Spasticity and Pain After Spinal Cord Injury: Relationships to Physiological, Functional, and Quality of Life Measures

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SPASTICITY AND PAIN AFTER SPINAL CORD INJURY:
RELATIONSHIPS TO PHYSIOLOGICAL, FUNCTIONAL, AND
QUALITY OF LIFE MEASURES

By
Jacqueline Anne Tibbett

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of the University of Miami
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SPASTICITY AND PAIN AFTER SPINAL CORD INJURY:
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QUALITY OF LIFE MEASURES

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Spasticity and chronic pain are both prevalent consequences of spinal cord injury (SCI), are commonly considered problematic, and are associated with reduced quality of life after SCI. This study investigated factors that contribute to the perceived impact of spasticity on daily life and how pain and spasticity are related. Analysis to characterize the strength of relationships between the impact of spasticity on life and physiological, environmental, and psychosocial factors can aid in identifying factors most strongly related to negative or positive impacts of spasticity. These factors may become candidates for experimental interventions aimed at reducing the problematic impact of spasticity on life. Therefore, the objective of this dissertation work was to improve understanding of the problematic impact of spasticity on life by characterizing associations between physiological, psychological, and functional measures of spasticity and pain in persons with SCI.

A need exists to focus spasticity research on its problematic aspects. Spasticity is commonly reported to interfere with daily activities such as transfers between seats, though spasticity has also been reported to be helpful for activities such as transfers. Characterizing the strength of relationships between physiological aspects of spasms
during transfers with the perceived impacts of spasticity can help guide spasticity research towards physiological aspects most related to problematic impacts. In Chapter 2, relationships between spasms evoked in a quadriceps muscle by seating transfers, the perceived impact of spasticity on activities of daily living, and clinically-rated spasticity severity were examined in persons with SCI and spasticity. There were no significant associations between the perceived impact of spasticity on daily activities and spasm duration, spasm magnitude, or clinical extensor spasticity score. However, the inter-day reliability of spasm magnitude and duration measured with electromyography was good to excellent, and spasm duration was positively associated with a clinical rating of extensor spasticity. The results imply that, for our non-ambulatory participants, involuntary muscle activity in quadriceps is not a strong determinant of the impact of spasticity on activities of daily living. Exploring other factors beyond physiological factors, such as pain and psychological characteristics, may lead to better understanding of how persons with SCI perceive the impact of spasticity on their lives.

Although the role of psychological factors in people with SCI and chronic pain is well-studied, their associations with the psychosocial impact of spasticity is largely unexplored. Spasticity is often experienced by individuals who also experience various chronic pain conditions. Spasms in these individuals can therefore cause or exacerbate pain, but little is known about how these sequelae of SCI influence each other. Interactions between pain, spasticity, and psychosocial impact are likely and need clarification in order to understand better how spasticity affects daily life. In Chapter 3, relationships between chronic pain and spasticity after SCI were examined with respect to severity, impact on daily life, and psychological factors. Significant relationships
between the severity of pain and spasticity, and between problematic impact of pain and of spasticity on daily life were found. Multiple factors explained variance in two measures of problematic impact of spasticity; specifically, greater self-rated spasticity severity, less resilience, greater time since injury, and greater difficulty of dealing with pain were associated with greater problematic impact of spasticity on life. In addition, persons who experienced painful spasticity had significantly higher overall chronic pain severity and more problematic impact of spasticity on sleep than persons who did not experience painful spasticity. The results suggest that spasticity and pain are strongly interrelated and painful spasticity may exacerbate chronic pain in persons with SCI. Another implication of the present studies is that interventions that target psychosocial factors may result in improved management of spasticity and pain after SCI.
DEDICATION

I dedicate this dissertation to the memory of my dear friend Jessica Palmieri. Jessica passed away from a chronic health issue decades too soon on September 30, 2017. During her last months of life, I witnessed many flaws in the American healthcare system. I strive to do Jessica’s kind soul justice by working towards better integration within American healthcare.

I would also like to dedicate this dissertation to the research participants who overcome many obstacles to participate studies like mine with the goal of improving quality of life for people living with spinal cord injuries.
ACKNOWLEDGEMENTS

So many people have helped me along this multi-year process. I must start by thanking my mentors, both planned and adopted. Both Dr. Edelle Field-Fote and Dr. Eva Widerström-Noga have believed in me, stood up for me, supported me, and given me freedom to follow an unconventional path. I have been continuously impressed by their knowledge and skills inside and outside of research. Thank you to Dr. Widerström-Noga for taking on the large responsibility of supporting an unplanned Ph.D. student without ever making me feel unwelcome. I must also thank my second adopted mentor, Dr. Christine Thomas; without her generous help and constructive feedback, I would not have made it through this Ph.D.

Thank you to my entire committee for their questions and support for my dissertation, despite its twists and turns. I couldn’t have asked for a more rigorous but caring scientist than Dr. Ellen Barrett to chair my committee. Thank you to my external examiner Dr. Mark Bishop for taking the time and effort to support my work.

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I would also like to thank my research participants; their willingness to participate and share their experiences despite daily obstacles is inspirational. Additionally, The
Miami Project to Cure Paralysis has been exceedingly generous in supporting me and I hope that my professional work will improve quality of life for persons in need.

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LIST OF ABBREVIATIONS

ADL: Activity of daily living
CBT: Cognitive behavioral therapy
CGRP: Calcitonin gene-related peptide
EMG: Electromyography
GABA: gamma-Aminobutyric acid
ICF: International classification of functioning in health and disability
MAP: Mitogen-activated protein
MPI-SCI: Multidimensional pain inventory for spinal cord injury
NMDA: N-Methyl D-Aspartate
P Difficulty: Difficulty dealing with pain
P Interference: Pain life interference subscale
P Severity: Pain severity subscale
SCATS: Spinal cord assessment tool for spastic reflexes
SCI: Spinal cord injury
SCI-SET: Spinal cord injury spasticity evaluation tool
S Difficulty: Difficulty dealing with spasticity
S Interference: Spasticity life interference subscale
SPASM: Support programme for assembly of a database for spasticity measurement
S Severity: Spasticity severity subscale
CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction to spasticity and pain after spinal cord injury and biopsychosocial models

An estimated 285,000 Americans live with a spinal cord injury (SCI), and about 17,500 more sustain injuries each year. SCI is caused by traumatic injury or damage to the spinal cord and results in impairment of sensory, motor, and autonomic function. Many chronic secondary conditions often result from injury, including bladder and bowel dysfunction, spasticity, pain, and pressure ulcers. Among the top-ranked problematic sequelae of SCI are spasticity and pain; both are considered difficult to deal with by significant portions of those living with SCI. Chronic pain interferes with life activities and participation and negatively affects quality of life. In some situations, such as for dressing, spasticity can be considered helpful, however it is more commonly reported to interfere with life activities and also has a negative impact on quality of life.

The biopsychosocial model is a theoretical and practical guide that attributes disease and health states to complex and non-linear interactions between biological, psychological and social factors. The concept was engendered by George Engel in the 1970s in response to the increasing dominance of a reductionist biomedical model in the 20th century. Engel embraced a systems viewpoint that straddled reductionism and holism but espoused neither: phenomena were not solely a product of molecular interactions nor solely a manifestation of ephemeral energies. As Borrell-Carrio et al. explain:

Rather, [mental and social phenomena] would be considered emergent properties that would be highly dependent on the persons involved and the initial conditions with which they were presented, much as large weather patterns can depend on initial conditions and small influences.
Relationships between factors in biopsychosocial models are generally not considered unidirectional. In fact, a hallmark of the biopsychosocial model is reciprocal determinism.\textsuperscript{14} The model has developed over time; for example, some believe that although interactions are non-linear, linear approximations must be made between factors for making treatment decisions.\textsuperscript{12}

In 2001, the World Health Organization published a biopsychosocial framework and classification system, called the International Classification of Functioning in Health and Disability (ICF).\textsuperscript{15} This conceptual framework and classification system provides a language and tools for healthcare professionals, researchers, economists, and policy makers, with the goal of facilitating achievement of the fullest life for individuals.\textsuperscript{16} In this model, “functioning” is the result of interactions between aspects of a health condition and contextual factors (see Fig 1.1). Health condition domains of the ICF model are divided into body structures and functions (anatomy and physiology), activities (tasks executed by an individual), and participation (an individual’s involvement in life situations). Contextual factors interact with each of these domains and are divided into environmental (including physical and social settings in which an individual lives) and personal (including sociodemographic characteristics, behavior patterns, and factors that influence how the disability is experienced).\textsuperscript{16}
Figure 1.1: Simplified biopsychosocial models applied to health conditions. (Top) Biological, psychological, and social domains are facets of a health condition and are interrelated themselves. (Bottom) Simplified diagram representing the domains of the World Health Organization’s International Classification of Functioning in Disability and Health. All domains are part of a health condition and are interrelated.
For chronic pain, the biopsychosocial model is the most widely accepted perspective and guide to understanding and treatment. However, for spasticity, the primary research and treatment focus has been on the physiological aspects rather than understanding the psychosocial aspects of spasticity. Research and treatment focus primarily on spasticity severity rather than on its impacts on daily life, including activity limitations and participation restrictions. However, to achieve optimal functioning, all domains of a health condition should be considered.

Characterizing the strength of relationships among factors in different domains may be useful for improving the treatment of problematic aspects of health conditions. Although relationships are viewed as non-linear in the biopsychosocial model, linear approximation is an important heuristic for making treatment decisions. Thus, if a factor is strongly and positively correlated with a negative health impact and that relationship is causal, downregulating that factor is likely to attenuate the negative impact.

In this dissertation, I attempt to further the understanding of spasticity within the biopsychosocial perspective and examine relationships between spasticity and pain. I will accomplish this in part by determining the strength of linear correlations between specific physiological and psychosocial factors related to spasticity and pain. Additionally, I will address how the well-researched biopsychosocial understanding of chronic pain after SCI can inform spasticity research. Though my research studies in this dissertation did not examine mechanisms of pain and spasticity, the mechanistic underpinnings of these conditions are important to understand. Examination of the existing literature regarding neuropathic pain and spasticity after SCI reveal that these
sequelae have many similar pathophysiological underpinnings. Additionally, a high co-
occurrence of chronic pain and spasticity after SCI\textsuperscript{7} suggests that the same psychosocial factors may play a role in both conditions.

1.2. Physiology of spasticity

1.2.1 Definition of spasticity

Spasticity is a collection of signs and symptoms resulting from an upper motor neuron lesion. The definition is still debated, likely because multiple mechanisms underlie involuntary motor activity after upper motor neuron injury.\textsuperscript{19} The traditional definition by Lance as a “velocity-dependent resistance to passive stretch”\textsuperscript{20} limits the focus to aspects of spasticity related to hyperactivity mediated by input from large Ia proprioceptive fibers and is commonly seen as too narrow.\textsuperscript{21} Inappropriate, involuntary motor activity may also occur in response to both proprioceptive and cutaneous afferent input.\textsuperscript{22,23} Some consider that spasticity includes passive elements conferred by changes in musculoskeletal architecture after injury,\textsuperscript{19,24,25} though structural changes in muscles are excluded from most definitions of spasticity.

For the purposes of this clinically-oriented dissertation that emphasizes the perspective of the person with spasticity, an inclusive definition will be utilized. An inclusive definition better matches wide-ranging nature of spasticity as characterized by those who experience it.\textsuperscript{26} The Support Programme for Assembly of a database for Spasticity Measurement (SPASM) consortium, which focuses on best practices and standardization for spasticity measurement, endorses the following definition: Spasticity is “disordered sensori-motor control, resulting from an upper motor neurone lesion, presenting as intermittent or sustained involuntary activation of muscles.”\textsuperscript{27,28} The
definition includes all neurological processes but excludes stiffness due to biomechanical changes. When engaging with participants, I presented Adams and Hick’s definition, which is in accordance with the SPASM definition:

When I talk about ‘spasticity symptoms’ I mean:
   a) uncontrolled, involuntary muscle contraction or movement (slow or rapid; short or prolonged)
   b) involuntary, repetitive quick muscle movement (up and down; side to side)
   c) muscle tightness, and
   d) whatever you might describe as ‘spasms’

1.2.2 Clinical presentations of spasticity after SCI

The most common clinical signs of spasticity include an exaggerated stretch reflex, increased tone, and muscle spasms in response to proprioceptive and/or cutaneous input. Persons with SCI report spasticity can be triggered most commonly by changing position, performing daily physical activities, bladder and bowel activity, emotional tension or stress, skin problems, vibration, cold and heat, and fatigue. Spasticity after SCI often involves multi-muscle and multi-joint responses, indicating the involvement of multiple types of reflex circuits. The most common manifestations of spasticity in the lower extremity after SCI are flexor spasms, extensor spasms, and clonus at the ankle.

Extensor spasms. Extensor spasms are the most common type of spasms reported by persons with SCI. In two studies, 82% and 84.6% of participants with spasticity due to SCI reported having extensor spasms. The typical pattern of extensor spasms in the lower extremity involves activation of muscles at the hip, knee extension, and plantarflexion, and spasms are often prolonged. The multi-joint phenomenon of lower extremity extensor spasticity is likely tied to dysregulation of locomotion networks.
after SCI. Improvements in lower extremity spasticity have been seen with locomotor training and sensory stimulation that activates locomotor networks.\textsuperscript{35–38}

Contraction of the quadriceps muscle group, which contributes to knee extension and hip flexion, is an integral part of extensor spasms. Experimentally, imposed hip extension\textsuperscript{31} as well as knee extension\textsuperscript{32} triggers extensor spasms in persons with SCI. Extensor spasms involve not only activity at multiple joints but also have a high rate of agonist-antagonist co-activation at knee and ankle joints.\textsuperscript{31} A high ratio of agonist and antagonist co-contraction is common in SCI, seen during lower extremity spasms in persons with complete SCI\textsuperscript{34} and during voluntary motor activity in persons with incomplete SCI.\textsuperscript{39}

**Flexor spasms.** Flexor spasms are somewhat less common than extensor spasms. In two studies, flexor spasms were reported by 68\% and 69.2\% of people with spasticity due to SCI.\textsuperscript{9,10} The typical response pattern involves flexion at multiple joints of the lower extremity.\textsuperscript{40} Persons with SCI report that flexor spasms are most common at night when lying flat and are most likely to interfere with sleep.\textsuperscript{10} Unlike extensor spasms and clonus, flexor spasms are commonly reported to occur when participants are in a stable body position for a long period of time.\textsuperscript{9}

Although they can seem to occur spontaneously, flexor spasms are likely triggered by activation of sensory afferents,\textsuperscript{41} and may be a result of dysregulation of flexor withdrawal reflexes and locomotor circuitry.\textsuperscript{42} Flexor withdrawal reflex responses can be elicited by cutaneous electrical stimulation of the foot in neurologically intact persons.\textsuperscript{43} In persons with SCI, this reflex response is hyper-excitable, with lower thresholds, longer duration, and increased area of the lower extremity responsive to
electrical and even mechanical stimuli. Thus, the flexor reflex response is thought to contribute to the flexor spasm pattern seen after SCI. Additionally, a convergence of locomotor circuitry on flexor reflex afferent pathways is thought to contribute to the pattern in persons with SCI. Evidence for this idea includes studies finding that imposed ankle rotation and hip extension (non-noxious stimuli) can trigger hip flexion, and that the flexor response is dependent on limb position.

**Clonus.** Clonus involves multiple repetitive short muscle contractions or “beats,” typically having a 5-8hz frequency. Clonus typically involves a single joint and occurs most often in ankle plantarflexors after SCI. Ankle plantarflexor clonus was reported in 80% of a sample of 60 individuals reporting spasticity symptoms after SCI. Although the mechanisms of clonus are still debated, activation of dysregulated locomotor circuitry by proprioceptive input plays a role in sustained clonus. Training via operant conditioning can improve voluntary activity and decrease ankle plantarflexor reflex excitability in persons with SCI, possibly by restoring sources of inhibition to maladapted reflex pathways.

**Perceived spasticity.** While clinicians and researchers dispute the definition of spasticity, people with spasticity also have varying definitions and experience of spasticity. In a series of semi-structured interviews of participants in an inpatient setting with multiple neurologic disorders and spasticity, Bhimani et al found that participants admitted they did not fully understand the word spasticity. They used a range of words to describe both tone and spasm. There was general ambiguity and a wide range of reported terms, definitions, and symptoms. Participants also felt that understanding the spasticity condition itself was “elusive.” One participant said:
Someone who hasn’t experienced severe spasticity has no frame of reference... every person feels it differently and although you can put inside the clinical box so to speak, it’s different for every person and their experiences that is different.

1.2.3 Basic mechanisms of spasticity

Clinical patterns of spasticity after SCI and other upper motor neuron disorders involve one or more basic mechanisms of spasticity. Altered supraspinal drive and secondary changes in cell properties contribute to the basic mechanisms of spasticity. These mechanisms may increase motoneuron excitability or impair inhibition of motoneurons to result in increased involuntary muscle activity.

**Reduced descending source of inhibition of Ia-mediated reflexes.** Damage to the corticospinal pathways directly results in reduced voluntarily activation and also reduced inhibition of motor systems. Of particular relevance to spasticity, damage to the corticospinal pathways reduces their input to interneurons that inhibit the monosynaptic Ia-mediated stretch reflexes, resulting in poor Ia-mediated stretch reflex inhibition.

Disynaptic reciprocal Ia inhibition normally allows for relaxation of an antagonist when agonist muscles are activated voluntarily. Reduced reciprocal inhibition has been implicated through neurophysiological testing as a pathway underlying the pathophysiology of spasticity, particularly in incomplete SCI. These studies demonstrate reduced reciprocal inhibition in persons with incomplete SCI, and that those with reduced inhibition also have more agonist/antagonist co-contraction.

**Reduced descending monoamine input and persistent inward currents.** In addition to corticospinal tract damage, SCI damages descending serotoninergic fibers and reduces their contacts on lumbar motoneurons. This damage can change motoneuron properties and contribute to spasticity: motoneurons adapt to reduced serotonin and other
monoamines (which normally facilitate activation of locomotor circuitry) by inserting constitutively active receptors, including the serotonin 5HT$_{2C}$ receptor.$^{55,56}$ The constitutively active receptors increase motoneuron excitability through persistent inward sodium and calcium currents.$^{55}$ Persistent inward currents contribute to prolonged stable depolarizations called plateau potentials.$^{57}$ Plateau potentials and receptors involved in maintaining persistent inward currents, including constitutively active 5HT$_{2C}$ receptors, have been linked to spasticity in animals and humans.$^{55,56,58}$

**Impaired intraspinal inhibition due to chloride dysregulation.** One mechanism linked to spasticity involves altered chloride homeostasis after injury.$^{59}$ The inhibitory effect of ionotropic chloride channels (GABA$_A$ receptors and glycine strychnine receptors) relies on a chloride equilibrium potential near or below the resting potential of the neuron. Changes in chloride transporter expression/activation leading to a positive shift (around 10 mV) in chloride equilibrium potential have been found in animals with hyperreflexia or spasticity after SCI.$^{60-62}$ A more positive chloride equilibrium potential reduces the ability of GABA and glycine to inhibit neurons. Interestingly, Redondo-Castro et al.$^{54}$ found more abundant inhibitory inputs (identified by the synaptic inhibitory marker gephyrin) on lumbar motoneurons after incomplete thoracic SCI in adult rats, and this may indicate attempted compensation for impaired inhibition.

