Sensory and motor correlates of stress urinary incontinence in women

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Imagine what you'll know tomorrow – Agent K, Men in Black

Preface

This research was approved by the University of Ottawa Health Sciences and Sciences Research Ethics Board, indicating compliance with national ethical standards for the conduct of human research (H-07-20-5945) and with COVID-19 safety precautions (Appendix A). The doctoral candidate completing this dissertation, Kaylee C. L. Brooks, participated in all aspects of the study conceptualization, design, data collection, data analysis and interpretation, and the presentation of the results. The findings of Chapter 4 and Chapter 6 were presented as podium presentations at the International Continence Society 2023 conference in Toronto, ON on September 28 and 29, 2023. The abstracts for these conference presentations were published in Continence, the journal of the International Continence Society.

Contribution of Collaborators

In compliance with the University of Ottawa Academic Regulation C-7 for theses, the contributions of the collaborators involved in the research process are outlined below.

The primary researcher, Kaylee C. L. Brooks (KCLB) conceptualized, led, and participated in all aspects of the research process. The main collaborator on the dissertation research was the thesis supervisor, Linda McLean, Ph.D. (LM), who collaborated on the design of the protocols for the components of the sensorimotor assessment that make up Chapters 3, 4, 5, and 6. LM also collaborated on the analysis and interpretation of the data in this dissertation. The Thesis Advisory Committee was selected for their specialties in stress urinary incontinence, motor control, and electromyography. They provided valuable feedback on study design at the dissertation proposal stage and reviewed each chapter of the thesis. The committee members included Duane Hickling, MD, Tony Carlsen, Ph.D., and Martin Bilodeau, Ph.D.. Methodology

for the genital sensation testing protocol was previously created by Caroline Pukall, Ph.D. (CP) and selected for use by KCLB in the study protocol. CP provided training for KCLB on proper techniques for data collection and provided a custom computer program for testing site randomization and data recording. This protocol was used in Chapter 5 of the dissertation and CP will be included as an author on the article that will come from this chapter when it is submitted for publication.

Abstract

Impairment of the sensorimotor system is suspected in women with stress urinary incontinence (SUI), but there is currently no consensus on its role in SUI pathophysiology. The primary aim of this dissertation was to explore differences in sensorimotor function of the pelvic floor muscles (PFMs) between women with and without SUI. The secondary aim was to explore which aspects of sensorimotor function (motor and sensory nerve function, PFM motor control and proprioception) may be different between women with SUI who were and were not cured of their symptoms with a physiotherapy intervention.

A single protocol was developed to gather data for four distinct studies. The sample consisted of 30 cis women who completed two data collection sessions to record information on their sensorimotor function. Fourteen participants were continent, and 16 participants had SUI. Twelve of the 16 participants with SUI then attended a pelvic floor physiotherapy clinic of their choice, with the specific treatment provided left to the discretion of each physiotherapist. These participants were then asked to complete the International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms and the Global Rating of Patient Satisfaction and Perception of Improvement Questionnaire 12 weeks after their first appointment to determine if they were cured.

The objective of the first study was to develop a standardized protocol for evaluating PFM proprioception. The assessments were based on tests used to evaluate limb proprioception and adapted for the pelvic floor. Using an intravaginal dynamometer (IVD), we identified an optimal signal processing protocol, and found that passive elongation and force-matching tasks provide different information about the proprioceptive function of the female-typical pelvic floor. We

also found that visual feedback and contractile intensity may independently influence performance on the force-matching task.

The objective of the second study was to compare, using an IVD, PFM motor function (e.g. strength, power, motor control) and proprioception between women with and without SUI, considering parity as a factor. Participants were asked to contract their PFMs with maximal effort and then perform one trial of a series of quick repeated contractions with the IVD. The protocol developed in objective one was used to assess proprioceptive function in women with and without SUI. The findings suggested that motor function and proprioception were not different between women with and without SUI. However, parous individuals displayed lower PFM force-generating capacity, a slower rate of force generation and relaxation, and no influence of visual feedback on the force-matching task compared to nulliparous women. This finding suggests that parity may influence PFM function, which may be important in understanding the pathophysiology of pelvic floor disorders. The secondary objective of the study was to determine which aspects of PFM function and proprioception may be different between women with SUI who were and were not cured of their symptoms through a physiotherapy intervention. The effect sizes suggested that women who were cured may demonstrate slower PFM force generation and relaxation and less accurate proprioception on a force-matching task at baseline compared to those who were not cured.

The third objective was to investigate differences in light touch genital sensory thresholds between women with and without SUI. Using monofilaments and a method of levels approach to threshold testing, the regression models indicated that SUI was associated with high sensory thresholds at the perianal skin. Outliers from this analysis were identified as individuals with extremely high sensory thresholds, which suggests that focal disruptions of the branches of the

pudendal nerve may be present, but impairment in the pudendal nerve as a whole is unlikely in women with mild to moderate SUI.

The final objective was to explore differences in voluntary and evoked PFM activation between women with and without SUI. This was accomplished through stimulating the pudendal nerve intravaginally and recording the resultant evoked potentials from the levator ani, bulbospongiosus, urethral rhabdosphincter, and external anal sphincter muscles. Electromyographic signals were also recorded during maximal voluntary contraction efforts. The results did not support the presence of pudendal nerve impairment in women with mild to moderate SUI. Nor did the findings suggest that voluntary and evoked PFM activation influence physiotherapy treatment outcomes.

When considered together, the results of these studies do not suggest that sensorimotor impairments of the PFMs are important to the pathophysiology of mild to moderate SUI. However, the impact of parity on PFM function warrants further study. The findings of this work may be used to direct future investigations of sensorimotor function in the pelvic floor to ultimately advance our understanding of pelvic floor disorders in women.

Key words: *stress urinary incontinence, quantitative sensation testing, nerve conduction testing, pelvic floor muscles, proprioception, intravaginal dynamometry*

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Abbreviations

ANOVA	Analysis of Variance
BSM	Bulbospongiosus Muscle
CMAP	Compound Muscle Action Potential
CPT	Current Perception Threshold
EAS	External Anal Sphincter
EMG	Electromyography
FSFI	Female Sexual Function Index
GTO	Golgi tendon organs
ICIQ-B	International Consultation on Incontinence Questionnaire – Bowel Symptoms
ICIQ-FLUTS	International Consultation on Incontinence Questionnaire - Female Lower Urinary Tract Symptoms
ICIQ-VS	International Consultation on Incontinence Questionnaire – Vaginal Symptoms
IVD	Intravaginal Dynamometer
LAMs	Levator Ani Muscles
MRI	Magnetic Resonance Imaging

MVC	Maximum Voluntary Contraction
PET	Positron Emission Tomography
PFM	Pelvic Floor Muscle
PFMT	Pelvic Floor Muscle Training
PMC	Pontine Micturition Center
PNTML	Pudendal Nerve Terminal Motor Latency
POP	Pelvic Organ Prolapse
PSC	Pontine Storage Center
QST	Quantitative Sensory Testing
RFD	Rate of Force Development
RFR	Rate of Force Relaxation
RMSE	Root Mean Square Error
SD	Standard Deviation
SUI	Stress Urinary Incontinence
UI	Urinary Incontinence
UR	Urethral Rhabdosphincter

Chapter 1: Introduction

1.1 Problem statement

Daily urine leakage affects up to 25-45% of the population[1] and is most common among women[*2]. Research suggests that with the aging population in the United States, the prevalence of urinary incontinence (UI) will increase by 55% by the year 2050[3]; with similar trends expected in Canada and Europe. UI in women is associated with an increased likelihood of comorbid chronic conditions such as cardiovascular disease, asthma, and/or diabetes[4,5] and it is considered a marker of frailty, with a higher risk of falls, hospitalization, and institutionalization among older women who experience UI compared to those who do not[6–8]. The Canadian healthcare system spends approximately $8.5 billion CAD annually on the direct (e.g. diagnosis, treatment, routine care, etc.) and indirect (e.g. decreased productivity, days off work, etc.) costs of UI[2], and further out-of-pocket expenses for affected individuals are estimated to be $1400-$2100 per year on routine symptom management (e.g. continence pads/diapers, extra laundry costs, etc.)[2]. As UI is often under-reported, these costs may be underestimated[9].

UI is classified into three subtypes: stress urinary incontinence (SUI), urgency urinary incontinence, and mixed urinary incontinence. The majority of women with UI are diagnosed with SUI, while 15-20% have urgency UI, and 30-35% have mixed UI [10]. The population of interest in this thesis is women with SUI, defined as those who experience involuntary leakage of urine during exertion (e.g. a sneeze, cough, laughter, high impact exercise, etc.)[11]. Major risk

[*] For the purposes of this thesis, the term woman refers to individuals who were assigned female at birth and identify as female (cis woman). The author recognizes and respects that those with female-typical anatomy may identify with different genders, however the consideration of gender effects is outside of the scope of this thesis.

factors for developing SUI include pregnancy, aging, lifestyle habits, and ethnicity[12]. Those who are most at risk of developing SUI include individuals who have had one or multiple pregnancies[13,14], long (>150min) active labour during childbirth[15], larger babies[13,14], and/or are of Hispanic or Caucasian ethnicity[16]. Additional risk factors include a history of previous urogynecological surgery[17], a family history of UI[18], moderate to heavy smoking[19], obesity[20], pelvic cancer[21,22], and/or participation in high impact physical activities[23,24]. SUI is most prevalent among middle-aged women and, while its prevalence declines with older age, this phenomenon appears to be related to the rise of concurrent urgency symptoms, resulting in a higher prevalence of mixed urinary incontinence with increasing age[25,26]. Importantly, SUI greatly reduces quality of life[27], sexual function[28–30], social interactions, and participation in physical activities[31–33].

As the symptoms of SUI are embarrassing, many affected individuals delay disclosing them and seeking treatment[12,34]. Feelings of embarrassment often lead those with UI to develop maladaptive coping strategies, such as avoidance, where they attempt to conceal their leakage by avoiding specific situations in which it typically occurs[33]. Embarrassment is often a barrier for consulting a primary care provider about urine leakage[12] and, when a primary care physician is consulted about UI, less than half report that they have a clear understanding of incontinence and only 40% of those physicians who report understanding UI have an organized plan for treatment[35]. Moreover, many women feel that UI is a normal part of aging, an expected result of childbirth, and/or they do not know that it is treatable[12,34]; while other women report that they simply do not have time to prioritize themselves over their family[12]. The development of a standard of care is important to educate those who do not know about UI and its treatment

options, to better manage those who do seek treatment, and to make UI treatment options more accessible to those seeking care.

Currently, the most common evidence-based treatment options for women with SUI include surgery[36–38] and physiotherapy, which most often includes supervised pelvic floor muscle (PFM) training (PFMT) as a major component[39]. Other conservative methods (e.g. pessaries[40], injectable urethral bulking agents[41], etc.) are available, with emerging evidence to support their use, but as of yet these have not achieved widespread adoption. Physiotherapist-supervised PFMT has a high level of evidence in SUI management and no known adverse effects[39]. As such, it is recommended by the International Continence Society and other major medical associations[42–45] as a first-line treatment for women with SUI. However, only approximately half of the women who undergo PFMT are cured of their SUI symptoms[39]. Indeed, developing a more thorough understanding of the pathophysiology of SUI in women may help to improve management through streamlining current treatment options and developing new, targeted, approaches to treatment.

SUI is often considered a mechanical problem, though its pathophysiology includes changes in structural support as well as neuromuscular alterations. Longstanding evidence suggests that poor bladder neck support and damaged connective tissues[46,47], urethral hypermobility[12,23,48], intrinsic sphincter deficiency[49], and PFM weakness or damage[39] are factors. Research has also found evidence of denervation in the urethral and anal sphincters among women with SUI[50–52]. The pudendal nerve, which innervates the urethral and anal sphincters, contains both motor and sensory fibers[53] and can be damaged during childbirth. Models of vaginal delivery have estimated that the branches of the pudendal nerve can experience strain between 13-33% during active labour—which often exceeds the strain known to cause damage

to peripheral nerves (15%)[54]. Women with SUI have demonstrated evidence of prolonged pudendal nerve terminal motor latencies (PNTMLs) [50,55–57] and an increased ratio of muscle fibers to nerve fibers (i.e., innervation ratio) in the urethral and anal sphincters[58,59], which are indicative of prior damage to and subsequent reinnervation of the muscles innervated by the pudendal nerve. Given the mix of sensory and motor innervation of the pudendal nerve, it is logical to hypothesize that changes in motor nerve conduction in women with SUI may be accompanied by changes in sensory nerve function. However, changes in sensation are not routinely evaluated in those with SUI and have only been reported in four studies. Two studies used quantitative sensory testing (QST)[60,61] and two used current perception threshold (CPT)[62,63] testing, reporting mixed results. Among these studies, one did not include a control group[62] and one assessed sensation only at the clitoris,[61] which is thought to have multiple sensory nerve contributions[64]. CPT testing methods were used in two of the studies, which may not be as reliable as QST methods[65]. As such, further research is required to better understand the role of sensory impairment among women with SUI.

Sensation plays an important role in motor control and motor learning[66,67]. Research into populations that have joint injuries at the ankle and knee show concurrent impairment to the sensorimotor system, where peripheral nerve injuries are associated with changes in proprioception and muscle function[68–70]. In terms of SUI, if the nerve fibers of the pudendal nerve are damaged, then motor control and motor learning in the PFMs and sphincters may be altered, which could lead to differences in the motor patterns employed to prevent urine leakage. That said, a recent study using intravaginal dynamometry[71] found that women with SUI demonstrated a more accurate sense of force output (an aspect of proprioception) compared to continent controls[72]. Yet the methods used to evaluate force-matching accuracy in the levator ani

muscles (LAMs) were not well described. Further research is needed to establish a standardized approach to the measurement of force-matching accuracy, and then to apply this approach in research to determine if impaired proprioception plays a role in SUI pathophysiology and/or treatment outcomes.

1.2 Objectives

Assessing the potential impact of sensorimotor impairments in women with SUI may enhance our understanding of SUI pathophysiology and the role that it may play in the success or failure of physiotherapy interventions. The primary aim of this thesis was to estimate the effect sizes of differences in PFM proprioception, muscle function, and sensory and motor nerve function between women with and without SUI. These effect sizes could then be used to direct future research to areas of sensorimotor function that hold the most promise for enhancing our understanding of SUI pathophysiology. This aim was accomplished through addressing four main objectives:

Objective 1: a) Develop protocols for assessing the ability to detect changes in PFM length and sense of force output in women using an intravaginal dynamometer (IVD); b) Determine if visual feedback and/or target force intensity affect performance on a LAM force-matching task.

Expected Outcome 1: Using our proprioception protocols, we expected to find that participant error in a passive elongation task was normally distributed. We also expected that the provision of visual feedback would improve performance on the force-matching task[73,74]. Lastly, we expected that the error on the force-matching task would be smaller at lower intensity targets and increase with the higher intensity targets[73,74].

Objective 2: Determine if there is evidence of a difference in PFM proprioception and/or force-generating capacity between women with and without SUI, considering parity as a factor. Measured characteristics included force matching accuracy during submaximal contractions [25%, 50%, 75% of maximum voluntary contraction (MVC) force], accuracy at detecting changes in PFM length, MVC force, maximal rate of force development achieved during MVC, relaxation of force after an MVC, and the number of quick contractions produced within 30s.

Expected Outcome 2: We expected that women with SUI would show evidence of impaired proprioception and motor output of the PFMs compared to continent women. Specifically, we expected that women with SUI would demonstrate higher error in force matching and would be less able to accurately identify tissue length compared to continent women[75]. Those with SUI would have a slower rate of force development during MVC and produce fewer quick contractions in 30 seconds but would not demonstrate lower MVC force compared to continent women[76].

Objective 3: Determine whether there is evidence of impaired genital sensation among women with SUI through measuring thresholds for light touch genital sensation at the right anterior section of the labia majora, the 6 o'clock position of the urethral meatus, the medial portion of the perineum, and the perianal skin to the right of the external anal sphincter (EAS); considering age as a covariate and parity as a factor.

Expected Outcome 3: We expected that, compared to continent women, women with SUI would demonstrate higher genital sensation thresholds to light touch when assessed at skin sites innervated by the pudendal nerve [60,63,77].

Objective 4: Determine whether there are differences in voluntary or evoked PFM activation between women with and without SUI. The primary outcomes were compound muscle action potential (CMAP) latencies recorded from electromyographic (EMG) signals recorded at the LAMs, urethral rhabdosphincter, bulbospongiosus, and EAS in response to intravaginal pudendal nerve stimulation.

Expected Outcome 4: We expected there would be differences in voluntary activation and CMAP latency between women with and without SUI[78]. Specifically, we expected those with SUI to demonstrate prolonged CMAP onset latencies[50,55,56] and slower signal rise times[79] during an MVC compared to continent controls.

A secondary aim of this thesis was to explore whether aspects of sensorimotor function might be associated with the outcome of a physiotherapy intervention for SUI:

Secondary Objective 1: Explore the effect sizes for differences in voluntary and evoked PFM activation, LAM passive forces, strength, power, motor control, and proprioception between women with SUI who were cured and those who were not cured of their symptoms through physiotherapy interventions.

