulators (0 or NT); 2) Slow Ambulators (0 to < .44); 3) Community Ambulators (≥ .44); and 4) grand total. Largest peak gait speeds occurred for community ambulators, yet the largest relative gain occurred in the initial non-ambulators and the slow ambulators.
Peak Gait Speed within Total Treatment Duration

The mean number of treatment sessions to reach peak gait speed was calculated for all functional categories and the overall sample (n=176) from the 10 Meter Walk Test (see Figure 9). On average, those entering the program unable to ambulate that converted to walking by discharge received the most sessions (~92 sessions) and those that entered the program as fast ambulators (≥0.44 m/s) received the fewest sessions (~41 sessions). On average, peak gait speed occurred between 72% and 82% of the total treatment duration. Those entering the program as fast ambulators achieved peak gait speeds closest to discharge (~34 sessions or ~82% of treatment duration) and those entering the program as non-ambulators achieved peak gait speeds earlier in the treatment duration (~ 67 sessions or ~72% of treatment duration) (Figure 9). Despite these values, 64% of those that ambulated (112/176) achieved peak gait speed at discharge (see Table 12). We determined the relative gain in gait speed between the next to last and last evaluation. The change over the final treatment period was larger than the MID for all ambulators. The largest relative change occurred in the slow ambulator group (55%; 0.17 m/s) and largest absolute change was found in the community ambulatory group (0.30 m/s).
Figure 9. Mean treatment session of peak gait speed for ambulators at discharge relative to total treatment duration based on maximum gait speed on 10 Meter Walk Test (n=176) per functional category as described by van Hedel: 1) Non-ambulators (0 or NT); 2) Slow Ambulators (0 to < .44); 3) Community Ambulators (≥ .44); and 4) grand total. Those initial non-ambulators required more sessions (67) to achieve peak gait speeds and did so earlier in the treatment duration compared to the other groups (72.3% of total treatment duration). Community ambulators achieved peak gait speeds much quicker (34 sessions) with shorter overall durations.
Table 12. For ambulators at discharge, the number and percentage of subjects achieving peak gait speed at final evaluation stratified by ambulation status at enrollment. Magnitude of change in gait speed from next to last and last evaluation expressed as percentages and mean values.

10 Meter Walk Test and 6 Minute Walk Test Final Gait Speed Comparisons

Final gait speeds were higher for 10 Meter Walk Test than 6 Minute Walk Test and these differences were statistically significant for each functional group and the overall sample (p<0.05) (Figure 10). Mean final gait speeds calculated for those entering the program as fast ambulators (≥0.44 m/s) showed the largest difference between 10 Meter Walk Test and 6 Meter Walk Test speeds (0.21 m/s; 22% of 6M speed) and those entering the program as non-ambulators showed very little difference (0.02 m/s; 23% of 6 Minute Walk Test speed). Final gait speeds on the 6 Minute Walk Test were 83% of final gait
speeds on the 10 Meter Walk Test for the total sample; 85% for those starting non-ambulatory; 84% for the slow ambulators and; 81% for the fast ambulators. The largest mean difference between the 6 Meter Walk Test final gait speeds and 10 Minute Walk Test final gait speeds were found for the fast ambulators (≥0.44 m/s) 0.22 ± 0.22 m/s and the smallest mean difference was found for the initial non-ambulators 0.04 ± 0.16 m/s (Figure 11). Interestingly, 34 of 169 (20%) final speeds were higher for the 6MWT compared with 16% found at initial evaluation. On average, those that walked faster on the 6MWT than the 10MWT at discharge had gait speeds of 0.45 ± 0.34 m/s and 0.36 ± 0.31 m/s, respectively (Table 13).

![Final Gait Speed 10M vs 6M](image)

Figure 10. Comparison of gait speeds at discharge calculated from the 10 Meter Walk Test and the 6 Minute Walk Test for each functional category as described by van Hedel ¹: 1) Non-ambulators (0 or NT); 2) Slow Ambulators (0 to < .44); 3) Community Ambulators (≥ .44); and 4) total (n=213). The largest difference in gait speeds occurred for the community ambulators while the smallest difference occurred for the initial non-ambulators.
Figure 11: Mean difference in gait speeds at discharge between the 6 Minute Walk Test and 10 Meter Walk Test (10MWT speed – 6MWT speed) for each functional category as described by van Hedel: 1) Non-ambulators (0 or NT); 2) Slow Ambulators (0 to < .44); 3) Community Ambulators (≥ .44); and 4) total (n=169). Positive values indicate that mean short bout gait speed was faster than long bout gait speed for all groups.
Table 13. Comparison of mean gait speed ±SD at discharge for subjects that walked faster on the 10 Meter Walk Test or faster on 6 Minute Walk Test.

