EXPLORING PELVIC FLOOR MUSCLE SPARING IN INDIVIDUALS WITH SPINAL CORD INJURY USING PELVIC FLOOR TRAINING EXERCISES AND TRANSCRANIAL MAGNETIC STIMULATION

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The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, a thesis/dissertation entitled:

Exploring pelvic floor muscle sparing in individuals with spinal cord injury using pelvic floor training exercises and transcranial magnetic stimulation

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Abstract

Background: The pelvic floor muscles (PFM) are crucial in maintaining urinary continence. Damage and denervation to this muscle group is associated with urine leakage. In able-bodied individuals, exercise programs intended to strengthen the core and PFM are considered the first line of treatment against urinary incontinence. However, limited research has explored applying these exercises to people with spinal cord injury (SCI), where more than 80% of individuals experience bladder dysfunction. PFM training programs may not have been attempted in people with SCI because of assumptions about remaining PFM function post-injury. Further, for those with high-thoracic motor-complete SCI (mc-SCI), it is often incorrectly assumed that they are unable to engage muscles of the core based on standard neurological assessment. Evidence from previous work has already shown that sparing in abdominal function can be detected using manual palpation, surface electromyography, and transcranial magnetic stimulation. It remains unknown to what extent the PFM may be similarly spared in this population.

Objectives: To a) characterize and compare activation patterns of pelvic floor, abdominal, and gluteal muscles during validated PFM training exercises in able-bodied individuals and those with mc-SCI and b) evaluate corticospinal excitability to the PFM via transcranial magnetic stimulation.

Methods: This study will use a two-part cross-sectional design. In both parts, EMG recordings will be taken bilaterally from rectus abdominis, external oblique, erector spinae, levator ani, and gluteus maximus muscles. In Part 1, participants will attempt a variety of validated maneuvers to
attempt to elicit PFM activity. In Part 2, participants will receive transcranial magnetic stimulation targeting the pelvic floor.

**Results:** Our results show that voluntary activation is possible for all AB and the majority of SCI participants. For AB participants, Kegels and gluteal contractions elicited the largest responses, but for SCI participants, abdominal exercises elicited the largest responses. MEPs were elicited in the PFM for all AB subjects and all but two SCI participants.

**Conclusion:** Our results suggest that those with mc-SCI retain functional sparing to the PFM after injury. This supports the application of PFM training programs to this population.
Lay Summary

The pelvic floor muscles (PFM) are important for bladder health by preventing urine leakage. Previous research has shown that exercises to strengthen the PFM (e.g. Kegels) can help individuals who suffer from urinary incontinence. Approximately 80% of those with spinal cord injury (SCI) experience bladder impairments, but we have yet to effectively apply PFM training programs to this population because we do not know how the PFM function after a SCI. The purpose of this study was to examine if people with SCI can voluntarily active their PFM and to evaluate if there is still a connection from the brain to these muscles after injury. Our results indicate that those with SCI may still have functional PFM activity. We hope that these results will support future research on the effects of PFM training programs on bladder health in this population.
Preface

The idea of this project was developed through discussions with my thesis supervisor Dr. Tania Lam about how the pelvic floor muscles may act as a target for improving neurogenic bladder symptoms after spinal cord injury. Dr. Mark Carpenter and Dr. Lynn Stothers contributed in the concept formation. The hypotheses and research design were developed by myself in consultation with Dr. Lam and Dr. Carpenter. All data collection and analysis were performed by myself under the guidance of Dr. Lam. This project was approved by the Clinical Research Ethics Board of UBC (“PFM study”, H17-00794).

At the time of thesis submission, the experiments contained in this thesis have not been submitted for publication. However, preliminary results were presented by myself at the 48th Alberta Motor Control Meeting (Jasper, Alberta; September 2017), the 10th World Congress for Neurorehabilitation (Mumbai, India; February 2018) and Neuroscience 2018 (San Diego, USA; November 2018).
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Chapter 1: Introduction

The pelvic floor muscles (PFM) play a crucial role in bladder control by facilitating the voluntary retention and voiding of urine (Ashton-Miller & DeLancey, 2007; Fowler, Griffiths, & de Groat, 2008). In able-bodied individuals, exercises intended to strengthen the pelvic floor are considered the first line of treatment in urinary incontinence (Bø, 2004, 2012). The spinal cord injury population experiences high levels of urinary incontinence; however, limited research has examined whether PFM training may improve bladder outcomes in this population (Elmelund, Biering-Sorensen, Due, & Klarskov, 2018; Vásquez et al., 2015).

For individuals with high-thoracic motor-complete spinal cord injury (mc-SCI), it is often incorrectly assumed that they are unable to engage muscles of the core based on standard neurological assessments (Kirshblum et al., 2011). Recent evidence has shown that sparing in abdominal muscle function can be detected by manual palpation and surface electromyography in these individuals (Altmann, Groen, van Limbeek, Vanlandewijck, & Keijsers, 2013; Bjerkefors, Carpenter, Cresswell, & Thorstensson, 2009; Pernot et al., 2011). Moreover, transcranial magnetic stimulation over the primary motor cortex can elicit motor-evoked potentials in the abdominal muscles, indicating preservation of corticospinal input to these muscles in people classified as mc-SCI (Bjerkefors et al., 2015; Squair, Bjerkefors, Inglis, Lam, & Carpenter, 2016). If people with mc-SCI have sparing of the PFM similar to sparing of other core muscles, then new interventions could be developed to target the PFM in this population to improve bladder function.
This introduction will begin by providing an overview of the lower urinary tract (1.1), followed by a review of the anatomy (1.2), innervation (1.3) and clinical implications (1.4) of the pelvic floor muscles.

### 1.1 Overview of the Lower Urinary Tract

The lower urinary tract (LUT) is comprised of two functional units: the urinary bladder and the urethra. The bladder is a hollow distensible organ composed of epithelium surrounded by layers of smooth muscle, collectively known as the detrusor (Mahadevan, 2016; Wei & DeLancey, 2004). The bladder operates in two phases in which it either stores urine (filling phase) or evacuates urine (voiding phase). During the filling phase, the smooth muscle layers of the bladder wall relax to allow for an increase in urine volume without increasing bladder pressure. In contrast, during voiding, the smooth muscles of the bladder wall contract to expel urine from this structure and into the urethra (Griffiths, 2015; Wei & DeLancey, 2004). The urethra functions as a channel to connect the bladder to the external world. The structure of the urethra differs greatly between the sexes as it reflects the variance in urogenital anatomy between men and women (Mahadevan, 2016). However, in both males and females, the urethra is surrounded by both an internal and external urinary sphincter. The internal urinary sphincter (IUS) is located at the inferior end of the bladder and is effectively a continuation of the detrusor muscle (Jung, Ahn, & Huh, 2012). As this sphincter is comprised of smooth muscle, it is not under voluntary control and is instead managed by the autonomic nervous system. The external urethral sphincter (EUS) lies distal to the IUS and is composed of striated skeletal muscle. This second sphincter is therefore under voluntary control through the somatic nervous system (Jung et al., 2012). Both the IUS and EUS function to close the urethra during bladder filling to prevent
urine leakage, but relax during voiding to allow for the release of urine (Fowler et al., 2008; Jung et al., 2012; Mahadevan, 2016; Wei & DeLancey, 2004).

At the peripheral level, the bladder is innervated by both sympathetic and parasympathetic nerves (Fowler et al., 2008; Griffiths, 2015). The sympathetic postganglionic nerves originate from the thoracolumbar (T11-L2) region of the spinal cord. These fibers release noradrenaline which activates β-adrenergic receptors in the detrusor muscle to relax the bladder, and α-adrenergic receptors in the urethra and bladder neck to contract these structures (Benevento & Sipski, 2002; Fowler et al., 2008; Griffiths, 2015). The parasympathetic postganglionic nerves arise from the sacral segments of the spinal cord (S2-S4) and release cholinergic neurotransmitters. The muscarinic cholinergic receptors of the detrusor are excited by these transmitters and in response, contract the detrusor muscle. (Benevento & Sipski, 2002; Fowler et al., 2008; Griffiths, 2015). Finally, somatic motor neurons also supply the striated muscle of the EUS. These fibers arise from the S2-S4 cells in the anterior horn of the spinal cord and are under voluntary control to close the urethral opening (Fowler et al., 2008).

Urinary continence is managed through a series of complex neural circuits in both the brain and spinal cord. During the filling phase, distension of the bladder produces afferent feedback that is conveyed back through pelvic nerves to interneurons in the lumbosacral spinal cord (Fowler et al., 2008). In response, the interneurons increase the sympathetic outflow to the bladder and somatic outflow to the EUS as a part of a spinal reflex pathway to prevent urinary leakage. While the existence of the pontine storage centre in humans is not certain, imaging studies have an activation near the expected location during the withholding of urine (Fowler et al., 2008; Seseke et al., 2006). As such, this structure within the rostral pons may play a role in increasing tonicity of the EUS as it does in other animals (Fowler et al., 2008). This increased
activity in the striated muscle aids in maintaining urethral closure during bladder filling (Fowler et al., 2008; Griffiths, 2015). As bladder filling continues, the conscious desire to void becomes stronger. However, the prefrontal cortex is activated to prevent micturition until it has been deemed ‘safe’ or socially appropriate to do so (Fowler et al., 2008). The prefrontal cortex has direct connections with periaqueductal grey (PAG) nuclei, which are involved in the control of the bladder and are part of the mechanism that drives the bladder to switch from storage to voiding phase (Fowler et al., 2008). Once it is time to void, afferent feedback from the bladder activates the spinobulbospinal reflex pathway, which passes through the PAG before reaching the pontine micturition centre (PMC). The PMC stimulates parasympathetic outflow to the bladder and urethral smooth muscle. The PMC also plays a role in inhibiting sympathetic outflow to bladder and both sympathetic and somatic outflow to the external urethral sphincter to aid in micturition (Fowler et al., 2008; Griffiths, 2015).

1.2 Anatomy of the Pelvic Floor Muscles

Physical structures that support the bladder and urethra also play a role in maintaining urinary continence (Griffiths, 2015). One such structure is the pelvic floor, which consists of a network of muscles and connective tissue that form the base of the abdomen to support the pelvic organs. The bladder sits on the superior surface of the pelvic floor, while the urethra extends through the pelvic floor muscles to the external environment (Ashton-Miller & DeLancey, 2007; Wei & DeLancey, 2004).

The levator ani muscle (LA), the most important muscle of the pelvic floor, remains one of the most poorly understood muscle groups in the human body (Barber et al., 2002; Margulies, Huebner, & DeLancey, 2007). Despite the high level of importance this muscle plays
in daily function, exact details of LA anatomy are still debated in the scientific community and a variety of terminology is used to describe similar structures (Kearney, Sawhney, & DeLancey, 2004; Margulies et al., 2007). It is generally accepted that there are three distinct muscle groups within the LA (Ashton-Miller & DeLancey, 2007; Kearney et al., 2004). The first is the iliococcygeus muscle which forms a relatively flat, horizontal shelf and spans the pelvic floor (Ashton-Miller & DeLancey, 2007; Wei & DeLancey, 2004). The iliococcygeus arises from the arcus tendineus levatoris ani (a thickening of pelvic fascia on the lateral pelvic wall) and inserts into the iliococcygeal raphe (Kearney et al., 2004). The second muscle is the puborectalis which arises from the right or left pubis and inserts into the contralateral pubis to form a sling like structure around the dorsal aspect of the rectum (Ashton-Miller & DeLancey, 2007; Kearney et al., 2004). The third structure is the pubococcygeus muscle, also known as the pubovisceral muscle, contains subdivisions which all originate bilaterally from the pubis and insert into the perineal body (puboperineus), the vaginal wall (pubovaginalis, women only), and the intersphincteric groove of the anal canal (puboanalis) (Ashton-Miller & DeLancey, 2007; Kearney et al., 2004; Margulies et al., 2007).