Secondary Expected Outcome 1: Among women with SUI who were not cured after a physiotherapy intervention, there would be evidence of pudendal neuropathy (i.e. prolonged CMAP onset latencies, lower EMG amplitude during MVC). In contrast, those who were cured would not show signs of pudendal neuropathy but would instead demonstrate better accuracy on the force-matching task and the passive elongation task, with slower force-generating capacity than women who were not cured.

Chapter 2: Literature review

This literature review highlights the potential role of sensorimotor impairment among women with stress urinary incontinence (SUI) and explores the potential impact of sensorimotor impairment on the effectiveness of exercise interventions. The databases searched included CINAHL, Embase, Medline, and PubMed, and search terms included genital sensation, sensory test, quantitative sensory test (QST), current perception threshold (CPT), pelvic sensation, pudendal nerve, perineal nerve, neuropathy, nerve injury, females, cis-female, woman/women, SUI, genuine stress incontinence, stress incontinence, urine leakage, urine loss, urine incontinence, levator ani muscles (LAMs), pelvic floor, force, strength, power, motor control, co-ordination, physiotherapy, pelvic floor muscle training (PFMT). The search was last updated in December 2022. Limits included female participants, English language articles, and SUI.

The narrative review includes an introduction to the anatomy and neural control of the female lower urinary tract and the pelvic floor muscles (PFMs), and what is known of the pathophysiology of SUI. It identifies a gap in knowledge regarding the role of sensory impairment and PFM proprioception in women with SUI. Specifically highlighted is the lack of data on the prevalence of nerve impairment among women with SUI and the potential impact of these nerve impairments on treatment outcomes associated with physiotherapist-supervised PFMT as an intervention for SUI.

2.1 Anatomy and neural control of the female-typical lower urinary tract

The female-typical lower urinary tract consists of the urinary bladder and the urethra. The urinary bladder collects, stores, and releases urine produced by the kidneys and is composed of an epithelium—known as the urothelium—surrounded by layers of smooth muscle referred to as the detrusor. The urothelium acts as the barrier between the body and urine and its associated

microorganisms, while also housing the nerve endings and blood vessels required for proper continence control[80–82]. The detrusor is smooth muscle which envelopes the urothelium in three layers: two longitudinal and one circular, to provide optimal compression of the bladder during micturition[83]. This muscle functions phasically, staying relaxed during bladder filling and actively contracting to squeeze the urine out when the individual deems it to be an appropriate time to urinate.

The female-typical urethra extends from the base of the bladder to the external meatus[84]; the lower two-thirds of the urethra adhere to the anterior vaginal wall[84]. The proximal portion of the urethra is supported by the endopelvic fascia surrounding the urethra and vagina[85,86] which is suspended from both the deep PFMs (LAMs) and the arcus tendinous fascia pelvis. In addition to fascia, the bladder neck—where the urethra joins the urinary bladder—is supported by smooth muscle; these muscle fibers are smaller than those of the detrusor, extending longitudinally and obliquely into the urethral wall[49,53]. The urethral sphincter is a complex muscular structure that surrounds an extensive vascular network within the subepithelial tissue. This vascular plexus contributes approximately one-third of the passive closure force of the urethra; it aids in the prevention of urine leakage by creating bulk pressure and hydrating the tissues to produce mucous to develop a hermetic seal[49,84,87]. Two different types of muscle create two sphincters in the urethra: the urethral rhabdosphincter (UR; striated sphincter) and the internal urethral sphincter (smooth muscle sphincter). The UR is comprised of a single layer of circular striated muscle beginning at the mid-point of the urethra and running to the level of the arch of the pubic bone where the fibers diverge and insert into the anterior vaginal wall and perineal membrane[84]. These striated muscle cells consist of slow twitch (type I) fibers with small diameters, allowing them to maintain a constant tone over prolonged periods of time[53,88]. Such continuous activity is

atypical for the striated skeletal muscle found throughout the rest of the human body, which normally operates in a phasic manner. The internal urethral sphincter is formed by a central layer of longitudinal and oblique smooth muscle fibers and extends from the bladder neck to the external urethral meatus, running deep to the circular, striated fibers[53]. The urethral musculature is under both voluntary (rhabdosphincter) and involuntary (rhabdosphincter and internal urethral sphincter) control.

Neural control of the female-typical lower urinary tract consists of a complex network controlled by both the central and peripheral nervous systems. Together, they coordinate muscle contraction and relaxation, integrating executive functions related to social micturition customs, learned behaviours, and the feelings of safety that are required for one to void their urinary bladder. The central nervous system, which consists of the brain and the spinal cord, is responsible for processing and integrating sensory information to respond to and interact with the environment. The peripheral nervous system includes the nerves that extend beyond the central nervous system and are responsible for relaying sensory information to the central nervous system and motor commands from the central nervous system to the appropriate muscles. The peripheral nervous system is further classified into sensory and motor components, the latter of which contains both voluntary (somatic nervous system) and involuntary (autonomic nervous system) pathways for control.

Central control of micturition primarily resides in the pons of the brainstem, specifically in an area referred to as the pontine micturition center (PMC)—also known as the M region or Barrington's area. In contrast to the PMC, the pons also houses the pontine storage center (PSC), also known as the L region, which plays a role in maintaining continence. As indicated by Blok and Holstege[89], micturition and continence are thought to be controlled separately, noting in

subsequent studies using positron emission tomography (PET) that the PMC was active during micturition, while the PSC was active when people were holding their urine[90,91]. Research in cats has also found unique connections between the UR and the PSC[92]. In cats, this area of the brain has a direct connection to Onuf's nucleus in the ventral horn of the S2 spinal segment, which innervates the urethral and anal sphincters and aids in the tonic activity required to prevent urine leakage[92]. Apart from the pons, other areas of the brain that are crucial to micturition and continence include the periaqueductal gray[93] and forebrain regions such as the anterior cingulate gyrus, prefrontal cortex, hypothalamus, amygdala, and the insula[89–91,93–98] (See Figure 2.1).

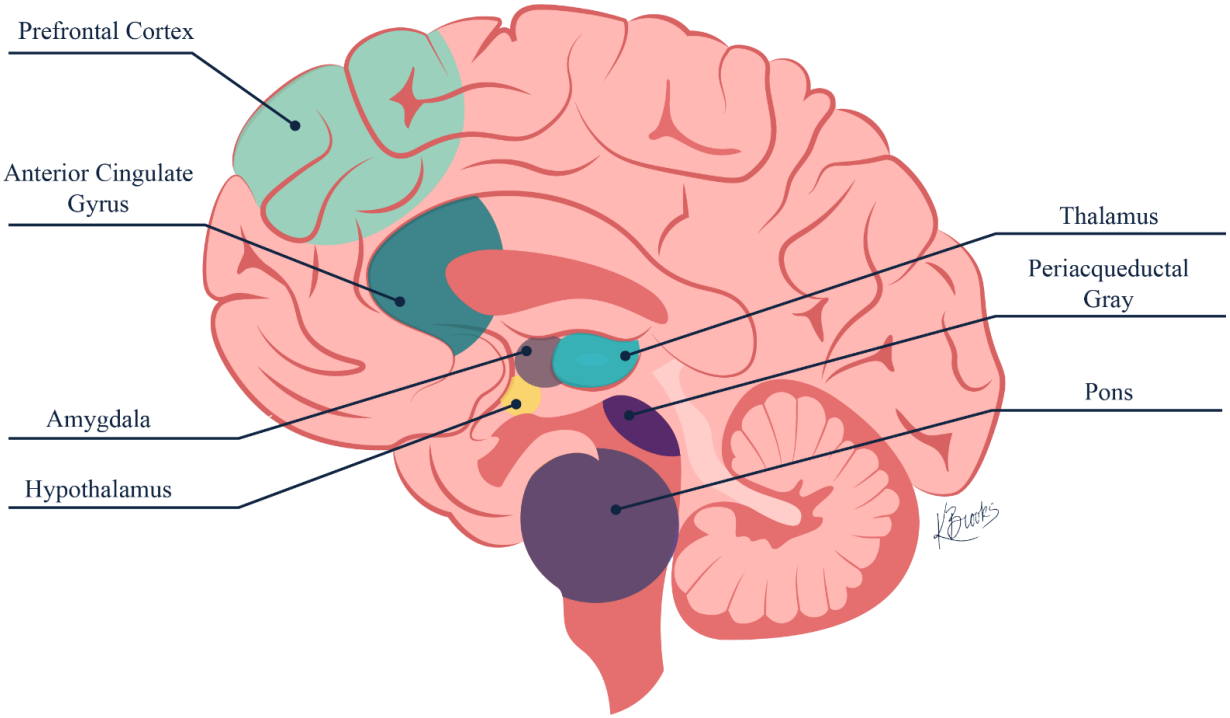

Figure 2.1 Areas of the brain involved in the central control of micturition.

These areas of the brain are used to coordinate the need, safety, and social customs required for one to urinate or store urine appropriately within the context of their environment. In particular, the periaqueductal gray is heavily involved in what Holstege[99] refers to as the emotional motor

system, in which the emotional state of the person strongly influences their motor responses[99,100]; for example, micturition can be effectively inhibited during sexual activity[100].

Peripheral control of the lower urinary tract involves an intricate balance of voluntary and involuntary control. The autonomic nervous system (involuntary) oversees the control of the smooth muscle (e.g. urinary bladder) through sympathetic and parasympathetic control, while the somatic nervous system (voluntary) controls the striated muscle. The involuntary aspect of lower urinary tract control is influenced by the hypogastric and pelvic nerves which are housed within the spinal column from the T11-T12 and S2-S4 segments[83,101]. These nerves convey information about bladder fullness and nociception to the central nervous system through myelinated Aδ-fibers and unmyelinated C-fibers. Aδ-fibers respond to passive bladder filling and contractions[101], while the C-fibers—often termed "silent C-fibers"—respond to noxious stimuli including chemical[102] or cooling irritants[103]. These messages travel up the spinal cord for further processing by the brain while triggering spinal reflexes, such as the guarding reflex, which keeps the urethral sphincters active during bladder filling[104]. The smooth muscles respond to the sympathetic and parasympathetic inputs from the central nervous system which control the phasic on-off behaviour of the urinary bladder through cholinergic, non-adrenergic, and non-cholinergic transmitters. These systems coordinate the neural control of the urethral sphincter, LAMs, and bladder.

The urethral sphincter receives dual innervation from the pelvic and pudendal nerves. The smooth muscle sphincter receives input from the autonomic system through the pelvic nerve and these muscle fibers contain a rich supply of cholinergic receptors identical to those embedded within the detrusor muscle of the bladder[53]. The UR receives somatic innervation via the pudendal nerve which originates from the S2-S4 spinal segments. The motor nerves of the

UR are densely packed in Onuf's nucleus, which is theorized to aid in the ability to simultaneously activate all sphincter motor units and may be related to the specialized function of a sphincter[104,105]. The striated muscle of the urethra does not contain muscle spindles or Golgi tendon organs (GTOs), as it lacks the small γ-motor neurons which typically innervate the muscle spindles or bony attachments for GTOs[104]. However, there have been Pacinian-like corpuscles found within the cat urethra, which may be used to sense urine flow for sphincter inhibition during urination[106] (See Figure 2.2).

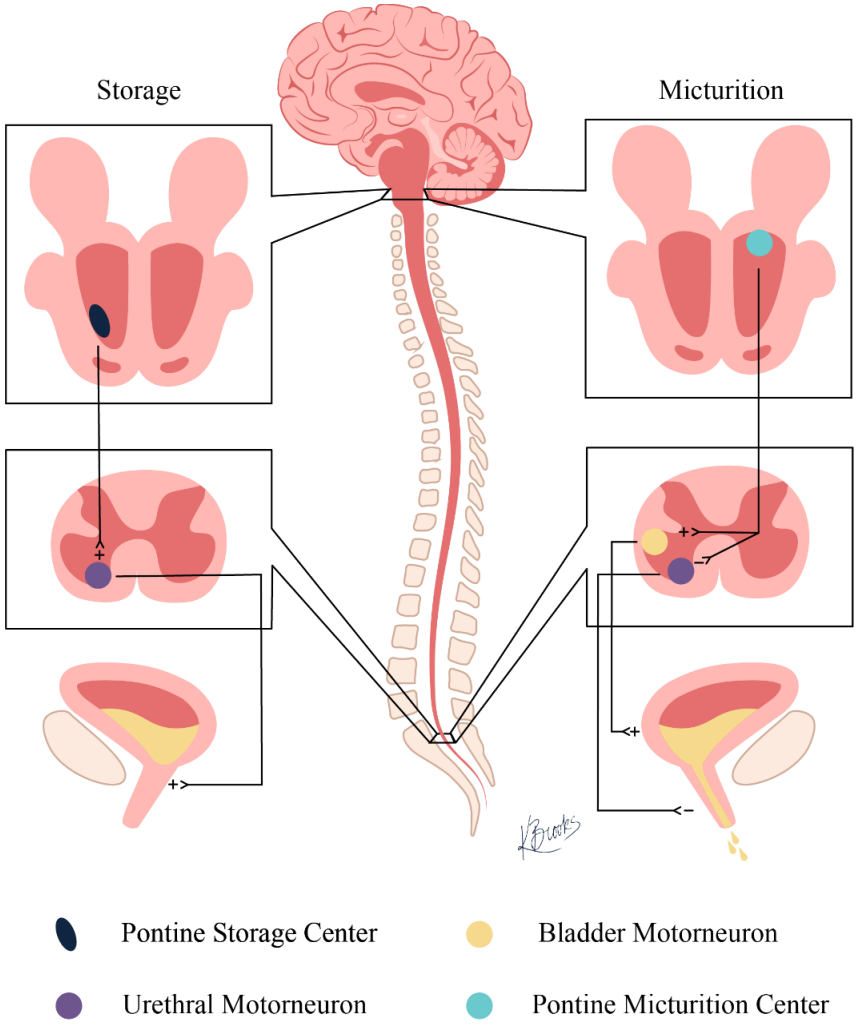

Figure 2.2 Neural control of the lower urinary tract in women. Highlighting the role of the Pontine Micturition Center in micturition and the Pontine Storage Center in urine holding.

2.2 The pelvic floor muscles and their role in continence control

The PFMs consist of superficial and deep layers that play a role in pelvic organ support[49], sexual functioning[107,108], micturition[84,104], and continence[49]. The deep layer—the striated LAMs and associated connective tissues—extend from the pubic symphysis to the coccyx and sacrum, with lateral attachments to the arcus tendinous levator ani and arcus tendinous fascia pelvis. The superficial layer is comprised of muscles located around the vulva and clitoris, including the superficial transverse perinei, the bulbospongiosus (BSM), and the ischiocavernosus[109]. Continence control is thought to mainly be enhanced by the deep layer of the PFMs, and as such this group will be one of the main foci in this thesis.

The deep PFMs include the LAMs, which, according to Ashton-Miller and Delancey, include three paired muscle groups. The iliococcygeal muscles span from each pelvic sidewall (arcus tendinous levator ani) and the arcus tendinous fascia pelvis to the coccyx, meeting in the midline, and are thought to augment the compression of the urethra and elevate the pelvic floor when they contract[49]. The pubovisceral muscles originate from the pubic symphysis and insert into the walls of the vagina (pubovaginalis), perineal body (puboperineus), and anus (puboanalis). This group of muscles compresses the urethra, vagina, and rectum against the anterior vaginal wall when they contract[49]. The puborectalis muscles originate from the pubic symphysis and inserts posterior to the rectum on either side, creating a sling around it such that contraction compresses the anorectum and provides an extrinsic closure force to the anorectum and the urethra[49] (See Figure 2.3). Like striated skeletal muscle throughout the rest of the body, the LAMs contain a mix of Type I and Type II muscle fibers[88] allowing them to produce sustained activity and quick contractions, respectively.

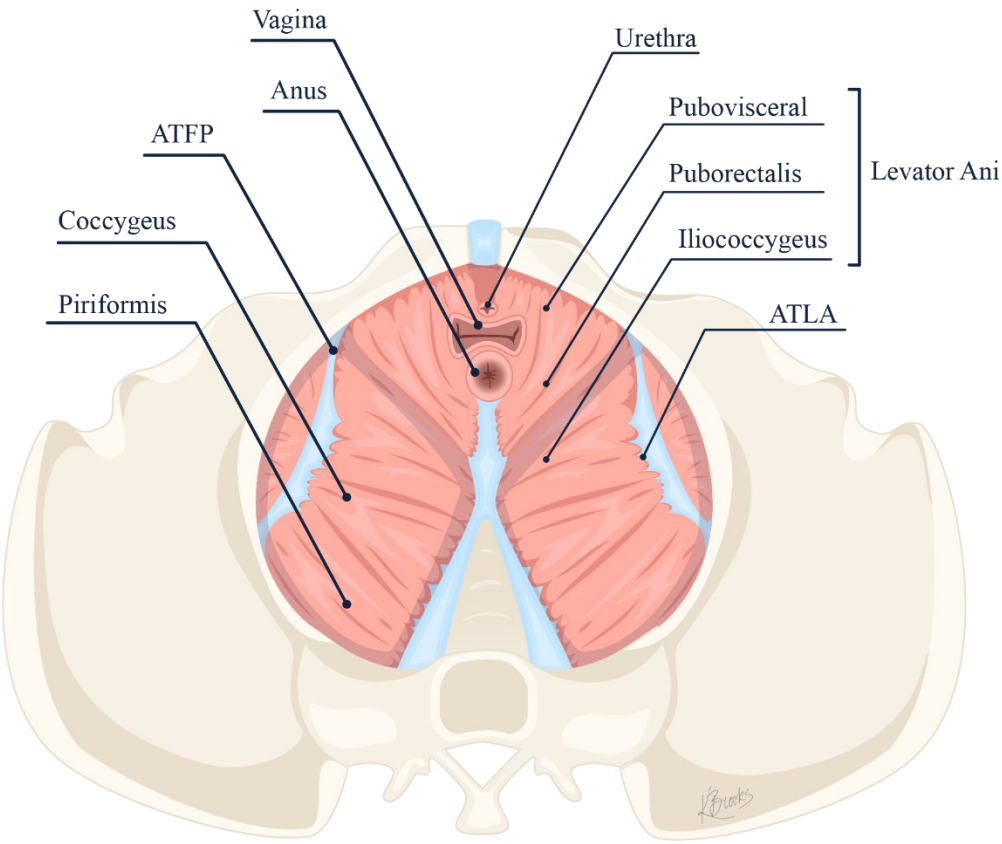

Figure 2.3 The levator ani muscles of the pelvic floor. Abbreviations: arcus tendinous fascia pelvis (ATFP), arcus tendinous levator ani (ATLA).