**Afferent sprouting.** Yet another secondary change implicated to underlie spasticity is collateral sprouting of sensory afferents, which may result in aberrant sensory and sensorimotor responses.$^{54,63,64}$ When the corticospinal tract is cut in animals, proprioceptive afferents sprout into denervated spinal gray matter, and markers of
proprioceptive Ia terminals are increased on motoneurons. Accompanying this plasticity are electrophysiological correlates of hyperreflexia (reduction in rate-dependent depression of the H-reflex). Similarly, after mid-thoracic transection in rats, there is site and time-dependent sprouting of multiple types of afferent fibers. For example, myelinated afferent arbors sprout into pain processing areas of the lumbar dorsal horn.

1.3. Physiology of pain

1.3.1 Definition of pain

Pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” Pain results from transduction, transmission and modulation of sensory information, and is filtered through personal and psychological factors such as genetics, prior learning, psychological state, and sociocultural influences. Importantly, pain is a subjective experience that requires perception. Pain is different from nociception, which is the neural process by which noxious stimuli are encoded. Nociception may result in pain sensation, or it may not. Additionally, nociception may have autonomic or motor outcomes.

Melzack and Casey proposed three necessary components in the subjective experience of pain: sensory-discriminative, motivational-affective, and cognitive-evaluative. Their proposal was based on evidence from experimental studies and clinical disorders of pain processing that indicated that each of the three components is comprised of different but interconnected parts of the nervous system. The sensory-discriminative component, related to the spatiotemporal analysis of sensation, involves mainly the spinothalamic projection system. The motivational-affective component, which activates pain response patterns based on sensory and cognitive input, involves the paramedial,
reticular, and limbic systems. The cognitive-evaluative component, comprised by neocortex structures, is the higher-level central processing that can modulate the other two components based on things such as prior history, anticipation, and evaluation of meaning.

Melzack and Casey\textsuperscript{67} considered “pain” to be a function of the interactions of all three aforementioned components. Melzack’s more current theories of pain still involve these three components but take a more complex understanding of the body and mind as a highly integrated “neuromatrix.”\textsuperscript{17} Importantly, the neuromatrix theory does not require somatosensory input to produce pain. This is particularly relevant to neuropathic pain after SCI, in which pain may be experienced in the absence of peripheral sensory input.

**Chronic pain** has no standardized definition,\textsuperscript{68} but is commonly defined or operationalized as persistent pain lasting at least 3 months or recurrent episodes of pain extending over months or years.\textsuperscript{17} Chronic pain has been recognized as distinct from acute pain since the 1970s,\textsuperscript{68} and it develops and is maintained through specific mechanisms. Because pain involves multiple components of the mind and body, chronic pain can be thought of as an all-encompassing experience. Pain is a powerful driver of behavior\textsuperscript{17} and therefore persistent pain can broadly influence one’s life. Drawing from Talcott Parsons’ work, Gatchel & Turk\textsuperscript{14(p4)} said of chronic pain:

Its continuous presence creates widespread manifestations of suffering, including demoralization and affective disturbance; preoccupation with pain; limitation of personal, social, and work activities; increased use of medications and of health care services; and a generalized adoption of the sick role (Parsons 1958).
1.3.2 Clinical presentations of chronic pain after SCI

Chronic pain after SCI is common, heterogeneous, and frequently severe; greater pain severity is usually associated with lower quality of life and life satisfaction. Chronic pain has been reported in different studies to be present in anywhere from 26-96% of persons with SCI. However, when all different chronic pain types that occur after an SCI are included, the most commonly reported frequencies are 60-80%.

Pain after SCI can be classified using a standard taxonomy published by Bryce et al. (See Table 1.1). The classification system divides pain into four types: nociceptive pain, neuropathic pain, other pain, and unknown pain. Nociceptive and neuropathic pain are the major types, however sometimes pain does not fit into the definition of either and must be classified as “other” or “unknown.” Individuals may experience more than one pain problem simultaneously, and those multiple pains may be of any type.

**Nociceptive Pain.** Nociceptive pain involves the activation of nociceptors via noxious stimuli or inflammatory molecules. Nociceptive pain mechanisms after SCI are the same as in the non-injured population, but some nociceptive pains are unique to or typical in the SCI population (See Table 1.1). For example, some individuals with SCI may experience recurrent visceral nociceptive pain due to frequent constipation as a secondary consequence of injury. The most common subtype of chronic nociceptive pain after SCI are musculoskeletal pains, which are often related to wheelchair or adaptive device use. Nociceptive musculoskeletal shoulder pain is especially common, reported in 30-51% of the SCI population.

**Neuropathic Pain.** Neuropathic pain develops as a result of a lesion or disease of the somatosensory system. In contrast to nociceptive pain, neuropathic pain does not require activation of peripheral nociceptors, but does require current or past damage to
some part of the somatosensory nervous system. Neuropathic pain after SCI is particularly refractory to treatment, even to pharmacological treatments that are effective for neuropathic pain in other populations. Subtypes of neuropathic pain are separated based on anatomical distribution of pain (See Table 1.1) but also have characteristics distinct from each other.

Accurate diagnosis of neuropathic pain based on symptoms and signs can be challenging, and therefore adherence to the international classification guidelines is important for consistent diagnoses. Diagnostic criteria are listed in Table 1.1. For my research, a standard SCI neurological exam was performed through The Miami Project to Cure Paralysis, which identified sensory and motor neurological level of injury and completeness of spinal injury. I assessed other required and supportive criteria used in pain diagnosis through interview.

Other Pain or Unknown Pain. Pain that does not fit any of the pain syndromes above (e.g. fibromyalgia) or pain with symptomology of unknown pathology can occur in persons with SCI as it does in neurologically intact persons (See Table 1.1).
Table 1.1 Pain Types after SCI. Classification adapted from International Spinal Cord Injury Pain Classification by Bryce et al. Diagnosis Criteria adapted from Bryce et al., Treede et al., and Finnerup & Baastrup. I argue the idea that pain from muscle spasms are not exclusively nociceptive-type pain in Chapter 3.

<table>
<thead>
<tr>
<th>Pain Type</th>
<th>Diagnosis criteria</th>
<th>Subtype</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nociceptive</td>
<td>Supportive evidence 1. Relationship with tissue injury/pathology or noxious stimuli (e.g. triggered by certain movement or by food intake) 2. Occurs in area with at least some preserved sensation 3. Responds to anti-inflammatory or opioid medications 4. Sensation qualities of dull, aching or tender 5. Tenderness on palpation</td>
<td>Musculoskeletal</td>
<td>Tendonitis, Muscle spasms†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Visceral</td>
<td>Pain from bowel impaction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other nociceptive</td>
<td>Migraine</td>
</tr>
<tr>
<td>Neuropathic</td>
<td>Required evidence: 1. Damage to somatosensory system (confirmed via history and diagnostic test) 2. Sensory signs within a topographically plausible distribution for the type of injury Supportive evidence: 1. Pain onset within 1 year of nerve injury 2. No relationship to movement, inflammation or other sources of damage 3. Sensation qualities fitting at least 1 of 10 particular descriptors (e.g. tingling, pins and needles) 4. Allodynia or hyperalgesia in pain areas</td>
<td>At-level SCI (occurs within 1 dermatome above and 3 below neurological level of injury)</td>
<td>Pain from spinal root compression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Below-level SCI (occurs more than 3 dermatomes below neurological level of injury)</td>
<td>Pain from spinal ischemia or lesion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other neuropathic pain (not related directly to SCI)</td>
<td>Diabetic neuropathy</td>
</tr>
<tr>
<td>Other pain</td>
<td>No identifiable noxious stimulus, inflammation, or damage (other than SCI) to the nervous system.</td>
<td></td>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>Unknown</td>
<td>Fits no category above with any certainty and has unknown etiology</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1.3.3 Basic mechanisms of chronic pain after SCI

Neuropathic pain has been the focus of much of the mechanism-based research related to pain after SCI because it is particularly refractory to available treatments and usually persists over a person’s lifetime. In this section, I will primarily review research on neuropathic pain mechanisms after SCI, noting that some of these mechanisms may occur across different pain types. General mechanisms of chronic pain and their role in different pain types as outlined by Woolf\(^1\) are summarized in Table 1.2. As noted previously in basic mechanisms of spasticity, alterations in inhibition and secondary changes in cell properties contribute to chronic neuropathic pain phenomena.

**Reduced descending pain inhibition.** Many supraspinal descending pathways are involved in pain processing circuits.\(^2\) Injury to these pathways can directly decrease endogenous spinal pain inhibition, or indirectly induce changes in cells that lead to maintenance of pain.\(^2\) Impaired endogenous pain circuitry may increase both the presence and severity of either nociceptive or neuropathic pain.

One type of descending pathway, serotonergic pathways, play a major role as descending sources of pain inhibition.\(^2\) For example, a major pain inhibition circuit is the periaqueductal gray-rostral ventromedial medulla-spinal cord circuit.\(^3\) Serotonergic cells in the raphe magnus nucleus and the reticular formation of the rostral ventromedial medulla are activated by the periaqueductal gray and project primarily to dorsal horn pain processing lamina I and II via the dorsolateral fasciculus.\(^4\) However, the role of serotonin and other monoamines involved in pain modulation is complex and context-dependent; monoamines may be anti-nociceptive or pro-nociceptive.\(^2\)
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Involves</th>
<th>Occurs in Pain Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nociception</td>
<td>Noxious stimuli activates nociceptors</td>
<td>Nociceptive</td>
</tr>
<tr>
<td>Peripheral sensitization</td>
<td>Chemical factors (eg. ATP, kinins) act on peripheral terminals → Intracellular kinases activated → 3 * 1 * 0 * 1 of ion channels and receptors, transcription changes → Altered membrane excitability and characteristics</td>
<td>Inflammatory nociceptive and some neuropathic (eg. post-herpetic)</td>
</tr>
<tr>
<td>Central sensitization</td>
<td>Central nerve injury or high peripheral input to dorsal horn → Intracellular kinases activated → 3 * 1 * 0 * 1 of ion channels and receptors, transcription changes → Altered membrane excitability and characteristics</td>
<td>Inflammatory nociceptive, neuropathic, “other”</td>
</tr>
<tr>
<td>Ectopic excitability</td>
<td>Transcriptional changes after inflammation processes lead to “inappropriate” neural firing</td>
<td>Neuropathic</td>
</tr>
<tr>
<td>Structural reorganization (eg. afferent sprouting)</td>
<td>Peripheral nerve injury → Central terminal reorganization → Alldynia or sensitivity (Eg., low-threshold afferent terminals sprout in nociceptive areas of dorsal horn, leading to mechanical allodynia)</td>
<td>Neuropathic</td>
</tr>
<tr>
<td>Decreased Inhibition</td>
<td>Central nerve injury → Death or phenotype change in inhibitory neurons → Loss of inhibition in pain transmission pathways (pre and post-synaptic)</td>
<td>Neuropathic</td>
</tr>
</tbody>
</table>

**Impaired intraspinal inhibition due to chloride dysregulation.** As noted previously in spasticity mechanisms, altered chloride homeostasis has been implicated as an important contributor to neuropathic pain and allodynia and may explain functional failures of inhibitory neurotransmission after injury. Chloride transporters have been linked to depolarizing shift of chloride equilibrium potential in animal models of neuropathic pain. Failure of the GABA system to properly inhibit has been proposed...
as an explanation for pain hypersensitivity and increased responsiveness of wide dynamic range neurons, which are involved in the sensory-discriminative aspect of pain, to myelinated afferents.87,88

Increased activity of GABAergic and glycinergic neurons has been observed in multiple animal pain models, including peripheral and central neuropathic pain.54,89 The persistence of pain sensitivity despite higher inhibitory activity may indicate attempted compensatory mechanisms.

Central sensitization. Though hyperexcitability and central sensitization can occur in other types of chronic pain, these are common features of neuropathic pain (see Table 1.2). Central sensitization is defined as “increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input.”65 Nerve injury leads to activation of signaling pathways, including MAP kinase pathways. Activation of these pathways results in changes in transcription and phosphorylation of proteins.90,91 Notably, increased NMDA channel phosphorylation is a source of the neural hyperactivity seen in central sensitization, similar to learning and memory pathways.91

Hyperexcitability in dorsal horn neurons and sodium channels.
Electrophysiological evidence from animal models of neuropathic pain after SCI demonstrate that spinothalamic tract dorsal horn neurons are hyperexcitable.91,92 Populations of dorsal horn neurons show greater response to noxious stimuli and increased ectopic activity.91 Increased sodium currents contribute to hyperexcitable dorsal horn neurons.92 Upregulated voltage-gated sodium 1.3 channels and associated hyperexcitability were found in dorsal horns in “multireceptive” (putatively wide
dynamic range) neurons in rats with allodynia and hyperalgesia after SCI compared to control rats. Transitory reduction of voltage-gated sodium 1.3 channel expression also temporarily reduced allodynia and hyperalgesia.

**Hyperexcitability in supraspinal pain processing neurons.** In addition to the spinal cord, supraspinal pain and sensory processing areas can also become hyperexcitable. After severe thoracic SCI, thalamic neurons in rats underwent a change in responsiveness that corresponded with pain behavior; specifically, a significantly greater percentage of ventral and posterior thalamic neurons responded to noxious pinch in rats with allodynia compared to controls.

**Astroglia and microglia reactivity in spinal cord.** Studies in animals link increased glial activity in the dorsal horn to neuropathic pain and allodynia after injury. Markers of increased glial reactivity are seen in lumbar segments after incomplete thoracic injuries. A molecular inhibitor of astrocytic and glial activation attenuated allodynia and hyperalgesia in animal models of neuropathic pain. Dysregulation of chloride homeostasis after nerve injury has been linked to brain-derived neurotrophic factor release from activated microglia, although the effect of this neurotrophic factor in chloride homeostasis is context-dependent.

**Glial reactivity in the brain.** In a rat model of SCI, inflammatory changes in the thalamus, hippocampus, and cortex were accompanied by memory impairment and depressive-like behavior that was linked to classical (M1) microglial activation. In humans with SCI, studies using non-invasive brain spectroscopy suggest a role of glial activation in the brain in severe neuropathic pain. Persons with severe neuropathic pain had greater concentrations of the glial marker myo-inositol (measured as a lower
ratio of glutamate-glutamine to myo-inositol) in the thalamus\textsuperscript{96} and anterior cingulate cortex\textsuperscript{97} compared to those with less severe pain or no pain. Lower ratio of glutamate-glutamine to myo-inositol was correlated with greater pain severity.\textsuperscript{96}

**Afferent sprouting.** Multiple studies in rats with spinal injuries have demonstrated evidence of increased nociceptive afferent terminals throughout the dorsal horn, and this may lead to increased input to second-order pain neurons or new connections with neurons that are normally not excited by nociceptive afferents. After incomplete thoracic injuries in adult rats, density of nociceptive sensory afferents increased in the lumbar dorsal horn laminae I-IV, with calcitonin gene-related peptide (CGRP)-positive fiber density increased in laminae I and II.\textsuperscript{54} Additionally, increased CGRP-reactive fibers in laminae III-V have been demonstrated in all cord segments 2 weeks after mid-thoracic transection.\textsuperscript{64}

1.4. Concordance between pathophysiological mechanisms of pain and spasticity

The same or similar pathophysiological mechanisms may occur in both spasticity and pain. For persons with SCI, spasticity is greater in persons with pain compared to those without pain, and is furthermore greater in those with neuropathic pain compared to nociceptive pain.\textsuperscript{7} Some mechanisms that may underlie both spasticity and neuropathic pain after SCI are central sensitization and neuronal hyperexcitability,\textsuperscript{46,86,98} dysregulated chloride homeostasis,\textsuperscript{60–62,85} loss of supraspinal input to the cord\textsuperscript{54,58,99} and primary afferent fiber sprouting.\textsuperscript{54,63,64} Additionally, the role of serotonergic pathways from the brainstem may play an important role in changes in both ventral and dorsal horns: injury to descending serotonergic tracks may contribute to decreased endogenous pain inhibition\textsuperscript{82,99} as well as increased spasticity via altered motoneuron properties.\textsuperscript{58,100}
Most studies examine mechanisms of neuropathic pain or spasticity separately. However, in some of the references I have cited, mechanisms related to neuropathic pain and spasticity after nerve injury are examined in the same animals. For example, Tashiro et al.\(^6\) found that in rats with allodynia and spasticity after SCI, exercise induced upregulation of chloride exporter KCC2. This increased KCC2 after exercise was accompanied by behavioral, electrophysiological, and immunohistochemical evidence of both reduced spasticity and allodynia compared to rats without exercise, indicating that the same exercise treatment resulted in improvements in both conditions. Connections between spasticity and pain mechanisms are discussed further in Chapter 3.

### 1.5. Roles of psychosocial factors in pain and spasticity

Pain and spasticity commonly co-occur in the same individuals with SCI.\(^7\),\(^{101–104}\) Pain is reported to occur with spasticity with a high frequency.\(^{101–104}\) In a study by Andresen et al.,\(^7\) 73% of persons with chronic pain also reported spasticity symptoms, and 19 out of 20 participants I analyzed in Chapter 3 had both spasticity and chronic pain. Thus, psychosocial factors that have been demonstrated to play a role in the impact of pain on life may also play a role in the impact of spasticity on life as these conditions are commonly occurring in the same persons.