<table>
<thead>
<tr>
<th></th>
<th>10MWT faster at DC</th>
<th>6MWT faster at DC</th>
</tr>
</thead>
<tbody>
<tr>
<td># and % of subjects</td>
<td>135(80%)</td>
<td>34(20%)</td>
</tr>
<tr>
<td>Mean gait speed 10MWT ± SD</td>
<td>0.80 ± 0.54 m/s</td>
<td>0.36 ± 0.31 m/s</td>
</tr>
<tr>
<td>Mean gait speed 6MWT ± SD</td>
<td>0.62 ± 0.43 m/s</td>
<td>0.45 ± 0.34 m/s</td>
</tr>
<tr>
<td>Mean difference between 10MWT and 6MWT</td>
<td>0.18 ± 0.17 m/s</td>
<td>0.08 ± 0.11 m/s</td>
</tr>
</tbody>
</table>

Discussion

Those entering the program walking ≥ 0.44 m/s typically attained higher gait speeds (1.21 ± 0.43 m/s) over fewer sessions (~41) than those that entered the program as non-ambulators (0.30 ± 0.36 m/s within ~92 sessions). Although absolute gains were similar between functional groups (0.31-0.35 m/s), relative gains were highest for the non-ambulators and the slow ambulators (<0.44 m/s). This indicates that subjects with chronic motor iSCI respond differently to Locomotor Training based on their functional ambulation ability at enrollment. Many of those entering the program as non-ambulators did not ambulate after Locomotor Training. The non-ambulators that become ambulators require twice as many sessions as people who enroll as fast walkers yet attain peak speeds that are 75% slower. Fast ambulators (≥ 0.44 m/s) at enrollment tend to gain faster speeds much quicker. This may help guide clinicians in resource utilization, time allocation, treatment planning and prognosis based on how patients present at initial evaluation. Also, future studies may look closer at the sub-group of subjects that never ambulate following Locomotor Training. It is possible that this group may have unique
characteristics such as high spasticity, low motor scores, poor sensation or a combination of these that prevents them from responding to Locomotor Training.

**Where in the Treatment Duration does Peak Gait Speed Occur?**

Subjects able to ambulate by discharge (n=176), typically obtained peak gait speeds around 72% to 82% of the total treatment duration regardless of functional ambulation category (Figure 2). At first glance this appears appropriate and expected based on typical physical therapy discharge criteria, where plateau of functional gains indicates readiness for discharge. Subjects that show gains in gait speed up until their “peak speed” and then plateau or slow slightly at subsequent re-evaluations would be discharged from the program. Such a strategy appears to occur in the NRN given that peak speed occurs in advance of discharge by 18-28% on average across functional classifications. However, on closer inspection of the overall sample, it is surprising to note that 64% (112/176) of subjects achieved peak gait speeds at discharge. The same trend was found for each functional category as well (see Table 12). In fact, there was typically a significant gain in gait speed during the final treatment period, especially for community ambulators (0.30 m/s). Thus, it appears that most people were discharged from the NRN while still making meaningful gains in gait speed. Importantly, those subjects obtaining peak gait speeds at the final evaluation certainly appear to have the potential to continue to improve with further Locomotor Training given that gains were about 3 to 5 times higher than the MID.

Discharge while making progress may be explained by several factors. Perhaps the fact that treating patients in the NRN occurs for such long durations is not currently the standard of practice and limitations of insurance reimbursement may have forced early discharge. It may be reasonable to assume that the community ambulators, although still making gains in gait speed at discharge evaluation, may have recovered sufficient gait
speed to equal their pre-injury functional status. Normal gait speed has been reported to be 1.31 m/s and this group achieved mean peak gait speeds of 1.21 m/s. However, this does not explain the findings for the other groups.

Our study treated subjects for longer overall treatment durations and provided more sessions than what is typically found in related studies analyzing gait speed gains for SCI with Locomotor Training. Most similar studies rarely treated subjects longer than 60 sessions, whereas our overall average was 60 sessions and the non-ambulators received an average of 67 sessions to achieve their peak gait speed with a total average treatment duration of ~92 sessions. It may be that in current clinical practice we are not providing those with chronic motor iSCI with a high enough dose of Locomotor Training to induce maximal gains in locomotor ability, especially those initial non-ambulators. Future studies may consider increasing the number of sessions or treatment durations for chronic iSCI, especially for those that are non-ambulatory in order to better capture maximal gains in gait speed as well as maximize the functional abilities of the subjects.