Central control of the PFMs resides mainly in the primary motor cortex, PMC, and PSC. Specifically, PET studies in humans show increased blood flow to the superomedial precentral gyrus—the most medial portion of the primary motor cortex—during voluntary LAM contraction[110]. This area of the brain has been implicated in the conscious holding of urine and the suppression of the micturition reflex[110]. Further work has noted that stimulation of the PSC in cats led to an increase in PFM EMG signals, while stimulation of the PMC led to a decrease in PFM activity on EMG[92], implicating a role for LAM inhibition in micturition[90]. Much like the UR, a unique connection exists between the LAMs and the pons, such that neurons in the pons project directly to Onuf's nucleus, where the motor neurons of the LAMs are housed with the

UR motor neurons[92,93]. This connection was first found in studies involving cats and eventually was noted in PET scans in humans[89,92,110]. Additional cortical regions that play a role in LAM control include the cerebellum, thalamus, supplementary motor cortex, and the anterior cingulate gyrus[110]. The cerebellum and the thalamus were active on PET scans in humans during PFM activation; the cerebellum is generally implicated in executing and coordinating learned motor patterns, while the thalamus usually plays a role in relaying sensory and motor information. The supplementary motor area is thought to play a role in the execution of simple motor tasks, such as a contraction or straining movement[110]. Lastly, the anterior cingulate gyrus was found to be very active during PFM activation and is implicated in goal-directed attention and alertness, especially during difficult or novel tasks[111].

Peripheral innervation of the PFMs is mixed and variable across women. Typically, the LAMs receive innervation from the somatic nervous system through the levator ani nerve (sacral roots S3-S5), while the superficial PFMs receive innervation from the pudendal nerve. However, there appears to be high variability in the innervation of the PFMs[104,112,113], where, at least in some individuals, the pudendal nerve appears to provide partial innervation to the LAMs. Like other skeletal muscles throughout the body, the PFMs (both deep and superficial) contain muscle spindles and GTOs, which provide sensory feedback regarding muscle length and tension, though there is an extremely low number of them in the superficial PFMs[88,104,114–116]. The levator ani nerve contains both large α-motor neurons and γ-motor neurons, which convey sensory information from muscle spindles, but evidence of these types of motor neurons has not been found in the pudendal nerve[104,117,118]. Further, sensory receptors reside within the layers of the genital epithelium, connective tissue, and muscle tissue, including Meissner's corpuscles, Pacinian corpuscles, free nerve endings, Merkel discs, and Ruffini corpuslces[114,119]. Meissner's

and Pacinian corpuscles both detect vibration, with Meissner's corpuscles working best at lower frequencies (2-60Hz) and Pacinian corpuscles favouring higher frequencies (60-400Hz)[120]. Free nerve endings detect nociceptive stimuli, while Merkel discs detect pressure (skin indentation) and Ruffini corpuscles favour low-frequency vibration or pressure. This information is relayed to the central nervous system for further processing and ultimately to coordinate muscle responses to the stimuli. Together they provide the important sensory feedback for the central nervous system to coordinate the appropriate LAM motor commands for continence, micturition, and sexual functioning.

2.3 Pathophysiology of stress urinary incontinence

2.3.1 Normal continence function in the female-typical continence system

The female-typical continence system is designed to prevent urine leakage during everyday activities. To do so, the continence system uses lower urinary tract structure and support, sphincteric function, and the PFMs[49,86]. When these components work in concert, urine leakage is prevented, even at times when high pressures are experienced in the bladder. For example, when the bladder is under stress (e.g. due to high forces caused by physical exertion, coughing, etc.) the urethral sphincters actively contract[53] to enhance the passive closure of the urethral hermetic seal[121]. The LAMs co-contract with the urethra[122] to further increase urethral closure force. Active extrinsic urethral compression is augmented by the optimal positioning of both the urethra and LAMs, which is maintained by the endopelvic fasciae and its attachment to the arcus tendinous fascia pelvis, pubic symphysis, and pelvic sidewalls[123]. This assembly of connective tissue, LAMs, and the anterior aspect of the vagina forms a hammock-like structural support to compress the urethra and prevent urine leakage[123]. Each component of the continence

mechanism appears to build redundancy into the system, such that if one aspect of the mechanism fails, it may be compensated for by the other components[77]. This suggests that multiple components of the continence mechanism may need to be compromised before SUI symptoms emerge. As such, it is thought that SUI pathophysiology is multifactorial[77,124] with precise deficits varying among affected individuals. Research suggests that defects in urethral and bladder neck structure and support, functional impairments of the UR and LAMs, and neuropathy contribute to the pathophysiology of SUI[77].

2.3.2 The bladder neck and urethra in stress urinary incontinence

Structure and support of the pelvic organs was the main focus of early research in SUI, often done through observations during surgical procedures, finding that SUI was associated with loose tissues at the bladder neck[46] and a loss of the urethrovesical angle[125]. With the emergence of ultrasound imaging in incontinence research, evidence of alterations in urethral and bladder neck morphology has been noted, which may be associated with the development of urine leakage. In women with SUI, it was found that the urethral sphincter complex is positioned more cranially and is shorter at rest[126] with a smaller area and circumference of the sphincter muscles[127] on ultrasound in comparison to continent controls. This is consistent with magnetic resonance imaging (MRI) findings that women with SUI display thinner URs than continent controls[128]. Further differences in the morphology of the bladder neck in women with SUI present as bladder neck funnelling—an opening of the proximal urethra[129]. A recent meta-analysis of 6 imaging studies found bladder neck funnelling to be 5-fold more prevalent among women with SUI (risk ratio = 5.23 at rest and 4.99 during straining tasks[77]) in comparison to controls. It is thought that bladder neck funnelling may develop from damage or denervation to the smooth muscle of the proximal (smooth) urethral sphincter[130]. However, bladder neck

funnelling currently has no standardized definition nor measure, and it is present in approximately 50% of continent women, which suggests that there are compensatory mechanisms such as UR function[130] or LAM contributions to maintain continence in these women[77].

Women with SUI also show changes in the connective tissues supporting the bladder neck and urethra. On ultrasound and MRI, evidence of damage to the periurethral, paraurethral, and pubo-urethral connective tissues has been noted[128,131] as well as lower bladder neck positioning[132–136] with more movement during mobile tasks[136]. This change in bladder neck and urethral position is thought to lead to poor urethral closure and result in urine leakage. One study did not show differences between women with SUI and controls in the resting position of the bladder neck in both the horizontal and vertical planes on ultrasound performed in supine[137], however, the SUI and control groups were significantly different in terms of age, parity, and menopausal status which may have impacted these findings. Moreover, research focused on urethral support[47] has found that women with SUI display urethral hypermobility[132,138–141]. As noted above, the optimal position of the urethra within the pelvis maximizes urethral closure pressure through external compression during dynamic tasks. It is thought that if the urethra moves out of its mid-sagittal position, it may receive ineffective pressure transmission from the abdomen and result in SUI symptoms[142]. Indeed, research has found that the urethrae of women with SUI tend to be more mobile on ultrasound than their continent counterparts[48,141] and that this is associated with a lower urethral closure pressure on urodynamic testing[141]. Urethral hypermobility is thought to be associated with damage incurred during vaginal childbirth[48,143,144], however, this trauma can also be a result of high-impact activities[23] or from strain induced by chronic coughing[12]. Vaginal delivery is also believed to be associated with paravaginal defects in

the arcus tendinous fascia pelvis (e.g. detachment from the ischial spine), which may alter urethral support and change the position of the PFMs in the pelvis and could lead to the development of SUI symptoms[138].

Research implicating impaired bladder neck and urethral support in SUI became the empirical basis for surgical interventions such as retropubic suspension (e.g. Marshall, Marchetti, and Krantz operation[145], the Burch colposuspension[146]) and bladder neck slings (e.g. pubovaginal slings using autologous tissues or synthetic materials[37]). The discovery of urethral hypermobility in women with SUI prompted the development of the mid-urethral sling surgical intervention, which was meant to stabilize the mid-urethra and, consequently, restore continence[38,147,148]. Interestingly, research has found no differences in urethral closure pressure on urodynamic testing after urethral support has been restored using a mid-urethral sling intervention, even if the patient reports some symptom alleviation[149]. Moreover, lower maximal urethral closure pressure has been associated with failure of mid-urethral slings, especially those inserted using a transobturator approach[150–152], though there have been some mixed opinions regarding this association[153,154]. Additionally, objective measures of SUI cure using mid-urethral slings suggest they have an 80% cure rate, but subjective measures reported by the patients show cure rates closer to 60% [155,156]. Thus, the loss of bladder neck and/or urethral support may be implicated in SUI pathophysiology, but they are unlikely to be the only factors at play.

2.3.3 Functional impairments of the urethra in stress urinary incontinence

Impaired urethral function in those with SUI is also thought to contribute to the development of urine leakage. Women with SUI show signs of poor urethral sphincter functioning, clinically known as intrinsic sphincter deficiency, the hallmarks of which include

reduced tonic activity and low maximum urethral closure pressure[157]. Intrinsic sphincter deficiency is typically assessed through urodynamic testing, with urethral pressure profiles and leak point pressures being considered key tests; a diagnosis of intrinsic sphincter deficiency is made when individuals display urethral pressure profiles of <60 cm H_2O and leak point pressures of <20 cm H_2O[158]. This loss of tone or inability to contract the urethral sphincters sufficiently can lead to urine leakage[159]. Intrinsic sphincter deficiency is thought to be the result of reduced hormone levels and/or damage to the pudendal nerve which innervates the UR[159]. The bladder and urethral tissues are rich in estrogen receptors[160], and as such, these tissues experience a reduction in vascularization and atrophy when levels of estrogen are low[161,162]. Estrogen therapies have been associated with increases in maximal urethral closure pressure[163,164] and urethral vascularization[161], however, they rarely provide a complete cure for SUI symptoms[165]. Apart from hormonal treatments, urethral bulking agents have also been used to combat poor urethral functioning. This procedure involves the injection of either synthetic material or autologous fat into the urethra at the bladder neck or the mid-urethra. The use of urethral bulking agents has resulted in reductions in urine leakage, but this effect is typically temporary, whereby treatment must be repeated every 12 months depending on the agent used[41,166]. Moreover, improvements in maximal urethral closure pressure after the use of urethral bulking agents have been minimal both at rest and during dynamic tasks (e.g. coughing or straining)[167] and there is currently not enough information available to make clinical recommendations for this approach[168].

Nerve damage may also affect the ability of the urethral sphincter to maintain tonic activity or to activate adequately to resist rises in intra-abdominal pressure (e.g. cough)[49]. This damage is often thought to be a result of stretch and compression trauma to the pudendal nerve

that occurs during vaginal childbirth[15]. Modelling work has estimated the strain that vaginal childbirth puts on the various pudendal nerve branches to be 13-33%, which is near or beyond the 15% strain threshold values known to cause permanent damage to appendicular nerves[54]. Indeed, among women with SUI, there has been some evidence of prolonged pudendal nerve terminal motor latencies (PNTMLs) to the urethra in comparison to continent controls[55,169]. Snooks et al.[55] found that women with SUI (n = 12) demonstrated longer PNTMLs to the urethra recorded from a custom surface electrode mounted on a Foley catheter compared to age and parity-matched controls (n = 31) using anal pudendal nerve stimulation, which had a large effect size (Cohen's d = 3.35). Additionally, Meyer et al.[169] found that among a group of women with SUI with urodynamically proven low-pressure urethras (n = 38), PNTMLs to the urethra were significantly longer compared to a continent group (n = 7) as measured by a custom surface electrode mounted on a Foley catheter in the urethra with anal pudendal nerve stimulation; this had a medium effect size (Cohen's d = 0.5). Moreover, individuals with SUI show lower responsiveness to urethral electrostimulation[170], prolonged urethroanal reflex latencies[170], and reduced electrosensitivity of the dorsal nerve and urethral mucosa[63] in comparison to continent controls. Using concentric needle EMG, through analysis of the EMG interference pattern, Kenton et al. [171] found medium to large effect sizes when they compared motor unit recruitment within the urethrae of continent women (n = 30) to those with SUI (n = 37), suggesting that neuropathic damage to the striated urethral sphincter is implicated in SUI. However, motor unit action potential duration was longer among controls than those with SUI[171], which may be attributed to pudendal nerve damage sustained during parturition and subsequent successful reinnervation of the urethra[171]. Neurophysiological investigations are few and heterogeneous,

and more research is needed to better understand the role of urethral neuropathy in SUI, as the currently available data have limited clinical applicability[156].

Apart from neuromuscular functioning, the function of the urethral hermetic seal is dependent on urethral vascularity, which is estimated to account for 8-33% of the maximal urethral closure pressure in animal models[87,172]. Amongst women with SUI, urethral vascularity was found to be reduced on 3D colour-Doppler ultrasound imaging, where they displayed fewer periurethral vessels and less periurethral blood flow than their continent counterparts[173]. Together, this indicates that urethral vascularity is another component of SUI pathophysiology but as research in this area is still in its early stages, further study is needed to better understand its role in women with SUI.

2.3.4 Levator ani muscles and stress urinary incontinence

The LAMs play an active role in continence by contracting synergistically with the urethral sphincter[122] in response to rises in intra-abdominal pressure to prevent urine leakage. While the evidence remains limited, LAM impairment is thought to contribute to urine leakage in SUI through changes in LAM morphology and positioning, LAM weakness, and/or poor coordination, as outlined below.

Biopsies of the LAMs of women with SUI show that they have less skeletal muscle content than their continent counterparts (continent n = 15; SUI n = 15, Cohen's d = 3.07) [174]. These changes in the LAMs can also be seen on MRI (continent n = 10, SUI n = 10[175]; continent n = 20, SUI n = 20, Cohen's d ranged from 0.3 – 2.0[176]) and ultrasound (continent n = 21, SUI n = 21, effect size could not be calculated[177]) such that women with SUI had a smaller LAM volume compared to controls; MRI specifically shows LAM degeneration in 45% of individuals

with SUI[178]. Moreover, LAM appearance in the transverse plane on MRI was found to be altered in those with SUI, such that in continent controls (n = 6), the LAMs typically show a sharp dorsally angulated or V-shaped levator sling, but this angulation is lost in 65% of individuals with SUI (n = 24)[178]. Further, puborectalis asymmetry and pubococcygeal muscle defects appear to be more common among those with SUI than continent controls[128]. However, other research has found no difference in overall levator defects (asymmetry, hypertrophy, or disruption) between continent and incontinent women (continent n = 50, SUI n = 33)[179]. Interestingly, direct muscle damage such as levator avulsion—a separation of the LAMs from the pubic symphysis—has no clear implications for urethral mobility or SUI [180–183]. Delancey et al.[184] found that levator avulsions were commonly found in primiparous women with SUI. However, when levator avulsions were separated into major and minor injuries, Morgan et al.[185] found that women with more severe avulsions had a lower risk of developing SUI, while women with more minor injuries had a higher risk of SUI. After a physiotherapy intervention, women with levator avulsion had a smaller area of their levator hiatus at rest and showed marked improvements in their ability to close the levator hiatus on PFM contraction when measured using 4-dimensional transperineal ultrasound[186–189], with values similar to those reported for women without avulsions[190,191]. Morphological changes to the LAMs may play a role in the development of SUI symptoms, but the heterogeneity of changes and the effects of these changes do not always appear to result in SUI, and as such, may not be the only factor involved.