Much about the psychosocial aspects associated with chronic pain after SCI are similar to findings in heterogeneous chronic pain populations, on which there is a wealth of research.\(^{105,106}\) However, pain after SCI has some unique mechanisms, unique co-morbidities, and unique psychosocial aspects.\(^{107}\) Therefore, relevant chronic pain research on both SCI and non-SCI populations is presented here in order to describe the psychosocial aspects of pain after SCI.
Importantly, I use the term “psychological factors” in this dissertation as a general category that includes cognitions, beliefs, appraisals, psychological resources, strategies, emotions, psychological traits, and psychological states. Many psychological factors have been investigated in relationship to chronic pain. Common psychological factors studied include negative factors such as depression, anger, catastrophizing, fear, and anxiety, and positive factors including self-efficacy, resilience, adaptive coping strategies, and optimism. As reflected in the biopsychosocial model, psychological factors have reciprocal relationships with the chronic pain experience; these factors may precipitate or be a consequence of pain development, and may modulate pain.¹⁷

Psychosocial research related to spasticity is minimal. Most of the psychosocial research related to spasticity focuses on perceived spasticity severity and interference with physical activities but does not assess relationships of psychological factors to these perceptions. The majority of psychosocial spasticity research has been performed in SCI populations, however some relevant results from studies in persons with stroke, multiple sclerosis, and cerebral palsy will be included here.

Despite the fact that spasticity is not by definition an inherently cognitive and affective experience, as is the case with pain, an individual’s perception of spasticity may be influenced by similar psychological factors. However, limited research exists on the role of psychological factors in the perception of spasticity. Only one study¹⁰⁸ has assessed the strength of relationships between psychological factors and perceptions of spasticity after SCI. Voerman et al.¹⁰⁸ utilized the Illness Cognition Questionnaire¹⁰⁹ and coping strategies from the Utrecht coping list¹¹⁰ to assess psychological factors in persons with spasticity due to SCI. The coping strategy of ‘reassuring thoughts’ and the illness
cognition of ‘helplessness’ contributed significantly to variance in perceived level of spasticity, with more reassuring thoughts and less helplessness related to lower levels of perceived spasticity. These results were important to indicate that psychological factors may play a role in the perception of spasticity in ways that mirror their role in pain. In Chapter 3 of this dissertation, I focus on specific psychological factors of importance in chronic pain that may be related to perception of activity limitations and participation restrictions in spasticity.

1.5.1 Negative psychological factors and pain

**Depression and affective distress.** Pain, under standard definitions, involves negative emotions and therefore much research has focused on negative psychological factors. Notably, depressive disorders are common for those with chronic pain; present in about 40-50% of people with chronic pain. There is evidence for all different types of causal and non-causal relationships between depression and chronic pain. For example, a prospective study found that men with chronic low back pain had over 9 times the risk of developing major depression compared to matched controls. In another prospective study, depressive symptoms more than doubled the odds of developing pain years later. A third study found no direct relationship between pain and depression but found that perceived interference of pain with life and lack of self-control mediated the relationship between pain and depression.

Symptoms of anxiety and depression are often referred to and measured as affective distress. In this dissertation, I use an affective distress scale from the West-Haven Yale Multidimensional Pain Inventory, which has also been adapted for use in SCI. This subscale asks an individual to rate his/her feelings of irritability, depressed
mood, and tension. (The affective distress questions can be seen in the Multidimensional Pain and Spasticity Inventory in the Appendix.) Pain after SCI is associated with more affective distress. Affective distress is more likely in persons who report that pain interferes with activities.

**Catastrophizing.** Catastrophizing is an exaggerated negative orientation towards an actual or expected experience. Although it is part of a common coping questionnaire, it is generally not considered a coping strategy. Catastrophizing is associated with increased pain and pain behaviors, more disability, and psychological dysfunction, including depression.

### 1.5.2 Positive psychological factors and pain

Positive psychological factors tend to protect against emotional distress due to pain. They are often related to a pain sufferer’s ability to feel in control of their pain or life. Less research has examined the relationships between positive psychological factors and pain than on the association with negative factors. Yet, identifying the psychosocial factors and strategies that can protect against or reduce the impact of chronic pain can be useful for treatment. Training in cognitive, behavioral, and emotional strategies to improve coping ability have been used successfully as interventions for chronic pain, including pain after SCI. Use of these interventions will be discussed further in Chapter 4.

**Control beliefs.** Health locus of control “is the degree to which the individual believes health outcomes are primarily the result of his own actions (internal locus of control), luck or chance, or the influence of powerful others (external locus of control).” In studies in SCI, higher internal locus of control has been associated with
positive outcomes, while higher external locus of control has been associated with negative outcomes. In Chapter 3, I used a related measure, the life control subscale from the West-Haven Yale Multidimensional Pain Inventory. In Kerns et al and in our study, the life control subscale consisted of 2 questions about control over life in general: perceived “amount of control over life” and “ability to deal with problems” during the past week. (See Multidimensional Pain and Spasticity Inventory in Appendix) Rudy et al found that a combined score they called ‘self-control,’ which was comprised of the life control scale and two other control-related scales, significantly mediated relationships between chronic pain and depression.

**Resilience.** Resilience allows a person to positively adapt, or “bounce back” in the face of adversity. Resilience has been conceptualized in many ways: as a psychological trait, a collection of factors (including cognitive appraisals and behaviors), and the process of engaging in said psychological factors. The concept of resilience as a process rather than a trait emphasizes the idea that “resilience mechanisms” (such as active coping, finding benefit, engaging in positive interpersonal events) can be taught and learned. In the face of pain, some individuals may develop greater resilience to improve or maintain function. Greater resilience is associated with favorable health outcomes in pain populations and specifically in SCI populations. In persons with SCI, resilience is associated with less depression, less stress, and greater self-efficacy. Lower resilience was one of the factors predicting more difficulty dealing with pain after SCI. I measure resilience as a “factor” in Chapter 3 using the Connor-Davidson Resilience Scale, although resilience is a dynamic process of adaptation.
**Self-efficacy.** Self-efficacy is “the belief in one's competence to cope with a broad range of stressful or challenging demands.”\(^{129}\) It is highly related to resilience as well as to beliefs related to internal locus of control.\(^{17,124}\) Given their similarities, it is not surprising that outcomes for self-efficacy are generally similar to those for resilience. Self-efficacy is associated with positive physical and psychological outcomes, and increased self-efficacy after interventions is associated with improvements in pain, function and psychological adjustment.\(^{17}\) Craig et al.\(^{130}\) found that persons with SCI with high chronic pain levels have lower self-efficacy, and that self-efficacy mediates the relationship between chronic pain and depression.

A study of experimentally-administered pain by Bandura et al.\(^{131}\) suggests that self-efficacy can inhibit pain through both opioid and non-opioid mechanisms. In this study, training in cognitive strategies of pain control strengthened perceived self-efficacy over pain and reduced pain levels in individuals. Stronger perceived efficacy was related to greater opioid activation, but persons who were “cognitive copers” were also able to achieve some increase in pain tolerance even when opioid mechanisms were blocked by naloxone.

**Coping strategies.** Coping strategies for pain are specific efforts to deal with pain.\(^{132}\) More specifically, Lazarus and Folkman\(^{130(p141)}\) defined coping as “constantly changing cognitive and behavioral strategies to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person.” Particular pain coping strategies and beliefs of control over pain have been positively associated with better markers of healthy psychological functioning.\(^{118}\) In a longitudinal study of coping behaviors after SCI, “acceptance” was the most common coping strategy at both 3
months and 10 years after injury, followed by “active coping” and “reinterpretation.”
Particular coping strategies that were utilized 3 months after injury predicted 33% of the
variance in depression scores at 10 years. Specifically, more use of positive
reinterpretation as a coping strategy was predictive of less depression, whereas behavioral
disengagement was predictive of more depression.

1.5.3 Social factors and pain

Literature on social factors will not be discussed at length in this dissertation, but
it is important to note that social factors are highly related to psychological factors and
vice versa. For example, chronic pain sufferers may be blamed as “complainers” by the
medical system, family, or society, and they may as a result feel self or societal
resentment and other negative emotions. Experience of pain and pain-related outcomes
are different across sexes, and social gender roles influence these experiences and
outcomes. Indeed, the disproportionate number of males who receive spinal injuries
highlights that sex even influences the likelihood of experiencing SCI and therefore SCI-
related pain. Our research participants were 86% male, similar to national average.

Understanding factors that restrict social participation is important in SCI
rehabilitation research, including research on chronic pain after SCI. For example, some
may avoid activities with which their condition interferes. This may reduce participation.
Multiple components of the Multidimensional Pain Inventory, including the life
interference subscales I use in Chapter 3, ask questions related to the influence of pain on
interpersonal relationships and social participation. (See Multidimensional Pain and
Rather than focusing on sociodemographics and other social classifications, I focus on how persons with pain and spasticity perceive the impact of pain and spasticity on participation in life.

1.5.4 Psychological factors and spasticity

Spasticity and stress. Reciprocal determinism is a feature of the biopsychosocial model. However, not enough research has been performed on spasticity and psychosocial factors to understand how they influence each other. Self-report studies indicate that the relationship between spasticity and psychological factors related to stress may be bidirectional. For example, participants have reported that stress triggers spasticity and that spasticity causes a great deal of psychological stress. Westerkam et al. speculate that, in addition to the perception of spasticity, psychological factors may influence involuntary muscle activity itself.

Emotional distress is reported to trigger spasticity. Fleuren et al. noted that in persons with SCI, 23% of participants reported that stress and negative emotions affected their spasticity. Little et al. and Mahoney et al. also noted that participants in their studies reported stress and emotions affected spasticity but did not report the frequency. In one study, 59% of participants with multiple sclerosis and 90% of participants with stroke said that stress and anxiety increased spasticity.

Spasticity is reported to cause psychological distress. Through interviews, Mahoney et al. found that spasticity had ramifications in emotional, interpersonal, and cognitive domains in addition to physical domains of experience. Interference of spasticity with mobility had a negative impact on emotions, and spasticity was embarrassing and socially stigmatizing. Similarly, some participants noted in Bhimani et
that uncontrollable jerks were misinterpreted by others as seizures, and felt embarrassed that they were perceived as not having control. The emotional distress from spasticity even made some question their faith in God or made them feel that God was punishing them.

Higher rates of anxiety, depression, and other psychiatric comorbidities than those in the general population are seen among disorders with spasticity, including stroke, multiple sclerosis, and SCI. However, spasticity was not significantly associated with development of depression in a study of 93 people with stroke. More research on relationships between spasticity and psychological disorders and factors is needed.

1.5.5 Impacts of spasticity on daily life

Spasticity severity versus impact on life. As noted previously, Voerman et al measured relationships of psychological factors different from those with perceived spasticity, specifically the participants’ self-rated “average level of leg spasticity” measured by a visual analog scale. It is reasonable to assume that perceived severity will have different relationships with particular psychological factors than the impact and interference of spasticity on life. Severity of spasticity and the impact of spasticity on daily life fall under different ICF domains. Even at the perception level, a person may recognize that his/her spasms are severe – i.e., strong or frequent contractions – yet not perceive that spasticity interferes with daily life. Instead of focusing on severity, I focus on psychological factors related to perceived impacts of spasticity on life activities and participation as well as difficulty dealing with spasticity in Chapters 2 and 3.

Interference of spasticity with life. It is well-documented that people with spasticity commonly feel that it interferes with daily life. Spasticity
may negatively impact life in numerous ways: by interfering with activities such as walking, seating transfers, self-care and sleep, by causing or exacerbating pain, by presenting a safety risk to self and caretakers, and by affecting self-image, interpersonal relationships, and economic situation. Spasticity after stroke has been reported to present a greater burden on persons with stroke and their caregivers\textsuperscript{145} as well as to be associated with higher levels of disability compared to persons with stroke who do not have spasticity.\textsuperscript{146} Spasticity after SCI is negatively associated with quality of life, even when correcting for demographic and injury-related factors.\textsuperscript{11}

Helpful aspects of spasticity. Although spasticity is generally considered a significant problem after SCI, some people with spasticity do not consider it problematic, and others consider it helpful for certain tasks, and for preventing muscle atrophy, improving circulation, or alerting of body problems.\textsuperscript{8,9,29,147} For example, some persons can trigger hip spasms to power a leg swing during ambulation or use extensor spasms to support their body weight.\textsuperscript{9,147} Spasticity is often used as an alternative way of receiving input from the body when sensation is impaired; spasms can alert a person to a bladder infection, need for bowel movement, or tissue damage due to heat, cold, or friction. For these beneficial reasons, some people prefer to have control over spasticity rather than to completely eliminate it.\textsuperscript{8}

Measurements of the impacts of spasticity on daily life are limited. Many argue that measurements of spasticity should better reflect how spasticity affects the individual’s life.\textsuperscript{8,9,27,148,149} Mahoney et al\textsuperscript{8} even argue that the definition of spasticity should be clarified based on its impacts on life. However, only limited measurement tools related to spasticity’s impact on life exist.\textsuperscript{150} The common and validated self-report
spasticity measures such as the Penn Spasm Frequency and Severity Scale\textsuperscript{151} focus on physiological aspects of spasticity rather than impact of spasticity.

A small number of studies have employed self-report measures that address activity limitations and participation restrictions due to spasticity in the SCI population. These measures are often single questions,\textsuperscript{102,152} or haven’t undergone extensive development and psychometric testing.\textsuperscript{101,148} Two comprehensive questionnaires that address activity limitations and participation restrictions are the Patient Reported Impact of Spasticity Measure\textsuperscript{144} and the Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET).\textsuperscript{29} The SCI-SET measure allows a participant to report either helpful or problematic impact of spasticity on specific daily activities and is therefore a useful counterpart to physiological measurements of spasticity during specific tasks. In Chapter 2, we assessed the impact of spasticity on daily life with the SCI-SET, and in Chapter 3, we utilized additional customized measures related to the impact of spasticity (as well as the impact of pain) on life.

### 1.5.6 Spasticity management may benefit from more investigations of psychosocial aspects of spasticity

While all common spasticity treatment approaches have some evidence of effectiveness, clinical spasticity management does not sufficiently address the needs of the individual. Medications and surgery present side effects and risks, and both may reduce desirable motor activity. (Medications used by our study participants are detailed in Chapter 4 Table 4.1) Use of prescription medications for spasticity, pain, depression and sleep present a greater risk of injury and mortality after SCI.\textsuperscript{153–155} To this point, participants report using different options than healthcare providers prescribe, such as massage, acupuncture, deep breathing, whirlpool, and cannabis.\textsuperscript{*8} Effects of spasticity
treatments on quality of life are unclear. Five years after treatment with an intrathecal baclofen pump, individuals who had pumps implanted actually had worse perceived levels of disability and health status despite improvements in clinically-rated spasticity severity. Furthermore, despite treatment options, spasticity is still largely considered problematic, even in recent studies. Therefore, more research to identify the factors that influence the impact of spasticity may help clarify why spasticity is problematic.

1.6. Research aims: Addressing gaps in the literature related to spasticity, pain and their relationships with physiological, psychological, and functional measures

There is general agreement in the literature that choices in spasticity management depend on many aspects, should involve input from the person experiencing spasticity, and should promote optimal quality of life. However, as noted previously, assessments that capture the impacts of spasticity on life are limited. Analysis to characterize the strength of relationships between impact of spasticity and factors (physiological, environmental, psychosocial, or otherwise) is necessary to identify factors related to the impacts of spasticity on life. If a strong candidate factor has a causal influence on impact, then interventions that upregulate positive factors or downregulate negative factors could increase positive impacts or attenuate negative impacts of spasticity. Therefore, treatment for spasticity may be improved through greater understanding of the factors affecting the impact of spasticity on life and their translation into interventions.

Much is still unclear about what factors contribute to the perceived impacts of spasticity on daily life. There are still many gaps in the understanding of spasticity within
and between domains of the ICF. My aims were to designed better understand activities limitations and participation restrictions in spasticity after SCI by characterizing associations between physiological, psychological, and functional measures of spasticity as well as pain.

1.6.1 Examining relationships between spasm duration and magnitude, clinical spasticity severity, and perceived impact of spasticity on daily life

Whether certain spasticity body functions are associated with impact of spasticity on activities of daily living (ADLs) is unclear. One of the most common ADLs with which spasticity is reported to interfere is transfer between seating surfaces,\(^9,10\) a task that is performed an average of 14 times per day.\(^159\) In particular, extensor spasms in the lower extremity are reported to interfere with transfers\(^9,10\) as well as other ADLs.\(^9,10,102,143\) However, some individuals find spasticity helpful during specific ADLs, including transfers.\(^8,9\) Are the magnitude or duration of spasms during transfers related to one’s perception of the impact of spasticity on transfers or daily activities in general? Are spasm duration and magnitude during transfers related to clinical ratings of spasticity severity?

**Aim 1: Quantify quadriceps spasms evoked by seating transfers and determine the day-to-day reliability of these spasms and their association with clinical spasticity severity and with the perceived impact of spasticity on activities of daily living.**

**H1.1:** EMG measurement of quadriceps spasms during transfers would be strongly correlated with a clinical measure of extensor spasticity.
H1.2: EMG measurements of quadriceps spasms during seating transfers would be significantly related to the perceived problematic impact of spasticity on activities of daily living.

1.6.2 Examining relationships between pain and spasticity and examining the role of psychological factors on the impact of spasticity on life

Despite reports of co-occurrence of pain and spasticity presentation, much is still unanswered about specific relationships between them. As noted previously, spasticity and pain have many similar pathophysiological mechanisms. Additionally, spasms are common reasons for both the cause and exacerbation of pain conditions after SCI. SCI participants who reported painful spasms had significantly greater clinically-rated extensor spasms than those who didn’t report painful spasms. How are spasticity and pain related to each other? What is the relationship between the presence of pain and the severity and psychosocial impact of spasticity?

Little is known about the role of psychological factors in the perception of spasticity and whether these are similar to or different from the role of psychological factors in a pain condition. Some evidence suggests that perceived spasticity severity is related to specific coping and illness-related thoughts and that perceived difficulties in dealing with muscle spasms, pain, abnormal sensations and feeling sad statistically cluster. To what extent do psychological factors contribute to one’s perception of the impact of spasticity on daily life?
Aim 2: Characterize relationships between chronic pain and spasticity after spinal cord injury, with respect to severity and impact on activities of daily living and psychological factors.

**H2.1**: Both pain severity and life interference would be strongly associated with the perceived severity and life interference associated with spasticity.

**H2.2**: A combination of perceived spasticity severity, pain-related factors, and psychological variables would significantly contribute to a person’s difficulty dealing with spasticity and the extent of life interference caused by spasticity.

**H2.3**: Persons who experience painful spasticity would experience greater chronic pain severity, greater spasticity severity, and greater interference of pain and spasticity on daily life than persons who do not experience painful spasticity.