### 1.3 Innervation of the Pelvic Floor Muscles

The LA is cortically represented within the primary motor cortex and supplementary motor area. Original research to map the somatotopic organization of the precentral gyrus with electrical stimulation failed to identify a motor area specifically related to the pelvic floor (Blok, Sturms, & Holstege, 1997; Penfield & Boldrey, 1937). However, more recent work with functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS) has demonstrated that the pelvic floor musculature is represented in the medial wall of the precentral
gyrus of the primary motor cortex (Asavasopon et al., 2014; Blok et al., 1997; Brostrøm, 2003; Schrum, Wolff, van der Horst, & Kuhtz-Buschbeck, 2011). This cortical area has been noted for its importance during the conscious withholding of urine as well as during voluntary activation of the pelvic floor (Blok et al., 1997; Yani et al., 2018). Other studies have also demonstrated that pelvic floor musculature has a broad representation in the supplementary motor area (SMA) (Asavasopon et al., 2014; Blok et al., 1997; Yani et al., 2018). It is thought that the SMA representation of the pelvic floor might be a part of a feedforward activation mechanism in which the SMA can activate the pelvic floor muscles if a voluntary motor task requires co-contraction of this muscle group (Asavasopon et al., 2014).

Limited work has been done to examine the descending pathway(s) responsible for transmitting motor commands to the pelvic floor from the motor cortex. While the corticospinal tract is likely responsible for this type of activation, it remains unclear whether it is the anterior corticospinal tract (ACST) or the lateral corticospinal tract (LCST) that plays a larger role in the innervation of this muscle group. While the LCST has been detected consistently through the lumbosacral spine, fibers of the ACST have been reported to terminate anywhere between the midthoracic to sacral levels of the spinal cord (Al Masri, 2011; Jang, 2014). As such, if the ACST does not reliably extend to the sacral spinal cord, then it is unlikely to play the predominant role in innervation of the LA (Al Masri, 2011; Nathan, Smith, & Deacon, 1990). However, work in primates has shown that the termination of corticospinal tracts to the pelvic floor may be bilateral in that some of the LSCT fibers re-cross the midline upon reaching the sacral spinal cord (Nakagawa, 1980). As the PFM cannot be unilaterally contracted, this bilateral cortical innervation could help explain how the pelvic floor operates as a functional unit instead of as distinct right and left paired muscles (Nakagawa, 1980).
There is also considerable controversy regarding the exact peripheral innervation of the LA (Barber et al., 2002; Guaderrama et al., 2005; Wallner, Maas, Dabhoiwala, Lamers, & DeRuiter, 2006). While various sources of innervation of the LA have been described grossly, there is a lack of evidence that has been verified experimentally and no clear consensus in the literature as to which spinal nerves innervate this muscle group (Barber et al., 2002; Guaderrama et al., 2005; Percy, Swash, Neill, & Parks, 1981; Timoh et al., 2018; Wallner et al., 2006). Many studies have suggested that the LA is innervated by a combination of direct branches from S3-S5 and/or the pudendal nerve, which are the same nerves that innervate the external urethral sphincter (Barber et al., 2002; Fowler et al., 2008; Griffiths, 2015; Grigorescu et al., 2008; Guaderrama et al., 2005; Timoh et al., 2018; Wallner et al., 2006). For instance, results from the cadaveric dissection of 17 subjects describe direct innervation of the LA from S3 or S4 ventral roots in addition to the pudendal nerve which innervates the LA from the caudal surface (Grigorescu et al., 2008). However, a second cadaveric study using 12 subjects found LA innervation from a combination of nerve branches from S3-S5, but no direct innervation from the pudendal nerve (Barber et al., 2002). Yet another study with 10 cadavers supported the pudendal nerve innervation of the LA, but made no reference to sacral nerve root innervation of any kind (Wallner et al., 2006). In vivo, one study using nulliparous women found that pudendal nerve blockage decreased pressure in the vaginal canal and decreased activity in the puborectalis muscle, supporting pudendal nerve innervation to the LA (Guaderrama et al., 2005). Yet once again in contrast, results from a nerve conduction study in humans undergoing surgery suggest that the LA is innervated directed from sacral branches whereas the pudendal nerve only innervates the external anal sphincter (Percy et al., 1981). Despite these inconsistent findings in both cadaveric and in vivo studies, it should be concluded that the LA receives innervation from
the sacral plexus. As the pudendal nerve arises from the sacral nerve roots of S2-4, perhaps it does not make a substantial difference if the LA is innervated by the pudendal nerve and/or directly by branches of sacral nerves (Tagliafico, Perez, & Martinoli, 2013). Ultimately, this muscle group is innervated by motor neurons located in the sacral spinal segments, which is the important conclusion to be drawn about the LA with respect to clinical outcomes.

There is also evidence for innervation of the PFM from the brainstem. Work in both monkeys and cats has shown a direct connection of the nucleus retroambiguus (NRA) to the PFM (Holstege & Tan, 1987; Vanderhorst, Terasawa, Ralston, & Holstege, 2000). Housed in the medulla, the NRA is a part of the ventral respiratory group (VRG) and receives input from respiratory centres in the brainstem and from the midbrain PAG (Feldman, Loewy, & Speck, 1985; Subramanian & Holstege, 2009). The NRA has shown to have direct connections to muscles involved in respiration including the diaphragm, intercostals, and abdominal muscles (Subramanian & Holstege, 2009). Work in felines has shown that projections from the NRA and VRG travel down through the ventral and lateral funiculus of the spinal cord to synapse with lower motor neurons, but they are not identified as a part of any distinct spinal tract (Feldman et al., 1985). The NRA has been shown to mediate a variety of motor functions including managing respiration rate, vocalization, coughing, vomiting, sneezing, childbirth, and mating posture (Subramanian & Holstege, 2009). With respect to the PFM, it is thought that NRA innervation may be important for activating the PFM during tasks that require straining against a closed glottis, such as vomiting, coughing, or sneezing (Subramanian & Holstege, 2009; Thor & de Groat, 2010; Vanderhorst et al., 2000). Clinical research has also shown the involvement of the PFM during respiration. During quiet breathing, expiration is associated with increase PFM activity. When breathing with an increased tidal volume, PFM activity is elevated at all stages of
respiration in comparison to quiet breathing (Hodges, Sapsford, & Pengel, 2007). However, it is unclear if this activity is a result of respiratory drive from the brainstem or if respiration activity causes muscles stretch, resulting in increased PFM activity (Hodges et al., 2007).

1.4 Clinical Significance of the Pelvic Floor Muscles

The structure and location of the PFM with respect to the bladder pose important implications for bladder health. The LA contains openings, collectively known as the urogenital hiatus, for the urethra, and the vagina in females, to pass through (Ashton-Miller & DeLancey, 2007; Wei & DeLancey, 2004). While the rectum also passes through the LA, it is not included as part of the hiatus as LA muscles insert directly into the anus (Ashton-Miller & DeLancey, 2007). During bladder filling, tonic activity in the LA pulls the urethra, vagina, and rectum towards the pubic bone. This LA activity, in combination with contractions of the external urethral sphincter, plays a crucial role in maintaining continence (Ashton-Miller & DeLancey, 2007; Fowler et al., 2008). Damage or denervation to the LA has been associated with pelvic organ prolapse, urinary incontinence, fecal incontinence, sexual dysfunction, and several chronic pelvic pain syndromes (Ashton-Miller & DeLancey, 2007; Barber et al., 2002; Heilbrun et al., 2010; Wei & DeLancey, 2004).

The LA is particularly important for maintaining continence during instances of high intra-abdominal pressure (IAP). During periods of high IAP, PFM activity increases to prevent downward displacement of the pelvic floor while amplifying urethral and anal closure (Hodges et al., 2007). This response of the LA muscle has been noted in individuals completing discrete tasks such as coughing, lifting, jumping, or resisted expiration, all of which increase IAP (Hodges et al., 2007; Moser, Leitner, Eichelberger, Kuhn, & Pierre, 2018; Neumann & Gill,
2002). Locomotion, including walking and running, is also associated with higher IAP due to the high impact nature of these activities (Luginbuehl et al., 2013, 2016). Indeed, three studies using female participants have noted that PFM activity during running and jumping tasks increased with higher speeds and more impactful jumps (Leitner, Moser, Eichelberger, Kuhn, & Radlinger, 2017; Luginbuehl et al., 2013, 2016).

1.5 Bladder Function after Spinal Cord Injury

Maintaining urinary continence is a complex process involving both the LUT and supporting structures such as the LA. As reviewed above, the ability to retain or void urine is managed through intricate neurophysiological pathways from both the autonomic and somatic nervous systems. Impairment in the neural pathways that supply the bladder, urethra, or pelvic floor could lead to adverse outcomes in bladder health and a loss of ability to maintain urinary continence. Spinal cord injury (SCI) is one such diagnosis where there is a dramatic interruption in these intricate pathways that control the bladder.

Sustaining a SCI is one of the most devastating and life-altering events that an individual can face. While the primary focus after a SCI diagnosis is often the immediate motor and sensory impairments, there are numerous other secondary health concerns which need to be addressed (Dijkers, 1997; Kennedy & Rogers, 2000; Kirshblum et al., 2011; McDonald & Sadowsky, 2002; Noonan et al., 2012). One of the most prevalent secondary outcomes of SCI is urinary dysfunction. Approximately 80% of those with SCI experience some form of neurogenic bladder dysfunction as a result of their injury (Ku, 2006; Manack et al., 2011; Taweel & Seyam, 2015). With more than 86,000 Canadians currently living with SCI and nearly 3,000 persons impacted by new cases each year, this chronic secondary health outcome poses a major concern for both the individuals affected and the national health care system (Noonan et al., 2012).
As reviewed in section 1.1, the bladder receives innervation from the thoracolumbar (T11-L2) and sacral (S2-S4) levels of the spinal cord, and communicates with both the brainstem and cerebrum. Thus, when a lesion to the spinal cord occurs, this damage can disrupt the pathway between the cortical control of the bladder and the peripheral nerves innervating this structure. As a result of this interference, patients may experience neurogenic bladder symptoms which are defined as a loss of voluntary control of the bladder secondary to a central nervous system injury (Benevento & Sipski, 2002; Manack et al., 2011). These symptoms vary between individuals but may result in differing degrees of incontinence and/or loss of coordination between the bladder and urinary sphincters (Benevento & Sipski, 2002; Manack et al., 2011; Taweel & Seyam, 2015). Neurogenic detrusor overactivity (NDO) is a common neurogenic bladder symptom in those with SCI characterized by involuntary detrusor contractions during bladder filling (Abrams et al., 2003; Stöhrer et al., 1999). Detrusor contractions as a result of NDO may be spontaneous due to overactive c-fiber afferents, or can be provoked when bladder filling causes a stretch reflex in the detrusor muscle (Abrams et al., 2003; Chapple, 2014; Hu, Granger, & Jeffery, 2016). Detrusor sphincter dyssynergia (DSD) is another common symptom in which detrusor contraction occurs concurrently with involuntary contraction of the urethral sphincters (Abrams et al., 2003; Stöhrer et al., 1999). In this case, the PMC is unable to effectively coordinate the sphincter relaxation with detrusor contraction and instead, spinal reflexes maintain closure of the urethra. DSD causes an inability to void effectively as well as increases in bladder pressure which if left untreated, may lead to permanent damage of LUT structures (Abrams et al., 2003; Agrawal, Joshi, Agrawal, & Joshi, 2015). These neurogenic bladder symptoms are incredibly common in the SCI population, with as many as 95% of individuals with suprasacral lesions experiencing NDO and/or DSD (Weld & Dmochowski,
In addition to neurogenic bladder symptoms secondary to a loss of function in autonomic nerve pathways, individuals with SCI may experience a loss of somatic innervation to the external urethral sphincter and the pelvic floor muscles (Kirshblum et al., 2011). This loss of voluntary control further compounds bladder dysfunction and can magnify the urogenital symptoms experienced by the individual (Fowler et al., 2008).