Past research on the implications of LAM strength in SUI has had mixed results. Some study findings indicate that the LAMs of women with SUI are weaker than continent controls such that during voluntary LAM contractions they display lower strength ratings on manual palpation testing (Continent n = 60, Incontinent n = 60, Cohen's d = 0.42)[192], lower pressure

measurements using perineometry (continent n = 23, SUI n = 10, Cohen's d ranged from 0.60 – 4.0[193]; continent n = 31, SUI n = 23, Cohen's d ranged from 0.17 – 0.81[194]; continent n = 21, SUI n = 13, Cohen's d = 0.22[195]), and lower force values using intravaginal dynamometry in the anteroposterior direction (continent n = 16, SUI n = 16, Cohen's d = 1.26[196]; continent n = 24, SUI n = 21, Cohen's d = 0.41[197]). All studies using perinometry demonstrated small effect sizes, apart from one[193] that had a large effect size. However, some of these studies did not age- or parity-match between their control and SUI groups[192–194,196,198] which could influence the observed strength differences. Several other studies have noted no difference in LAM strength between women with and without SUI using palpation (continent n = 25, SUI n = 23, r = .18)[199], pressure measurements (continent n = 35, SUI n = 52, η^2 = n/a)[200] and dynamometry (continent n = 30, SUI n = 59, d = .10)[76]. When LAM strength is assessed in female athletes, those reporting SUI symptoms were found to have higher LAM strength than controls[201], yet among runners who regularly ran ≥20km a week there was no difference in LAM strength between those who were continent and those with SUI[202]. One study also noted no associations between the extent of improvements in LAM strength assessed using palpation before and after a 12-week pelvic floor muscle training (PFMT) intervention and the extent of improvements in SUI symptoms[203]. These conflicting results and a general lack of assessor blinding in studies comparing individuals with and without SUI indicate that there is limited evidence for impairments in LAM strength in women with SUI.

Motor control of the LAMs has also been investigated. Indeed, studies have noted slower rates of force development on voluntary force generation using dynamometry[76] and slower rates of muscular activation in response to a cough using surface EMG[204] among women with SUI compared to continent women. Moreover, motor coordination between the LAMs and abdominal

muscles, which typically co-contract during a cough or voluntary contraction in continent individuals, displays asynchronous activation among those with SUI (particularly those with moderate to severe symptoms) during a cough[204] and delays in abdominal muscle recruitment during voluntary maximum LAM contractions[200]. Conversely, Leitner et al.[79] noted no differences in the LAM rate of recruitment using EMG when comparing women with (n = 22) and without SUI (n = 28), but they did note that those with SUI took longer to return to their resting state after performing a fast maximum PFM contraction. Changes in coordination were also found during postural perturbations, such that women with SUI (n = 16) demonstrated increased LAM and abdominal muscle activity prior to and during a postural response to unexpected loading compared to continent women (n = 14) assessed through surface EMG[205]. Further, using fine-wire EMG to evaluate PFM responses to coughing and voluntary contractions, the right and left sides of the LAMs of women with SUI (n = 8) showed poor coordination and shorter periods of activation during active tasks both when the bladder was full and when it was empty compared to continent individuals (n = 10)[206]. More research is required to better understand the role of LAM coordination and recruitment in SUI and how the severity of symptoms may alter these motor patterns.

2.3.5 Role of nerve function in women with stress urinary incontinence

As discussed in Section 2.3.3, there is some evidence of motor nerve impairments in the URs of women with SUI, and these changes have been observed in the LAMs as well. Alterations in motor nerve conduction are thought to be a result of the traumatic damage that can occur during vaginal delivery[12,104,207] due to the positioning of the pudendal and levator ani nerves in relation to the birth canal. Indeed, women who are 6 weeks or less postpartum show prolonged PNTMLs[207–211], neurogenic patterns of injury on EMG interference pattern

analyses[51,144,212], and increased fibre densities innervated by a single motor axon in both the UR and LAMs[207,208]; all of which indicate motor neuropathy. Interestingly, for the majority of women, much of this damage appears to recover by approximately 6 months[51,144,212], apart from the UR EMG interference pattern, which in one study was found to demonstrate persistent abnormalities at 6 months postpartum[212]. However, longitudinal neurophysiological investigations of multiparous women at 5 and 15 years postpartum suggested that there might be a return of the prolonged PNTMLs even among individuals whose values were within typical ranges when they were assessed at 2 months postpartum. While these changes were not always associated with SUI symptoms, 3 to 36% of the women in these studies did develop SUI[208,211]. As such, it has been hypothesized that aging may intensify the effects of any existing nerve damage[213], which may account for the delayed onset of SUI symptoms[58,211]. Histological studies have also found some evidence for neurogenic[214] and myogenic[214,215] changes to the LAMs among parous women—none of whom had recently given birth—noting the presence of centrally located nuclei in muscle cells, fibrosis, and variation in fibre diameter and distribution of fibre type in the LAMs[214,215]. While age alone was associated with these changes, there was a distinct increase in the prevalence of the above alterations among parous women compared to their nulliparous counterparts[214,215].

Similarly, in comparison to continent women, women with SUI have demonstrated prolonged PNTMLs (Snooks et al.[55] control n = 31, SUI n = 12, d = 3.35; Smith et al.[57] control n = 42 SUI n = 34, d = 0.80; Meyer et al.[169] control n = 7, SUI n = 38, d = 0.68), increased fibre densities in the EAS (Snooks et al.[55] control n = 31, SUI n = 12, d = .45; Smith et al.[58] control n = 69, SUI n = 28, d = n/a), lower turns per amplitude and turns per second in the urethra (control n = 30, SUI n = 37, d = .77[171] the EAS (control n = 20, SUI n = 9, r = n/a[216]), and LAMs (control

n = 20, SUI n = 9, r = n/a[216]), and lower levels of motor unit recruitment on concentric needle EMG of the urethra (control n = 30, SUI n = 37, d = .82[171]). In contrast, two studies have noted no difference in PNTMLs between those with SUI and controls[55,170]. Specifically, using anal pudendal nerve stimulation techniques outlined by Kiff and Swash,[217] Snooks et al.[55] found prolonged onset latencies only in the perineal branch of the pudendal nerve (i.e., the branch which innervates the urethra; d = 2.94) but not in the branch that innervates the EAS (control n = 20, SUI n = 12, d = .00). Similarly, de Aguiar et al.[170] found no significant differences in PNTML using intravaginal stimulation and recording from circumvaginal musculature (control n = 19, SUI n = 33, effect size = n/a[78]), but they did find prolonged urethroanal reflex latencies (effect size = n/a) and reduced urethral electrosensitivity (urethral sensation; effect size = n/a).

Further evidence of the role of innervation changes can be seen in the histological abnormalities of the posterior portion of the LAMs in women with SUI (n = 16) which include more centrally located nuclei in the muscle fibers, and a greater proportion of Type I muscle fibers that have a larger diameter in comparison to controls (n = 11)[214]. In contrast, Jundt et al.[215] found that all histological changes (e.g. centrally located nuclei, fibrosis, and variation in fibre diameter) of the muscle fibers of the LAMs were associated with age and parity, but they did note evidence of neuropathic changes (i.e. decreased intramuscular nerve density) in the LAM biopsies as well (n = 94 female-typical cadavers, n = 24 women with prolapse and/or incontinence). The conflicting findings of pudendal nerve damage and reinnervation may reflect the wide variability in the type and severity of nerve damage that may occur, as well as the difficulty in assessing its impact reliably. As such, motor nerve alterations in the lower urinary tract and LAMs appear to play a role in SUI pathophysiology but require further research to understand.

In summary, the pathophysiology of SUI in women is a complicated mixture of alterations in urethral and bladder neck structure and support, functional impairments of the UR and LAMs, and nerve impairment[77]. The precise deficits likely vary among individuals, which makes it difficult to assess and study in its entirety.

2.4 The potential role of sensory neuropathy in stress urinary incontinence and implications for management through exercise interventions

The pudendal nerve contains both motor and sensory fibers which run in parallel[53], therefore, if the motor fibers display evidence of nerve damage, then the sensory fibers may also be affected[218,219]. Sensory nerve impairment may manifest in increased sensory thresholds of various modalities (e.g. vibration, temperature, light touch, etc.) and changes in proprioception, the perception of afferent (sensory) information of joint position, the force generated within a joint, and joint movement[220]. Moreover, reinnervation after an injury is not a specific process and in some instances cross innervation may occur, where mechanoreceptors and sensory afferent axons mismatch. For example, muscle spindle afferents may reinnervate cutaneous mechanoreceptors or vice versa, as found in a study of the transection and repair of a feline tibial nerve[221,222]. As such, it may be important to assess both cutaneous and proprioceptive mechanoreceptors when evaluating peripheral nerve impairments.

Research on injuries to other areas of the body, such as the ankle and knee, display concurrent impairment to the sensorimotor system, whereby peripheral nerve injuries are associated with changes in proprioception and muscle function[68–70]. When persistent, proprioceptive deficits can contribute to ongoing joint dysfunction[223–230]. Like injuries to the knee and ankle, sensory changes may be important to the outcome of PFMT interventions for women with SUI, as impaired sensation can lead to altered motor control, motor learning, and

motor programs for which the sensorimotor system is responsible[66,67]. Individuals with SUI may have altered motor control and motor learning of the LAMs and/or UR if the nerve fibers within the pudendal or levator ani nerves are damaged. Changes in motor nerve function and sensation with subsequent changes in motor control may also impact the effectiveness of PFMT interventions for those with SUI.

However, sensory nerve function is not routinely evaluated among women with SUI and a search of the literature revealed only four studies. The first study assessed women with self-reported sexual dysfunction who either did (n = 63) or did not (n = 114) present with concurrent SUI symptoms. Quantitative sensory testing (QST) techniques showed that women with SUI had higher sensation thresholds at the anterior and posterior vaginal wall and the clitoris for both thermal and vibratory stimuli when compared to those without SUI (d = .80)[60]. A second genital sensation study, also using QST, assessed the vibratory thresholds in women with SUI as compared to age-matched controls, finding no differences in vibratory thresholds between continent (n = 44) and incontinent (n = 66) individuals (effect size = n/a); however, only one genital site (at the clitoris) was used to assess genital sensation, which may not be representative of overall pudendal nerve sensory function[61]. A third study assessed the urethral sensation of women with SUI, urgency urinary incontinence, and mixed urinary incontinence using current perception threshold (CPT) testing. They found no differences in thresholds among the different subtypes of urinary incontinence but did note that thresholds were higher in older individuals (n = 61, effect size = n/a)[62]. However, the lack of a symptom-free control group limits the interpretability of these results. The fourth study assessed CPTs in the dorsal clitoral nerve and the urethral mucosa in women with SUI (n = 28) and continent controls (n = 28), finding that those with SUI displayed higher thresholds than the controls (effect size = n/a)[63]. However, CPT

testing may not be a reliable method of sensation testing in comparison to QST methods[65]. There remains a low number of studies and a lack of consensus in the literature regarding sensory impairment in women with SUI.

Pelvic floor proprioception is a new area of study and there were no protocols for assessing it reported in the literature at the time of initial protocol development for this dissertation. The role of pelvic floor proprioception in everyday function in women is currently unknown, so the potential implications of proprioception in the pathophysiology of pelvic floor disorders is theoretical. Currently, there is only one study that has reported on pelvic floor proprioception in women with SUI through the creation of a force-matching task [72]. The results suggested that women with SUI demonstrated more accurate target force reproduction measured using an intravaginal dynamometer (IVD) than continent controls[72]. However, the methods of this assessment were poorly described, limiting their repeatability, and no assessor blinding was reported. Further research is needed to understand pelvic floor proprioception.

PFMT for women with SUI is typically administered by trained pelvic health physiotherapists and targets improved strength, power, endurance, and/or motor control of the PFMs. PFMT programs often include aspects of strength, endurance, and behavioural training and vary based on the specific needs of the patient. PFMT is the recommended first-line treatment for women with SUI[42,43] even though only up to 56% of the women who complete the intervention are cured[39]. PFMT has been shown to reduce involuntary urine leakage, and improvements in symptoms are attributed to hypertrophy of the LAMs and concurrent improvements in PFM strength[231]; it has also been suggested to hypertrophy the UR[232] and possibly improve motor control through teaching “the knack” maneuver, which trains women to contract their LAMs before a rise in intra-abdominal pressure (e.g. a cough)[233]. Furthermore, the

long-term outlook for maintaining continence after PFMT is good, with a 66% chance that improvements will last at least 10 years if the initial training is successful[234]. However, as the cure rate is modest, there may be an aspect of training that is missing among certain individuals, which may affect the success rate of PFMT. It is hypothesized that PFMT may be less effective for the treatment of SUI if the individual has extensive tissue and nerve damage, as exercise therapy can only compensate to a certain extent[235]. As such, the motor and sensory nerve damage found in some women with SUI may impact the success of PFMT interventions. Only one study has assessed the role of pudendal nerve function and corticomotor control of the PFMs in physiotherapy treatment outcomes, finding that women with SUI who were (n = 9) and were not cured (n = 9) did not differ on pudendal nerve function[236]. Women who were cured with a physiotherapy intervention demonstrated higher corticomotor excitability at the EAS and circumvaginal musculature than women who were not cured (effect size = n/a)[236]; however, this study recruited women who had already completed a physiotherapy intervention. As such, no research has systematically and prospectively studied signs of motor and sensory neuropathy among women with SUI and whether such defects are associated with the success or failure of PFMT intervention.

2.5 Conclusion

The female-typical continence system is robustly designed, combining active and passive mechanisms intended to resist urine leakage at times of increased intra-abdominal pressure. Damage to this system does occur and is thought to typically happen during vaginal delivery, during which, damage to the muscle, connective tissue, and nerves can co-occur. Damage may also occur due to other acute or repetitive forces experienced at the female-typical pelvic floor. Both the motor and sensory components of the nerve, particularly of the pudendal and levator ani

nerves, may be damaged, which may alter proprioception and motor control within the LAMs and UR which may impact the effectiveness of PFMT interventions for women with SUI.

The aim of this dissertation was to explore sensorimotor function in women with SUI and investigate the effect sizes of any differences in motor and sensory nerve function, pelvic floor proprioception and muscle function between those with and without SUI. The data in this dissertation could be used to power future research on areas of sensorimotor function that demonstrate the most potential for improving our knowledge of SUI pathophysiology. The findings of this dissertation may also be used to direct future studies on the potential relevance of sensorimotor impairments on physiotherapy intervention outcomes among women with SUI.

Chapter 3: Overview of data collection and study sample

3.1 Data collection protocol

A single data collection protocol was used to record the pelvic floor sensorimotor function using an observational, cross-sectional study design in a sample of 30 participants for all studies included in this dissertation. The sensorimotor assessment consisted of an evaluation of pelvic floor muscle (PFM) proprioception using novel tasks developed in Chapter 4, an assessment of proprioception and PFM passive and active function in Chapter 5, an investigation of perineal tactile sensation (Chapter 6), and an assessment of pudendal motor nerve function (Chapter 7). The study received ethics approval from the University of Ottawa Health Sciences and Sciences Research Ethics Board, indicating compliance with national ethical standards for the conduct of human research (H-07-20-5945) and with COVID-19 safety precautions (Appendix A).

The sensorimotor assessment occurred over the course of two separate data collection sessions: session one consisted of the PFM proprioception and muscle function testing using an intravaginal dynamometer (IVD), followed by the motor nerve function evaluation using pudendal nerve stimulation and surface electromyography; session two consisted of a sensory threshold assessment using custom-made monofilaments to assess genital light touch sensation. Each data collection session was 2-hours in length. An initial telephone screening was performed to determine eligibility (Appendix B). Eligible women were sent, via e-mail, a web link to a series of questionnaires used for descriptive purposes: the International Consultation on Incontinence Questionnaire (ICIQ)-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS; Appendix C), the ICIQ-Vaginal Symptoms (ICIQ-VS; Appendix D), the ICIQ-Bowel (ICIQ-B; Appendix E), and the Female Sexual Function Index (FSFI; Appendix F) which they were asked to complete before attending the laboratory assessment.

At the first data collection session, the researcher acquired informed consent (Appendix G) before recording demographic information (e.g. height, weight, parity, etc.) using standardized methods (Appendix H). A visual genital inspection was then performed to ensure that there were no obvious signs of infection, pelvic organ prolapse beyond the hymen, or pelvic masses that would make the assessment uncomfortable. No participants were excluded for these reasons.

3.2 Participant recruitment

Women with stress urinary incontinence (SUI) were recruited from local physiotherapy clinic waitlists and continent women were recruited from the community through posters and word of mouth; all participants were over the age of 18 years. Participants were excluded if they did not have female-typical pelvic anatomy, were pregnant or had given birth within the past 6-months, reported fecal incontinence, had known neurological disorders or impairments, had known connective tissue disorders, were on medications that affect continence, had a previous pelvic surgery to treat SUI or pelvic organ prolapse, had known pelvic organ prolapse or reported pain on the insertion of tampons or during sexual activities. Participants were not compensated for their time but did benefit from the education on the PFMs they received over the course of the data collection period.

3.3 Sample

In total, 30 women completed both data collection sessions. Fourteen participants were continent, and 16 participants had SUI. Twelve of the 16 participants with SUI then attended a local pelvic floor physiotherapy clinic of their choice. Four participants were excluded from the analyses of women who were cured and those who were not because one participant decided not to attend physiotherapy due to a lack of financial support, two participants reported a lack of

time/desire to undergo physiotherapy treatment after the laboratory-based assessment, and one participant was lost to follow-up (25% attrition rate).