1.7. Recruitment note

A total of 21 participants were evaluated in Chapters 2 and 3, with 18 overlapping between Chapter 2 (Aim 1) and Chapter 3 (Aim 2). Two participants who were excluded from analysis in Aim 1 because they had voluntary motor function in the quadriceps were included in Chapter 3 analysis, while one participant who was analyzed in Chapter 2 did not complete the questionnaires used in Chapter 3 analysis and was therefore excluded. The specific inclusion and exclusion criteria for recruitment and analysis are described within each chapter.
CHAPTER 2: IMPACT OF SPASTICITY ON TRANSFERS AND ACTIVITIES OF DAILY LIVING IN INDIVIDUALS WITH SPINAL CORD INJURY

2.1. Overview

Spasticity develops in approximately 60-80% of individuals after a spinal cord injury (SCI) and is considered problematic by many of those who experience it.\(^2,73,102,160\) Spasticity has been defined as “disordered sensori-motor control, resulting from an upper motoneuron lesion, presenting as intermittent or sustained involuntary activation of muscles.”\(^21,27,28\) This definition encompasses clinical signs of spasticity after SCI, including increased tone or stiffness and muscle spasms in response to proprioceptive or exteroceptive inputs. While spasticity commonly interferes with activities of daily living (ADLs),\(^8–10,102,143\) some individuals find spasticity helpful during specific ADLs (e.g. during transfers,\(^8,9\) likely by providing postural stability or body weight support) or as a signal of problems in insensate parts of the body.\(^8–10,29,102,147\) One of the most common ADLs with which spasticity interferes is transfer between seating surfaces,\(^9,10\) a task that is performed an average of 14 times per day\(^159\) and that is critical for independence after SCI.\(^161\) Extensor spasms in the lower extremity (knee extension, plantar flexion, and activation of muscles at the hip)\(^10,31–34\) is the most common presentation of spasticity after SCI\(^10\) and is reported to interfere with transfers in particular\(^9,10\) as well as other ADLs.\(^9,10,102,143\)

Many researchers have advocated for spasticity research to focus on its problematic aspects,\(^8,9,148,149\) however few physiological measures of spasticity that are relevant to ADLs exist, especially for non-ambulatory individuals. A small number of studies\(^34,162–164\) have used electromyographic (EMG) recordings from leg muscles paralyzed by SCI to measure involuntary muscle spasms during ADLs. EMG and other
measures of involuntary muscle activity fall within the physiological or “body functions” domain of the World Health Organization’s International Classification of Functioning in Disability and Health (ICF). The ICF model provides a biopsychosocial framework for understanding and treating health conditions. Characterizing the relationships between body functions and the impacts of spasticity on activities and participation may help identify physiological factors that influence the problematic impact of spasticity on life.

In a recent study by Mayo et al. in which EMG was recorded during seating transfers, the authors found associations between the duration and time of agonist-antagonist muscle coactivity and self-reported spasm frequency, as well as the intensity of agonist-antagonist coactivity and self-reported spasm severity. These associations support the utility of EMG measurement during transfers as an objective measure relevant to the subjective experience of spasms. However, EMG measures of spasms during transfers have not been compared with a comprehensive measure that reflects the impact of spasticity on ADLs. We focused on an extensor muscle group (quadriceps) during an ADL (seating transfers) with which extensor spasticity often interferes. We hypothesized that the duration and magnitude of spasms evoked in a quadriceps muscle during transfers would be strongly associated with more problematic impact of spasticity on transfers and ADLs in general.

Additionally, the day-to-day reliability of EMG recordings during transfers have not yet been evaluated, nor has this measure been compared with a clinical test of spasticity severity. Good day-to-day reliability for EMG measures and a strong
relationship between EMG during transfers and clinical spasticity tests would further support the value of EMG recorded during transfers as a tool in a multimodal assessment of spasticity.

2.2 Methods

2.2.1 Study Design

Non-ambulatory participants with SCI and spasticity performed seated pivot transfers on two separate days while spasms (involuntary muscle contractions) were recorded using EMG from a quadriceps muscle. On separate days, participants performed transfers once or three times (Fig. 2.1). Even though individuals do not perform multiple transfers in succession during ADLs, repeating 3 trials for a measure is common (e.g. the pendulum test) and allowed us to quantify the stability of repeat measurements. The number of transfers performed on each day was counterbalanced into two groups to prevent potential order effects, and participants were assigned to the groups using a randomization generator. Intra-test periods spanned between one and 10 days.

2.2.2 Participants

Male and female volunteers between the ages of 18 and 65 with chronic SCI (>1 year) were recruited over 20 months from The Miami Project’s SCI research volunteer database. Participants had to exhibit knee extensor spasms, either after imposed knee and hip extension during the SCATS test or by experimenter observance of extensor spasms evoked by position change. One participant who scored 0 on the SCATS extensor score had visually observable quadriceps spasms invoked by positional change. Potential subjects were excluded if they needed lifting assistance to complete seating transfers, or had evidence of voluntary quadriceps function, defined as the ability to elicit any increase in EMG amplitude during intentional voluntary contraction of the quadriceps.
Fig 2.1: Study design and participant exclusions

The study was performed at The Miami Project to Cure Paralysis and was approved by the Institutional Review Board of the University of Miami Miller School of Medicine. The investigation was conducted according to the principles expressed in the Declaration of Helsinki. Written informed consent was obtained from each participant.

2.2.3 Measures

Demographic information, injury characteristics and medications, were collected by both examination and interview. The data presented in this article are part of a larger data set.

2.2.3.1 Transfers

Each participant was given standardized instructions to perform seated pivot transfers between his/her wheelchair and a mat table adjusted to the participant’s
preferred height. Participants used their upper extremities to place their feet on the floor and to push from the seating surface and swing their body to the adjacent mat table. Participants then used their upper extremities to place their lower extremities onto and off of the mat table. For data analysis, a single transfer was defined as the movement from wheelchair to the mat table (with legs on table) and then back to the wheelchair (see representative EMG trace in Fig. 2.2). Transfer duration was defined as the time to complete a single transfer. On the day of three successive transfers, participants rested less than one minute between transfers.

2.2.3.2 EMG recordings of spasms

We recorded spasms in the quadriceps, a muscle group involved in extending the knee during extensor spasticity. We chose to record from vastus lateralis based on superior signal quality and innervation zone uniformity compared to rectus femoris. To record surface EMG from the vastus lateralis, a preamplifier with electrodes (Motion Lab Systems Z03, Baton Rouge, LA, USA) was placed on the vastus lateralis of the leg with the greater SCATS extensor score. The distal electrode was placed approximately 15 cm proximal to the patella at a 20° angle from midline and affixed with medical tape. A 3 cm diameter ground electrode was positioned on the anterior thigh. The electrodes were placed in the same locations on both testing days. EMG data were sampled at 2000Hz with a Power 1401 interface, DC offset-corrected, and filtered from 30-500Hz using Spike2 software (Cambridge Electronic Design, Cambridge UK). EMG recordings were time-synchronized with video for post hoc evaluation of pivot transfer start/end times and for quality control.
Fig 2. Example transfer and automated EMG analysis of spasms. EMG activity in vastus lateralis and time-synchronized videos were recorded during transfer from wheelchair to mat table and back to wheelchair. Raw EMG was filtered, rectified, and integrated offline. Integrated EMG was analyzed in MATLAB according to the parameters in Thomas, et al. Lower panel: individual spasms are highlighted with light gray background.
2.2.3.3 Maximal compound muscle action potentials (M-Max)

M-max was used to normalize EMG amplitude during spasms across our participants. Normalization reconciles biological differences (such as differences in subcutaneous fat) and experimental differences (such as different electrode spacing or placement on muscle) across participants. The M-max of vastus lateralis was elicited by electrical stimulation of the femoral nerve with a DS7A stimulator (Digitimer Ltd, Welwyn Garden City, UK). The cathode was placed in the femoral triangle at the site that achieved the greatest evoked EMG at the lowest intensity. The current intensity was increased in a step-wise manner until the maximal M-wave amplitude was stable for five pulses (i.e. no further increase in amplitude despite increasing stimulus intensity).

2.2.3.4 Impact of spasticity on ADLs

Impact of spasticity on daily life was measured with the SCI-Spasticity Evaluation Tool (SCI-SET). Participants rated the impact of spasticity from -3 (extremely problematic) to +3 (extremely helpful) on 35 items related to ADLs. The SCI-SET demonstrates internal consistency, test-retest reliability, face validity and construct validity and has been recommended based on these psychometric properties to be useful for assessing the impact of spasticity on daily life in people with SCI. Responses are averaged to provide a measure of the overall impact of spasticity on ADLs for an individual. Correlations were performed separately for participants with SCI-SET scores in the “problematic” and “neutral” range (≤0), from those in the “helpful” range (>0).
2.2.3.5 Clinical spasticity severity

The Spinal Cord Assessment Tool for Spastic reflexes (SCATS) is a clinical spasticity measure with adequate construct validity and inter-rater reliability. Unlike the modified Ashworth scale, it is designed to measure three presentations of spasticity typical in SCI: evoked extensor spasticity, evoked flexor spasticity, and evoked clonus. A trained evaluator applies a stimulus (passive muscle stretch or pinprick) and then scores the response from 0-3 based on the test criteria. For comparisons with vastus lateralis EMG, the SCATS extensor spasticity score for the corresponding leg was utilized throughout this study. The evaluator of the SCATS score was blinded to all of the other assessments, which were performed by a different investigator.

2.2.4 Data Analysis

2.2.4.1 Spasm Analysis

All EMG acquired during transfers was considered involuntary, as participants had no perceived control of vastus lateralis, and no visible contraction or increased EMG activity occurred in the muscle during requested maximal voluntary contractions. The methodology of Thomas et al. was employed with slight modifications for spasm analysis. Briefly, filtered and rectified EMG was integrated over 10ms. To separate spasms from baseline noise, a threshold was calculated based on the 30s rest period prior to transfer. A spasm was defined as having ≥50ms of above-threshold integrals in a period of at least 100ms, preceded and followed by at least 1s of below-threshold integrals (see Fig. 2.2). “Spasm duration” was defined as the temporal sum of discrete spasms during a given transfer. “Spasm magnitude” was defined as the total integrated EMG area (mV*s) during spasms for a given transfer, normalized to M-max. When a
participant did not experience spasms during a particular transfer (based on EMG activity, N=3), spasm duration and magnitude were “0” for that transfer.

EMG records were visually reviewed for quality. Seven records from five participants were excluded because they had continuous motion artifacts (abnormally high amplitude spikes, N=5), low signal to noise ratio (N=1), or the video failed to record (N=1).

2.2.4.2 Statistical Analysis

An a priori sample size of 19 was determined\textsuperscript{168} using a two-tailed test with an alpha level of 0.05, a power of 80\%, and a correlation coefficient of 0.6. A coefficient of 0.6 would represent a strong correlation between SCI-SET scores and EMG measures, as hypothesized. Data analysis was performed in SPSS 22 (SPSS Inc, Chicago, IL, USA). Shapiro-Wilkes tests revealed transfer and EMG variables (spasm duration, spasm magnitude, and transfer duration) were not normally distributed, therefore nonparametric tests were used to analyse EMG data, as well as ordinal SCATS and SCI-SET data. Specific tests utilized (all 2 tails) are described in the Results. For tests with multiple comparisons, p-values were adjusted with a Bonferroni correction. No significant order effects were found for the four transfer variables (absolute and normalized spasm duration, spasm magnitude, transfer duration) using carryover effects analysis described by Welleck.\textsuperscript{169} Thus, subject data were combined for all analyses regardless of group assignment (see Fig. 2.1).
**Table 2.1: Participants included in analysis.** AIS, American Spinal Injury Association Impairment Scale; LEMS, Lower Extremity Motor Score (in the leg tested, max score=25); SCATS, Spinal Cord Assessment Tool for Spastic reflexes; qid, four times daily; tid, three times daily; bid, twice daily; sid, once daily; prn, as needed.

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2.3. Results

2.3.1 Participants

Nineteen participants were included in the final analysis (17 males, 2 females, Table 2.1). Mean age was 39.5 years (SD=10.2) and mean time since injury was 15.6 years (SD=11.0). Participants contacted and excluded at each stage are noted in Fig. 2.1.

2.3.2 Spasm characteristics during transfers

All participants exhibited spasms during at least one of the transfers, although one participant exhibited a brief spasm during only one of the four transfers. On average, participants took 75.4s (SD=47.4) to complete a single transfer and quadriceps spasms were present 23.1s (SD=23.6). When normalized to transfer duration, spasms were present an average of 31.4% (SD=30.3) of the transfer time. Means, medians and ranges for each variable and each transfer are depicted in Fig. 2.4. No significant differences were detected between a single transfer and the first of three transfers for any of these variables (Wilcoxon signed rank tests, Fig. 2.4).

A single transfer and the first of three successive transfers are similar tasks in that they are both a first transfer (whereas the second and third transfers may be influenced by the muscle history of prior transfers). Thus, we compared the day-to-day-reliability of our variables for these two transfers. The single transfer and first of three transfers demonstrated good or excellent test-retest reliability (Spearman’s rho, Fig. 2.5) for all four variables. Thus, each participant’s values for the single transfer and first of three transfers were averaged over the two testing days to create a single, more robust value for use in correlations to other measures.
Successive transfers demonstrated good-to-excellent internal consistency for spasm duration, magnitude and transfer duration variables (Cronbach’s α, Table 2.2). Significant differences were found among three successive transfers for all 4 of these variables (Friedman’s ANOVA by ranks, Fig. 2.3A, B, and C, respectively), but not when spasm duration was normalized to transfer duration (Fig. 2.3D).

**Fig. 2.3 Transfer-related responses from single transfers and repeated transfers.** Boxplots represent median, 25th and 75th percentiles for each variable. Whiskers represent ranges and “X”s represent means. A) Spasm duration, B) Spasm magnitude, C) Transfer duration, and D) Spasm duration as a percent of transfer duration. Wilcoxon signed rank tests performed between single and first of three transfers for each variable. Friedman’s ANOVA performed between first, second and third successive transfers. *P < 0.05, ** P < 0.01. N=14 with EMG data on both days tested.
Fig 2.4. Day-to-day reliability of transfer-related variables. Responses from single transfer plotted against responses from the first of 3 successive transfers. A) Spasm duration, B) Spasm magnitude, C) Spasm duration as a percent of transfer duration, and D) Transfer duration. Spearman rank correlations; * P < 0.05, ** P < 0.01, *** P < 0.001. N=14 with EMG data on both days.

Table 2.2: Internal Consistency of 3 successive transfers measured by Cronbach’s α. Results were calculated from N=15 participants with EMG data on 3-transfer day. *all P < 0.001

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<th>95%CI</th>
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<tr>
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<td>Spasm Duration, % of Transfer Duration</td>
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2.3.3 Impact of spasticity on ADLs is not associated with measures of spasms evoked during a common ADL

The impact of spasticity on ADLs (mean SCI-SET score) was perceived as “problematic” for 16 participants and “helpful” for three participants. No significant relationships were found between the duration or magnitude of quadriceps spasms during transfers and the perceived problematic or helpful impact of spasticity on ADLs (Spearman’s rho, Fig. 2.5A). Similarly, spasm duration normalized to transfer duration did not correlate with either problematic or helpful impact (rho = 0.008, P = 0.978, and rho = 0.500, P = 0.677, respectively). Clinically-rated spasticity severity measured by SCATS did not correlate significantly with impact on ADLs for either (unilateral) extensor scores alone or bilateral sum scores, which also included flexor spasms and clonus (rho value range: 0.000 to 0.866; P value range: 0.333 to 1.000).

Specifically regarding the impact of spasticity on transfers (SCI-SET question #3), 15 participants with EMG records considered it problematic or neutral while four considered it helpful. Neither duration nor magnitude of quadriceps spasms during transfers were significantly associated with the perceived impact of spasticity on transfers (Fig. 2.5B), although spasm duration demonstrated a strong positive correlation with helpful impact that approached significance (rho = 0.949, P = 0.051, Fig. 2.5B).

A greater time since injury was significantly associated with less problematic impact of spasticity on ADLs overall (rho = 0.501, P = 0.029) and specifically on transfers (rho = 0.568, P = 0.011). Controlling for time since injury did not significantly change correlations between impact scores and transfer-related variables, which remained non-significant. Age, injury level, and dosage of antispastic medications were not significantly related to transfer-related variables or impact of spasticity on daily life.
**Fig. 2.5. Impact of spasticity is not associated with quadriceps spasm EMG during seating transfers.** Impact of spasticity on ADLs (SCI-SET mean) plotted against A) Spasm duration (left) and spasm magnitude (right). B) Impact of spasticity on transfers (SCI-SET question #3) plotted against spasm duration (left) and spasm magnitude (right). Participants with “Problematic” and “No Effect” ratings analyzed separately from those with “Helpful” ratings using Spearman rank correlations.

X axis values: -3=Extremely Problematic, -2=Moderately Problematic, -1=Mildly Problematic, 0=No Effect, +1=Mildly Helpful, +2=Moderately Helpful, +3=Extremely Helpful.
### 2.3.4 Spasms evoked by transfers correlate with a clinical measure of spasticity severity

The extensor score of the SCATS was positively associated with average spasm duration (Fig. 2.6A) and spasm duration normalized to transfer duration (Fig. 2.6C). Average spasm magnitude did not significantly correlate with SCATS extensor score but the trend was similar to that for spasm duration (Fig. 2.6B). Transfer duration did not correlate significantly with SCATS extensor score (rho = -0.253, P = 0.327).

#### Fig 2.6. Spasms measured with EMG correlate with a clinical score of spasticity severity.

SCATS extensor score plotted against individual two-day averages for each spasm variable. A) Spasm duration (B) Spasm magnitude C) Spasm duration as a percent of transfer duration. Spearman rank correlations; *P < 0.05, **P < 0.01. N=17 with EMG data from at least one day.

### 2.4. Discussion

Spasticity is a multidimensional phenomenon,\(^{152,157,170}\) therefore it is important that a combination of self-reported perceptions and objective measures is considered when assessing spasticity or changes in spasticity due to treatment.\(^{157,164}\) This study addressed the lack of characterized associations among measures of involuntary muscle activity and the impact of spasticity on transfers and ADLs in general by investigating relationships among spasm duration and magnitude during transfers, perceived impact of
spasticity on ADLs, and clinically-rated spasticity severity. Even though extensor spasticity is often reported to interfere with ADLs,\textsuperscript{9,10,102,143} we found no significant relationships between problematic impact scores and quadriceps spasm duration or magnitude measured with EMG or clinically-rated extensor spasticity measured with the SCATS. We found that greater time since injury was associated with less problematic impact of spasticity on both ADLs in general and on transfers, which has been noted in some studies,\textsuperscript{2,9,102} but not others.\textsuperscript{148} In another study of individuals with SCI, high self-reported spasm frequency during transfers, pain, and the combined scores for spasm frequency and pain were associated with greater perceived interference with function.\textsuperscript{34}

Interestingly, the impact of spasticity on ADLs for most of our participants was minimally problematic (Fig. 2.5A). However, for the question related to transfers, participants gave a full range of responses from “extremely problematic” to “extremely helpful” (Fig. 2.5B). For the four participants reporting a helpful impact of spasticity on transfers, the relationship of impact with spasm duration was strongly positive and nearly significant (Fig. 2.5B). Helpful influence of spasticity on transfers has been noted in other studies,\textsuperscript{8,170} as spasms can provide postural stability or body weight support for some individuals during this task.