Recovery of bladder function has been regarded as a top recovery priority for individuals with SCI (Anderson, 2004; Simpson, Eng, Hsieh, Wolfe, & Team, 2013). In a meta-analysis of studies examining the health priorities of those living with SCI, the most commonly expressed priorities included improvements in bladder, bowel, and motor function (Simpson et al., 2013). Bladder concerns also place a large cost on our health care system as rehospitalization for urogenital complications is common after SCI (Cardenas, Hoffman, Kirshblum, & McKinley, 2004; McKinley, Jackson, Cardenas, & DeVivo, 1999; Savic, Short, Weitzenkamp, Charlifue, & Gardner, 2000). One Ontario-based model reported that 47% of all rehospitalizations after the initial SCI were due to diseases of the genitourinary system, including urinary tract infections and bladder infections (Krueger, Noonan, Trenaman, Joshi, & Rivers, 2013). While urinary complications and renal failure are no longer the leading cause of death after SCI, urinary dysfunction is associated with a higher level of morbidity and occasionally mortality in this population (Agrawal et al., 2015; Ku, 2006). Proper techniques to manage bladder symptoms that optimize health and minimize social limitations are greatly needed in this population to improve quality of life (Ku, 2006).
1.6 Management of Bladder Symptoms after Spinal Cord Injury

Many different therapies may be used to manage micturition and overcome neurogenic bladder symptoms post-injury. The most common means of bladder draining is the use of intermittent or indwelling catheterization techniques (Benevento & Sipski, 2002). While these strategies are effective in allowing for voiding, they provide opportunities for bacterium to enter the bladder and increase the likelihood of infection (Ackery, Tator, & Krassioukov, 2004; Cardenas & Hooton, 1995; Foxman, 2002). As a result, urinary tract infections (UTIs) are highly prevalent in the SCI population (Agrawal et al., 2015; Cardenas & Hooton, 1995). In the acute stages of SCI care, UTIs are the most frequent medical complication, occurring in about 20% of patients (Ackery et al., 2004; Cardenas & Hooton, 1995). Further, one study examining symptomatic and non-symptomatic cases of UTIs in community-dwelling SCI participants reports a prevalence rate of 57% across one year (Waites, Canupp, & DeVivo, 1993). However, other sources have reported the rate of contracting at least one bacterial UTI over one year to be as high as 67-100% (Agrawal et al., 2015).

Pharmacologic management of bladder dysfunction may also be required post-injury depending on the specific bladder symptoms an individual is experiencing. A common class of drugs given to those with SCI who are experiencing NDO or general failure to store urine properly are anticholinergics, such as oxybutynin and propantheline (Benevento & Sipski, 2002; Ku, 2006; Taweel & Seyam, 2015). These medications suppress bladder contractions, reduce bladder pressure, increase bladder capacity, and increase urethral resistance (Benevento & Sipski, 2002; Taweel & Seyam, 2015). However, these medications are not without side effects. Anticholinergic drugs may cause dry mouth and constipation, as well as require patients to drink large volume of liquids per day, further complicating the daily routine of those who rely on
intermittent catheterization techniques (Benevento & Sipski, 2002). More seriously, anticholinergic drugs may produce impairments in memory, tachycardia and arrhythmias, or visual blurring depending on the class of muscarinic acetylcholine receptors the prescribed drug binds with (Taweel & Seyam, 2015).

Surgical innervations are the last resort in a bladder management plan and are generally for those who cannot use or tolerate catheterization or pharmacological treatment of their bladder symptoms (Benevento & Sipski, 2002; Ku, 2006; Taweel & Seyam, 2015). The goals of surgical treatments are to achieve continence while protecting the upper and lower urinary tracts. A range of surgical procedures are available, extending from minimally invasive measures to permanent and complex surgeries (Taweel & Seyam, 2015). A common minimally invasive treatment is the use of botulinum toxin injections to treat NDO. The effects of each injections last approximately nine months, but this treatment seems to have promising effects in improving bladder capacity and reducing urinary incontinence (Taweel & Seyam, 2015). Another surgical option includes bladder augmentation in which an intestinal or colonic segment is transplanted into the bladder to improve bladder capacity (Taweel & Seyam, 2015). Finally, a more aggressive surgical means to manage urinary dysfunction is to surgically impair the urethral sphincters by conducting a sphincterotomy. This allows the individual to utilize a passive collection system such as a condom catheter, but any future treatments to manage urinary dysfunction that require use of urinary sphincter may no longer be utilized (Taweel & Seyam, 2015).

1.7 Core and Pelvic Floor Muscle Training to Manage Incontinence

Because of the important role the PFM plays in maintaining continence, PFM training is considered to be a first line of defense treatment against urinary incontinence in other
populations (Bø, 2012). PFM training refers to any exercise that requires voluntary contraction of the pelvic floor, such as Kegels (Bø, 2004, 2012). Multiple randomized control trials have demonstrated PFM training as an effective technique to reduce urine leakage, especially during instances of high IAP, in those who are able-bodied (Bø, 2004, 2012). Further, a handful of randomized control trials have shown promising results in training the PFM to prevent organ prolapse (Braekken, Engh, & Bø, 2010; Ghroubi et al., 2008; Hagen, Stark, Glazener, Sinclair, & Ramsay, 2009) and there is limited data that this type of training could have a positive effect on sexual dysfunction (Bø, 2012; Braekken et al., 2010). Moreover, there have been no reported adverse effects as a results of PFM training, indicating that this therapeutic strategy is generally well tolerated (Bø, 2012).

One concept behind PFM training is to increase the structural support to pelvic organs by elevating the LA within the pelvic cavity and enhancing hypertrophy and tone of this muscle group (Bø, 2004). This would effectively improve neural function by improving motor unit firing and prevent the depression of the LA during moments of increased IAP (Bø, 2004). The LA also provides urinary continence by working in synergy with the EUS to directly compress the urethra. The amount of force the LA can apply to the EUS increases with PFM training, thereby mechanically supporting the prevention of urine leakage (Ashton-Miller & DeLancey, 2007; Bø & Stien, 1994).

PFM training may also be effective in treating overactive bladder symptoms, specifically detrusor overactivity (DO), by inhibiting detrusor muscle contractions (Bø & Berghmans, 2000). Activation of the LA leads to a reflex inhibition of the bladder wall which in turn reduces bladder pressure and increased bladder capacity. One study by Godec et al. (1975) showed that in 31 of 40 participants, hyperactivity of the detrusor was diminished or abolished during
functional electrical stimulation of the PFM. Further, one minute after stimulation ceased, this inhibition remained present and bladder capacity increased significantly during this time (Godec, Cass, & Ayala, 1975). Clinical experience has also shown that patients may reduce voiding urgency and detrusor contractions by engaging the PFM. This strategy has been previously used in interventions to improve urge urinary incontinence (Burgio et al., 1998).

Part of PFM training often involves engaging the core muscles alongside the LA. The core has been described as a box with the abdominals on the anterior side, the paraspinals and gluteals on the posterior side, the diaphragm as the superior surface, and the PFM as the inferior surface (Akuthota, Ferreiro, Moore, & Fredericson, 2008; Akuthota & Nadler, 2004). Effectively, the core may be considered a muscular “corset” to stabilize the trunk and spine either during or in the absence of limb movement (Akuthota & Nadler, 2004). This stabilizing mechanism has been given particular attention in athletics where it is believed that the core provides “proximal stability for distal mobility” (Akuthota et al., 2008; Kibler, Press, & Sciascia, 2016). In this sense, the core acts as an anatomical base for motion in the limbs including throwing, kicking, and locomotion activities (Kibler et al., 2016; Willson, Dougherty, Ireland, & Davis, 2005).

There is a great deal of evidence suggesting that muscles of the core act synergistically during functional tasks. In able-bodied individuals, the PFM strongly co-activate with the abdominals during trunk flexion and abdominal hollowing (Asavasopon et al., 2014; Neumann & Gill, 2002; Sapsford & Hodges, 2001). Further, some evidence has suggested that it is not possible for individuals to contract the PFM effectively while maintaining relaxation of the deep abdominal muscles including transverse abdominis and the internal obliques (Neumann & Gill, 2002). The PFM also co-activate with voluntary gluteal muscle activation (Asavasopon et al.,
2014; Bø & Stien, 1994; Peschers, Gingelmaier, Jundt, Leib, & Dimpfl, 2001). However, unlike the deep abdominals, it is possible to activate the PFM without the gluteal muscles being co-activated (Asavasopon et al., 2014).

Despite the success of using PFM and core training in able-bodied individuals, limited work has explored the possibility of using this type of training in a neurologically impaired population. One study showed significant improvements in bladder function in participants with multiple sclerosis (MS) who used PFM training in combination with electromyography (EMG) biofeedback and neuromuscular electrical stimulation vs. a control group of PFM training alone (McClurg, Ashe, Marshall, & LOwe-Strong, 2006). Significant improvements in bladder function were seen in the group who used PFM training in combination with the biofeedback and stimulation as measured by the number of urine leaks experienced by the participants over a 24-hour period. (McClurg et al., 2006). Another randomized control trial examined the effect of PFM training in women with urinary incontinence after ischemic stroke (Tibaek, Gard, & Jensen, 2005). The results from this study showed that PFM training had a significant improvement on urinary incontinence as measured by frequency of voiding during daytime, leakage over a 24-hour period, and PFM strength. (Tibaek et al., 2005). In SCI, a case study of two males with chronic incomplete SCI reported promising preliminary results that PFM training may improve NDO and urinary incontinence (Vásquez et al., 2015). After 6 weeks of PFM training up to three times per day, PFM contractions suppressed DO by 81% and 16% in each subject respectively. Further, one participant experienced a 10% improvement in incontinence as measured by the International Consultation on Incontinence (ICIQ-UI) questionnaire (Vásquez et al., 2015). Finally, a recent randomized control trial explored the use of PFM training alone or in combination with intravaginal electrical stimulation on urinary incontinent women with
incomplete SCI. After a 12-week intervention, only the PFM training group showed significant improvements in daily urine leakage episodes, ICIQ-UI score, and opening urethral pressure (Elmelund et al., 2018). These improvements persisted 3 months after the training intervention had ceased which suggests that PFM training may produce both meaningful and long-lasting functional improvements in the SCI population (Elmelund et al., 2018).