3.4 Physiotherapy intervention

The physiotherapy intervention was not standardized, allowing the treatment plan to be customized to the participant, however, all physiotherapists used supervised PFM training (PFMT) and a home exercise prescription. Twelve weeks after their first physiotherapy appointment, participants were asked to complete the ICIQ-FLUTS and the Global Rating of Patient Satisfaction and Perception of Improvement Questionnaire (Appendix N) to determine if they were cured. A cure with the physiotherapy intervention was defined as a score of ≤4 on the urinary incontinence subscale of the ICIQ-FLUTS. This questionnaire was selected based on its strong measurement properties[237] and recommendation by the International Continence Society[238]. The criterion for cure was based on previous research[239,240] and allows for comparison across studies. Based on this definition, five were considered cured and seven were not cured indicating a 42% cure rate. Only nine women provided further details on the types of exercises performed in treatment: one participant stated that she was taught “The Knack”, two participants reported performing PFM contractions in different positions and exercises, and five participants reported instruction on breathing and the pelvic floor. Participants were instructed to try to complete at least four sessions with their physiotherapist in the 12 week period, however the number of visits ranged from 1—5 with an average of 3.22 sessions within the designated time period.

Chapter 4: A novel dynamometry-based method to assess female-typical levator ani muscle proprioception.

Authors: Kaylee C. L. Brooks, Linda McLean

4.1 Abstract

Aims: The goal of this study was to develop standardized methods for assessing levator ani muscle (LAM) proprioception. Two tests were developed using an automated intravaginal dynamometer (IVD), an active force matching task and a passive elongation awareness task. For the active force-matching task, we aimed to determine the optimal window length and location for the extraction of root mean square error (RMSE) to assess accuracy, and to examine the effects of feedback (visual feedback or no visual feedback) and target force level (25, 50 and 75% maximal voluntary contraction [MVC]) on participant accuracy. For the passive LAM elongation task, we aimed to determine whether the test provided an adequate distribution of data for group-level comparisons. A third aim was to determine the association between performance on the active force-matching task and the passive elongation task. **Methods:** Adult women naïve to LAM contractions were recruited from the local community. In a supine position, the passive elongation awareness test was performed first. A reference IVD diameter was determined for each participant as the extent of arm-opening that elicited a passive force between 1.4 and 1.5 N. To conduct the test, the IVD arms were first opened to the reference diameter, then closed, and reopened to a test diameter that was either the same, 5mm smaller or 5mm larger than the reference diameter. Participants were asked to identify the size of the test diameter relative to the reference diameter. The percentage of correct responses was retained as the primary outcome, and descriptive statistics were used to report on participant performance. To conduct the force-matching task, the participant's MVC force was determined first. Participants were then asked to

contract their LAMs to match target forces of 25%, 50%, and 75% of their MVC, presented in a random order, first with visual feedback and then without visual feedback. The RMSE was calculated for each target force from the first force peak to 2.5s after the first force peak of the contraction using 3 different window lengths (0.25s, 0.50s, and 1.00s). The optimal window length to use in signal processing was assessed with a linear mixed model analysis of variance (ANOVA) and the optimal location along each window length was assessed with repeated measures ANOVAs. A 2-way repeated-measures ANOVA was used to examine the impact of feedback and target force on participant accuracy. A difference measure was calculated for each participant to represent the difference in accuracy between the visual and no visual feedback conditions, and a one-way repeated-measures ANOVA was used to evaluate the impact of target force on this outcome. **Results:** Thirty women (44±13 years) completed the assessment. Participants correctly identified the IVD diameter relative to the reference diameter 77.8% ± 25% of the time, and there was a large range in accuracy (22% – 100%). For the force-matching task, RMSE did not differ across the three window lengths, but the smaller window lengths (0.25s and 0.50s) demonstrated a plateau in RMSE between 1.0 and 1.5s after the initial force peak. Using a window between 1.0 and 1.5s after the initial force peak, both feedback and target force were found to independently influence accuracy in reaching the desired target. Women were most accurate at reaching and holding the target force at 25% MVC and with visual feedback. There were no observed differences across the target forces ($p = .62$) when the difference between visual feedback and no visual feedback was computed for each individual. The passive and active measures of proprioception as described were not correlated ($p > .05$). **Conclusion:** This study presents a systematic and objective approach to assessing LAM proprioception in women. Performing both passive elongation and force-matching tasks is

recommended when assessing proprioception, as they provide different information. Active force protocols should include different target forces and feedback conditions, and signal processing parameters should be standardized as they can influence outcomes. The information gained from LAM proprioceptive assessments may improve our understanding of the role of LAM proprioception in pelvic floor disorders and may help to refine targeted treatment strategies.

4.2 Introduction

The levator ani muscles (LAMs) are thought to contribute to continence control by supporting the bladder neck and urethra, and externally compressing the urethra between the pubic symphysis and the anterior vaginal wall during tasks that challenge continence[1–4]. Indeed, training the LAMs cures or improves continence function and reduces symptoms in close to 70% of women with mild to moderate stress urinary incontinence (SUI) [5], which has led to a longstanding assumption that LAM strength and/or power is important to continence control. However, studies have failed to support this assumption empirically[6–8]. Indeed, research suggests that there may be no difference in LAM strength between women with and without SUI[6–8], but rather that there are differences in women's capacity to generate force rapidly during voluntary contractions[7,9] and to perform repeated quick contractions of the LAMs[7]. These latter findings suggest that testing beyond muscle strength should be considered when assessing LAM function in women with SUI, as there may be aspects of proprioceptive function or motor control that play a role in continence.

Motor control is a complex process that relies on sensory information to provide ongoing feedback on muscle length and tension for the optimization of movement[10]. The process of interpreting and utilizing this information is often referred to as proprioception[11] which is defined as the perception of joint/limb position, force generation, and joint/limb movement[12,13].

Injured individuals often exhibit changes in the proprioception of the injured joint/limb[14], and impaired proprioception has a demonstrated impact on motor function[13,15] and rehabilitation outcomes[14,15]. In fact, in joints such as the ankle[16] or knee[17], injured individuals demonstrate a reduced capacity to control force output[16] and a decreased ability to recognize and reproduce specified joint angles[17] compared to uninjured individuals. Changes in proprioceptive feedback may lead to some immediate alterations in motor control and dysregulation of muscle stiffness[14]; long-term effects may result in changes to previously established motor programs, leading to a reduction in muscle performance and an increase in the risk or recurrence of injury[14].

In the case of SUI, LAM proprioception may be of importance[18]. Changes in LAM control have been identified as a potential factor in cases of SUI[3,19], including altered muscular activation patterns compared to continent women during voluntary contractions[6], coughing[9], and postural perturbations[20], asymmetry during LAM contractions[21], and a slower relaxation of the LAMs after a quick contraction[22]. Moreover, women's "awareness" of the force generated during a LAM contraction and the ability to perform a correct contraction is low and they often require external feedback to improve their performance[23–28]. Yet there has been only one objective assessment of proprioception in the LAMs and one assessment of intravaginal stretch sensation[29,30] reported in the literature. In a recent study, women with SUI demonstrated more accurate target force reproduction measured using an intravaginal dynamometer (IVD) than continent controls[31]. However, the methods of this assessment were poorly described, limiting their repeatability. Another study used the inflation of an intravaginal balloon to create a stretch sensation, reporting that sensory threshold was reliable[30] and that pregnancy and delivery method induced changes in intravaginal stretch sensation thresholds[29]. However, this study used a

method of limits approach, which, while faster for data collection, can be less accurate in determining thresholds[32].

While there is research interest in LAM proprioception, currently this area is in an early stage of development. To facilitate comparisons among studies, it is important to develop valid and standardized approaches for the evaluation of LAM proprioception. Given that IVDs have emerged as the criterion standard for the objective examination of passive (stiffness) and active (strength/power/endurance) LAM characteristics[3,33,34], they may also be useful for the objective assessment of LAM proprioception[18]. However, there has been no systematic examination of methods to test LAM proprioception described in the literature. The goal of this study was to develop a systematic method for assessing LAM proprioception and sensory acuity during active LAM contractions and passive LAM elongation based on methods previously used to evaluate proprioception in peripheral joints. The objectives were to:

1) Develop a passive LAM elongation task to assess the proprioception and sensory acuity of the LAMs.
    a. Describe the distribution of performance on the passive elongation task and evaluate potential ceiling and floor effects.
    b. Determine if the reference LAM elongation value, age, and/or parity influence accuracy during a passive LAM elongation task.
2) Develop a standardized approach for a force-matching task to be used to assess LAM proprioception during active contraction.
    a. Determine the optimal time window length and location for the extraction of root mean square error (RMSE) from the target force to assess accuracy at a fixed IVD aperture of 35mm.

b. Use the time window found in objective 2a to assess the effect of visual feedback and target force level (25%, 50%, 75% of MVC) on RMSE when individuals perform the LAM force-matching task, and to investigate proprioception using the difference in force matching accuracy between the visual feedback and no visual feedback conditions.
c. Determine if peak and relative peak force values reached during a maximum voluntary contraction (MVC), age, and/or parity influence RMSE measured during the force-matching task.

3) Investigate whether performance on the passive elongation task is associated with performance on the active force-matching tasks to determine if these tests are measuring different constructs of LAM proprioception.

4.3 Methods

4.3.1. Protocol development

While different definitions are presented in the literature[10,35], for this study, proprioception is defined as the perception of sensory information of joint/limb position, force generation, and joint/limb movement[12,13]. A general literature search of CINAHL, Medline (Ovid), and Google Scholar between the years 1980 and 2022 retrieved a variety of methods for evaluating proprioception in peripheral joints. Due to the complexity of the sensorimotor system, there is no single measure to quantify proprioception. As such, we narrowed our focus to methods for evaluating joint position sense and sense of force[13], as these approaches best translate to methods that could be implemented for the female-typical pelvic floor using an automated IVD.

No test for assessing the ability to detect passive changes in LAM length has been previously reported in the literature, however, one study reported on intravaginal stretch sensation[29,30]. This study used an intravaginal balloon that was slowly inflated until the participant stated that they felt the first sensations of stretch. The method was found to produce a reliable assessment[30] and the outcome was affected by pregnancy and delivery method[29]. However, this test used the method of limits which is known to be affected by participant reaction time and thus may overestimate sensation thresholds[32]. The protocol in this study was based on methods used to evaluate knee joint position sense[36,37]. At the knee, position sense is typically evaluated through a participant's ability to detect movement of the joint, including the direction and/or the range of motion threshold or the accuracy in recognizing a reference position when the limb is passively moved[10]. However, there are no joints in the LAMs that could be repositioned and due to the nature of the IVD, only one plane of movement (sagittal plane) is available in which to assess LAM length/position. As such, we developed a passive elongation task for the LAMs in which participants were asked to identify whether the extent of IVD arm opening was the same, more, or less than a reference diameter that was based on the resistance to passive elongation determined *apriori*.

Sense of force reflects an individual's ability to sense and interpret the force being applied around a joint[13] and often includes assessments of the impact of different feedback techniques (e.g. visual feedback, kinesthetic feedback, etc.)[38,39]. Only one study was found that evaluated LAM sense of force output; it only included kinesthetic feedback. This study used a force-matching task to compare performance between women with SUI and those who were continent[31]. Yet the methods used to determine accuracy in the force-matching task were not clearly described—in particular, the signal processing methods were not described with adequate

detail to replicate the approach. It has been recommended in the literature to discard the first second of data during which participants attempt to match a target force due to high variance[40], yet it is not clear whether this was performed, nor whether assessor blinding or target force randomization was included. The force-matching task developed for this study was based on methods reported for the shoulder and ankle[16,41]. Participants were first asked *apriori* to generate a maximal voluntary contraction (MVC), and then customized target forces of 25%, 50%, and 75% of the participant's maximal contractile force were created. Participants were asked to contract their LAMs to match these target forces, which were presented in a random order. The impact of visual feedback on target-matching performance was also assessed by having participants perform the tasks with and without visual feedback provided through a computer display.

The custom mechatronic IVD used in this study has been previously described; it demonstrates valid load measurement and speed control in bench testing[42] and is reliable[43] when used to test active and passive tissue properties in vivo. Following the development of the methods, the test protocol was implemented into the IVD driver software (MatlabTM R2022a, Mathworks, Natick, MA) and data acquisition software (LabChart 8, ADInstruments, Colorado Springs, CO).

4.3.2 Protocol evaluation

An observational, cross-sectional study design was implemented after receiving approval from the University of Ottawa Health Sciences and Sciences Research Ethics Board, indicating compliance with national ethical standards for the conduct of human research (H-07-20-5945) and with COVID-19 safety precautions (Appendix A).

All laboratory assessments were carried out by a researcher who had received >20 hours of one-on-one training from an experienced pelvic health physiotherapist (>10 years of clinical experience and > 3 years of research experience using the IVD) on the assessment of LAM contraction and the use of the IVD. This researcher remained blinded as to whether or not participants reported any lower urinary tract symptoms.

4.3.3 Participants

See Chapter 3 for a description of the sample and recruitment. As there were no previous studies available in the literature on which to estimate sample size at the time of the protocol development, a sample size of n = 30 was deemed adequate to inform on the feasibility of the methods because it would likely generate data with normal distributions for parametric analyses[44].

4.3.4 Intravaginal dynamometer preparation

Prior to each participant's visit, a new set of IVD arms was 3D printed (Ultimaker 2+/Ultimaker S5, Ultimaker B.V., Geldermalsen, Netherlands) in biocompatible plastic (PLA). After printing, they were washed in soap and water, air dried, mounted on the stainless-steel bar mounts of the IVD, and covered with a separate condom on each arm. See Figure 4.1.

4.3.5 Procedure

See Chapter 3 for a description of the initial assessment and recording of demographic information. The proprioception assessment then proceeded with participants in supine.

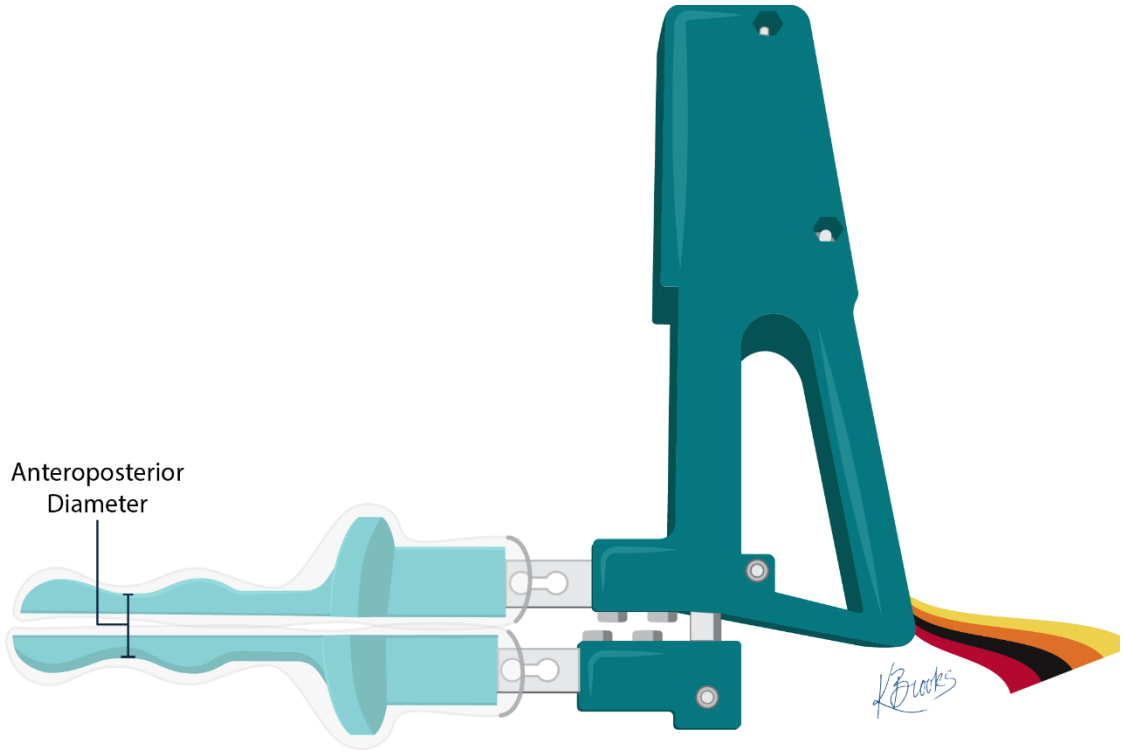

Figure 4.1 Intravaginal dynamometer with condom-covered arms attached displaying the anteroposterior diameter measurement points.

4.3.5.1 Dynamometry protocol

The researcher first provided instruction on how to perform a proper LAM contraction, using visual inspection and digital palpation to ensure that participants could demonstrate visible and palpable closure of the levator hiatus and lifting of the perineum with minimal use of hip/gluteal muscles without bearing down or breath-holding. If a participant was unable to contract their LAMs after coaching, they were to be withdrawn from the study, however, no participant was withdrawn based on this criterion.

4.3.5.2 Passive elongation task assessing position sense

The dynamometer was first calibrated outside of the body. Then lubricant was then applied to the condom-covered arms of the IVD and either the participant or the researcher (at the participant's

request) guided the IVD arms into the participant's vagina. Device positioning and participant comfort were confirmed visually by the researcher and verbally by communicating with the participant.