This study demonstrates that EMG measurement of spasm duration during seating transfers is positively associated with clinically-rated spasticity severity. Other studies have found that EMG activity recorded during a clinical spasticity test correlated with the corresponding score\textsuperscript{30,31,33,171}; however, our EMG measures were not recorded during the SCATS test itself but instead during seating transfers. The relationships we found provide evidence that the SCATS extensor score has relevance to involuntary muscle activity
during a real-life activity. The positive relationship between EMG variables and SCATS extensor score was strongest when spasm duration was normalized to the overall time to complete the transfer. Normalizing spasm duration may have reduced variability due to factors that influence transfer mobility, such as upper extremity strength, body mass, and transfer technique.\textsuperscript{172,173}

Our EMG measurements of quadriceps spasm duration and magnitude during seating transfers were reliable day-to-day (Fig. 2.4) and had internal consistency across repeated trials (Table 2.2), supporting prior evidence that EMG is a useful method for objectively quantifying spasms during transfers.\textsuperscript{34} Despite adequate internal consistency, both spasm duration and magnitude decreased after the first transfer (Fig. 2.3A and B). Previous research has demonstrated that both active and passive muscle movement increases post-activation depression and leads to a decrease in spasticity.\textsuperscript{174,175} Therefore, muscle activation during initial spasms and peripheral stimulation during transfers may have elicited post-activation depression or other sources of segmental inhibitory feedback, resulting in shorter spasm duration during subsequent transfers.

Similar to EMG measures, SCATS scores were not correlated with the impact of spasticity on ADLs. This contrasts with a study by Bravo-Esteban \textit{et al.}\textsuperscript{143} In their study, SCATS extensor scores inversely correlated with SCI-SET scores. Differences between studies may be due to differences in participant inclusion -- notably, their inclusion of ambulatory individuals. Extensor spasms strongly interfered with gait function in their study\textsuperscript{143} and have been associated with slower walking speeds.\textsuperscript{36} Thus, perceived problematic impact of spasticity may be influenced by gait interference in ambulatory individuals.
This study has some limitations. We recorded EMG responses from a single muscle during one task, and it is possible this task or muscle did not fully reflect the varied nature of spasticity encountered in daily life. In future studies, multiple channel EMG should be used along with the SCI-SET to determine the influence of various muscle groups on perceived impact of spasticity. Further, EMG can reliably capture spasms, but EMG, clinical tests such as the SCATS, and biomechanical tests do not detect common sensations associated with the experience of spasticity (i.e. feeling of muscle tension or pain)\textsuperscript{9,101} that may influence the problematic impact of spasticity.

The small sample size in this study can be considered a limitation; the present sample size was calculated to detect strong correlations. Due to the small number of participants who reported a helpful impact of spasticity on ADLs (N=3) or transfers (N=4), inferential statistics in this subset should be interpreted with caution. Additionally, we did not include individuals with voluntary quadriceps function to avoid any confounding effects of voluntary activity on EMG recordings. Therefore, results obtained from this sample of participants without voluntary function may not be generalizable to all individuals with SCI. Further research in larger and more diverse study samples are needed to elucidate factors that may influence the perceptions of spasticity and its impact on daily life.

2.5 Conclusions

We have demonstrated that the duration and magnitude of quadriceps spasms during transfers are not directly related to the perceived problematic impact of spasticity on transfers or ADLs in general. However, quadriceps spasm duration and magnitude measured with EMG during a seating transfer are reliable, and EMG measures of spasm...
duration are directly associated with a clinical measure of extensor spasticity. Exploring more complex interactions between body function measures of spasticity and other factors such as pain and psychological characteristics may help identify factors that strongly influence the impact that spasticity has on daily life. Further understanding may help direct treatment strategies to reduce the problematic impact of spasticity in persons with SCI and may also be useful across neurological conditions that involve spasticity, including stroke, multiple sclerosis, cerebral palsy, traumatic brain injury, vasculitis, CNS tumors, and muscular dystrophies.
CHAPTER 3: SPASTICITY AND PAIN AFTER SCI: IMPACT ON DAILY LIFE AND THE INFLUENCE OF PSYCHOLOGICAL FACTORS

3.1 Overview

Spasticity and pain are both common and problematic consequences of spinal cord injury (SCI). Approximately 60-80% of individuals with SCI experience spasticity.73,102,160 The proportion of those who consider it “problematic” typically ranges from 27% to 43%,2,73,102,142 although spasticity after SCI has been reported to interfere with some aspect of daily life in up to 91% of participants.10 Spasticity has traditionally been defined by exaggeration of the tonic stretch reflex.20 Clinically, however, the term ‘spasticity’ has been used broadly to describe a range of involuntary motor activities in response to a range of proprioceptive and exteroceptive inputs.10,23,142 The 2005 SPASM Consortium promoted a broader definition of spasticity as “disordered sensori-motor control, resulting from an upper motoneuron lesion, presenting as intermittent or sustained involuntary activation of muscles.” 21,28 This definition better matches the clinical use of the term as well as the use of the term in questionnaires that measure perceived spasticity in daily life 29. Spasticity has been reported to interfere most frequently with activities such as seating transfers, changing positions, sleeping and walking.9,10

Like spasticity, prevalence of chronic pain after SCI is approximately 60-80%.71–73 Pain after SCI is frequently severe and greater pain severity is usually associated with lower quality of life and life satisfaction.7,69 Pain after SCI is heterogeneous and may be nociceptive or neuropathic in nature.74 Nociceptive pain involves the activation of nociceptors and can be of inflammatory origin (Pain Taxonomy Working Group, IASP 2011). Pain from shoulder injury due to overuse is a common type of nociceptive pain...
for wheelchair-dependent individuals. In contrast, neuropathic pain develops as a result of a lesion or disease of the somatosensory system and is therefore common after SCI. Neuropathic pain after SCI is particularly refractory to treatment, even to pharmacological treatments that are effective for neuropathic pain in other populations. The incidence of neuropathic pain gradually increases to about 60% at one year after injury.

Both animal and human studies point towards important relationships between pain and spasticity after SCI. For example, those individuals who experience spasticity after their injury also frequently report pain associated with their spasms. Spasms or excessive tone may both cause pain or exacerbate existing pain. Among individuals with SCI, those with chronic pain have a higher prevalence of spasticity and muscle spasms compared to those without pain. Furthermore, the prevalence of spasticity is greater still in those with neuropathic pain compared to those with nociceptive pain. In human and animal studies related to pain, hyperreflexia, or spasticity, similar pathophysiological processes have been reported such as central sensitization and the disruption in chloride homeostasis and GABAergic interneuron transmission in the spinal cord, disruption in serotonergic descending transmission, and fiber sprouting after injury.

Despite similarities in terms of co-occurrence and potential mechanisms, little is known about how these sequelae of SCI influence each other, and whether their impacts on daily life are associated with similar or independent factors. Sensations such as pain and paresthesias are often associated with the experience of spasticity but are not captured by common physiological and clinical tests for spasticity. This may be one
reason why physiological and clinical measures often correlate poorly with self-report measures of spasticity.\textsuperscript{102,152}

The association between psychological factors such as coping abilities, symptoms of depression and the perception of spasticity and its impact on daily life is largely unexplored. A study in 430 people with SCI statistically clustered ratings of perceived difficulty in dealing with common consequences of injury.\textsuperscript{3} The study showed that difficulty in dealing with muscle spasms, pain, and abnormal sensations was particularly associated with feeling sad. Evidence suggesting a relationship between cognitive factors and spasticity was provided by Voerman et al.\textsuperscript{108} who examined associations between perceived spasticity intensity, coping thoughts, and illness-related thoughts. This study found that “reassuring thoughts” and “helplessness” explained 44\% of the variance in the perceived intensity of spasticity.

The understanding of the association between spasticity, pain, and psychological factors, and the role of pain and psychological factors in the impact of spasticity on daily life is incomplete. In order to design optimal treatment strategies and assess patient-centered treatment outcomes for these difficult conditions post-SCI, the potential for an interaction between pain and spasticity and psychosocial impact should be considered. The present study aimed to address this gap in knowledge. Specifically, we wanted to address aspects of “body structures and functions,” “activities limitations” and “participation restriction” components of the International Classification of Function in Health and Disability,\textsuperscript{141} a theoretical and practical framework based on the biopsychosocial model. Our primary goals were three-fold:

First, we aimed to characterize the relationships between severity and impact of pain and spasticity. We expected that both pain severity and life interference would be
strongly associated with the perceived severity and life interference associated with spasticity. Second, we aimed to determine which factors are associated with the perceived difficulty of dealing with spasticity and the extent of life interference caused by spasticity. We expected that a combination of perceived spasticity severity, pain-related factors, and psychological variables would significantly contribute to a person’s difficulty dealing with spasticity and the extent of life interference caused by spasticity. Third, we aimed to examine the impact of painful spasticity on the severity of chronic pain and spasticity, and on the interference of pain and spasticity with daily life. We expected that persons who experience painful spasticity would experience greater chronic pain severity, greater spasticity severity, and greater interference of pain and spasticity on daily life than persons who do not experience painful spasticity.

3.2. Methods

3.2.1 Participants

Twenty-one participants with cervical or thoracic SCI and lower extremity spasticity were assessed with respect to chronic pain, spasticity, and relevant psychological factors (resilience, self-efficacy, affective distress, life control) by examination and interview. Demographic information, injury characteristics, and medications were also documented. Participants were male and female volunteers from The Miami Project to Cure Paralysis’s SCI research volunteer database. Participants were between the ages of 18 and 65 with chronic SCI (>1 year), exhibited leg extensor spasticity, and had the ability to transfer independently between sitting surfaces.

The study was carried out in accordance with the recommendations of The University of Miami Miller School of Medicine Human Subjects Research Office. All
subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Institutional Review Board.

3.2.2 Chronic pain history

To document chronic pain, the characteristics of up to 3 of a participant’s worst chronic pains were collected using the International Spinal Cord Injury Pain Basic Data Set v2.0.\textsuperscript{179} This data set is a standardized and recommended method for collecting the minimal clinically relevant information to classify pain in persons with SCI in accordance with the taxonomy of the International Spinal Cord Injury Pain Classification.\textsuperscript{74} The interviewer was trained using the pain data set through the Widerstrom-Noga laboratory and an understanding of the indicators of neuropathic pain (see Table 1.1 Pain Types after Spinal Cord Injury). Participants marked the locations of any persistent pain using a frontal and dorsal body map. Body maps have been demonstrated to be reliable.\textsuperscript{180,181}

3.2.3 Clinical spasticity severity

Clinical spasticity severity was assessed with the Spinal Cord Assessment Tool for Spastic Reflexes (SCATS).\textsuperscript{30} This tool is designed to measure 3 common presentations of spasticity exhibited after SCI (extensor spasms, flexor spasms, and ankle clonus) and demonstrates construct validity and inter-rater reliability. A trained evaluator applies a stimulus (passive muscle stretch or pinprick) and then scores the response observed. In this study, the experimenter collecting other spasticity measures was blind to the SCATS score, and the evaluator of the SCATS score was not involved in other assessment measures.
3.2.4 Physiological measure of spasms during seating transfer

We recorded surface electromyographic activity in a quadriceps muscles, vastus lateralis, while participants performed seated pivot transfers between their wheelchair and a mat table. Since participants were individuals with chronic SCI for whom surface-to-surface transfers are a common daily activity, they were allowed to use their preferred wheelchair positioning and mat table height during the transfers. The same instructions were given to each participant. Participants used their upper extremities to place their feet on the floor and push from the seating surface, pivoting their bodies to the adjacent mat table. They used their upper extremities to place the lower extremities onto and off of the mat table and then push from the table, pivoting their bodies to return to their wheelchair.

The methodology of Thomas et al\textsuperscript{163} was employed to quantify spasms from vastus lateralis EMG activity. “Spasm duration” was the total time a participant spent in quadriceps spasm during a single seating transfer between wheelchair and a mat table and back to mat table. Data were analyzed only from participants with no evidence of voluntary motor activity in the recorded muscle.

3.2.5 Questionnaires

3.2.5.1 Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET)

The SCI-SET\textsuperscript{29} is a measure of perceived impact of spasticity on activities of daily living. The scale allows for bi-directional (ie, helpful or problematic) assessment of the impact of spasticity on 35 different items and ranges from -3 (extremely problematic) to +3 (extremely helpful). The SCI-SET demonstrates internal consistency, test-retest reliability, face validity, and construct validity.\textsuperscript{29} Scores obtained for each participant’s responses were averaged over the 35 questions to provide a measure of overall spasticity
impact. The definition of spasticity in the SCI-SET\textsuperscript{29} was retained throughout the study when defining spasticity to participants:

- uncontrolled, involuntary muscle contraction or movement (slow or rapid; short or prolonged),
- involuntary, repetitive, quick muscle movement (up and down; side to side),
- muscle tightness, and
- what you might describe as ‘spasms.’

3.2.5.2 Pain and spasticity inventories

The Pain Severity, Life Interference, Life Control, and Affective Distress subscales from the Multidimensional Pain Inventory, SCI version (MPI-SCI)\textsuperscript{69,114} were used to evaluate psychosocial impact. The MPI-SCI has been validated for internal consistency, stability, and construct validity.\textsuperscript{69} Each question is rated numerically from 0-6.

To adequately compare pain severity and its impact on daily life to spasticity severity and its impact on daily life using the same metrics, we created spasticity specific items using the MPI-SCI framework. Specifically, where needed the word “pain” was replaced with “spasticity,” keeping all other original wording and anchors of the MPI-SCI identical (See Multidimensional Pain and Spasticity Inventory in Appendix). Both evaluators and participants agreed that the substitution had face validity.

Thus, the six pain and spasticity subscales included: Pain Severity ($P_{\text{Severity}}$), Pain Life Interference ($P_{\text{Interference}}$), Spasticity Severity ($S_{\text{Severity}}$), Spasticity Life Interference ($S_{\text{Interference}}$), Life Control, and Affective Distress (See Multidimensional Pain and Spasticity Inventory in Appendix).
3.2.5.3 Difficulty dealing with pain and spasticity

Two questions were used to evaluate the difficulty in dealing with pain ($P_{\text{Difficulty}}$) and spasticity ($S_{\text{Difficulty}}$): “Overall, how hard is it to deal with your pain/spasticity?” Responses ranged from 0: “not hard at all” to 10: “extremely hard.” These questions have been previously used to evaluate muscle spasms and pain\textsuperscript{3,182} but have not been compared with more comprehensive questionnaires such as the SCI-SET that measure the impact of spasticity on multiple aspects of daily life.

3.2.5.4 Self-efficacy and resilience

A person’s confidence in overcoming challenges (eg, self-efficacy, resilience) may influence the perceived impact of spasticity on daily life. We assessed self-efficacy, or “the belief in one's competence to cope with a broad range of stressful or challenging demands”\textsuperscript{129} as well as the related factor of resilience, which has been defined as “the qualities that enable individuals to positively adjust in the face of a significant adversity.”\textsuperscript{124} We measured self-efficacy in our participants with the Moorong Self-efficacy Scale,\textsuperscript{183} which measures an individual with SCI’s confidence in performing functional, social, leisure, and vocational activities. The scale has been demonstrated to be valid, consistent, and sensitive.\textsuperscript{183} Resilience was assessed with the 10-question version of the Connor-Davidson Resilience Scale,\textsuperscript{125,184} which measures an individual’s ability to cope with and adapt to general life challenges. This scale has been demonstrated to be valid and consistent,\textsuperscript{184} and both full-length and short versions have been utilized in SCI populations.\textsuperscript{124,185,186}
3.2.5.5 Painful spasticity

To determine the extent to which pain due to spasticity has a measurable impact on aspects of daily life, we asked participants to rate the pain intensity (0-10), duration (<1 minute, 1-10 minutes, 11 minutes to 1 hour, >1 hour), and location of any regularly occurring painful spasticity.

3.2.6 Timeline

The SCATS, spasm duration, the SCI-SET, and the Pain History were completed in the laboratory. A follow-up phone interview was completed to collect the psychological questionnaires, and the Pain and Spasticity Inventories (Figure 3.1). All questionnaires were given in an interview-style.

Figure 3.1. Study Timeline

- **Contacted from Database** (N=79)
  - Did not meet inclusion criteria (N=17)
    - Not interested or available (N=41)
- **In-Lab Testing** (N=21)
  - SCATS
  - SCI-SET
  - Pain History
  - Spasm duration
  - Declined questionnaire (N=1)
- **Phone Interview** (N=20)
  - Multidimensional Pain and Spasticity Inventories
  - Self-Efficacy Scale
  - Resilience Scale
- **Final Analysis** (N=20)
3.2.7 Data Analysis

Data analysis was performed in SPSS 22 (SPSS Inc, Chicago, IL). All tests were 2-tailed. Sample size was not calculated *a priori* for the current aims, however, for a 2-tailed correlation with an alpha level of 0.05 and a correlation coefficient of 0.6, power would be 80% with our sample size.168

One of our main goals was to determine which factors had the strongest relationships with impact of spasticity on life in our sample. This research was largely explanatory and meant to direct future research. Exploratory data analysis can be used for “determining relationships among the explanatory variables, and assessing the direction and rough size of relationships between explanatory and outcome variables.”187 It is common not to adjust p-values in studies of this type.104,108 Adjusting all p-values in a related set of comparisons (for example, correlations of multiple variables with Difficulty Dealing with Spasticity) using the same multiplier would not affect the ranking of variables as candidate factors in future analysis.

**Internal consistency**: Internal consistency of questionnaire subscales was measured by Cronbach’s $\alpha$. Cronbach’s $\alpha$ is a common measure to determine how well a set of items/events are grouped together, or the extent to which items measure the same underlying dimension.188 Identical items have a score of 1, while completely uncorrelated items have a score of 0. We used the following valuation categories for $\alpha$ (Shrout, 1998): fair consistency, $\alpha=0.41-0.6$; moderate consistency, $\alpha=0.61-0.8$, and substantial consistency, $\alpha=0.81-1.0$.

**Comparisons and correlations**: Mann-Whitney U tests were utilized to compare the distribution of scores across independent groups. Spearman correlations were utilized
to quantify bivariate correlations between variables. Because the present study is mainly exploratory in nature, p-values were not adjusted for multiple bivariate correlations.