**10MWT and 6MWT Gait Speed Comparisons**

Overall final gait speeds were higher during the 10MWT than the 6MWT but those that entered the program as fast ambulators (≥ 0.44 m/s) showed the largest difference between 10MWT and 6MWT speeds (Figure 10,11). The non-ambulators and slow ambulators generally ambulated shorter distances on the 6MWT so it is not surprising that gait speeds achieved on the 10MWT and the 6MWT were similar for these groups. Also, since subjects in the fast ambulator (≥ 0.44 m/s) category are more likely to be ambulating in the community, their ambulation endurance should be higher than subjects in the other two functional groups; hence they should be more likely to sustain higher gait speeds for longer distances. In general, this is true for our sample, whereby the mean
6MWT (long distance) speeds for fast ambulators were higher than 10MWT (short distance) speeds for the other two groups. It might be surprising, however, that this difference in speeds was largest for those that enter the program ambulating relatively fast. Barbeau found similar results with acute iSCI subjects from the SCILT trial where no significant difference in speeds between the 15.2 Meter Walk Test and the 6 Minute Walk Test were found except when a threshold of 0.9 m/s was reached\textsuperscript{81}. This may be explained by the fact that as certain subjects are able to walk longer following Locomotor Training, levels of endurance, individual subject characteristics, and responsiveness to Locomotor Training become increasingly variable. On average, after locomotor training, the ability to sustain higher gait speeds for longer distances becomes increasingly difficult especially for the community ambulators. For those ambulating at community speeds, it may be valuable to compare 10MWT and 6MWT speeds pre- and post-intervention as an indicator of improvement in endurance. A decrease in the difference between the 10MWT and 6MWT speeds or an increase in the percent of subjects walking faster on the 6MWT than the 10MWT indicates an improvement in endurance, specifically the ability to sustain higher gait speeds for longer distances.

It appears that Locomotor Training not only increases overall walking endurance (distance) but also increases the ability of some subjects to cover greater distances faster. Indeed, we found that 20% of subjects walked faster during long bout locomotion than short bout locomotion after training. Although past studies have reported no difference between 10MWT and 6MWT speeds measured for those with SCI\textsuperscript{1,81}, our study does not support this for chronic iSCI following Locomotor Training. Instead, our results support the notion that the 6MWT may be a better measure of community ambulation than the 10MWT especially for those ambulating at community speeds. The sustainability of higher gait speeds for longer distances may be of value in indicating true community endurance. Hence, short distance 10MWT speeds should not be considered a surrogate for long bout locomotor tests.
Limitations

A primary limitation of this study was that gait speed alone may not be an accurate determinant of functional or locomotor independence for people with incomplete SCI. Scientists propose that a single measure is probably insufficient to reflect recovery of ambulation while others support the use of only one gait measure. Recently a call for the use of a combination of outcome measures occurred in order to accurately describe the complexity of locomotor recovery in terms of gait speed, gait quality and functional independence in the community and the home. Unfortunately, performing multiple tests and measures may be too time consuming and impractical in our current rehabilitation environment. Many studies that utilized BWSTT for treatment of incomplete SCI to induce walking used gait speed as a primary outcome measure to show improvement in ambulation. Also, walking speed has been validated as a predictor of ambulation ability in this population. Therefore, although gait speed may not be the best descriptor of overall gait quality and ability in the SCI population, it may be a practical and inexpensive estimation of independent functional walking ability.

A second limitation of this study is that our findings only generalize to people with higher potential for recovery (ie ASIA C or D). The efficacy of Locomotor Training and predictive factors for functional recovery in people with more severe injuries such as AIS A or B remain undetermined.
Chapter 5 – Conclusions

To conclude, manual-assisted Locomotor Training improves gait speed, distance, balance and functional ambulation ability in individuals with chronic motor incomplete SCI. Sensory and motor scores derived from the ASIA examination and AIS classification may be poor indicators for recovery of walking ability and care should be taken when using them to determine treatment efficacy or functional improvement following Locomotor Training. Functional classification based on gait speed as described by van Hedel \(^1\) may be a more effective way to determine treatment efficacy or functional improvement following Locomotor Training. Also, different functional severities may require different doses of Locomotor Training to maximize locomotor abilities and this should be considered when determining if an individual has reached maximal locomotor gains or determining potential for recovery. Lastly, speeds derived from the 6MWT may be a better indicator of community ambulation ability than the 10MWT and each test describes different domains of walking ability in those with chronic incomplete SCI following Locomotor Training.

Clinical Implications

These findings can help guide clinicians in determining appropriateness of Locomotor Training for their patients as well as determining expected overall treatment duration, potential locomotor outcomes and allocation of resources to maximize locomotor outcomes as efficiently and effectively as possible.
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Ref Type: Unpublished Work


Ref Type: Unpublished Work