The researcher held the IVD in place and provided instruction to the participant while a research assistant operated the device using a custom computer program (Matlab^{TM} R2022a, Mathworks, Natick, MA). The protocol is illustrated in Figure 4.2. First, a reference diameter was determined by incrementing the opening diameter of the IVD arms until a passive force between 1.4-1.5N was recorded while the participant kept their LAMs relaxed; the diameter that produced this passive force was deemed the reference diameter for the assessment. During testing, the IVD arms began from a closed position. They were first opened to the reference diameter, held for 7s, and then closed. Approximately 30 seconds later, the IVD arms were opened to the test diameter, which was either 5mm larger, 5mm smaller or the same as the reference diameter, held for 7s, then closed. After the arms closed, the participant was asked to identify the extent of the change in LAM length relative to the LAM length perceived at the reference diameter (e.g. same, smaller, or larger). Each test diameter was presented three times in a random order, for a total of nine trials.

4.3.5.3 Force-Matching Task

The IVD arms remained inserted in the vagina and were opened to a diameter of 35mm at a speed of 20mm/s. Once the force was stable based on inspection of the real-time data presented on the computer display (e.g. the stress relaxation response had stabilized), the participant was instructed to contract their LAMs as strongly and as quickly as possible and to hold the force for at least 3 seconds. The specific instructions to the participant were: "Breathe in….breathe

out….and Squeeze, Squeeze, SQUEEZE, HARD, HARD, HARD!", and then "Relax, let the contraction go." This was repeated 3 times. The maximum relative peak force (i.e. peak minus

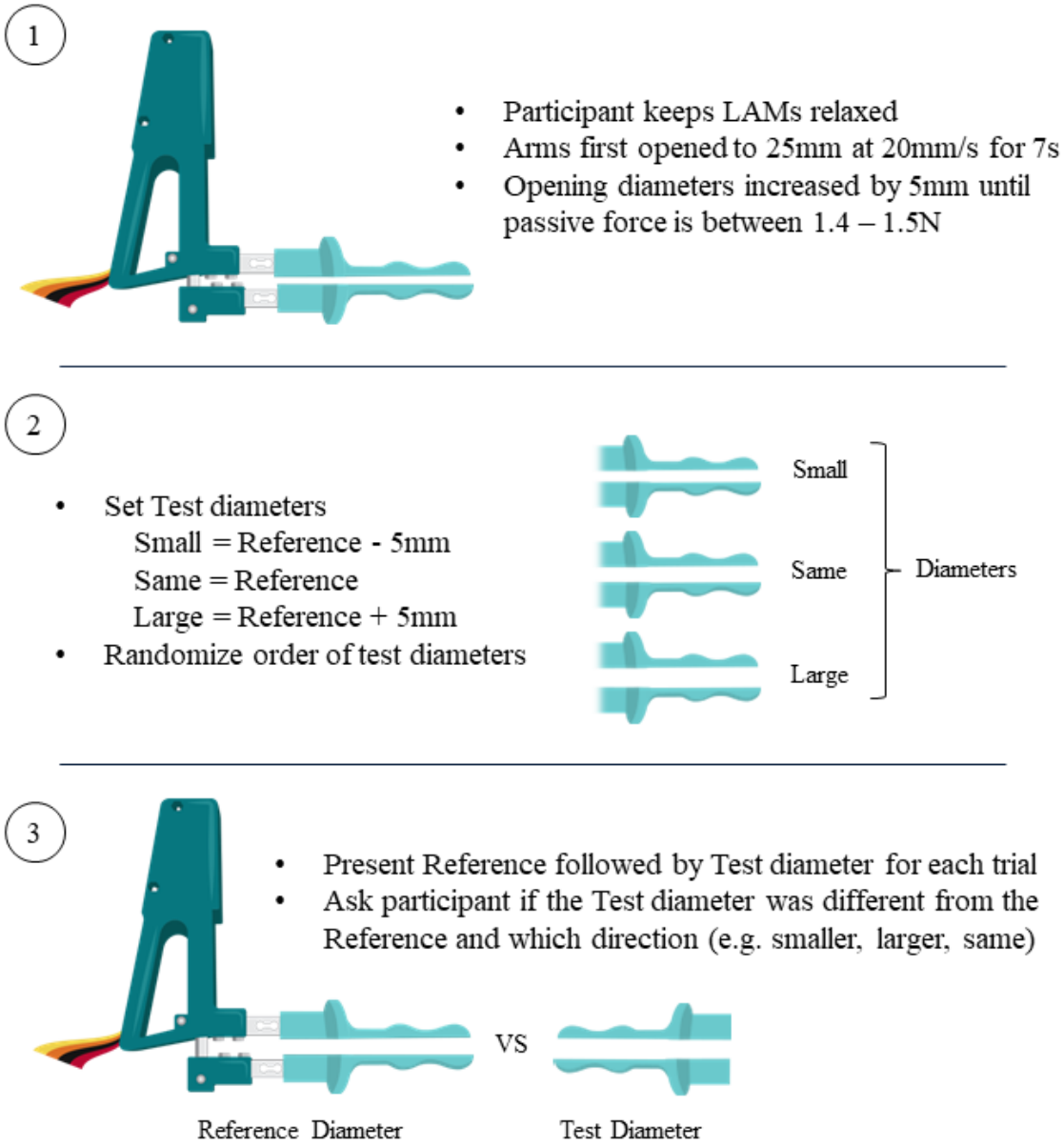

Figure 4.2 Illustrated protocol for the novel levator ani muscle elongation comparison task using an intravaginal dynamometer. Abbreviations: levator ani muscles (LAMs).

baseline) achieved across the three trials was retained as the MVC and using visual inspection, the lowest baseline value while the participant was at rest prior to their contraction was used as the lowest baseline force in Equation 3.1.

Personalized targets for the force-matching task were created based on each participant's MVC. Equation 3.1 was used during the force-matching task to present force output as a percentage of MVC in real time on the computer display. Force targets of 25%, 50%, and 75% of the MVC force were displayed with boundaries of ±5% MVC indicated by a coloured band along with the real-time force output.

Equation 4.1

$$Force\ (t)(\%) = \left(\frac{(Force(t) - Lowest\ Baseline\ Force)}{MVC}\right) \times 100$$

During each force-matching trial, the IVD arms opened to a standardized diameter of 35mm at a speed of 20mm/s. The researcher and research assistant watched the baseline force closely on the screen to ensure that the baseline force remained within ±10% of zero to ensure that participants always started their contraction from 0% of their MVC. If the baseline force exceeded this range, the trial was stopped and repeated, after advising the participant to completely relax their LAMs. Adjustments to the equation depending on changes in passive forces of the LAMs were made as needed during data collection to ensure that participants' baseline force was always nominally the same before they started their contraction.

During each task, participants were instructed to contract their LAMs enough to reach but not to exceed the target displayed on the computer screen and then to hold the force level as steady as possible for approximately 5s, at which point they were prompted to "Relax, let the contraction

go" (See Figure 4.3). Participants were provided with up to 3 practice trials at each target force. During the practice trials, the participant attempted to contract their LAMs to match the force target, first with visual feedback provided on the computer screen and then with their eyes closed and/or the computer screen moved outside of their line of sight (no visual feedback). The participant was allowed to select the order of the target forces and choose when to end the practice session when they felt confident in their ability to perform the task, or the researcher ended the practice session at a maximum of 3 trials per target force.

During the force-matching assessment, the target forces were presented in a randomized order. At each force level, the participant performed the trials with visual feedback first and then without visual feedback, with approximately 1-minute of rest provided between trials. Each target was presented three times under each condition (visual feedback/no visual feedback). Completion of these tasks marked the end of the assessment.

4.3.6 Data processing and outcome measures

The outcome measure of interest from the passive elongation task was the percentage of correctly identified IVD opening diameters, and thus no data processing was required. For the force-matching task, data processing was conducted using custom MATLAB (R2022a, Mathworks, Natick, MA) programs. Each raw force-time curve was smoothed using a 2nd order, dual pass, low pass (5 Hz 3dB cut-off) Butterworth filter. Participant accuracy was measured using the RMSE of each force curve relative to the target force. This was done using three different time window lengths (0.25s, 0.5s, and 1.0s) starting from the first force peak of the contraction (determined through visual inspection) to 2.5s after the first force peak, with this

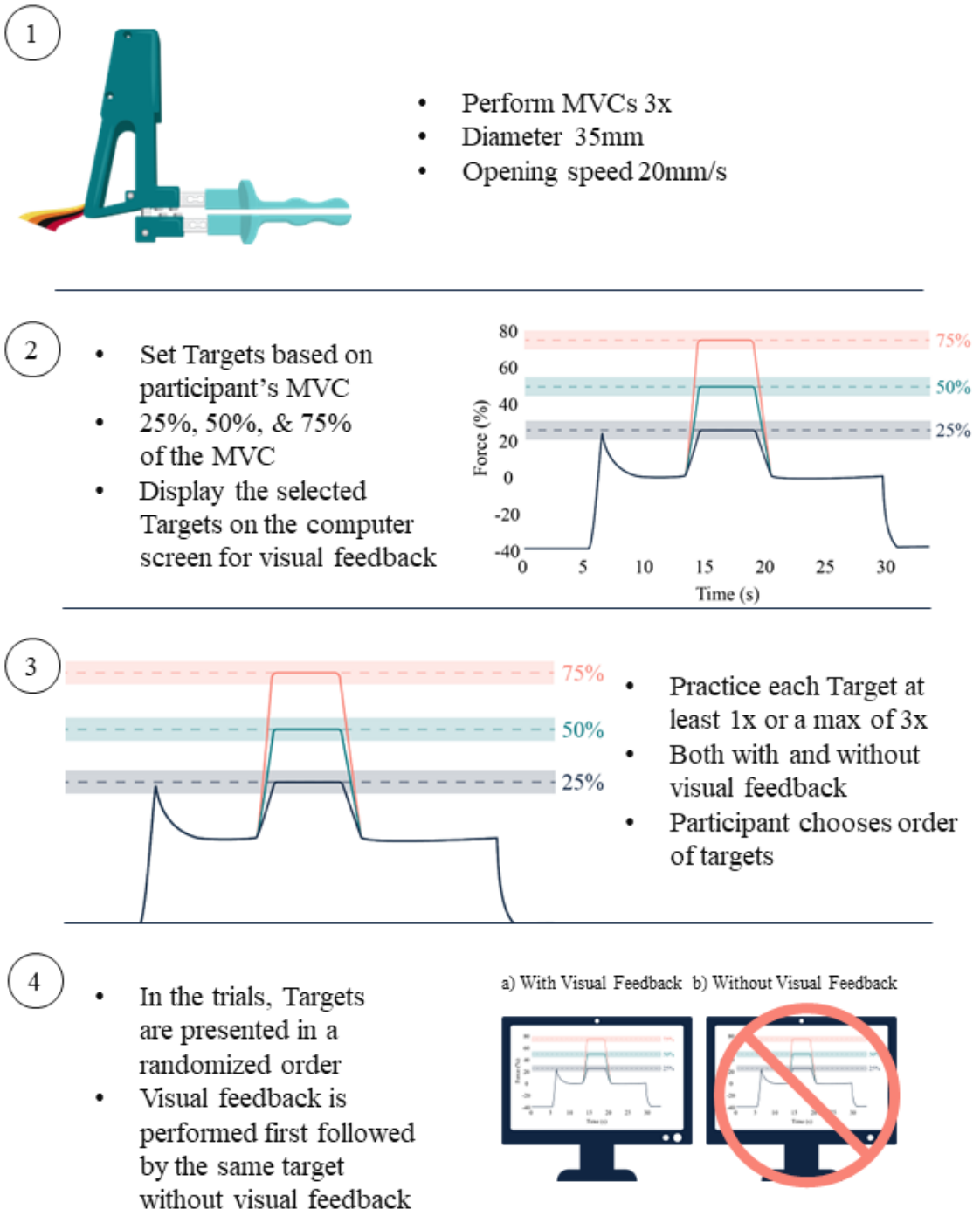

Figure 4.3 Illustrated protocol for the novel force-matching task in the levator ani using an intravaginal dynamometer. Abbreviations: Maximal voluntary contraction (MVC); levator ani muscles (LAMs).

endpoint selected based on all participants having held the contraction for at least 2.5s (See Figures 4.4 and 4.5). In addition, a difference score between the two feedback conditions was computed by subtracting the mean RMSE across the three trials with visual feedback from the mean RMSE across the three trials with no visual feedback for each participant.

4.4 Data Analysis

All statistical tests were performed using IBM SPSS Statistical Software Version 25 (IBM Corp; Armonk, NY, USA). Continuous data were tested for normality using the Shapiro-Wilks test and visual inspection. The data were found to be non-normal, however, because analyses of variance (ANOVAs) are known to be robust to normality violations[45,46], ANOVA models were used. The outcomes from the passive elongation task and the force matching task are reported as mean ± standard deviation and $\alpha = .05$ unless otherwise specified. Partial eta-squared effect sizes were reported following the classification of 0.01 as a small effect, 0.06 as a moderate effect, and 0.14 as a large effect.

Descriptive statistics were used to report participant accuracy on the passive elongation task as well as to evaluate potential ceiling or floor effects in the data (Objective 1a). Spearman correlations were used to assess the relationships between reference IVD diameter and accuracy as well as between accuracy and age and accuracy and parity (Objective 1b).

A linear mixed model ANOVA was used to assess the impact of window length (0.25s, 0.50s, 1.00s) on the calculated RMSE across both feedback conditions (visual and no visual) and target force levels (25%, 50%, 75%) to determine the best window length for assessing participant accuracy in the force-matching task. Following this, a series of repeated measures ANOVAs

were used to determine the most stable location for RMSE along the force-time curve to assess participant accuracy (Objective 2a).

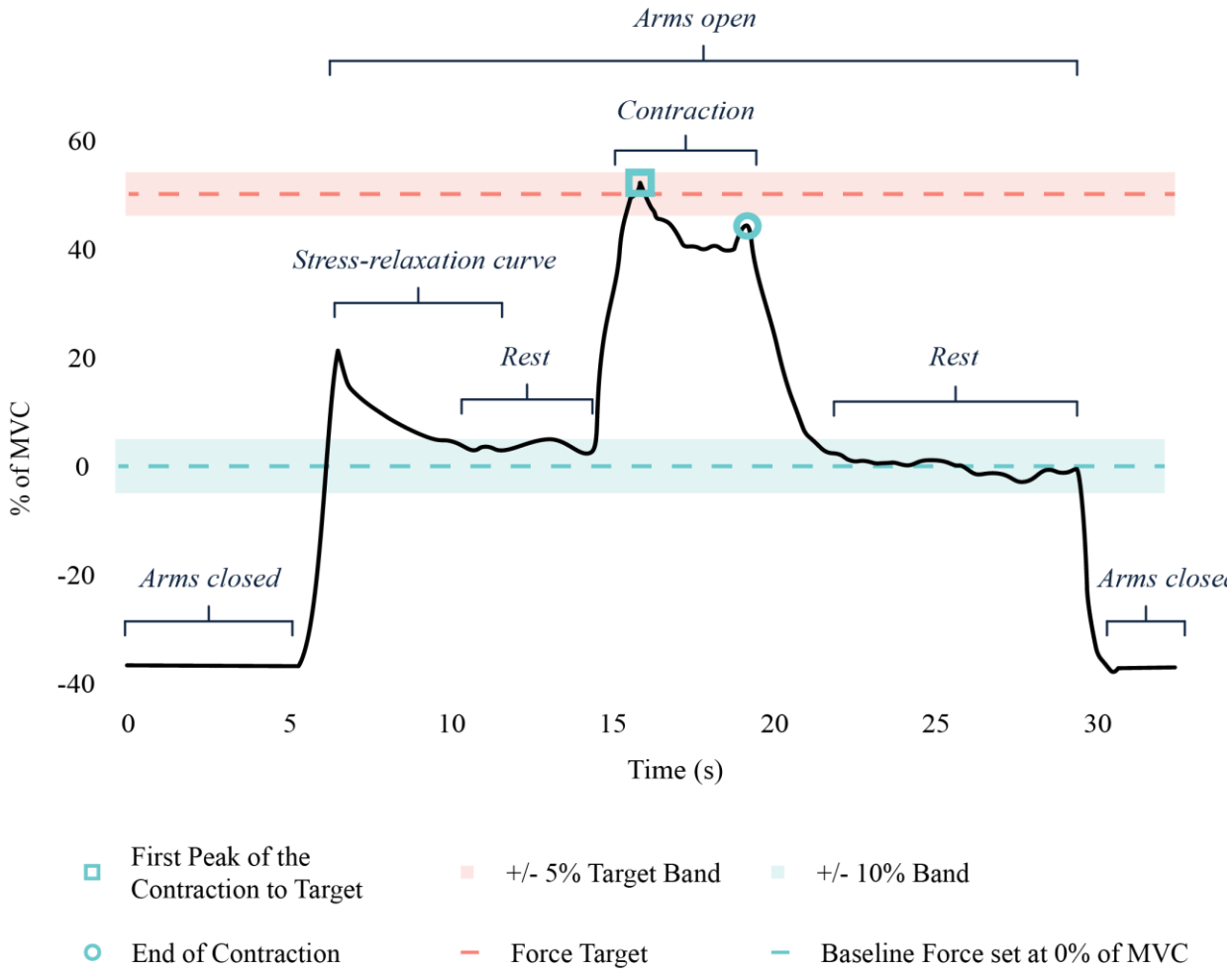

Figure 4.4 Percent of MVC by time curve with features of the curve labelled.