**Multiple linear regressions:** Multiple regressions performed for explanatory purposes explore relationships between multiple variables in a sample to “shed light” on a phenomenon. We utilized multiple forward regression models to quantify the amount of variance explained in 2 measures related to the impact of spasticity on life due to our independent variables (spasticity measures, pain measures, and psychological measures).

A multiple linear regression model uses a linear equation to fit the dependent variable to the independent variables ($I_i$), as noted in the following regression equation:

$$\text{Dependent variable} = \text{Constant} + (B_1*I_1) + (B_2*I_2) + (B_3*I_3) + \ldots (B_i*I_i)$$

Where,
- $I_i$ is the value of independent variable $i$
- $B_i$ is the unstandardized slope coefficient for variable $i$, expressed in the units of variable $i$.
- The Constant is the intercept and has no real-world significance to the variables.

$B_i$ denotes the relative contribution of an independent variable, $I_i$, to the equation. In Table 3.4B, we also report the standardized slope coefficient Beta (as opposed to B). Beta values are expressed in units of standard deviation, similar to correlation coefficients. A change in 1 standard deviation of an independent variable $I_i$ would result in a change in the dependent variable equal to the value of Beta; standard deviations.

In each regression, self-rated spasticity severity ($S_{\text{Severity}}$) was entered into the regression model and other independent variables were allowed to proceed forward only if the model F value including that variable was $\leq 0.05$ (i.e., the model was significant).
The amount of variance explained in the model is represented by $R^2$. Adjusted $R^2$ values were reported instead of unadjusted $R^2$ values, as adjusted $R^2$ values have minimal bias with as little as 2 subjects per variable.$^{192}$

3.3 Results

3.3.1 Participants

Twenty-one participants were recruited; 20 completed the follow-up interview and were included in final analysis. All participants recruited had spasticity as per inclusion criteria; 19 of the 20 analyzed participants also experienced chronic pain. One of these 19 participants with pain reported non-painful chronic tingling in the legs during the initial pain history that was later reported as painful (pain intensity 1/10) when the follow-up phone interview was conducted. Demographics, injury characteristics, and pain and spasticity information for each participant are displayed in Table 3.1.

3.3.2 Pain profiles of participants

We mapped the prevalence of both chronic pain and spasticity-related pain in each body region for our participants (Figure 3.2). For both cervical and thoracic participants, chronic pain was most common in the upper extremities and back, while painful spasticity was the most common in the lower extremities and back. For 8 out of the 11 participants with painful spasticity, body regions where painful spasticity occurred overlapped with a body region where chronic pain was present. Five of these 8 participants noted that painful spasticity was associated with chronic pain and either triggered or exacerbated the pain. In 4 cases, the chronic pain occurring in the area of the painful spasticity was neuropathic, while in the remaining case it was musculoskeletal.
Table 3.1 Participant Demographics. AIS = American Spinal Injury Association Impairment Scale. SCATS = Spinal Cord Assessment Tool for Spastic Reflexes. A=At-level neuropathic pain, B= Below-level neuropathic pain, M=Musculoskeletal pain, V=Visceral pain. sid, once daily; bid, twice daily; tid, three times daily; qid, four times daily; prn, as needed.

<table>
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<th>ID</th>
<th>Sex</th>
<th>Age</th>
<th>Years Post SCI</th>
<th>Injury Level</th>
<th>AIS grade</th>
<th>SCATS total</th>
<th>Prescription Medications</th>
<th>Pain types (worst 3)</th>
<th>Painful Spasticity</th>
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<td>1</td>
<td>F</td>
<td>28</td>
<td>2</td>
<td>T2</td>
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<td>2</td>
<td>T2</td>
<td>B</td>
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<td>13</td>
<td>C2</td>
<td>C</td>
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<td>B</td>
<td>7</td>
<td>None</td>
<td>1. V</td>
<td>No</td>
</tr>
</tbody>
</table>
Figure 3.2. Chronic pain and spasticity-related pain occurrence in participants by body region. Pain frequency for participants with cervical (left) and thoracic (right) injuries were counted separately. Pain did not need to encompass the entire body sub-region to be included in count, and a single pain could be present in more than one location. Darker shade indicates higher frequency. (A) Percent of participants with chronic pain in each body region. Up to 3 worst chronic pains were included for each participant. (B) Percent of participants with spasm-related pain in each body region.
3.3.3 Descriptive statistics and consistency of multidimensional pain and spasticity inventories

This is the first study to utilize a Spasticity Inventory measuring perceived severity and interference of spasticity consistent with the domains frequently used in pain studies. The spasticity questionnaires had Cronbach’s alpha values ranging from 0.80 to 0.95, which demonstrated moderate to substantial internal consistency (Table 3.2) and support some psychometric properties of this new measure. Means, medians, ranges, and interquartile ranges for the inventory subscores are displayed in Figure 3.3. The alpha values for pain subscales were similar to or more consistent than those reported previously.69,114

Table 3.2: Consistency of inventory subscales. aWiderstrom-Noga et al 2006. bKerns et al 1985. *All significance values <0.001 using 2 way mixed model.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Number of Questions</th>
<th>Alpha</th>
<th>Low</th>
<th>Hi</th>
<th>Prior Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>PInterference</td>
<td>8</td>
<td>0.93</td>
<td>0.88</td>
<td>0.97</td>
<td>0.94a</td>
</tr>
<tr>
<td>SInterference</td>
<td>8</td>
<td>0.95</td>
<td>0.90</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>PSeverity</td>
<td>3</td>
<td>0.88</td>
<td>0.74</td>
<td>0.95</td>
<td>0.76a</td>
</tr>
<tr>
<td>SSeverity</td>
<td>3</td>
<td>0.80</td>
<td>0.57</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>Affective Distress</td>
<td>3</td>
<td>0.82</td>
<td>0.62</td>
<td>0.92</td>
<td>0.60a</td>
</tr>
<tr>
<td>Life Control</td>
<td>2</td>
<td>0.92</td>
<td>0.80</td>
<td>0.97</td>
<td>0.79b</td>
</tr>
</tbody>
</table>
**Figure 3.3 Inventory subscales.** Boxplots represent interquartile ranges divided by the median. Whiskers represent full range and diamonds represent means. Number of questions in subscale are indicated in parentheses. Scales range from 0 to 6, with 6 generally indicating the worst score. In the case of LC, 6 indicates best sense of control over life. PS: Pain Severity, SS: Spasticity Severity, PLI: Pain Life Interference, SLI: Spasticity Life Interference, AD: Affective Distress, LC: Life Control.

### 3.3.4 Comparison of impact-related spasticity measures

The scores from impact-related spasticity questionnaires (SCI-SET, 35 questions; S\textsubscript{Interference}, 8 questions; S\textsubscript{Difficulty}, 1 question) were evaluated with bivariate correlations to examine the strength of relationships among these questionnaires (Table 3.3). S\textsubscript{Difficulty} correlated strongly with SCI-SET averages (rho = -0.748, p < 0.005), indicating that the more problematic spasticity was perceived to be for daily activities, the more difficult spasticity was to deal with. This supports the validity of both the SCI-SET and the S\textsubscript{Difficulty} question, suggesting that the S\textsubscript{Difficulty} may be useful as a very brief screening measure. In contrast, S\textsubscript{Interference} was not significantly related to the SCI-SET (rho = -0.125, p = 0.601, Table 3.3), therefore, these measures may capture different domains of the perception of spasticity.
Table 3.3 Correlations between measures of impact of spasticity. Values are Spearman correlation coefficients (rho values). **p<0.01.

<table>
<thead>
<tr>
<th></th>
<th>SCI-SET</th>
<th>S_{Interfere}</th>
<th>S_{Difficulty}</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCI-SET</td>
<td>1.000</td>
<td>-0.125</td>
<td>-0.748**</td>
</tr>
<tr>
<td>S_{Interfere}</td>
<td>-0.125</td>
<td>1.000</td>
<td>0.370</td>
</tr>
<tr>
<td>S_{Difficulty}</td>
<td>-0.748**</td>
<td>0.370</td>
<td>1.000</td>
</tr>
</tbody>
</table>

3.3.5 Relationships between severity of pain and spasticity and impact of pain and spasticity

Self-rated severity of pain and spasticity were positively correlated (rho=0.573, p<0.01, Figure 3.4A). Impact-level measures were also correlated between pain and spasticity: (P_{Difficulty} and S_{Difficulty}, rho=0.673, p<0.01, Figure 3.4B; P_{Interference} and S_{Interference}, rho=0.514, p<0.05, Figure 3.4C). The SCI-SET also correlated strongly with P_{Severity} and P_{Interference} (rho= -0.653 and -0.668, both p<0.01), indicating that greater chronic pain severity and pain interference was associated with greater problematic impact of spasticity on daily activities. Neither the physiological measure (spasm duration) nor clinical measure of spasticity (SCATS) was significantly associated with any of the self-report measures, including self-rated pain and spasticity severity. However, SCATS total score and spasm duration were strongly correlated with each other (rho=0.658, p<0.01).
Figure 3.4. Relationships between severity and impact of chronic pain and of spasticity. (A) Data points represent individual PSeverity and SSeverity subscores. (B) Data points represent individual PDifficulty and SDifficulty scores. (C) Data points represent individual PInterference and SInterference subscores. *p<.05 and **p<0.01, Spearman correlations.

3.3.6 Factors associated with impact of spasticity on life

Affective distress positively correlated with SInterference, and SDifficulty, (rho=0.448 and 0.497 respectively, p values <0.05, Table 3.4A), denoting that more distress was associated with worse impact of spasticity on life. Resilience was negatively correlated with SInterference, implying that factors related to overcoming challenges were associated with less impact of spasticity (rho= -0.519, p<0.05, Table 3.4A). Self-efficacy was not significantly correlated with either SInterference or SDifficulty.

To determine which factors, in addition to spasticity severity, influence the impact of spasticity on daily life, we performed forward multiple regressions for 2 measures: SDifficulty and SInterference. (See Data Analysis for information on interpreting outcomes of multiple regression.) Independent variables included are listed in Table 3.4A. SSeverity, Years Since Injury, and PDifficulty together explained 60.9% of the variance in SDifficulty (F(3, 16)=10.848, p<0.001, Table 3.4B). SSeverity had a stronger relationship with SDifficulty.
scores than the other variables (Beta=0.453, p=0.009, Table 3.4B). Severity and resilience together explained 71.6% of Interference (F(2, 17)=24.94, p<0.001, Table 3.4B), and Severity had a stronger relationship with Interference than resilience (Beta=0.517, p=0.004, Table 3.4B). Other variables did not meet model inclusion criteria, even those variables with significant pairwise correlations with the respective dependent variables.

3.3.7 Impact of painful spasticity on severity and interference of pain and of spasticity

Fifty-five percent of participants (11/20) reported having painful spasticity (Figure 3.2B). Most participants reported painful spasticity as short-lasting painful spasms (<10 minutes), but some participants had longer-lasting pain, which they reported was triggered by or associated with muscle activity. Muscle activity at the time of perceived painful spasticity could not be assessed as the questions were based on recall. Painful spasticity had moderate-high pain intensity (mean: 6.09 out of 10, SD: 2.1).

3.3.8 Participants with painful spasticity experienced greater chronic pain severity and worse interference of spasticity with sleep

Participants who reported having painful spasticity had significantly higher Severity than those without painful spasticity (p=0.020, Figure 3.5A). Group differences for Interference approached significance (p=0.067, Figure 3.5B). Neither the Interference nor SCI-SET average was different between groups (p=0.882 and p=0.131, respectively, Figure 3.5A and B). However, when the individual items of the SCI-SET were compared between groups, two items related to sleep differed between groups: spasticity had a more problematic effect on the ability to get to sleep and quality of sleep (p=0.025 and p=0.031, respectively). Additionally, spasticity had a more problematic effect on pain (p=0.008, Figure 3.5) for persons with painful spasticity.
Table 3.4: Factors related to impact of spasticity on life. (A) Bivariate correlations with 2 measures of the impact of spasticity on life. Values represent Spearman rho coefficients. (B) Outcomes and coefficients for forward regression models. †Spasticity severity was entered into equation while other variables were only carried forward if F for model including that variable was significant at ≤ 0.05. *p<0.05 **p<0.01 ***p<0.001.

(A) Bivariate Spearman correlations

<table>
<thead>
<tr>
<th></th>
<th>P Severity</th>
<th>P Interference</th>
<th>P Difficulty</th>
<th>S Severity</th>
<th>S Difficulty</th>
<th>Resilience</th>
<th>Self-Efficacy</th>
<th>Affective Distress</th>
<th>Spasm Duration</th>
<th>SCATS</th>
<th>Years Since Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Interference</td>
<td>0.418</td>
<td>0.514*</td>
<td>0.209</td>
<td>0.747**</td>
<td>0.370</td>
<td>-0.519*</td>
<td>-0.162</td>
<td>0.448*</td>
<td>0.031</td>
<td>-0.015</td>
<td>0.086</td>
</tr>
<tr>
<td>S Difficulty</td>
<td>0.649**</td>
<td>0.702**</td>
<td>0.673**</td>
<td>0.527*</td>
<td>1.000</td>
<td>-0.188</td>
<td>-0.334</td>
<td>0.497*</td>
<td>-0.173</td>
<td>-0.213</td>
<td>-0.389</td>
</tr>
</tbody>
</table>

(B) Regression outcomes

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Adj. R²</th>
<th>Unstandardized Coefficient</th>
<th>Standardized Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>SEₘ</td>
</tr>
<tr>
<td></td>
<td>(Constant)</td>
<td>2.245</td>
<td>0.752</td>
</tr>
<tr>
<td></td>
<td>S Severity†</td>
<td>0.695</td>
<td>0.233</td>
</tr>
<tr>
<td>SDifficulty</td>
<td>0.609**</td>
<td>-0.066</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>Years Since Injury</td>
<td>0.323</td>
<td>0.143</td>
</tr>
<tr>
<td></td>
<td>P Difficulty</td>
<td>0.323</td>
<td>0.143</td>
</tr>
<tr>
<td>S Interference</td>
<td>0.716**</td>
<td>3.425</td>
<td>1.416</td>
</tr>
<tr>
<td></td>
<td>(Constant)</td>
<td>0.516</td>
<td>0.155</td>
</tr>
<tr>
<td></td>
<td>S Severity†</td>
<td>-0.098</td>
<td>0.034</td>
</tr>
</tbody>
</table>
3.3.9 Greater pain reported by persons with painful spasticity was not due to greater evoked spasm duration

To determine whether higher pain ratings in persons with painful spasticity were because participants with more pain also had more spasticity in general, we compared spasticity levels between groups using SSeverity, the SCATS, and the duration of quadriceps spasms measured by EMG. No significant group differences were detected in these measures (Figure 3.5C-E).

3.4 Discussion

We investigated relationships among pain, spasticity, and psychological factors in 20 persons with spasticity due to SCI. Our results suggest that spasticity and chronic pain are strongly related, and that personal and psychological factors play an important role in the perception of the impact of spasticity on life. We found strong relationships between chronic pain and spasticity regarding their self-rated severity, life interference, and how difficult they were to deal with. We also found that affective distress, self-efficacy, resilience, and injury duration were differentially associated with self-rated spasticity severity and impact of spasticity on daily life. Resilience and self-rated spasticity severity significantly contributed to the perceived interference of spasticity with life, while injury duration, difficulty dealing with pain, and self-rated spasticity severity significantly contributed to difficulty in dealing with spasticity. Finally, chronic pain severity but not spasticity severity was higher in persons with painful spasticity than in persons with non-painful spasticity.
Figure 3.5. Severity and interference of pain and of spasticity in persons with and without painful spasticity. Graphs represent means + SE. *p<0.05 **p<0.001 using the Mann-Whitney U test. (A) Pain and spasticity subscale means. (B) Mean responses to the sleep and pain-related SCI-SET questions with a significant difference between groups. More negative scores indicate more problematic impact of spasticity. (C) Self-rated spasticity severity means. (D) Quadriceps spasm duration, measured as vastus lateralis EMG activity during a seating transfer. Two persons from the painful spasticity group were missing EMG data, resulting in N=9. (E) Clinical spasticity severity, measured by the bilateral SCATS scores. Max =18 for SCATS total score and 6 for SCATS extensor score.

3.4.1 Associations between chronic pain and spasticity

The present study showed significant relationships between ratings of pain and spasticity, suggesting that these phenomena are highly related in persons who experience spasticity and pain after their injuries. However, there was no significant relationship
between pain and clinically-rated spasticity or EMG of spasms. Although no causality can be inferred, our results suggest that pain may contribute to perceived spasticity severity and impact, even though pain is not associated with physiologically and clinically-measured spasticity. Thus, evaluating pain will be helpful in better understanding the subjective experience of spasticity. Our results correspond with the few studies that have examined the strength of relationships between pain and spasticity. For example, Voerman et al.\textsuperscript{108} found a moderate correlation between self-rated pain and leg spasticity (measured by a visual analog scale of pain and spasticity “levels”). However, Shaikh et al.,\textsuperscript{193} failed to find a relationship between numerical rating scores of pain intensity and the Modified Ashworth Score, a clinical test of spasticity severity.

### 3.4.2 Factors that influence the impact of spasticity on daily life

We used a biopsychosocial framework to explore factors that influence the impact of spasticity on daily life. In order to examine the relationship between the perceptions of pain and spasticity, we adapted the Pain Severity and Life Interference subscales of the Multidimensional Pain Inventory to address spasticity. Our methodology of using Difficulty Dealing and Interference scales, in addition to the SCI-SET, allowed for better more multi-dimensional understanding the impact of pain and spasticity on life, and our analysis indicated that the $S_{\text{Interference}}$ measure was not the same as SCI-SET or $S_{\text{Difficulty}}$. It is not a given that different questionnaires that are all related to impact on life will all measure the same construct. Questionnaires designed to measure the impact of a health condition on daily life are not necessarily interchangeable, and depend on the questions asked in that measure. The $S_{\text{Interference}}$ subscale appeared to have face value and
demonstrated strong internal consistency, however its lack of correlation with the SCI-SET and SDifficulty suggests that the SInterference measures a different domain of perceived spasticity.

Both the SCI-SET and SInterference address aspects of both the “activities limitations” and “participation restriction” components of the International Classification of Function in Health and Disability.\textsuperscript{141} However, most SCI-SET items relate to physically-based activities (e.g., showering, transfers, exercise, wheelchair use, body control), while SInterference includes more items that involve participation in society (e.g., relationships with family and friends, planning activities, see Multidimensional Pain and Spasticity Inventory in Appendix). The differences in our regression outcomes for SDifficulty (which was highly related to the SCI-SET) and SInterference also supports the idea that these measures address different domains, and may give insight into which specific factors are more related to the impact of spasticity on physical activities versus social participation (see Table 3.4B). For example, experience dealing with spasticity over time may reduce its perceived difficulty as people learn how to avoid triggers or learn physical adaptation techniques\textsuperscript{9}; however, time since injury may not lessen the impact spasticity has on personal relationships. Indeed, some participants spontaneously mentioned social-related impacts of spasticity, including feeling embarrassed by spasticity when in public, or that friends/family did not understand how one’s limbs could move if one could not walk.