1.8 Classification of Core Muscles After Spinal Cord Injury

One reason why PFM training has not been commonly applied to the SCI population could be that we lack the tools to properly assess trunk and core muscle function post-injury. While a SCI can occur anywhere along the length of the spinal cord, the vertebral level at which the lesion occurs in addition to the severity of the lesion will determine the potential sensory and motor deficits post-injury (Kirshblum et al., 2011; McDonald & Sadowsky, 2002). An injury to the cervical level is labeled as tetraplegia and can result in impairment to all four limbs and the trunk, including the core muscles (Kirshblum et al., 2011). An injury at the thoracic level or lower is classified as paraplegia and could impact lower limb function as well as trunk or core function depending on the level of injury (Kirshblum et al., 2011).

In both tetra- and paraplegics, motor impairments can range from partial to complete paralysis below the level of injury. Similarly, sensory deficits present on a spectrum from which an individual may only experience a mild difference in sensation to a complete loss of sensory function (Kirshblum et al., 2011; McDonald & Sadowsky, 2002). A motor-complete injury (mSCI) is defined as one in which there is an absence of motor function below the neurological level of injury. In contrast, a motor-incomplete injury describes an SCI in which there is partial preservation of motor function below the neurological level (Kirshblum et al., 2011). To classify
injuries as complete or incomplete, clinicians use the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) exam which is an internationally recognized gold standard exam for the neurological and functional classification of SCI. Developed in the 1990s, this exam assesses both motor and sensory function to score the level and completeness of injury (Kirshblum et al., 2011).

While the motor component of the ISNCSCI exam directly assesses motor function in the upper and lower limbs, this assessment falls short in its ability to assess core muscle function (Kirshblum et al., 2011). For injuries that occur between T2-L1, which are the spinal segments supplying the majority of the core, clinicians rely solely on the results of the sensory testing to make conclusions about the motor function of muscles in these regions (Kirshblum et al., 2011). Considering that sensory and motor neurons travel within different compartments of the spinal cord, it is entirely possible for an individual to experience impairments in sensation while still maintaining a degree of motor functionality in the same region. Thus, relying on sensory tests to evaluate core muscle function has the potential to greatly misjudge the extent of spared muscle function post-injury (Bjerkefors et al., 2015).

1.9 Evidence for Core Muscle Sparing After Spinal Cord Injury

To address the gap in the ISNCSCI exam, other means to functionally assess trunk and core muscles have been developed by clinicians and researchers. When classifying wheelchair sport athletes, manual palpation of the abdominal muscles during trunk movements has been used to assist in determining the extent to which a player may retain muscle function in this region (Altmann et al., 2013; Pernot et al., 2011). In individuals with SCI, the use of transcranial magnetic stimulation (TMS) has been used in combination with electromyography (EMG) to
examine abdominal muscle function (Bjerkefors et al., 2015; Squair et al., 2016). In a study by Bjerkefors et al., (2015) TMS was delivered over the abdominal region of the primary motor cortex in participants classified with the ISNCSCI exam as high-thoracic (C5-T3) mc-SCI. In all participants, motor evoked potentials in the abdominal muscles in response to TMS could be elicited (Bjerkefors et al., 2015). A similar study using TMS to examine preserved muscle activity in the trunk, hip, and leg muscles of 16 individuals classified as mc-SCI found that almost all participants had TMS-evoked muscle activity below the clinically classified level of injury (Squair et al., 2016). Further, in most cases, voluntary muscle activation was also found in these muscles with TMS activation, but on occasion TMS activation was still present in muscles that could not be voluntarily activated (Squair et al., 2016). In another study by Bjerkefors et al (2009), activation of the abdominal and erector spinae muscle groups was assessed in a single high-thoracic mc-SCI subject (T3) during voluntary contractions and in response to balance perturbations (Bjerkefors et al., 2009). In the results from this study, the EMG data showed that the individual was able to activate all of the muscles assessed in both conditions (Bjerkefors et al., 2009). Not only has recent research proposed that the core muscle may be spared after injury, some evidence suggests that function in these spared muscles may be trained. This was shown in a study by Chisholm et al (2017) who assessed abdominal and erector spinae muscle activity in motor-complete SCI subjects from C7-T4 during overground walking with a robotic gait training device. In this study, not only were all participants able to voluntarily engage trunk muscles, but activation of these trunk muscles was seen during walking in the robotic exoskeletons. Furthermore, the participants who trained in the exoskeleton, which required a high degree of balance and trunk movement, experienced improved seated postural stability (Chisholm, Alamro, Williams, & Lam, 2017).
The collective message from these recent publications support the notion that abdominal and paraspinal muscle function is spared to some extent in individuals who have sustained a SCI at or above the T6 level and have been classified by the ISNCSCI exam as motor-complete (AIS A or B) (Alamro, Chisholm, Williams, Carpenter, & Lam, 2018; Bjerkefors et al., 2009, 2015; Chisholm et al., 2017; Squair et al., 2016). However, there has yet to be any work examining whether this type of sparing extends to the other muscle groups of the core, including the gluteal muscles and PFM, in people with SCI.

1.10 Summary and Rationale

The vast majority of individuals with SCI experience some form of bladder dysfunction (Ku, 2006; Manack et al., 2011; Taweel & Seyam, 2015). Very few treatments are available today to improve bladder function, and the most common management technique, catheterization, is associated with high levels of bladder infections and a high likelihood of rehospitalisation (Benevento & Sipski, 2002; Cardenas et al., 2004; Taweel & Seyam, 2015). New treatments are urgently needed in the SCI population to manage bladder symptoms post-injury.

In able-bodied individuals, PFM training is the most common means of managing urinary incontinence (Bø, 2004, 2012). Limited work has applied these training programs to neurologically impaired populations and only two previous studies have examined the possibility of using PFM training in SCI and those were in individuals with motor-incomplete injuries (Elmelund et al., 2018; Vásquez et al., 2015). The paucity of research in this direction may be due to underestimations about the extent to which the PFM are spared post-injury. Standard clinical exams for those with SCI do not directly assess muscles of the core, including the PFM,
which may lead to false assumptions on their spared motor function after a SCI (Kirshblum et al., 2011).

While traditional PFM training program exercises have been shown to improve continence in able-bodied populations, no work has yet examined how the PFM might function during these exercises in the SCI population. No study to date has recorded PFM during attempted PFM contraction concurrently with other trunk muscles including those of the abdomen, back, or gluteal regions. If voluntary or even synergistic activation of the PFM can be seen in SCI participants, then these results could inform the creation of PFM training programs for this population.

Recent work using EMG and TMS has shown that other muscles of the core, including the abdominal and paraspinal muscles, do retain a certain degree of descending input and voluntary motor function after injury. Even in individuals with motor-complete injuries above the level of T6, where abdominal innervation begins, sparing of abdominal muscles can still be noted during both voluntary contractions and detected in the EMG responses to TMS (Bjerkefors et al., 2009, 2015; Chisholm et al., 2017; Squair et al., 2016). No work has yet assessed if the PFM can be similarly activated after a SCI through voluntary contractions. Further, TMS could confirm if there is still supraspinal input to these muscles post-injury. Any evidence of spared PFM function would have important implications for the neurogenic bladder community as these findings could open new avenues for the development of treatments to target urinary dysfunction after SCI.

Thus, the overall purpose of this study was to evaluate the presence of sparing of motor function in the PFM in people with SCI. We evaluated this in two ways: a) by characterizing the
activation of the pelvic floor during discrete maneuvers commonly used to recruit the PFM and b) by exploring the corticospinal excitability to the pelvic floor during TMS.
1.11 Specific Aims and Hypotheses

**Aim 1:** To compare the activation level of the pelvic floor muscles among different validated PFM training exercises in those with motor-complete SCI and able-bodied participants.

**Hypothesis 1:** PFM amplitude elicited during voluntary contractions will be larger than background activity at rest across all maneuvers for both the able-bodied and spinal cord injured participants.

**Aim 2:** To characterize the corticospinal tract excitability to the pelvic floor via transcranial magnetic stimulation (TMS) in individuals with motor-complete SCI and able-bodied participants.

**Aim 3:** To determine if there is a relationship between voluntary activation or TMS response and neurogenic bladder symptoms in SCI participants.

**Hypothesis 3:** Participants with more severe bladder symptoms will have a reduced voluntary activation of the PFM and a reduced response to TMS.
Chapter 2: Methods

2.1 Study Design

Cross-sectional.

2.2 Participants

SCI participants were recruited for this study who met the study inclusion criteria: 1) They were between 19-60 years of age; 2) they had a chronic (≥12 months post-injury) SCI; 3) they were in a stable medical condition; 4) they had a motor-complete injury (AIS A or B) at or above the level of L1. Able-bodied participants were included if they 1) were between 19-60 years of age; 2) were in a stable medical condition.

Participants were excluded from participation if they met any of the following exclusion criteria: 1) they were currently pregnant, or had been pregnant and/or given birth within the last 6 months; 2) they had experienced prolonged pelvic dysfunction as a result of being pregnant or giving birth; 3) they had urogenital or abdominal surgery within the last 12 months; 4) they were currently experiencing menses; 5) they were currently experiencing acute vaginal infection or bladder infection; 6) they had been diagnosed with cervical cancer; 7) they were unable to provide consent and/or follow instructions; 8) they were unable to speak or understand English.

The following additional exclusion criteria related to the TMS component of the study: 1) they had any permanent metal fixtures within the head excluding dental fillings; 2) they had recurring or severe headaches; 3) they had a history of seizures, had an immediate family member with a history of seizures, or were taking medications that lower the seizure threshold; 4) they had a history of skull fracture or brain/head injury including concussions; 5) they had
head or brain surgery; 6) they had a hearing impairment; 7) they had a psychiatric disorder and/or experience sleep deprivation; 8) they had heart disease or diabetes; 9) they had electrodes implanted within the central or peripheral nervous system.

2.3 Procedures

All measurements took place in Human Locomotion Research Laboratory at the Blusson Spinal Cord Centre. For all participants, data for Part 1 and 2 were collected in a single session.

2.3.1 Demographics and ICIQ-UI

All participants were asked to complete a brief form about their relevant medical history including age, sex, height, weight, and history of childbirth. The SCI participants were further asked to provide their date of injury, and information on their bladder routine and management history. The International Consolation on Incontinence Modular Questionnaire (ICIQ-UI short form) was also administered to all participants. This brief questionnaire asks users if they experience urine leakage, how much urine they think they leak, how urine leakage interferes with daily life, and when urine leakage occurs (Avery et al., 2004). The maximum possible score is 21, with higher scores indicating worse symptoms. Previous work has demonstrated that the ICIQ-UI shows good construct validity, convergent validity, and reliability (Avery et al., 2004).

2.3.2 ISNCSCI Exam

A standard neurologic examination, the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), was used to assess the motor and sensory function of the upper and lower extremities of the SCI participants (Kirshblum et al., 2011). The
Upper and Lower Extremity Motor Score (UEMS, LEMS) of the ISNCSCI measures muscle strength in 10 myotomes using a 5-point grading scale ranging from 0 (total paralysis) to 5 (active movement through full range of motion against full resistance). A score out of 25 is summed for each limb, giving the examiner a total motor score out of 100. The sensory score of the ISNCSCI measures light touch and pin prick sensation at each dermatome using a 3-point grading scale ranging from 0 (absent) to 2 (normal). A score out of 112 is recorded for each light touch and pin prick sensation. A trained nurse performed the ISNCSCI exam for all participants.