Abbreviations: maximal voluntary contraction (MVC).

A 2-way repeated-measures ANOVA was used to assess the impact of visual feedback (yes/no) and target force level (25%, 50%, and 75% of MVC) on participant accuracy (RMSE) using the window length and location that was determined in objective 1a. Pairwise comparisons with a Bonferroni correction were used to assess significant main effects. (Objective 2b).

A one-way repeated-measures ANOVA was used to assess the difference in RMSE between visual feedback and no-visual feedback conditions across target forces (25%, 50%, and 75% of MVC) with using the window length and location determined in objective 1a. Pairwise comparisons with a Bonferroni correction were used to assess significant main effects. (Objective 2b).

Spearman correlation coefficients were used to evaluate the associations between participant accuracy on the force-matching task and peak and relative peak contractile force reached during the MVC. Spearman correlations were also used to evaluate potential influences of age and parity (Objective 2c).

Lastly, Spearman correlations were used to evaluate the association between performance on the passive elongation task and performance on the force matching task (Objective 3).

4.5 Results

4.5.1 Sample characteristics

Thirty women (44 ± 13 years) participated; however, one participant did not finish all trials of the force-matching task due to an equipment failure during data collection, resulting in n = 29 for the force-matching task analysis (See Figure 4.6). Sixteen of the participants reported SUI symptoms. Twelve of the participants were nulliparous and 18 were parous, with a mean of 2 ± 1 deliveries. None of the participants reported a history of smoking. See Table 4.1 for demographic data, Table 4.2 for questionnaire results, and Table 4.3 for LAM strength and passive resting force prior to testing.

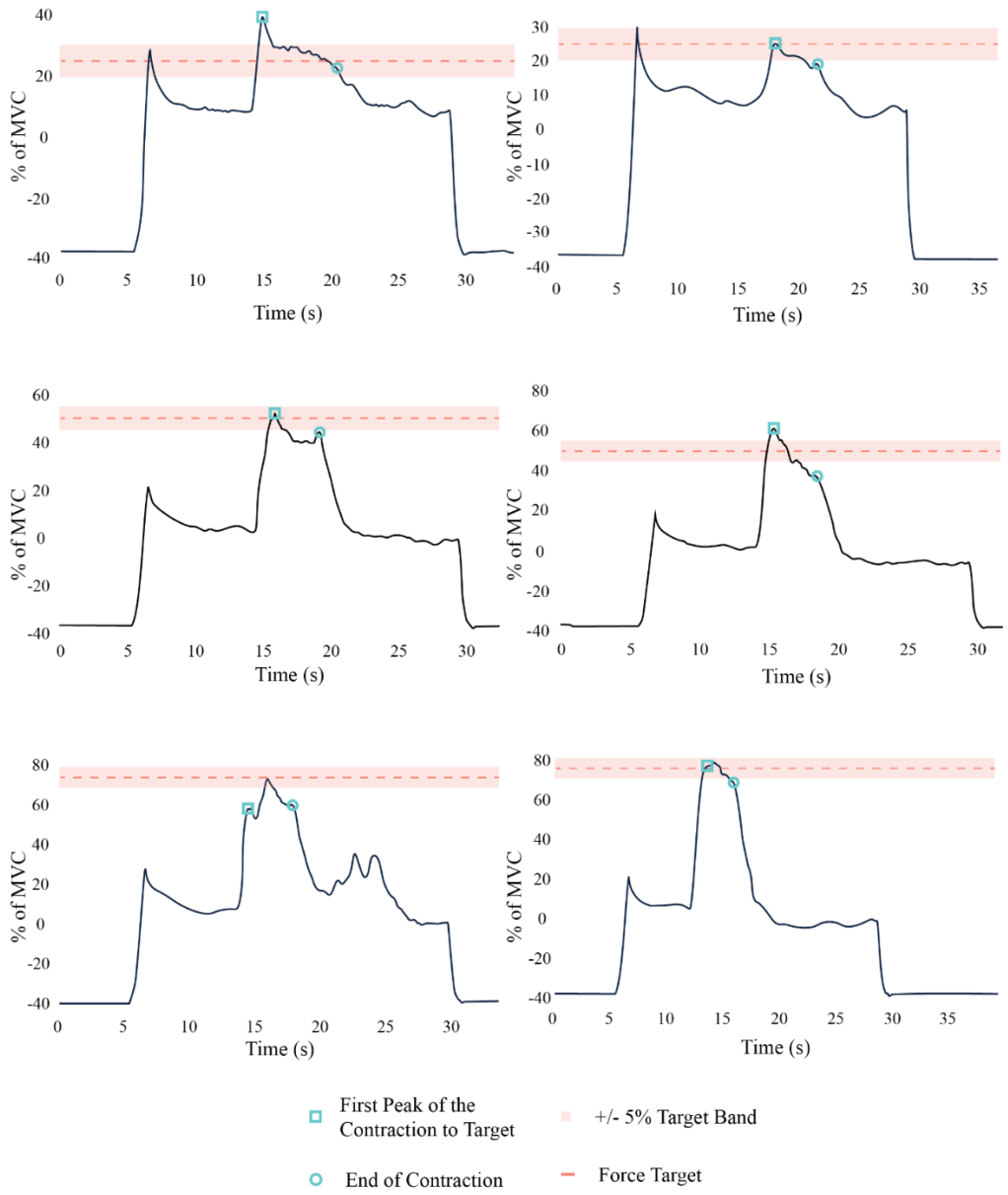

Figure 4.5 Sample percentage of MVC vs time curves recorded during the force-matching task from one participant. The force target is indicated as the dotted red line surrounded by ±5% on either side. The scale on the force axis was adjusted for each individual to set the baseline force before contraction (i.e. at the end of the stress relaxation response) at 0 N; a) Target force was 25% of MVC, visual feedback provided, b) target force was 25% of MVC no visual feedback provided c) target force was 50% of MVC visual feedback provided, d) target force was 50% of MVC no visual feedback provided, e) target force 75% of MVC visual feedback provided, f) target force was 75% of MVC no visual feedback provided. Abbreviations: maximal voluntary contraction (MVC); levator ani muscle (LAM).

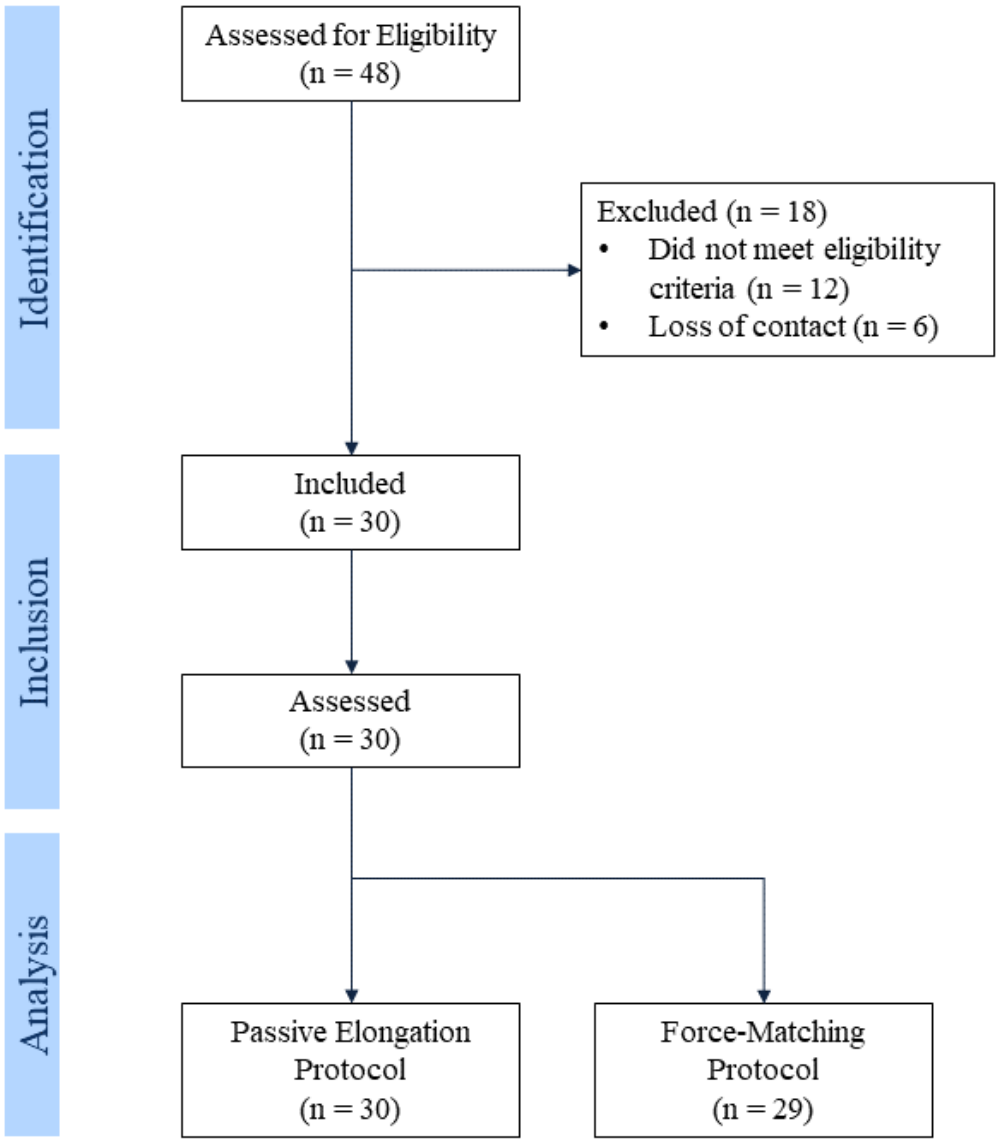

Figure 4.6 Flowchart participant recruitment and analysis.

Table 4.1 Sample characteristics and demographic information

Demographics	**mean ±SD**
Height (m)	1.66 ± 0.55
Weight (kg)	68.61 ± 16.23
Body Mass Index (kg/m^2)	24.99 ± 6.09
Wasit-Hip Ratio	0.79 ± 0.06
Parity	
0	10
1	3
2	10
>2	7
Menopause	
Yes	12
No	18
Ethnicity	
White	25
Middle Eastern	1
East/Southeast Asian	1
Mixed (Mediterranean/White)	1
Mixed (Indigenous/White)	1
Mixed (Black/White/French Canadian)	1
Highest Level of Education	
High School	2
College	1

Bachelors	16
Masters	9
Doctorate (MD or PhD)	2
Contraceptive Use	
Yes	5
No	25
Hormone Replacement Therapy Use	
Yes	3
No	27
Phase of Cycle During Testing	
Menstrual Cycle Days 1 – 14	6
Menstrual Cycle Days 15 – 28	12
No Cycle	12

Abbreviations: Standard deviation (SD); stress urinary incontinence (SUI).

Table 4.2 Questionnaire results describing the urinary, vaginal, bowel, and sexual functioning of the sample.

Questionnaire	Overall (Mean ± SD)
ICIQ-FLUTS	
Urinary Incontinence (0 – 20)	2.55 ± 3.91
Filling (0 - 16)	2.79 ± 2.01
Voiding (0 - 12)	1.14 ± 1.53
ICIQ-VS	
Total (0 - 53)	4.17 ± 3.95
Sexual Matters (0 - 58)	6.21 ± 9.41
Quality of Life (0 - 10)	0.79 ± 1.63
ICIQ-B	
Bowel Pattern (1 – 21)	5.38 ± 1.80
Bowel Control (0 - 28)	1.66 ± 1.32
Quality of Life (0 - 26)	1.17 ± 2.27
FSFI[+]	
Total (2 - 36)	25.13 ± 5.24

[+]the total score does not include the three individuals who reported no sexual activity within that last 4 weeks.
Abbreviations: Standard deviation (SD); International Consultation on Incontinence Questionnaire (ICIQ) - Female Lower Urinary Tract Symptoms (ICIQ-FLUTS); ICIQ-Vaginal Symptoms (ICIQ-VS); ICIQ-Bowel (ICIQ-B); Female Sexual Function Index (FSFI); stress urinary incontinence (SUI).

Table 4.3 Sample levator ani muscle function characteristics measured using an intravaginal dynamometer.

LAM Function	Overall (Mean ± SD)
Baseline force before Contraction (N)	1.21 ± 0.63
Peak force attained during MVC (N)	3.57 ± 2.25
Relative Peak force of MVC (N)	2.36 ± 1.75

Abbreviations: maximal voluntary contraction (MVC); levator ani muscle (LAM); standard deviation (SD); stress urinary incontinence (SUI).

4.5.2 Passive elongation task

The average reference IVD diameter was 36.00mm ± 3.25mm. While women correctly identified the IVD opening diameter relative to the reference diameter 77.8% ± 25.0% of the time, there was a large range in scores (22% – 100%; See Figure 4.7). Four of the 30 participants demonstrated 100% accuracy and no participant demonstrated 0% accuracy, although 4 individuals were accurate less than 50% of the time. The Spearman correlations indicated that there was no significant association between the reference diameter and the percentage of correctly identified opening diameters ($r(28) = -0.29$, $p = .13$), nor were there associations between the percentage of correctly identified opening diameters and age ($r(28) = -0.02$, $p = .94$) or parity ($r(28) = 0.03$, $p = .86$).

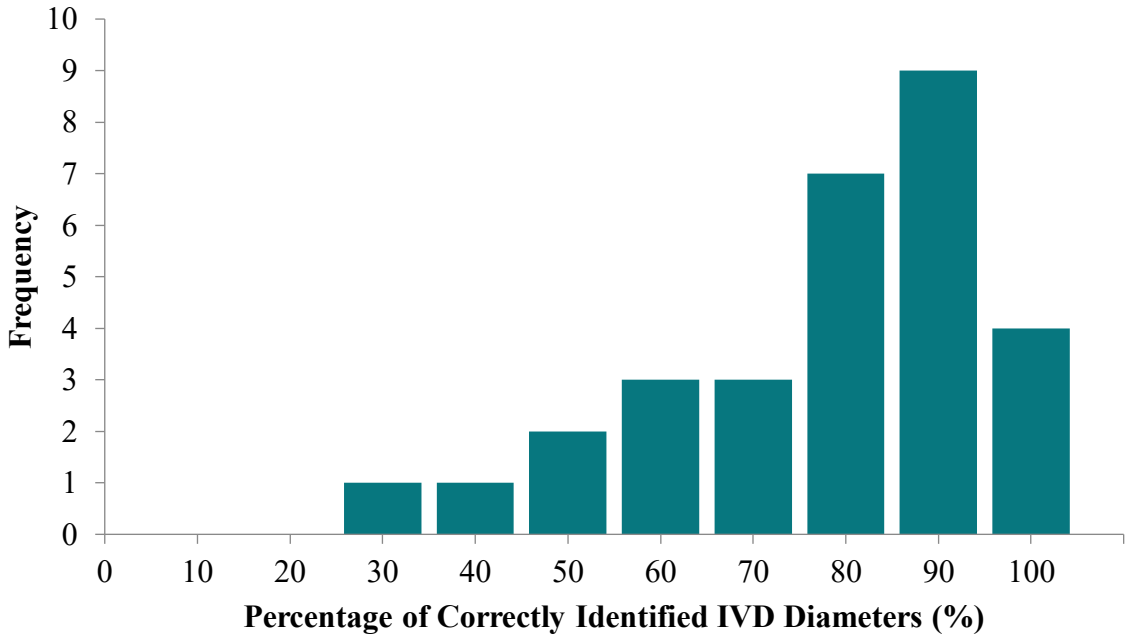

Figure 4.7 Histogram representing the distribution of correctly identified intravaginal dynamometry (IVD) diameters among women on a passive muscle elongation task to assess the ability to detect changes in muscle length in the levator ani muscles.

4.5.3 Force-matching task

3.5.3.1 Optimal window length for determining participant accuracy in target matching

The window length over which RMSE was calculated did not significantly change the outcome of participant accuracy (F (2, 2945) = 1.84, p = .16; Figure 3.8). There were no significant interaction effects between target force and window length (F (4, 2945) = 0.32, p = .86) nor feedback condition and window length (F (2, 2945) = 0.00, p = .99). There was a significant interaction between target force and feedback condition on RMSE (F (2, 2945) = 3.71, p = .03).

4.5.3.2 Window location for determining participant accuracy in target matching

All ANOVAs violated the assumption of sphericity; therefore, a Greenhouse-Geisser correction was used. With visual feedback, the 0.25s window length showed increasing RMSE for the

duration of the task. At the 25% and 50% MVC target forces, there were periods of stability between 0.75s and 1.50s after the first force peak, where RMSE did not differ across windows. At the 75% MVC target force, RMSE continued to increase over time without evidence of a plateau like the lower force targets. Without visual feedback, the 0.25s window length demonstrated a similar trend to the one observed with visual feedback (See Table 4.4 for models). At the 25% target force, the RMSE stabilized between 1.00s and 2.00s after the first force peak. However, the 50% and 75% MVC target forces demonstrated increasing RMSE throughout the task. Both feedback conditions demonstrated a progressive reduction in accuracy when attempting to maintain a target force at each level. The plateaus in RMSE observed between 1.00 and 1.50s at most of the target forces suggest that this may be the best location to assess participant accuracy when using a 0.25s window length.