Our finding that resilience significantly predicted SInterference suggests that greater ability to overcome challenges decreases the interference of spasticity with social participation in life. Other studies\textsuperscript{194–196} emphasize the role of self-efficacy in general life
participation for persons with SCI. It is not clear why resilience but not self-efficacy was associated with S\text{Interference} in our study. One possibility is that the Moorong Self-Efficacy Scale measures self-efficacy specifically in the SCI population, with topics including bowel movements and sex, whereas the Connor-Davidson Resilience Scale measures general resilience, such as “adapting to changes.” Furthermore, both Geyh et al.\textsuperscript{194} and Peter et al.\textsuperscript{195} utilized a general self-efficacy scale rather than the Moorong scale. Motor disabilities may influence Moorong Self-Efficacy scores more directly than Connor-Davidson Resilience and general self-efficacy scores.

Our results add to the existing literature that spasticity has complex relationships with multiple contributing factors.\textsuperscript{8,9,108,148} Pain severity and affective distress were significantly associated with spasticity interference and difficulty in dealing with spasticity (S\text{Interference}, S\text{Difficulty}) in pair-wise analyses. However, these variables did not contribute over and above that of other factors (spasticity severity and resilience, or spasticity severity, time since injury, and difficulty dealing with pain) in multivariate models. Similarly, Voerman et al.\textsuperscript{108} found that while pain severity was correlated with perceived spasticity, it did not significantly explain variance in perceived spasticity. Instead, psychological variables related to coping and helplessness contributed significantly to their model.

Extensive literature exists in which the biopsychosocial model of pain is applied\textsuperscript{14,17,197}; however, studies of psychosocial and cognitive influences on spasticity perception and impact are limited. According to the biopsychosocial model and the existing literature, pain intensity is not the only predictor of pain’s impact on life. For example, similar to other chronic pain populations,\textsuperscript{198–200} we have previously found that
individuals with spinal cord injury and pain can be clustered into subgroups based on their psychosocial profiles. Interestingly, the SCI pain population includes a subgroup not found in other pain populations: “interpersonally supported.”

Persons in this subgroup have moderately low levels of pain disability despite experiencing moderately high pain severity. Based on the research findings in pain populations, researchers and clinicians should include measures of the impact of spasticity along with other spasticity measures in order to assess whether a spasticity treatment has a positive outcome for an individual.

### 3.4.3 Painful spasticity

We found that chronic pain, but not severity of spasticity or duration of spasms during a common daily activity, was significantly greater for persons with painful spasticity than for those without. Painful spasticity was commonly reported by our participants as temporary and intermittent spasms, yet our results suggest that painful spasticity affects overall pain severity.

In a handful of persons with painful spasticity, at least one of a participant’s worst chronic pains directly coincided with an area with perceived involuntary muscle activity. Painful spasticity is generally attributed to activation of skeletomuscular nociceptors during muscle contractions. It is possible that in some cases painful spasticity may be partially related to neuropathic pain mechanisms; in fact, persons with neuropathic pain have more spasticity than those with other pain types. Links between chronic pain and painful spasticity need mechanistic exploration.

The more severe chronic pain that we found in persons with painful spasticity may involve a multitude of causes at peripheral, spinal, and brain levels. For example, injury to serotonergic pathways from the brainstem, which descend to both ventral and
dorsal horns, may contribute to decreased endogenous pain inhibition\textsuperscript{82,99} as well as increased spasticity via altered motoneuron properties.\textsuperscript{58,100} Neuroplasticity after injury, such as primary afferent terminal sprouting\textsuperscript{54,63,64} may alter connections between non-noxious sensory pathways (proprioceptive and exteroceptive) and nociceptive pathways. In persons with complete SCI, the nociceptive withdrawal reflex exhibits signs of central sensitization and can undergo further sensitization in response to noxious stimuli.\textsuperscript{46} Thus, activation of muscle nociceptors during bouts of spasticity may also lead to sensitization of spinal pain projection neurons and therefore pain in persons with preserved sensation.

\textbf{3.4.4 Limitations}

Although we quantified evoked spasms using EMG as well as spasticity evoked by passive muscle movement (SCATS) in this study, we were not able to quantify more sustained muscle contractions. Sustained muscle contractions sometimes manifest after SCI even during resting states,\textsuperscript{202} thus, it is possible that persons with painful spasticity in our study did have higher sustained EMG. Additionally, we did not measure self-reported symptoms of spasticity other than pain associated with its occurrence. Considering reports that 62.8\% of persons with SCI and spasticity report the sensation of “tension,”\textsuperscript{101} if sustained muscle contractions are responsible for these sensations, the sustained contractions may have associations with our self-report measures of pain and spasticity. Additionally, recent data support the idea that individuals with spinal cord injury describe their spasticity by both the duration and intensity of involuntary agonist-antagonist muscle co-activity during everyday tasks. Intense co-activation was associated with high tone, while intense contraction of one muscle of an agonist-antagonist pair likely induced joint movement and was associated with severe spasms.\textsuperscript{34}
Our study included a group with high self-efficacy and resilience which may have confounded our results. Means values for self-efficacy (98.2±16.4) and resilience (34.9±5.7) in our participants were significantly higher than those reported in other published studies of spinal cord-injured individuals using the same self-efficacy scale\textsuperscript{124,196,203} or resilience scale.\textsuperscript{124} However, self-efficacy scores of participants in our study was not significantly greater than those considered “high participation” in Craig et al.\textsuperscript{196} (Figure 6, student’s t-test, adjusted p<0.05). The other studies were survey-based, while our participants were required to come to the laboratory and answer questions over the phone, which may have self-selected more self-efficacious individuals.

We may have failed to detect important statistical relationships and differences due to our small sample size. Despite a small sample size, our study highlights several important relationships that can be further investigated in larger sample sizes.

**Figure 3.6.** Means for (A) self-efficacy and (B) resilience from the present study and other studies.*adjusted p<0.05 and **adjusted p <0.01 compared to the present study using student’s t-tests with Bonferroni correction of p-values. HP= High participation group, LP=Low participation group. NS= Not significant. Graphs represent means + SE
3.5 Conclusions

This study helps fill the gap in literature regarding relationships between spasticity and pain. The strong relationships between self-rated pain and spasticity measures suggest that pain and spasticity are intimately related in how they impact daily life and may have underlying mechanistic relationships. These relationships should be further examined in larger studies. Given the strength of relationships between pain and spasticity, and the findings that those with painful spasticity have worse chronic pain and worse impact of spasticity on sleep, it would be informative to investigate pain and spasticity together, including a more detailed investigation of painful spasticity. Treating painful spasticity may reduce chronic pain or improve quality of sleep, and may therefore synergistically improve quality of life. These relationships and their treatment implications in the SCI population are worthwhile to evaluate in other neurological conditions associated with spasticity and pain, including stroke and multiple sclerosis.
CHAPTER 4: SUMMARY OF FINDINGS AND FUTURE DIRECTIONS

4.1 Overview

Chapter 1 introduced the common secondary consequences of pain and spasticity after SCI, reviewed physiological mechanisms and psychosocial literature related to pain and spasticity, and introduced the research aims. In Chapter 2, I aimed to fill gaps in spasticity research by characterizing relationships between physiological measures of spasms during a common daily activity with the perceived impact of spasticity on daily activities. I also characterized the relationships between physiological measures of spasms in a quadriceps muscle with a clinical test of extensor spasticity. In Chapter 3, I further investigated what factors, including pain and psychological factors, are related to the problematic impact of spasticity on life. Additionally, I characterized relationships between subjective measures of spasticity and chronic pain, and compared spasticity and chronic pain in people with and without painful spasticity.

In this chapter, I will summarize the findings in Chapters 2 and 3, discuss novel aspects of the studies, and discuss future implications of the research. In particular, I will focus on implications of psychosocial aspects of spasticity research. I will also discuss the role of common medications prescribed to treat pain and spasticity after SCI and their potential effects in our research participants.

4.2 Summary of findings

4.2.1 Physiological and clinical measures of spasms were significantly related to each other but not with the perceived impact of spasticity on daily life or self-rated spasticity severity.

The results of research related to Aim 1 (Chapter 2) demonstrated that spasm duration in a knee extensor muscle during transfers and clinically-rated extensor
spasticity severity were strongly related to each other, but that neither were significantly associated with the impact of spasticity on life. While it is possible that the lack of a significant relationship of spasm duration with impact of spasticity was because I measured activity in a single muscle during a single task, I had chosen a muscle group (quadriceps) and a task (seating transfers) that were frequently reported to be problematic in spasticity literature.

In Chapter 3, I broadened the investigation into the relationships between spasms and perceived problematic impact of spasticity by utilizing multiple measures of the problematic impact of spasticity on life (Spasticity Interference and Difficulty Dealing with Spasticity) and a clinical measure of total lower extremity spasticity (SCATS total score) rather than a unilateral extensor score. I also included participants with voluntary motor function in order to better represent less severe injuries. The results were similar to Chapter 2 findings: clinical and physiological measures of spasms were associated with each other but were not significantly associated with the impact of spasticity on daily life. Interestingly, the clinical and physiological measures were also not significantly associated with self-rated spasticity severity. In contrast, greater self-rated spasticity severity was associated with more difficulty dealing with spasticity as well as greater interference of spasticity on life (Table 3.4).

The sample means for the measures of the impact of spasticity on life indicated that study participants overall perceived spasticity as mildly problematic (Chapter 2, Figure 2.5, Chapter 3, Figure 3.3). Yet, spasticity is known to be a significantly
problematic issue which negatively influences quality of life.\textsuperscript{2,3} It is therefore important to consider that the participants in this sample represents a subset of the SCI population who perceive spasticity as mildly problematic overall.

4.2.2 Personal factors, including psychological factors and chronic pain, were significantly related to an individual’s perception of the impact of spasticity on activities of daily living.

The finding in Chapter 2 that impact of spasticity on daily life was unrelated to measures of involuntary muscle activity lead us to hypothesize that personal factors would influence the perceived impact of spasticity on life. Indeed, the findings from Chapter 3 demonstrated that the perceived impact of spasticity on daily life was related to several personal factors. In addition to self-rated spasticity severity, greater pain severity, interference of pain with life, and perceived difficulty dealing with pain, as well as greater affective distress and less resilience were significantly associated with more problematic scores for measures of impact of spasticity on life (Table 3.4A). Self-rated spasticity severity and less resilience together explained 71.6\% of the variance in the ratings of the interference of spasticity with life (Table 3.4B), while injury duration, spasticity severity, and difficulty dealing with pain explained 60.9\% of the variance in how difficult spasticity was to deal with.

Importantly, the influence of psychological factors in our participants should be considered when interpreting the low means for perceived impact of spasticity. Study participants had significantly higher levels of self-efficacy and resilience compared to their SCI peers in other studies (Figure 3.6),\textsuperscript{124,196,203} and our results indicate that greater resilience was associated with less perceived interference of spasticity. High resilience and self-efficacy likely contributed to the low perceived impact of spasticity. Another
possibility should be considered: that persons with chronic injury may learn to avoid activities that evoke spasms and this may lead to lower perceived impact of spasticity due to lack of exposure to activity-evoked spasms.

The results reported in Chapter 3 suggest that spasticity and pain are strongly interrelated, in that greater pain severity was associated with greater spasticity severity (Figure 3.4A). This was consistent with the relationship between greater negative impact of pain on life and greater negative impact of spasticity on life (Figure 3.4B and C). Moreover, the more severe pain in persons with painful spasticity than persons without painful spasticity (Figure 3.5A) suggested that painful spasticity may exacerbate chronic pain in this population.

4.2.3 Persons with painful spasticity had greater chronic pain levels and greater impact of spasticity on pain and sleep than those without painful spasticity.

In Chapter 3, physiological and self-report measures of spasticity and pain were compared between those who reported having painful spasticity and those who did not find their spasticity painful. Clinically-rated and self-rated severity of spasticity were not greater in persons with painful spasticity, nor did they experience greater spasms in an extensor muscle during seating transfers (Figure 3.5 C-E). However, persons who experience painful spasticity had significantly higher overall pain severity (Figure 3.5A). Persons with painful spasticity reported a more negative impact of spasticity on pain and sleep.

4.3 Novelty of findings

For chronic pain research, the biopsychosocial model is widely accepted. A biopsychosocial perspective can be applied to other conditions such as spasticity,
however, there have been few other investigations involving people with spasticity that have used a biopsychosocial perspective. My results highlight that the impact of spasticity on life for people with SCI has complex relationships with multiple contributing factors, similar to what is established in the pain field.

In Chapter 3, I demonstrated several relationships between chronic pain and spasticity. There have been few in-depth characterizations of the relationships between pain severity and impact with spasticity severity and impact in studies that address both sequelae of SCI. Most other studies that have investigated both pain and perceived spasticity report descriptive statistics of the proportion of individuals who experience pain associated with spasticity. Only a few studies have characterized relationships between them. Several novel aspects of Chapter 2 and 3 are enumerated here:

**Aim 1/Chapter 2 novelty**

1. To my knowledge, no studies published in persons with SCI have assessed relationships between a comprehensive measure of the activity limitations and participation restrictions due to spasticity with the body functions of spasm duration and magnitude. This may be because the SCI-SET is one of only two comprehensive, validated measures of activity limitations and participation restrictions for SCI, and these measures have had limited use, despite recommendations for inclusion in spasticity assessment.

2. To my knowledge, no studies have assessed relationships between EMG specifically recorded during transfers and a clinical test of spasticity severity. EMG has instead been recorded during clinical Ashworth tests and the SCATS test itself.
Aim 2/Chapter 3 novelty

1. To my knowledge, the study in Chapter 3 is the first to investigate whether persons with SCI with painful spasticity have higher levels of chronic pain than persons for whom spasticity is not painful.

2. I utilized a novel measure of spasticity with a rating scale that was consistent with common and validated scales used in SCI pain research. This scale may thus have value as a measure of the impacts of spasticity on social participation.

3. To my knowledge, this is the first study to characterize associations between the impact of spasticity after SCI and affective distress, life control, resilience and self-efficacy. One other study quantified the influence of psychological factors in the perception of spasticity. That study addressed the role of factors on perceived spasticity “level” rather than impact of spasticity on daily life.

4.4 Implications of research findings and future directions

4.4.1 Implication: Measuring the psychosocial aspects of spasticity is important

Utilizing a combination of subjective (self-report) and objective (physiological) measures of spasticity is important for a comprehensive evaluation and to better understand the clinical problem. The results from Chapters 2 and 3 highlight the importance of the personal perspective and individual psychological factors in understanding spasticity. Involuntary muscle activity, measured with an objective physiological measure and a clinical test, was not related to perceived impact of spasticity on life. In contrast, personal factors were related to this impact. This finding suggests that the severity of a medical condition alone does not determine impact on life and participation but relies on personal abilities to adapt and cope.
4.4.2 Implications: Painful spasms

Chapter 3 results demonstrated that pain and spasticity were strongly interrelated and that persons with painful spasms had worse impact of spasticity on chronic pain levels and sleep. These finding may be useful for clinicians, as treating painful spasticity may reduce chronic pain or improve quality of sleep, and may therefore synergistically improve quality of life.

4.4.3 Future directions: Explore relationships between spasticity and stress

As discussed in Chapter 1, persons report that emotional distress both triggers spasticity and results from spasticity.8–10,26,136 In persons with spasticity, it is not known whether stress and anxiety actually increase involuntary motor activity, whether stress merely causes perception of increased spasticity, or whether a combination of factors accounts for the perceived influence of stress on spasticity. It is possible that spasticity and negative emotional have bi-directional relationships, similar to relationships of pain and negative psychological factors such as depression.17,111–113,115,116 In Chapter 3, we found that a negative impact of spasticity on life was associated with more affective distress. In addition to a potentially large role of psychological factors in the perception of spasticity, it is possible that psychological factors also influence involuntary motor activity. The relationships between stress and involuntary muscle activity after SCI could be explored experimentally using EMG.

4.4.4 Future directions: Can psychological approaches used in pain management improve problematic aspects of spasticity?

In terms of both mechanistic and psychosocial aspects, findings from nociceptive and pain research can inform sensorimotor research and vice versa. Nociception and
proprioception are integrated systems. As discussed in Chapter 1 and 3, in SCI, pain and spasticity share some of the same pathophysiological mechanisms. Additionally, pain and spasticity are both sensory experiences filtered and modulated by the brain. Pain by definition involves one’s emotional, cognitive state; however, one’s experience of spasticity or any health condition happens within the context of one’s psychological state and therefore psychological factors may be able to be targeted in spasticity management.

If negative psychological factors such as stress causally influence involuntary muscle activity, degree of perceived spasticity, or both, then increasing positive psychological factors may target any of these mechanisms. Increasing positive psychological factors such as resilience or coping ability related to spasticity might make an individual feel that spasticity has a less problematic impact on daily life, even if one’s underlying pathophysiology does not change. If the correlation of greater resilience with less interference of spasticity represented a causal influence of resilience on interference of spasticity, then increasing resilience in persons with spasticity could reduce the perceived impact of spasticity on life.

As spasticity generally does not present a health threat (although consequences such as falling do), interventions can focus on reducing the perceived problematic aspects of spasticity. Future studies should explore whether problematic impact of spasticity can be reduced by targeting psychological factors. Cognitive and behavioral therapies such as those utilized for chronic pain may be able to upregulate positive factors such as resilience and coping. Findings from the literature on cognitive behavioral therapy in persons with pain may be useful to apply to behavioral management of spasticity.
4.4.4.1 Cognitive Behavioral Therapy has been used to improve quality of life in persons with chronic pain

Biopsychosocial approaches in chronic pain management aim to increase adaptive coping skills and improve quality of life.\textsuperscript{17} Treatments often focus on improving a person’s ability to cope with and adapt to pain. Cognitive Behavioral Therapy (CBT) is one such type of approach with some evidence of effective results for a variety of chronic pain conditions.\textsuperscript{205} Interventions vary widely, but all try to change behavioral response through positive or negative reinforcement and additionally utilize attention to the cognitive and affective factors that influence behavior.\textsuperscript{14(p131)} The underlying idea supporting this approach is that treatment interventions for a particular problem will be most effective if the individual actively addresses emotional, cognitive and behavioral dimensions of the problem.\textsuperscript{14(p131)}

A study\textsuperscript{121} indicated that a CBT intervention in persons with neuropathic pain after SCI had a beneficial effect on factors that influence pain intensity and pain-related disability. Three months after the intervention, participants scored higher on measures of coping strategies and optimism and lower on catastrophizing and reliance on healthcare. While pain intensity and pain disability scores themselves were not significantly reduced after the intervention, participants with greater adoption of positive pain coping strategies in the course of the intervention also had less pain intensity and pain-related disability after the intervention. Considering that neuropathic pain after SCI is particularly refractory to treatment and difficult to deal with\textsuperscript{3} and that the trial enrolled participants with moderate and severe neuropathic pain, the results are very significant.