2.3.3 EMG Set-up for Part 1 and Part 2

Surface EMG signals were recorded to measure the amplitude of PFM and other core muscle contractions. All recordings were made using Delsys’ Trigno EMG system (Delsys Inc, Boston, USA) at a sampling frequency of 2000Hz.

For the PFM, muscle recordings were taken from the LA group. All participants had four surface electrodes placed on their perineum in a square pattern, approximately 1.5cm from the anus, by a registered nurse. To confirm that the electrodes had been placed in the correct position, participants were asked to cough a number of times during a test recording (Neumann & Gill, 2002). The nurse also placed surface EMG bilaterally to record from gluteus maximus (GM) 2cm inferior and lateral to the line drawn between the posterior superior iliac spine and the third sacral spine. This was done in a private setting without the presence of other research staff. Additional surface electrodes were also placed bilaterally to record EMG from the rectus abdominis (RA; 1cm lateral and 3cm superior of navel), external oblique (EO; 2cm inferior of the lowest rib on the anterior side), and erector spinae (ES; 2cm lateral of the vertebral column at L4). These surface electrodes were placed by research staff.
2.3.4 Data Collection Protocol for Part 1

Participants completed a series of validated maneuvers to examine pelvic floor activity (Bø et al., 1990; Neumann & Gill, 2002; Sapsford & Hodges, 2001). To control for changes in intra-abdominal pressure during the movements, participant’s breathing pattern was timed to each exercise. Before each maneuver, participants were given the following instructions: “breathe out (2 sec), breathe in (2 sec), breathe out (2 sec) while [performing the requested movement]”. During the procedure, correct breathing was verified using a thermocouple affixed below one of the nostrils to record changes in temperature as related to inhalation/exhalation. Participant were asked to attempt complete the following maneuvers isometrically and hold the position for approximately 5 seconds:

1) *Quiet rest* – participants lay quietly in supine for 30 seconds.
2) *Trunk Flexion* - while in supine with their knees flexed and feet flat, participants were asked to attempt to perform a sit-up.
3) *Side Bend (right and left)* – while in supine with legs extended and arms at their sides, participants were instructed to perform lateral trunk flexion.
4) *Back Extension* – while prone with their arms by their sides, participants were instructed to perform a back extension movement.
5) *Abdominal Hollowing* – while supine with their knees flexed and feet flat, participants were asked to perform abdominal hollowing (abdominal compression, drawing the naval toward the spine).
6) *Kegel* – while in supine with their knees flexed and feet flat, participants were asked to contract their pelvic floor.
7) **Gluteal Contraction** – while in supine, participants were asked to maximally contract their gluteal muscles.

For trunk flexion, lateral flexion, and back extension, a member of the research team provided resistance to the participant by stabilizing them against the plinth.

### 2.3.5 Data Collection Protocol for Part 2

Participants then completed a series of TMS trials to examine PFM activity. A double cone coil attachment on the Magstim 200 stimulator (MagStim Company Ltd, Dyfed, UK) was used in this part of the study. The coil was placed tangentially to the scalp, parallel to the mid-sagittal plane, and with the central aspect of the coil over the stimulation site (medial aspect of the precentral gyrus) (Asavasopon et al., 2014; Brostrøm, 2003). To ensure that the coil position was consistent between trials, an Optotrak (Northern Digital Inc, Waterloo, Canada) rigid-body was secured on both the coil and participant’s forehead and their real-time positions were streamed into a custom-made navigation program (Unity Technologies, San Francisco, USA) that allowed for tracking of the position of these rigid bodies relative to each other in all three planes. The navigation program provided visual feedback of the real-time 3D position of the rigid-bodies relative to each other. The trial-to-trial consistency of coil position was within a 2mm range of error of the target position.

Participants were given blocks of 5 pulses separated by 5-10 seconds each. The timing between blocks was selected by the participant for their comfort, but generally lasted between 15-180 seconds. Pulses began submaximally and increased in intensity by 5-10% each block. The test ended when 100% maximum stimulator output (%MSO) was reached, the participant
MEP amplitude reached a plateau in amplitude, or if the participant requested to discontinue the experiment.

Participant lay supine on a plinth with a small foam block under their head for support and to allow proper coil positioning. During each stimulation, participants were asked to attempt a submaximal contraction of their pelvic floor by attempting a sit-up at 10% of their maximal effort.

To control for changes in intra-abdominal pressure, participant’s breathing was timed to the TMS pulse. Before each stimulation, participants were given the following instructions “breathe in (2sec), breathe out (2sec) while gently contracting your abdominal muscles without moving your head”. The stimulation was delivered during the last exhalation. During the entirety of the procedure, correct breathing patterns were verified using a thermocouple affixed below one of the nostrils to record changes in temperature as related to inhalation/exhalation.

2.4 Data Analysis

2.4.1 Part 1

EMG data from Part 1 were band-stop filtered at 60 Hz and then high-pass filtered at 30 Hz with an eighth-order dual-pass Butterworth filter and rectified. The thermocouple signal was low-pass filtered at 6 Hz with a fourth-order dual-pass Butterworth filter. All signal processing was completed offline using custom-written routines in MATLAB (Mathworks, Natick, MA, USA).

For each participant and each trial, the filtered data were used to calculate the root mean square (RMS) over a 2 second window for each muscle during rest and the attempted voluntary contraction. The mean and standard deviation of all the rest windows across all trials were used
to create a threshold. If the RMS value for a given muscle during the contraction phase exceeded 2 SD above this global mean RMS resting value, muscle activity was considered ‘present’ for this maneuver. Because participants attempted each maneuver twice, the participant was given an ‘activation score’ of 0 (no activity on either trial), 1 (activity on only one of the trials), or 2 (activity on both trials). The activation score for each participant was then reported as a percentage (total score for right and left PFM divided by number of maneuvers).

2.4.1 Part 2

Data from all TMS trials were analyzed off-line using custom written MATLAB routines. For the RA and PF bilaterally in each trial, a 100ms sample of baseline EMG was taken 50ms before the TMS stimulation and rectified. MEP onset (latency) was defined as the time at which the MEP exceeded 2 SD above the mean of this baseline EMG activity and remained beyond this threshold for at least 2ms. MEP amplitude was calculated as the peak-to-peak amplitude of the raw EMG activity after MEP onset. All MEP onset times and peak MEP points were visually confirmed by the experimenter and manually adjusted as required.

To examine the differences in latency between the RA and PF while accounting for individual characteristics in participants, the difference between the PFM and the RA was then calculated for each subject where a positive value would represent a longer MEP latency in the PFM.

The MEP peak-to-peak amplitudes at a given intensity were averaged and plotted against stimulation intensity to produce a recruitment curve. Each participant was also given a ‘MEP presence score’ based on the five trials completed at their individual maximum %MSO.
Participants received a score of 0 if no MEP was present in any of the final trials, a score of 1 if a MEP was present in one to four of the trials, and a score of 2 if the MEP was present in all trials.

2.5 Statistical Analysis

For statistical analyses, the right and left responses of each muscle were averaged together. All statistical analyses were performed using SPSS (IBM, Armonk, USA) with an alpha of 0.05 across all tests. For Part 1, EMG amplitude for each maneuver were compared within both the SCI and AB groups using a one-way repeated measures ANOVA. A pairwise comparison using a Bonferroni corrected alpha was used to compare each maneuver against rest (total of 7 pairwise comparisons; adjusted alpha of 0.007). Prior to conducting the ANOVA, a normal distribution of data was checked through a Shapiro-Wilk test and log transformed as necessary.
Chapter 3: Results

3.1 Participant Characteristics

9 SCI and 7 AB subjects participated in this study. All subjects enrolled in both Part 1 and Part 2. Key participant characteristics are summarized in Table 1a, 1b, and 2 for SCI and AB participants, respectively.
Table 1a: Characteristics of SCI Participants

<table>
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<tr>
<th>ID</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Height (cm)</th>
<th>Weight (cm)</th>
<th>Years Post Injury</th>
<th>Level of Injury</th>
<th>AIS</th>
<th>ZPP R/L</th>
<th>Light Touch</th>
<th>Pin Prick</th>
<th>Total Motor Score</th>
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<td>M</td>
<td>178</td>
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<td>T6/T6</td>
<td>48</td>
<td>46</td>
<td>50</td>
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<td>1</td>
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<td>A</td>
<td>T9/T11</td>
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<td>F</td>
<td>178</td>
<td>49</td>
<td>22</td>
<td>C6</td>
<td>A</td>
<td>T3/T2</td>
<td>26</td>
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<tr>
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<td>T4</td>
<td>A</td>
<td>T6/T7</td>
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<td>77</td>
<td>33</td>
<td>T3</td>
<td>A</td>
<td>T4/T4</td>
<td>42</td>
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<tr>
<td>SCI09</td>
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<td>M</td>
<td>170</td>
<td>68</td>
<td>21</td>
<td>C6</td>
<td>B</td>
<td>-</td>
<td>60</td>
<td>29</td>
<td>37</td>
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Note: M = male; F = female; ZPP R/L = zone of partial preservation right/left; AIS = American Spinal Cord Injury Association Impairment Scale; A = motor and sensory complete; B = motor complete and sensory incomplete
Table 1b: Bladder Characteristics of SCI Participants

<table>
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<tr>
<th>ID</th>
<th>Voiding Strategy</th>
<th>Frequency of Catheterization (hr)</th>
<th>History of Childbirth</th>
<th>Months Since Last Botulinum Toxin Treatment</th>
<th>ICIQ-UI</th>
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<td>CIC</td>
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<td>-</td>
<td>Never</td>
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<td>3 Caesarians</td>
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<td>-</td>
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<td>-</td>
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<td>6</td>
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<td>CIC</td>
<td>4</td>
<td>-</td>
<td>24</td>
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</tbody>
</table>

Note: CIC = clean intermittent catheter; CC = condom catheter; IC = indwelling catheter; Y = Yes, N = No; ICIQ-UI = International Consultation on Incontinence Questionnaire Score, a higher score indicates worse bladder symptoms
### Table 2: Characteristics of AB Participants

<table>
<thead>
<tr>
<th>ID</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Height (cm)</th>
<th>Weight (cm)</th>
<th>ICIQ-UI</th>
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</tr>
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<td>AB08</td>
<td>19</td>
<td>F</td>
<td>162</td>
<td>54</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: M = male; F = female; ICIQ-UI = International Consultation on Incontinence Questionnaire Score, a higher score indicates worse bladder symptoms.

### 3.2 Maneuvers Results

EMG results from the left PFM for one AB (AB08) and one SCI (SCI06) were excluded due to technical problems processing this data. Sample EMG data from one AB and one SCI participant are displayed in Figure 1. EMG data for all SCI participants can be found in Appendix A.
Figure 1: Sample EMG Data from Maneuvers

**AB03**
31 y.o. Female

**SCI03**
49 y.o. Male
T9 AIS A, 1 year post-injury

**Figure 1:** Right and left pelvic floor muscle (rPF; lPF) EMG data from an able-bodied (AB03) and spinal cord injured (SCI03) participant. The dotted line represents the thermocouple signal, where downward deflections represent exhalation. The grey boxes represent the period during which the participant was instructed to attempt the given maneuver.
3.2.1 Maneuvers Results – Activation Score

All AB participants were able to successfully recruit their PFM during the majority of the targeted maneuvers as seen in Figure 2a. The total activation score ranged from 64-100% with an average of 90%. The gluteal contraction produced the highest PFM activation score where all participants received 100% for both the right and left pelvic floor. This was followed closely by the Kegel maneuver where all participants scored 100% for the right and left pelvic floor with the exception of AB05 who scored a 50% unilaterally.

All but one SCI subject were able to successfully recruit their PFM during the attempted maneuvers (Figure 2b). However, successful recruitment varied between subjects. The total activation score ranged from 3-64% with an average score of 27%. Trunk flexion was the most effective for recruiting the PFM among the SCI group, where 5 participants received a score of 100% at least unilaterally. Unlike the AB subjects, the Kegel maneuver and gluteal contraction were the least effective in recruiting the PFM, producing only a small activation response from two participants.
Figure 2a: Activation Score Summary for AB Participants

<table>
<thead>
<tr>
<th>ID</th>
<th>PF</th>
<th>Trunk Flexion</th>
<th>Right Side Bend</th>
<th>Left Side Bend</th>
<th>Trunk Extension</th>
<th>Abdominal Hallowing</th>
<th>Kegel</th>
<th>Gluteal Contraction</th>
</tr>
</thead>
<tbody>
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<td>AB01</td>
<td>rPF</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td></td>
<td>lPF</td>
<td></td>
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<td></td>
<td></td>
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<td>rPF</td>
<td></td>
<td></td>
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<td></td>
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<tr>
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<td>lPF</td>
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<td></td>
</tr>
<tr>
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<td>rPF</td>
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Figure 2a: Frequencies of activation of the right and left pelvic floor (rPF; IPF) during the attempted maneuvers for all AB participants. Each participant completed 2 trials for each maneuver and were awarded a score of 2 if their rPF/IPF was active during both trials (black), a score of 1 if their rPF/IPF was active during one of the trials (grey), or a score of 0 if their rPF/IPF was not active in either trial (white). Cells with diagonal lines represent data that was not included in the analysis.
**Figure 2b: Activation Score Summary for SCI Participants**

<table>
<thead>
<tr>
<th>ID</th>
<th>PF</th>
<th>Trunk Flexion</th>
<th>Right Side Bend</th>
<th>Left Side Bend</th>
<th>Trunk Extension</th>
<th>Abdominal Hallowing</th>
<th>Kegel</th>
<th>Gluteal Contraction</th>
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</table>

*Figure 2b:* Frequencies of activation of the right and left pelvic floor (rPF; lPF) during the attempted maneuvers for all SCI participants. Each participant completed 2 trials for each maneuver and were awarded a score of 2 if their rPF/lPF was active during both trials (black), a score of 1 if their rPF/lPF was active during one of the trials (grey), or a score of 0 if their rPF/lPF was not active in either trial (white). Cells with diagonal lines represent data that was not included in the analysis.
3.2.2. Maneuvers Results – Differences Among Maneuvers

Figure 3a and Figure 3b summarize the EMG results for the AB and SCI subjects while completing the targeted maneuvers. In the AB group, there was a statistically significant difference among the maneuvers as determined by the one-way repeated measures ANOVA (F(7,49) = 23.730, p < 0.0001). The pairwise comparisons revealed a significant difference in EMG amplitude between rest and all maneuvers (p < 0.0001).

In the SCI group, the one-way repeated measures ANOVA also showed a statistically significant difference among the maneuvers (F(7,56) = 8.831, p < 0.001). The pairwise comparison revealed a significant difference in EMG amplitude between rest and right side bending (p = 0.0069), left side bending (p = 0.003), and trunk extension (p = 0.006). Trunk flexion also showed a trend towards significant activation of the PFM (p = 0.008).
Figure 3a: Comparison of the average root mean square (RMS) EMG amplitude for the AB participants across all maneuvers. The grey bars represent the average RMS amplitudes across all AB participants in the right and left pelvic floor (rPF; lPF) and the error bars represent the standard deviation. The results from each participant is also individually plotted (coloured circles). * indicates $p < 0.007$ when comparing each maneuver against rest.
Figure 3b: Comparison of the average root mean square (RMS) EMG amplitude for the SCI participants across all maneuvers. The grey bars represent the average RMS amplitudes across all SCI participants in the right and left pelvic floor (rPF; lPF) and the error bars represent the standard deviation. The results from each participant is also individually plotted (coloured circles). * indicates p < 0.007 when comparing each maneuver against rest.
3.3 TMS Results

The %MSO ranged from 30-100% across the SCI and AB subjects. The total number of stimulations applied to each subject varied from 45 to 138 and were well tolerated by both SCI and AB subjects. All stimulations were delivered over the medial aspect of the precentral gyrus, approximately 1cm anterior to the auricular plane for all participants (Asavasopon et al., 2014; Brostrøm, 2003). Results from one AB subject (AB04) were excluded due to technical problems processing this data.
Figure 4: Superimposed raw EMG responses at incrementing levels of TMS from PFM in one able-bodied (AB01) and two SCI subjects (SCI02, SCI08). Intensity of stimulus (%MSO) is rainbow colour coded. Time of stimulation is indicated by the dotted line. Background EMG used to calculate MEP threshold was determined from the period outlined by the grey boxes.
3.3.1 TMS Results – Able-Bodied Group

TMS elicited MEPs in all subjects in the PFM. Emergence of a MEP was evident between 30-50%MSO in the AB group. The size of the MEP corresponded well to the intensity of stimulation where higher percentages of MSO correspond to a larger MEP amplitude as seen in the recruitment curves (Figure 4, 5b). Further, participants were generally able to maintain a consistent background contraction, indicating that changes in MEP amplitude were not a function of changes in background EMG (Figure 4, 5b). Despite targeting the PFM, MEPs were also elicited for the RA bilaterally in all AB participants.

Average latency for the PFM and the RA were 17.5ms and 17.9ms respectively (Figure 5c). The average difference between the RA and PFM latency ranged from -2.6ms to 2.3ms with an average of 0.4ms.

For all participants, the MEP response score was 100% in both the RA and PF bilaterally at the maximum %MSO individually achieved (Figure 5a).
### Figure 5a Summary of MEP Responses for AB Participants

<table>
<thead>
<tr>
<th>ID</th>
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<th>RA</th>
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<th>PF</th>
<th>PF Presence</th>
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<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
<tr>
<td>AB02</td>
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<td>rRA</td>
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<td>rPF</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
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<td>rRA</td>
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<td>rPF</td>
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</tr>
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<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
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<td></td>
<td></td>
<td>lRA</td>
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<td>IPF</td>
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</tr>
<tr>
<td>AB06</td>
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<td>rRA</td>
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<td>rPF</td>
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<td></td>
<td></td>
<td>lRA</td>
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<td>IPF</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 5a:** Frequencies of MEP observation in the right and left rectus abdominis (rRA; lRA) and pelvic floor (rPF; lPF) during the highest achieved stimulus intensity. Participants received a score of 2 (black) for MEP presence in all trials, a score of 1 for MEP presence in some of the trials, and a score of 0 for no MEP presence. %MSO = percentage of maximum stimulator output. Cells with diagonal lines represent data that was not included in the analysis.
Figure 5b: Recruitment Curve Plots for AB Participants

Figure 5b: TMS recruitment curves for AB participants. Both the right and left pelvic floor are plotted (rPF/lPF; green and blue dots respectively) with error bars representing standard deviation. Below each recruitment curve, background EMG is plotted with error bars representing standard deviation to show consistency of EMG activity across different stimulus intensities.
Table 3: Latency Values for AB Participants

<table>
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<th></th>
<th>rRA</th>
<th>lRA</th>
<th>rPF</th>
<th>lPF</th>
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<td>17.3</td>
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</tr>
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</tr>
<tr>
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</tr>
<tr>
<td>AB05</td>
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<td>15.6</td>
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</tr>
<tr>
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<td>20.2</td>
</tr>
<tr>
<td>AB07</td>
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<td>-</td>
</tr>
<tr>
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</tr>
<tr>
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</tr>
<tr>
<td>Grand Average</td>
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<td></td>
<td>18.1</td>
<td></td>
</tr>
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</table>

Table 3: Latency values for the right and left rectus abdominis (rRA; lRA) and pelvic floor (rPF; lPF). An ‘X’ indicates that data was not included in the analysis.
3.3.2 TMS Results – Spinal Cord Injured Participants

Of the nine participants, TMS elicited MEPs bilaterally in six individuals and unilaterally in one individual (SCI06). Emergence of a MEP ranged from 35-70% MSO. Of the two participants who did not produce a MEP response (SCI01, SCI03), they reached a maximum TMS intensity of 90% MSO and 80% MSO. For most subjects, the size of the MEP corresponded to the intensity of stimulation, but this relationship was not as well defined in comparison to the AB group (Figure 4, 6b). However, participants were generally able to maintain a consistent background contraction using the attempted trunk flexion maneuver (Figure 4, 6b). TMS also elicited MEPs bilaterally in the RA in eight participants and unilaterally for one participant.

Average latency for the PFM and the RA were 20.3ms and 22 (Figure 6c), respectively. The average difference between the RA and PFM latency ranged from -3.6ms to 9.2ms with an average of 2.4ms.

MEP response score varied heavily across participants. All but two participants received a score of 100% for the RA bilaterally, but the remaining participants scored a 50% and 75% respectively. For the PFM, MEP presence scores, four participants scored 100%, two scored 75%, one scored 25%, and the remaining two scored 0% each (Figure 6a).
Figure 6a Summary of MEP Responses for SCI Participants

<table>
<thead>
<tr>
<th>ID</th>
<th>Maximum %MSO</th>
<th>RA</th>
<th>RA Presence</th>
<th>PF</th>
<th>PF Presence</th>
</tr>
</thead>
<tbody>
<tr>
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<td>rRA</td>
<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
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<td>SCI02</td>
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<td>rRA</td>
<td></td>
<td>rPF</td>
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<td>rPF</td>
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<td></td>
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<td></td>
<td>IPF</td>
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<td></td>
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<td>rRA</td>
<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
<tr>
<td>SCI06</td>
<td>90</td>
<td>rRA</td>
<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
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</tr>
<tr>
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<td>rRA</td>
<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
<tr>
<td>SCI08</td>
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<td>rRA</td>
<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
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</tr>
<tr>
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<td>rRA</td>
<td></td>
<td>rPF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lRA</td>
<td></td>
<td>IPF</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 6a**: Frequencies of MEP observation in the right and left rectus abdominis (rRA; lRA) and pelvic floor (rPF; lPF) during the highest achieved stimulus intensity. Participants received a score of 2 (black) for MEP presence in all trials, a score of 1 for MEP presence in some of the trials, and a score of 0 for no MEP presence. %MSO = percentage of maximum stimulator output.
Figure 6b: Recruitment Curve Plots for SCI Participants

Figure 6b: TMS recruitment curves for SCI participants. Both the right and left pelvic floor are plotted (rPF/lPF; green and blue dots respectively) with error bars representing standard deviation. Below each recruitment curve, background EMG is plotted with error bars representing standard deviation to show consistency of EMG activity across different stimulus intensities.
Table 4: Latency Values for SCI Participants