A systematic review found that CBT interventions for different chronic pain conditions had significantly greater improvements in multiple domains compared to no
treatment and alternative treatments. While it is not clear whether CBT is always associated with better long term outcomes relative to other approaches, cognitive therapies are safe and cost-effective compared to other therapies such as surgeries and can be used in conjunction with other approaches.

4.5. Discussion: Mechanisms and effects of prescription medications used by the participants

Although examining the effects of medication on spasticity and pain were outside the scope of the studies in Chapters 2 and 3, I discuss them here as they relate to spasticity management and potential effects on our participants. A table of prescription analgesic, antispastics and antidepressant medications used by the participants are listed in Table 4.1.

4.5.1 Common treatments for spasticity and pain management

Pharmacological, invasive, and non-pharmacological, non-invasive treatments are used clinically to reduce spasticity symptoms. Systemic pharmacological agents are commonly prescribed; of these, GABA receptor agonists or modulators (baclofen and diazepam), α2 adrenergic agents (tizanidine and clonidine) and muscle agents (dantrolene) are the most common. Invasive treatments block afferent nerves, motor nerves, or muscle contraction using ablation, targeted application of agents, or insertion of electrical stimulators. For example, intrathecal baclofen pumps may reduce systemic pharmacological side effects compared to oral baclofen but also present risks such as infection and equipment malfunction. Non-invasive management methods include therapies to improve range of motion, improve voluntary control, or provide movement
strategies. Additionally, non-invasive electrical stimulation, transcranial magnetic stimulation, and vibration target neuromodulation as a means to reduce spasticity.

The Canadian SCI pain working group clinical practice recommended pregabalin, gabapentin and amitriptyline as first line therapies for neuropathic pain after SCI, and tramadol and lamotrigine as second-line therapies. Non-invasive electrical stimulation, visual illusion, oxycodone, and surgical ablation of the dorsal root at the entry zone were third-line recommendations.

### 4.5.2 Why can the GABA agonist baclofen be effective in persons with SCI?

Baclofen is a commonly prescribed antispastic medication and was the most widely-used medication in my study participants. It is a GABA\textsubscript{B} receptor agonist. The GABA\textsubscript{B} receptor is a metabotropic receptor that increases inhibition through activation of potassium channels and is slower than the ionotropic GABA\textsubscript{A} receptors. Inhibition via GABA\textsubscript{B} receptors does not directly depend on the chloride reversal potential like GABA\textsubscript{A} receptors. As discussed in Chapter 1, evidence of dysregulated chloride homeostasis is linked to both neuropathic pain and spasticity after SCI. However, SCI affects GABA\textsubscript{B} receptors as well; their density is reduced after SCI but recovers with exercise.

In the spinal cord, the majority of GABA\textsubscript{B} receptors are presynaptic, located on primary afferent terminals. Activation of GABA\textsubscript{B} receptors on I\textsubscript{a} neurons can presynaptically inhibit the monosynaptic stretch reflex on motoneurons, reducing this type of hyperreflexia associated with spasticity.

### 4.5.3 Medications can have off-target effects

Due to the majority of persons with spasticity also having chronic pain, many persons with spasticity will also take pain medications and vice versa. Medications
prescribed for spasticity or pain are usually centrally-acting and therefore most have off-target effects. For example, baclofen is sedating when taken orally, and has some antinociceptive effects when taken orally or intrathecally.\textsuperscript{210,211} Additionally, most antispastic medications weaken muscles and may have long term negative effects on motor units.\textsuperscript{142,212} Analgesics can affect motor function and psychological function. For example, the anticonvulsant gabapentin commonly used for pain after SCI can reduce spasticity,\textsuperscript{213,214} and early use of anticonvulsants for pain after SCI predict greater motor recovery.\textsuperscript{215} Conversely, use of opioids in acute stages of SCI attenuates motor recovery in animal models.\textsuperscript{216,217} Long-term pregabalin (but not gabapentin or baclofen) use impairs memory in rats.\textsuperscript{218}

4.5.4 Medications as potential mediators or confounders of relationships

Whether medication should be considered a potential confounder of results depends on the research questions, study design, and relationships measured. My main research questions were not mechanistic, experimental, nor predictive. This research intended to describe and explain relationships in our participants rather than predict future behavior. Furthermore, medications may not always fit the definition of a potential confounder.\textsuperscript{219–221}

1. Confounders predict the outcome even in the absence of exposure.
2. Confounders are associated with the exposure and the outcome but are not surrogates for the exposure.
3. A confounder is not an intermediate between the exposure and the outcome.

In an observational study, the exposure can be a risk factor or prognostic factor.\textsuperscript{220} In the primary hypothesis in Chapter 2, spasm duration/magnitude would be the exposure and
the impact of spasticity on life (SCI-SET score) would be the outcome. A medication used to alleviate spasticity symptoms is not a confounder of the relationship between spasticity (exposure) and perception of spasticity (outcome). Instead it may be a mediator between the relationship, a causal link between the condition and a related measurement. A medication could be a potential confounder of relationships between spasticity and a medication prescribed for something other than spasticity, but would have to fit all the criteria. In the context of Aim 1, I did not investigate antispastics as a confounder because it better fits the definition of an intermediate. Additionally, as noted in Chapter 2, dosage of antispastic medications (along with age and injury level) were not significantly associated with transfer-related variables or impact of spasticity on daily life. However, I listed medications used by study participants in the demographic table.
Table 4.1. Mechanisms of prescription medications used by participants. To see which participants used which medications, see Chapter 3 Table 3.1 Participant demographics. Of the 21 subjects included in both studies, 9 used no prescription medications and 1 used only an occasional bladder antispastic (Solifenacin).

<table>
<thead>
<tr>
<th>Type</th>
<th>Medication (# using)</th>
<th>Effects on spasticity and pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Prescribed for spasticity (skeletal muscle)</strong></td>
<td></td>
</tr>
<tr>
<td>GABA analogue</td>
<td>Baclofen (6)</td>
<td>GABA$_A$ receptor agonist. Increases pre and post synaptic inhibition, resulting in reduced activation of motor neurons. $^{142}$ Anti-nociceptive.$^{210}$</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Diazepam (1)</td>
<td>Modifies GABA$_A$ receptor function to facilitate GABA-mediated chloride conductance. Increases effectiveness of pre-synaptic inhibition of mono and polysynaptic reflexes.$^{142}$</td>
</tr>
<tr>
<td>Barbiturate-like</td>
<td>Carisoprodol (1)</td>
<td>Modifies GABA$_A$ receptor function, but exact mechanism unknown. Depresses motor function and pain perception.$^{222,223}$</td>
</tr>
<tr>
<td>Tricyclic antidepressant-like</td>
<td>Cyclobenzaprine (1)</td>
<td>Mechanism unknown. May be 5HT$_2$ antagonist. Depresses motor function and pain perception.$^{222}$</td>
</tr>
<tr>
<td>Antiadrenergic</td>
<td>Clonidine (1)</td>
<td>$\alpha_2$ adrenergic receptor agonist. Increases presynaptic inhibition of polysynaptic reflexes. $^{142}$</td>
</tr>
<tr>
<td>Peripherally-acting muscle relaxant</td>
<td>Dantrolene (1)</td>
<td>Inhibits muscle contraction by blocking the release of calcium from sarcoplasmic reticulum.$^{142}$</td>
</tr>
<tr>
<td></td>
<td><strong>Prescribed for bladder spasticity (smooth muscle)</strong></td>
<td></td>
</tr>
<tr>
<td>Antimuscarinic</td>
<td>Oxybutnin (2) Solifenacin (1) Darifenacin (1)</td>
<td>M3 acetylcholine receptor antagonist. Inhibits smooth muscle spasms.$^{224}$</td>
</tr>
<tr>
<td></td>
<td><strong>Prescribed for pain</strong></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsant</td>
<td>Pregabalin (1) Gabapentin (2)</td>
<td>Inhibits calcium currents by binding to voltage-dependent calcium channel $\alpha_2\delta$ subunit. Reduces excitatory pro-nociceptive transmitter release and dorsal horn neural hyperactivity.$^{225}$ Gabapentin can reduce spasticity.$^{213,214}$ Pregabalin use may impair memory.$^{218}$</td>
</tr>
<tr>
<td>Opioid</td>
<td>Oxycodone (3) Hydrocodone (1)</td>
<td>Binds to opioid receptors throughout CNS and body. Analgesia achieved in part by increasing pain inhibition pre and post-synaptically in the dorsal horn. Decreases neural excitability through various mechanisms. Many other central and peripheral effects.$^{226}$</td>
</tr>
<tr>
<td>Opioid-like</td>
<td>Tramadol (1)</td>
<td>Multiple, including $\mu$-opioid agonist and monoamine reuptake inhibitor. Analgesia linked most strongly to opioid actions.$^{227,228}$</td>
</tr>
<tr>
<td></td>
<td><strong>Prescribed for depression</strong></td>
<td></td>
</tr>
<tr>
<td>Selective Serotonin Reuptake Inhibitor</td>
<td>Sertraline (1)</td>
<td>Reduces depression. Some evidence of pain reduction.$^{229}$</td>
</tr>
</tbody>
</table>
4.5.5 Comparing outcomes between medication users and non-users

In the multivariate models assessing the impact of spasticity on daily life in Chapter 3 (Table 3.4B), I did not include medication use. There is a risk of obscuring a true relationship between exposure and outcome when adding too many intermediate variables into the model.221 Instead, I used Mann-Whitney U tests to compare the distribution of scores in my measures between people who took prescription medications (regular use of analgesics, antispastics, and antidepressants) and those who did not take these medications (Table 4.2). Those taking prescription medications regularly had greater pain severity, difficulty dealing with spasticity, and affective distress. Other variables were not significantly different between groups (age, years injured, pain life interference, spasticity severity, spasticity life interference, difficulty dealing with pain, life control, SCATS extensor scores and quadriceps spasm duration). Greater scores for pain severity are consistent with the understanding that current medication treatments are not fully effective at reducing pain after SCI.72,230,231
Table 4.2 Outcomes for regular prescription medication users and non-users. Differences were measured with Mann-Whitney U-test. †bilateral extensor score. * P < 0.05

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Years Injured</th>
<th>P_Severity</th>
<th>P_Interference</th>
<th>P_Difficulty</th>
<th>S_Severity</th>
<th>S_Interference</th>
<th>S_Difficulty</th>
<th>Affective Distress</th>
<th>Life Control</th>
<th>SCATS†</th>
<th>Spasm Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription Non-users (10)</td>
<td>Mean</td>
<td>41.30</td>
<td>19.90</td>
<td>1.73</td>
<td>1.46</td>
<td>2.20</td>
<td>1.77</td>
<td>0.93</td>
<td>2.60</td>
<td>1.47</td>
<td>5.25</td>
<td>3.90</td>
</tr>
<tr>
<td></td>
<td>SE</td>
<td>4.07</td>
<td>4.16</td>
<td>0.45</td>
<td>0.45</td>
<td>0.73</td>
<td>0.40</td>
<td>0.40</td>
<td>0.67</td>
<td>0.34</td>
<td>0.34</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>35.50</td>
<td>18.00</td>
<td>1.83</td>
<td>1.06</td>
<td>1.50</td>
<td>1.67</td>
<td>0.38</td>
<td>2.00</td>
<td>1.50</td>
<td>5.50</td>
<td>4.00</td>
</tr>
<tr>
<td>Prescription Users (10)</td>
<td>Mean</td>
<td>38.60</td>
<td>9.50</td>
<td>3.23</td>
<td>2.06</td>
<td>3.30</td>
<td>2.10</td>
<td>1.06</td>
<td>4.40</td>
<td>2.60</td>
<td>4.50</td>
<td>3.00</td>
</tr>
<tr>
<td></td>
<td>SE</td>
<td>2.59</td>
<td>1.42</td>
<td>0.49</td>
<td>0.47</td>
<td>0.68</td>
<td>0.41</td>
<td>0.42</td>
<td>0.40</td>
<td>0.37</td>
<td>0.48</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>37.00</td>
<td>11.50</td>
<td>3.50</td>
<td>1.81</td>
<td>3.50</td>
<td>1.67</td>
<td>0.44</td>
<td>4.50</td>
<td>2.33</td>
<td>5.00</td>
<td>3.50</td>
</tr>
<tr>
<td>Significance</td>
<td>0.97</td>
<td>0.09</td>
<td><strong>0.04</strong></td>
<td>0.22</td>
<td>0.32</td>
<td>0.63</td>
<td>0.85</td>
<td><strong>0.04</strong></td>
<td>0.03</td>
<td>0.32</td>
<td>0.28</td>
<td>0.54</td>
</tr>
</tbody>
</table>
4.6. Concluding remarks

In conclusion, my results indicate that there is a need for further study of the roles of psychosocial factors and chronic pain conditions in people who experience spasticity after their SCI. When performing spasticity research, a biopsychosocial perspective that is inclusive of psychosocial factors and pain can provide a framework for finding factors that may influence the impact of spasticity on life. Interventions that modulate factors that are strongly related to impact may result in less problematic impact and better management of spasticity and pain after SCI.

Figure 4.1: How measured variables related to spasticity fit into ICF domains
APPENDIX

Multidimensional Pain and Spasticity Inventory (SCI version subscales). Questions belonging to specific subscales (eg. Pain Severity) are labelled. Modified from Widerström-Noga et al.69

Definitions

The term “your spasticity” could mean: uncontrolled, involuntary muscle contraction or movement (slow or rapid; short or prolonged); or involuntary, repetitive quick muscle movements; or muscle tightness, or whatever you might describe as spasms. The term “your pain” includes all pain that you may have, meaning anything that feels painful to you, or anything you would describe as pain, even if it is very low-level pain.

Pain Inventory

Now I will ask you questions about you and your pain. I want you to take into account all of your pains when I ask these next questions, and think about your pain overall, not separately. Listen to each question carefully and then choose a number to indicate how that question applies to you. These questions range from 0 to 6. For each question, I will tell you what the numbers mean.

<table>
<thead>
<tr>
<th>Pain Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Rate the level of your pain at the present moment.</td>
</tr>
<tr>
<td>No pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pain Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. How much has your pain changed the amount of satisfaction or enjoyment you get from taking part in social and recreational activities?</td>
</tr>
<tr>
<td>No change</td>
</tr>
</tbody>
</table>
### Pain Severity

3. On the average, how severe has your pain been during the past week?

<table>
<thead>
<tr>
<th>Not at all severe</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Extremely severe</th>
</tr>
</thead>
</table>

### Pain Interference

4. How much has your pain changed your ability to take part in recreational and other social activities?

<table>
<thead>
<tr>
<th>No change</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Extreme change</th>
</tr>
</thead>
</table>

### Pain Interference

5. How much do you limit your activities in order to keep your pain from getting worse?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Very much</th>
</tr>
</thead>
</table>

### Pain Interference

6. How much has your pain changed the amount of satisfaction or enjoyment you get from family-related activities?

<table>
<thead>
<tr>
<th>No change</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Extreme change</th>
</tr>
</thead>
</table>

### Pain Severity

7. How much suffering do you experience because of your pain?

<table>
<thead>
<tr>
<th>No suffering</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Extreme suffering</th>
</tr>
</thead>
</table>

### Pain Interference

8. How much has your pain changed your relationship with your spouse, family, or significant other?

<table>
<thead>
<tr>
<th>No change</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Extreme change</th>
</tr>
</thead>
</table>

### Pain Interference

9. How much has your pain changed your ability to do household chores?

<table>
<thead>
<tr>
<th>No change</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Extreme change</th>
</tr>
</thead>
</table>
10. How much has your pain interfered with your ability to plan activities?
No interference  0  1  2  3  4  5  6 Extreme interference

11. How much has your pain changed or interfered with your friendships with people other than your family?
No change  0  1  2  3  4  5  6 Extreme change

Spasticity Inventory

The next 12 questions are about you and your spasticity. The questions still range from 0 to 6. Please listen carefully to the questions and then choose a number to indicate how the question applies to you.

12. Rate the level of your spasticity at the present moment.
No spasticity  0  1  2  3  4  5  6 Very intense spasticity

13. How much has your spasticity changed the amount of satisfaction or enjoyment you get from taking part in social and recreational activities?
No change  0  1  2  3  4  5  6 Extreme change

14. On the average, how severe has your spasticity been during the past week?
Not at all severe  0  1  2  3  4  5  6 Extremely Severe
15. How much has your spasticity changed your ability to take part in recreational and other social activities?

| No change | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extreme change |

16. How much do you limit your activities in order to keep your spasticity from getting worse?

| Not at all | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Very much |

17. How much has your spasticity changed the amount of satisfaction or enjoyment you get from family-related activities?

| No change | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extreme change |

18. How much suffering do you experience because of your spasticity?

| No suffering | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extreme suffering |

19. How much has your spasticity changed your relationship with your spouse, family, or significant other?

| No change | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extreme change |

20. How much has your spasticity changed your ability to do household chores?

| No change | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extreme Change |
21. How much has your spasticity interfered with your ability to plan activities?
No interference  0  1  2  3  4  5  6  Extreme interference

22. How much has your spasticity changed or interfered with your friendships with people other than your family?
No change  0  1  2  3  4  5  6  Extreme change

General Inventory

The next questions are about you in general. The range is still from 0 to 6. Please listen carefully to the questions and then choose a number to indicate how the question applies to you.

23. Rate your overall mood during the past week.
Extremely low  0  1  2  3  4  5  6  Extremely high

Note: The score for this question is inverted for analysis

24. During the past week, how much do you feel that you have been able to deal with your problems?
Not at all  0  1  2  3  4  5  6  Extremely well

Affective Distress

25. During the past week, how irritable have you been?
Not at all irritable  0  1  2  3  4  5  6  Extremely irritable
26. During the *past week*, how tense or anxious have you been?

| Not at all tense or anxious | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extremely tense or anxious |

27. During the *past week*, how much control do you feel that you have over your life?

| No control | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Extreme control |
WORKS CITED