<table>
<thead>
<tr>
<th>Participant</th>
<th>rRA</th>
<th>IRA</th>
<th>rPF</th>
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<td>29.2</td>
<td>-</td>
<td>-</td>
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<tr>
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<td>23.9</td>
<td>29.9</td>
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<tr>
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<td>23.6</td>
<td>20.6</td>
<td>24.5</td>
</tr>
<tr>
<td>SCI06</td>
<td>-</td>
<td>18.7</td>
<td>-</td>
<td>24.1</td>
</tr>
<tr>
<td>SCI07</td>
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<td>26.6</td>
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</tr>
<tr>
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<tr>
<td>SCI09</td>
<td>16.0</td>
<td>15.5</td>
<td>15.6</td>
<td>22.1</td>
</tr>
<tr>
<td>Average</td>
<td>20.7</td>
<td>20.2</td>
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<tr>
<td>Grand Average</td>
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<td>21.8</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Latency values for the right and left rectus abdominis (rRA; lRA) and pelvic floor (rPF; IPF). A ‘-’ symbol indicates that no MEP was elicited for this participant in that particular muscle.
Chapter 4: Discussion

This study sought to examine the presence of PFM activity in individuals with mc-SCI. Previous work has already shown sparing of trunk muscles (rectus abdominis, external obliques, erector spinae) in this population (Bjerkefors et al., 2009, 2015; Squair et al., 2016), and the presence of PFM activity post-injury could support the development of new treatments and management techniques for neurogenic bladder dysfunction. PFM sparing in this study was examined by asking participants to attempt to voluntarily contract the PFM (Part 1) and by measuring corticospinal excitability through TMS (Part 2). Although all of the SCI participants who enrolled in this study were not clinically expected to have PFM activity as per the ISNCSCI examination, evidence of PFM activity was apparent in all participants during Part 1, 2, or both.

4.1 Voluntary Activation of the Pelvic Floor Muscles

All AB participants and all but one SCI participant were able to activate their PFM while attempting the validated maneuvers in Part 1 (Bø et al., 1990). However, the patterns of activation varied between the two groups. Among the SCI participants, we consistently found that they were unable to contract their PFM directly (no response during the Kegel maneuver) but they were able to access this muscle group through other maneuvers such as trunk flexion or side bending. We have already seen from work in able-bodied literature that there is a strong co-activation of the PFM during these trunk maneuvers (Asavasopon et al., 2014; Hodges et al., 2007; Neumann & Gill, 2002; Sapsford & Hodges, 2001), which is further supported by the results from the AB group who also demonstrated synergistic PFM activation during these tasks. However, if we are able to elicit contraction of the PFM by trunk maneuvers, how is it that we are unable to elicit an isolated contraction of the PFM in the SCI group?
4.1.1 Could Pelvic Floor Activation by Trunk Maneuvers Be Reflexive?

Previous work has shown that the PFM are active during tasks that require abdominal activation such as sit-ups, abdominal hollowing, coughing, and forced expiration (Neumann & Gill, 2002; Sapsford & Hodges, 2001). It is thought that PFM are active during these tasks in order to maintain urinary continence when intra-abdominal pressure is increased by this abdominal muscle activity to ensure closure of the urethra and maintenance of the bladder neck position (Ashton-Miller & DeLancey, 2007; Bø, K, Lilleas, & Talseth, 1997; Christensen et al., 1995; Sapsford & Hodges, 2001). However, there is also evidence that this PFM activity increases prior to an increase in intra-abdominal pressure driven by abdominal activation. For example, during a cough, urethral pressure increases 120-200ms prior to increased bladder pressure (Pieber, Zivkovic, & Tamussino, 1998). Similarly, in Sapsford et al (2001), recordings of intra-abdominal pressure were made in conjunction with recordings of vaginal pressure during attempted abdominal maneuvers. Their results confirmed that vaginal pressure increased in advance of an increase in intra-abdominal pressure (Sapsford & Hodges, 2001). These results suggest that PFM activity occurs in advance of both involuntary (e.g. cough) and voluntary contraction of the abdominal muscles. As such, co-activation of the PFM with abdominal muscle activity could not be a reflexive response due to muscle stretch of the PFM during moments of increased intra-abdominal pressure when the PFM might be downwardly displaced. These previous results support that the activity we see in the PFM of participants during abdominal maneuvers might not be due to reflexive contraction, but is instead part of a pre-programmed response in the central nervous system in preparation for an increase in intra-abdominal pressure. This is further supported by our use of the thermocouple in this study to track breathing during the attempted maneuvers. As our participants maintained an open glottis during the voluntary
contractions, we prevented an increase in intra-abdominal pressure which in turn should have prevented a reflexive contraction of the PFM due to downward pressure on this muscle groups.

4.1.2 Why are Spinal Cord Injury Participants Unable to Perform Kegels Effectively?
If there is still central nervous system innervation to the PFM during co-activation of the abdominal muscles, then how is it our participants are unable to perform effective Kegel contractions? It is possible that learning to perform this maneuver was simply too difficult, especially when an individual lacks sensation, and therefore feedback, from this region of the body due to neurological injury. One study examined urethral pressure in 47 women during rest and during a Kegel contraction after a brief standardized verbal instruction. They found that only 49% of participants had an ideal Kegel response in that they were able to increase the force of urethral closure, and concerningly 25% of respondents actually displayed a Kegel technique that would potentially promote incontinence (Bump, Hurt, Fantl, & Wyman, 1991). Another study examined 107 female participants who were currently undergoing a regular PFM training program by assessing vaginal strength using the Oxford scale. The majority of these women were initially given either written or verbal instruction on how to perform these exercises, but only 45% of women in this group could perform Kegels correctly (Kandadai, O’Dell, & Saini, 2015). The conclusions from these works suggest that verbal or written instruction may not be adequate in teaching individuals to effectively perform Kegels. This is likely compounded for individuals with SCI who are unable to use sensory feedback to confirm if their activation is targeting their PFM. In comparison, abdominal maneuvers such as trunk flexion, side bending, and trunk extension may be simpler for individuals to understand and perform. These movements are part of common exercise programs that individuals likely performed prior to injury (e.g. sit-
ups) which provides prior knowledge of performance. Further, feedback for these exercises is more obvious as the participant will be able to see and, depending on their injury level, feel their torso move with respect to the plinth.

4.2 MEPs in Response to TMS

MEPs were elicited in the PFM for all AB subjects and for seven of the SCI participants. These results suggest that despite thoracic or cervical level mc-SCI injuries, these individuals retain direct pathways from the cortex to the PFM which bypass the injury site. Moreover, the SCI participants also displayed strong MEPs in the RA muscles which supports previous research that muscles of the trunk maintain cortical connections post-injury (Bjerkefors et al., 2015; Squair et al., 2016).

4.2.1 Differences in Latency

As the PFM are innervated at a lower level than the abdominal muscles, it would be expected that the latency values for the RA would be shorter in both the SCI and AB groups. This was the case for most subjects, but for two AB participants and three SCI participants, their average PFM latency was shorter than the latency for their RA response. It is possible that this is a function of coil positioning. The purpose of this study was to explore PFM activity and so we target the PFM in our TMS protocol but placing the coil over the medial aspect of the precentral gyrus which is directly along the midsagittal plane (Asavasopon et al., 2014; Yani et al., 2018). However, the abdominal muscle representation in the cortex is not directly along this midline and is instead at least 2cm lateral of the precentral gyrus (Bjerkefors et al., 2015). Thus, it is possible then that there was a delay in the cortex for the signal to travel from the targeted
position to the abdominal representation when, in comparison, we would have targeted the PFM directly.

Previous work reported the average latency for RA during activation to be around 16-19ms in AB participants (Tunstill, Wynn-Davies, Nowicky, McGregor, & Davey, 2001) and 17-22ms in those with SCI (Bjerkefors et al., 2015). These previous data are consistent with our results; we calculated latencies of 17ms and 20ms for AB and those with SCI, respectively. Similarly, two studies have previously reported the latency of the PFM response to TMS. One study reported a single AB male subject as having a latency of 23ms, and a second study reported PFM latency to be between 18-19ms while contracted and 21-20ms while relaxed in 30 healthy women. Again, our results fall well within these ranges for both the SCI and AB groups with mean PFM latencies of 18ms and 22ms, respectively.

While all reported latencies fell within normal ranges, the latencies for both the RA and PFM were consistently shorter in the AB compared to the SCI group. It is possible that this delay is a result of the SCI as the signal passes through the injury site which may suffer from poor conduction velocity. Evidence has shown that after a SCI there is reduced myelination of axons around the injury site due to both initial mechanisms of injury and secondary nerve damage (Mcdonald & Belegu, 2006; Totoiu & Keirstead, 2005). While there is evidence of remyelination post injury, many of these axons remain demyelinated permanently (Totoiu & Keirstead, 2005). As myelination is key for rapid nerve conduction, this demyelination or partial myelination of axons around the injury site may result in increased MEP latency (Salzer & Zalc, 2016).
4.2.2 Not All Spinal Cord Injured Participants Had a MEP Response

Of the nine SCI participants, two showed no MEP response (SCI01, SCI03). However, both of these participants showed strong MEP responses in their RA bilaterally, which is below the level of injury in SCI01 (T4 AIS A) but may be partially preserved in SCI03 (T9 AIS A). SCI01 had poor PFM activation during the maneuvers in Part 1 of this study where activity was detected in only one of the trunk extension trials and not during any other maneuver. It is possible that this subject has not retained a functional connection to the PFM from the cortex. In contrast, SCI03 demonstrated strong PFM activity during the attempted maneuvers with an activation score of 64% and was the only participant to show PFM activation during the gluteal contraction. The PFM has a very small cortical representation and without better guidance software, it is possible that we were unable to target their PFM effectively (Asavasopon et al., 2014). However, this participant also asked to end the TMS portion of the study after reaching 80%MSO due to a strong dislike for the stimulus sensation, and so it is also possible that at a higher %MSO, we could have elicited a MEP in this participant.

SCI06 was the only participant who showed a unilateral response in the PFM to the TMS. However, we also noticed that we were only able to elicit a MEP from the RA on the ipsilateral side. It is possible that the coil was not placed perfectly over this participants’ median sulcus and as such we recruited one side and not the other. However, Nakagawa et al (1980) observed in monkeys that the PFM are bilaterally innervated; assuming that there is a similar pattern of connectivity in humans, we should have expected to observe some response in the right PFM of SCI06.
4.2.3 MEP Responses Without Voluntary Activation

MEPs were noted in SCI subjects who had very limited voluntary activation in the PFM including SCI06 (0%), SCI07 (4%) and SCI02 (18%). While it may be clear that some maneuvers, such as the Kegels, were challenging for all participants to perform, it is surprising that these participants had such little activation during other tasks. However, similar results were found by Squair et al (2016) where they also explored the presence of muscle sparing below the level of injury in those with SCI. In this study, they reported 22 cases in which a voluntary response was absent despite a present MEP response in the same muscle (Squair et al., 2016). It is possible that these participants simply had difficulties performing all of the movements, and not just the Kegel maneuver.

4.3 Clinical Implication of MEP Presence & Activation Score

This study showed that most SCI participants have potential voluntary activation of and cortical sparing to the PFM after injury. However, these measures do not indicate the strength of the PFM. As it is PFM strength that is directly related to bladder function and not degree of PFM sparing, we are unable to make assumptions that the individuals in this study with higher degrees of PFM sparing will have the least bladder symptoms. Future work could explore the degree of strength that these individuals retain in the PFM and correlate this against measures of neurogenic bladder symptoms. However, there is no current gold standard methodology for measuring PFM strength (Deegan, Stothers, Kavanagh, & Macnab, 2018). Common techniques include digital palpation, perineometers, EMG recordings, and the use of dynamometers (Deegan et al., 2018). Considering the denervation and expected weakness of the PFM in the mc-SCI population, the given technique would need to be sensitive enough to record the potentially poor
strength of the PFM from these participants. Further, the majority of these techniques to examine PFM strength are specialized to women using intravaginal devices. Adaptation of these devices and techniques may be required for those with SCI where the majority of the population is male (Ackery et al., 2004).

4.4 Methodological Considerations

4.4.1 TMS Landmarking and Navigation

The PFM has a small cortical representation as seen in previous studies using MRI (Asavasopon et al., 2014; Blok et al., 1997; Schrum et al., 2011; Yani et al., 2018). Earlier work attempting to elicit MEPs of the PFM have utilized guidance systems incorporating fMRI mapping in order to increase the accuracy of accessing a precise stimulation site (Asavasopon et al., 2014; Yani et al., 2018). This research did not utilize similar technology and instead used surface landmarks of the skull to approximate the location of where the median sulcus meets the precentral gyrus. Further, custom Unity software allowed us to relocate our target position for each stimulus within a 2mm range. Based on the results from this study with respect to MEP latency and size, we are confident that we were able to consistently identify an appropriate area for stimulation in line with previous work. However, the use of technology that offer more precise navigation would only improve performance. This could have improved our chance of producing a response for the two SCI participants who did not elicit a MEP (SCI01, SCI03), especially SCI03 who demonstrated strong voluntary activation of this muscle group.
4.4.2 Crosstalk

Recording EMG from the PFM is challenging based on the location of this muscle group within the pelvis in addition to participant discomfort in accessing the perineum. Previous work exploring PFM activity while performing exercises, locomotor activity, and in response to TMS have often utilized vaginal or anal recording probes (Asavasopon et al., 2014; Hodges et al., 2007; Leitner et al., 2017; Moser et al., 2018; Neumann & Gill, 2002; Sapsford & Hodges, 2001; Yani et al., 2018). We chose to use surface EMG electrodes to minimize participant discomfort and facilitate participant recruitment. Further, the use of perineal surface EMG allows us to examine the right and left PFM independently instead of as a singular unit like vaginal/anal probes. Perineal surface EMG is commonly used as a part of urodynamic studies to monitor PFM activity and to make clinical decisions about the functionality of this muscle group with respect to the bladder (Kirby et al., 2011; Stöhrer et al., 1999). One study also examined the differences in signal between an intravaginal sensor and perineal surface EMG during Kegel contractions and determined there was no difference in mean or peak RMS between the two sensor types (Moretti, de Moura Filho, de Almeida, Araujo, & Lemos, 2017). However, both vaginal/anal probes and perineal surface recordings are prone to crosstalk from the gluteal muscles and anal sphincter (anal probe and perineal surface only) (Flury, Koenig, & Radlinger, 2017; Keshwani & McLean, 2015; Moretti et al., 2017). For the gluteal muscles, potential crosstalk is harder to identify as there is a strong co-activation between the gluteals and LA (Asavasopon et al., 2014; Yani et al., 2018). As such, and as seen our AB data, when a participant attempts to contract their gluteals we see an extremely strong PFM response. It is possible that crosstalk between the gluteals and PFM is responsible for the higher RMS values that we see in the PFM during a gluteal contraction in the AB group (Fig 3a) in comparison to the Kegel contraction.
Alternatively, it could be that gluteal contraction is simply easier to perform for subjects than a Kegel maneuver which is why we see such a strong response during this exercise.

To determine if there is crosstalk between the gluteals and the PFM, we could perform a secondary analysis to examine when PFM activity is initiated with respect to the pelvic floor. We know that during abdominal maneuvers and other co-contraction activities, the PFM is active prior to the targeted muscle in those maneuvers (Pieber et al., 1998; Sapsford & Hodges, 2001). As such, if the PFM is active in advance of the gluteals during a gluteal contraction, we can confirm that the activity we see in the PFM is not due to cross talk of the gluteals and is instead independent activity. Alternatively, the presence of crosstalk in our EMG set-up could be confirmed/excluded by examining the signal recorded during gluteal contractions from a bipolar electrode configuration running perpendicular to the PFM muscle fiber. If there is no crosstalk from the gluteal muscles, then the signal recorded from the perpendicular configuration should not be affected by gluteal contractions.

4.4.2 Instructing Kegel Performance

When instructing participants on how to perform a Kegel, this study used simple verbal instruction based the American Urological Association guidelines and previous work in this field (Kandadai et al., 2015). As previously discussed, evidence from the literature suggests that verbal or written instructions on how to perform a Kegel maneuver might not be sufficient coaching to elicit proper performance (Bump et al., 1991; Kandadai et al., 2015). This is especially true for those with SCI where they are unable to use sensory feedback to confirm if they are targeting the right muscles. On top of this, many of the existing Kegel instructions use language that might not be suitable for those with SCI. For example, a common instruction is to
have the person imagine they are squeezing their anus to prevent flatulence or to imagine they are actively voiding urine and need to stop the flow of urine mid-stream (Kandadai et al., 2015). For individuals with mc-SCI who might be using alternative techniques to manage bowel and bladder function, this imagery is not effective or applicable. Further work needs to explore the best mode for educating patients on how to perform a Kegel exercise effectively. The application of PFM training programs for those with stroke and MS have incorporated the use of electromyographical or manual bio-feedback and/or neuromuscular electrical stimulation (McClurg et al., 2006; Tibaek et al., 2005). Perhaps the integration of these techniques would more effective for those with SCI than PFM exercises alone.

4.4.3 Systemic Effects of Botulinum Toxin

It is possible that the lower activation scores observed in the SCI participants could be due to previous botulinum toxin (BTX) injections of the detrusor to help manage their bladder symptoms. Of the 9 SCI participants enrolled in this study, 7 reported receiving an injection, from 1 to 9 months previously. Although it is a targeted injection, there is evidence that BTX injections may spread to adjacent muscles or further migrate throughout the body (Ramirez-Castaneda et al., 2013; Wyndaele & Van Dromme, 2002; Yaraskavitch, Leonard, & Herzog, 2008). In animals, effects on adjacent muscles have been shown to persist for at least four weeks following the initial injection (Yaraskavitch et al., 2008). In the SCI population, there have been reports of generalized full-body muscle weakness for upwards of three months (Wyndaele & Van Dromme, 2002). SCI01 and SCI05 had BTX treatments one and three months prior to participating in this study, respectively. While SCI05 had a slightly below average activation score, we still saw clear activation of her PFM during the attempted maneuvers and a consistent
MEP in response to the TMS. In contrast, SCI01 had a poor activation score at 3% and no MEP response, and we cannot discount the possibility that this subject was experiencing systemic effects of his recent injection that could have influenced his results.

4.5 Potential Clinical Implications and Future Directions

PFM training is used to increase hypertrophy and tone of the PFM (Bø, 2004). Improved functionality of this muscle groups helps maintain continence by structurally supporting the bladder and allowing for increased compression of the urethra to prevent urine leakage (Ashton-Miller & DeLancey, 2007; Bø & Stien, 1994). Activation of the LA also leads to reflex inhibition of the bladder wall which further supports bladder function by reducing bladder pressure and increasing bladder capacity (Bø & Berghmans, 2000). Previous work has already shown that PFM training may be effective for those with motor-incomplete SCI (Elmelund et al., 2018; Vásquez et al., 2015). With regular PFM training, Elmelund et al (2018) showed an improvement in ICIQ-UI score and a reduction in leakage while Vásquez et al (2015) demonstrated a reduction in bladder over-activity with PFM contractions. Our results are the first to present evidence for both voluntary control of and cortical sparing to the PFM in the mc-SCI population. Based on these findings, it is possible that the application of a PFM training program to this population may improve bladder function. However, our voluntary activation results from Part 1 showed that the most effective means to activate the PFM in the SCI group was to perform trunk maneuvers, but otherwise the PFM was not consistently activated. As such, development of PFM training programs for the mc-SCI population may have to rely on synergistic activation strategies as opposed to direct maneuvers such as Kegels. Future work could explore how the
application of these effective PFM training programs may improve neurogenic bladder symptoms.

This work also adds to the growing body of literature to suggest that those who are diagnosed as clinically complete may still maintain functional muscle sparing below the injury level (Alamro et al., 2018; Bjerkefors et al., 2009, 2015; Chisholm et al., 2017; Squair et al., 2016). Previous work has shown strong evidence for abdominal muscle sparing in those with mc-SCI and recent work has also shown that these muscles may be trainable post-injury (Chisholm et al., 2017). This study shows that the PFM is similarly spared after a mc-SCI diagnosis and hopefully future work can demonstrate that they can be similarly trained. This is of importance to clinicians within the rehabilitation field as other muscle groups might maintain functional sparing post-injury which is not captured by standard neurological exams.
Chapter 5: Conclusion

The PFM are essential for both the effective retention and voiding of urine (Ashton-Miller & DeLancey, 2007; Fowler et al., 2008). Previous work has also shown that training programs to strengthen these muscles in able-bodied individuals is effective as a non-invasive treatment of urinary incontinence (Bø, 2004, 2012). Recent work has explored using PFM training programs for those with motor-incomplete SCI (Elmelund et al., 2018; Vásquez et al., 2015), but due to an assumption that the PFM cannot be recruited in those with mc-SCI (Kirshblum et al., 2011), this type of treatment has not yet been translated to those with more severe injuries.

In this study, we demonstrate that many people who have been classified as mc-SCI by standard neurological exams are in fact able to voluntarily contract their PFM by attempting abdominal exercises. Further, using TMS, we were able to show a connection to these muscles from the cortex for the majority of these participants. These results support the growing body of literature that those diagnosed as mc-SCI retain functional sparing below the injury level. Future studies could investigate the effectiveness of PFM training for those with mc-SCI to improve neurogenic bladder symptoms.
References


Appendix A1: EMG responses for SCI01 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A2: SC102 EMG Response to Maneuvers

Appendix A2: EMG responses for SC102 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A3: SCI03 EMG Response to Maneuvers

Appendix A3: EMG responses for SCI03 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A4: SCI04 EMG Response to Maneuvers

Appendix A4: EMG responses for SCI04 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A5: EMG responses for SCI05 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A6: SCI06 EMG Response to Maneuvers

Appendix A6: EMG responses for SCI06 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A7: EMG responses for SCI07 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A8: SC108 EMG Response to Maneuvers

Appendix A8: EMG responses for SC108 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.
Appendix A9: SCI09 EMG Response to Maneuvers

EMG responses for SCI09 for each attempted maneuver. EMG traces from the right side of the body are coloured blue, and muscles from the left side are coloured orange. RA = rectus abdominis; EO = external oblique; ES = erector spinae; PF = pelvic floor; GM = gluteus maximus.