The 0.50s window length yielded results that were similar to the 0.25s window length. With visual feedback, contractions targeting 25% and 50% of MVC were stable between 0.50s and 1.50s (See Table 3.5 for models). Without visual feedback, the RMSE generally increased with each consecutive window but was stable between 1.0 and 2.0s at the 25% MVC target force (See Table 3.5). Again the 75% target force demonstrated no period over which the RMSE was stable in either feedback condition. The plateaus in some of the targets suggest that a time window between 1.00s-1.50s may be the best location to assess participant accuracy using a 0.50s window over which RMSE is calculated. RMSE increased over time across all target forces and feedback conditions when a 1.0s window was used, except for the 25% MVC force target when visual feedback was provided (See Table 4.6).

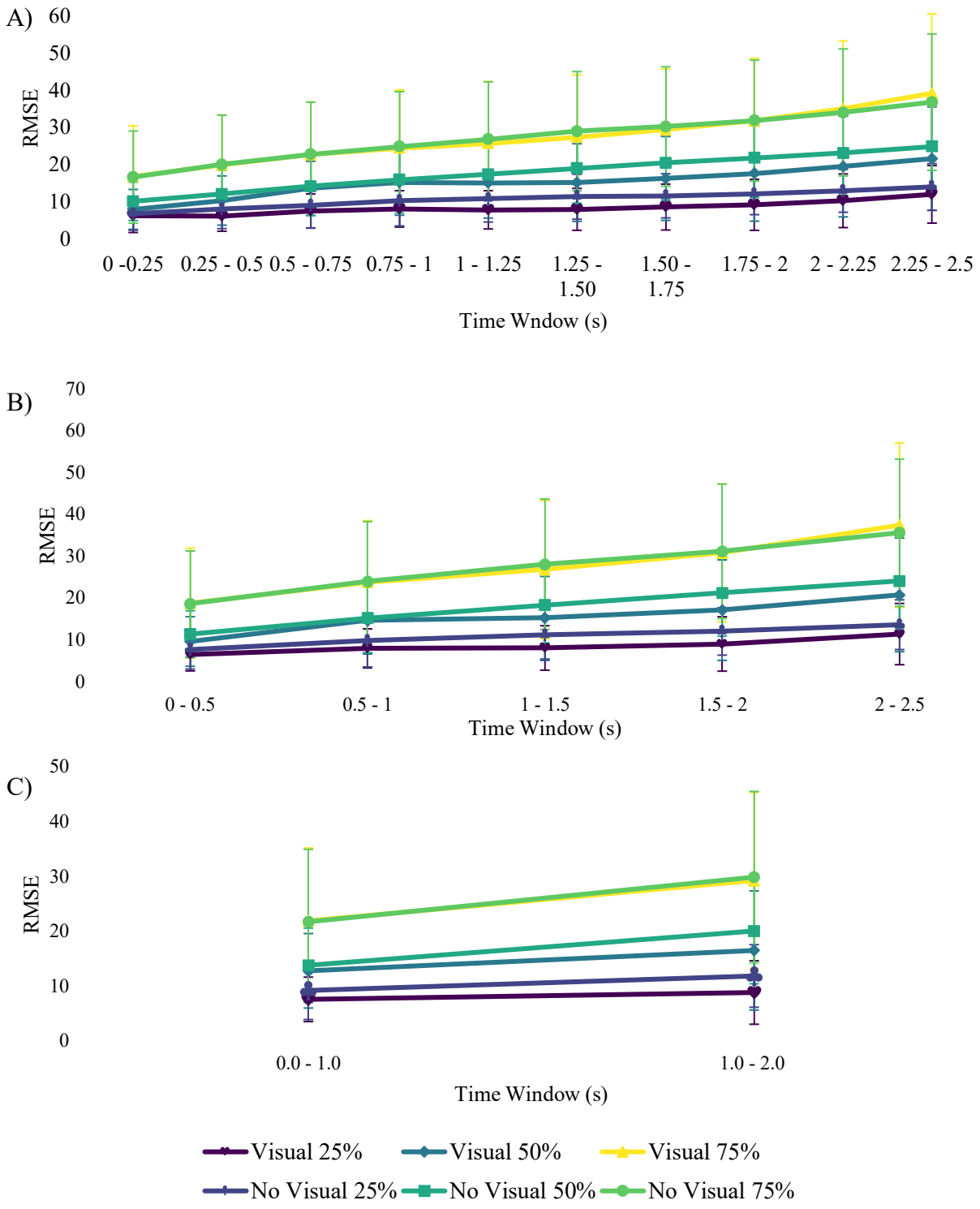

Figure 4.8 Root mean square error in different window lengths from the first peak of the force curve to 2.50s of the levator ani contraction. A) 0.25s window, B) 0.50s window, and C) 1.00s window.

As the RMSE was stable between 1.0 and 1.50s after the first force peak when both the 0.25s and 0.50s windows were used to calculate RMSE, we chose to evaluate RMSE using a 0.50s window between 1.00 and 1.50s to assess the impact of feedback and target force on force-matching accuracy for objectives 2b and 2c.

4.5.3.3 Effect of feedback and target force on accuracy in the force-matching task

Sphericity was assumed for all variables except for the target force level ($\chi^2(2) = 14.87$, p = .00), which used the Greenhouse-Geisser correction ($\varepsilon = 0.70$).

Both feedback ($F(1, 28) = 7.58$, $p = .01$, $\eta^2 = .21$) and target force level ($F(1.41, 39.34) = 35.16$, $p = .00$, $\eta^2 = .56$) significantly affected participants' ability to accurately match target LAM forces; yet there was no interaction between feedback and target force ($F(2, 56) = 0.49$, $p = .62$, $\eta^2 = .02$). Participant accuracy was significantly better with visual feedback (p = .01; See Figure 4.9) compared to without visual feedback, and participants were more accurate at the lower target forces (25% and 50% MVC; p = .00; See Figure 4.9) relative to the higher (75% MVC) target force. Participants were most accurate in reaching the 25% MVC target with visual feedback and least accurate in reaching the 75% MVC target without visual feedback.

Both peak and relative peak MVC force were not associated with accuracy across the target forces and feedback conditions except for the 25% MVC target force when visual feedback was provided (Peak $r(27) = -.36$, $p = .06$; Relative Peak $r(27) = -.45$, $p = .02$), where those with higher peak and relative peak forces were more accurate than those with lower relative peak forces. Accuracy on the force-matching task was not correlated with age ($p > .05$) nor parity ($p > .05$).

Table 4.4 Repeated Measures ANOVA of root mean square error by feedback condition, target force, and 0.25s window location. Planned repeated contrasts between consecutive time windows are also displayed to indicate plateaus of error from the target.

	Overall Model	0.00 – 0.25 vs 0.25 – 0.50	0.25 – 0.50 vs 0.50 – 0.75	0.50 – 0.75 vs 0.75 – 1.00	0.75 – 1.00 vs 1.00 – 1.25	1.00 – 1.25 vs 1.25 – 1.50	1.25 – 1.50 vs 1.50 – 1.75	1.50 – 1.75 vs 1.75 – 2.00	1.75 – 2.00 vs 2.00 – 2.25	2.00 – 2.25 vs 2.25 – 2.50
Visual Feedback										
25%	F (2.37, 66.43) = 7.68, p = .00	F (1, 28) = 0.003 p = .96	F (1, 28) = 10.84 p = .00	**F (1, 28) = 2.57 p = .12**	**F (1, 28) = 0.41 p = .53**	**F (1, 28) = 0.16 p = .70**	**F (1, 28) = 2.83 p = .10**	**F (1, 28) = 3.08 p = .09**	F (1, 28) = 7.08 p = .01	F (1, 28) = 10.81 p = .00
50%	F (1.80, 50.27) = 17.63, p = .00	F (1, 28) = 15.71 p = .00	F (1, 28) = 28.23 p = .00	F (1, 28) = 9.39 p = .01	**F (1, 28) = 0.15 p = .70**	**F (1, 28) = 0.04 p = .85**	F (1, 28) = 6.59 p = .02	F (1, 28) = 4.58 p = .04	F (1, 28) = 10.33 p = .00	F (1, 28) = 21.48 p = .00
75%	F (2.20,63.68) = 28.19, p = .00	F (1, 29) = 9.29 p = .01	F (1, 29) = 10.58 p = .00	F (1, 29) = 8.68 p = .01	F (1, 29) = 6.10 p = .02	F (1, 29) = 7.03 p = .01	F (1, 29) = 8.88 p = .01	F (1, 29) = 21.76 p = .00	F (1, 29) = 20.71 p = .00	F (1, 29) = 11.88 p = .00
No Visual Feedback										
25%	F (2.66, 74.40) = 14.12, p = .00	F (1, 28) = 2.91 p = .10	F (1, 28) = 5.45 p = .03	F (1, 28) = 7.09 p = .01	F (1, 28) = 4.57 p = .04	**F (1, 28) = 2.31 p = .14**	**F (1, 28) = 1.01 p = .32**	**F (1, 28) = 3.28 p = .08**	F (1, 28) = 5.21 p = .03	F (1, 28) = 11.80 p = .00
50%	F (1.83, 51.27) = 43.00, p = .00	F (1, 28) = 8.41 p = .01	F (1, 28) = 20.08 p = .00	F (1, 28) = 19.27 p = .00	F (1, 28) = 9.11 p = .01	F (1, 28) = 18.46 p = .00	F (1, 28) = 13.74 p = .00	F (1, 28) = 21.74 p = .00	F (1, 28) = 10.91 p = .00	F (1, 28) = 18.65 p = .00
75%	F (1.75, 50.68) = 35.81, p = .00	F (1, 29) = 15.85 p = .00	F (1, 29) = 19.67 p = .00	F (1, 29) = 18.03 p = .00	F (1, 29) = 10.38 p = .00	F (1, 29) = 11.65 p = .00	F (1, 29) = 10.12 p = .00	F (1, 29) = 10.12 p = .00	F (1, 29) = 21.38 p = .00	F (1, 29) = 15.64 p = .00

Bolded values are time windows that were not significantly different from each other, indicating a plateau of root mean square error from the target; the Greenhouse-Geiser correction was applied to the model because sphericity was violated.

Table 4.5 Repeated Measures ANOVA of root mean square error by feedback condition, target force, and 0.50s window location. Planned repeated contrasts between consecutive time windows are also displayed to indicate plateaus of error from the target.

	Overall Model	0.00 – 0.50 vs 0.50 – 1.00	0.50 – 1.00 vs 1.00 – 1.50	1.00 – 1.50 vs 1.50 – 2.00	1.50 – 2.00 vs 2.00 – 2.50
Visual Feedback					
25%	F (2.03, 56.82) = 8.26, p = .00	F (1, 28) = 5.04 p = .03	**F (1, 28) = 0.04 p = .85**	**F (1, 28) = 2.79 p = .11**	F (1, 28) = 12.34 p = .00
50%	F (1.60, 44.67) = 17.88, p = .00	F (1, 28) = 30.79 p = .00	**F (1, 28) = 0.93 p = .34**	F (1, 28) = 5.27 p = .03	F (1, 28) = 16.53 p = .00
75%	F (1.92, 55.73) = 29.99, p = .00	F (1, 29) = 11.95 p = .00	F (1, 29) = 12.34 p = .00	F (1, 29) = 15.79 p = .00	F (1, 29) = 21.43 p = .00
No Visual Feedback					
25%	F (2.15, 60.11) = 15.16, p = .00	F (1, 28) = 7.53 p = .01	F (1, 28) = 7.77 p = .01	**F (1, 28) = 2.96 p = .10**	F (1, 28) = 10.97 p = .00
50%	F (1.62, 45.41) = 45.97, p = .00	F (1, 28) = 22.32 p = .00	F (1, 28) = 23.57 p = .00	F (1, 28) = 25.38 p = .00	F (1, 28) = 21.68 p = .00
75%	F (1.56, 45.26) = 28.77, p = .00	F (1, 29) = 25.57 p = .00	F (1, 29) = 20.14 p = .00	F (1, 29) = 17.86 p = .00	F (1, 29) = 25.48 p = .00

Bolded values are time windows that were not significantly different from each other, indicating a plateau of root mean square error from the target; the Greenhouse-Geiser correction was applied to the model because sphericity was violated.

Table 4.6 Paired t-tests of root mean square error by feedback condition, target force, and 1.00s window location.

	0.0 – 1.0s	1.0 – 2.0s	P Value	Cohen's d
Visual				
25%	7.55 ± 4.05	8.80 ± 5.80	**.10**	**.25**
50%	12.76 ± 6.79	16.47 ± 10.87	.00	.41
75%	21.88 ± 13.28	29.24 ± 16.07	.00	.50
No Visual				
25%	9.17 ± 5.30	11.81 ± 5.70	.00	.48
50%	13.77 ± 6.79	20.02 ± 9.62	.00	.75
75%	21.71 ± 13.21	29.86 ± 15.63	.00	.56

Bolded values are time windows that were not significantly different from each other, indicating a plateau of root mean square error from the target.

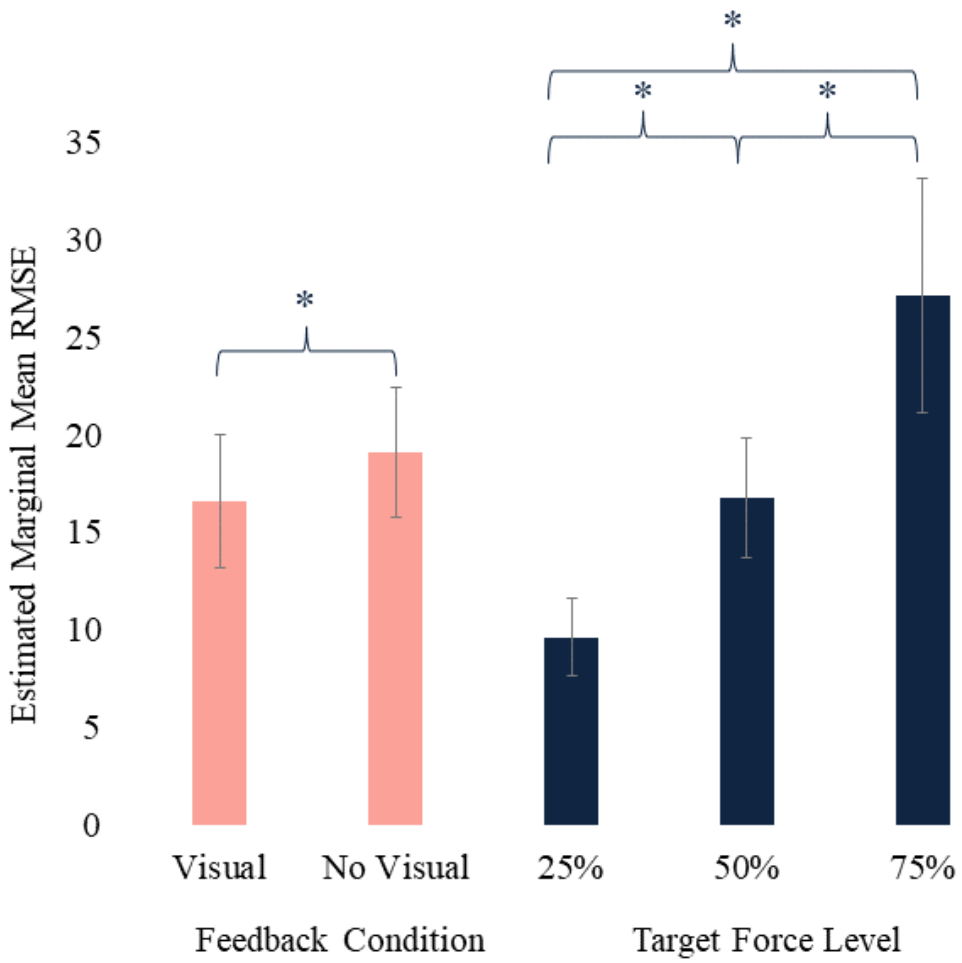

Figure 4.9 Effect of feedback (visual or no visual) and target force (25%, 50%, and 75% MVC) on accuracy measured as root mean square error (RMSE) from the target. Bars represent estimated marginal mean values and 95% confidence intervals for the mean.

Abbreviations: maximal voluntary contraction (MVC); * denotes a $p < .05$.

4.5.3.4 Difference between feedback conditions used as an outcome measure

Sphericity was assumed ($\chi^2(2) = .60$, p = .74) for the model. Using this measure, the difference between the feedback conditions was not different across force targets at 25%, 50%, and 75% MVC ($F(2, 56) = .49$, $p = .62$, $\eta^2 = .02$).

4.5.4 Relationship between passive elongation and active force-matching tasks

There was no significant association between performance on the force-matching task and accuracy in the identification of changes in muscle length regardless of target force or the presence of visual feedback ($p > .05$; See Figure 3.10).

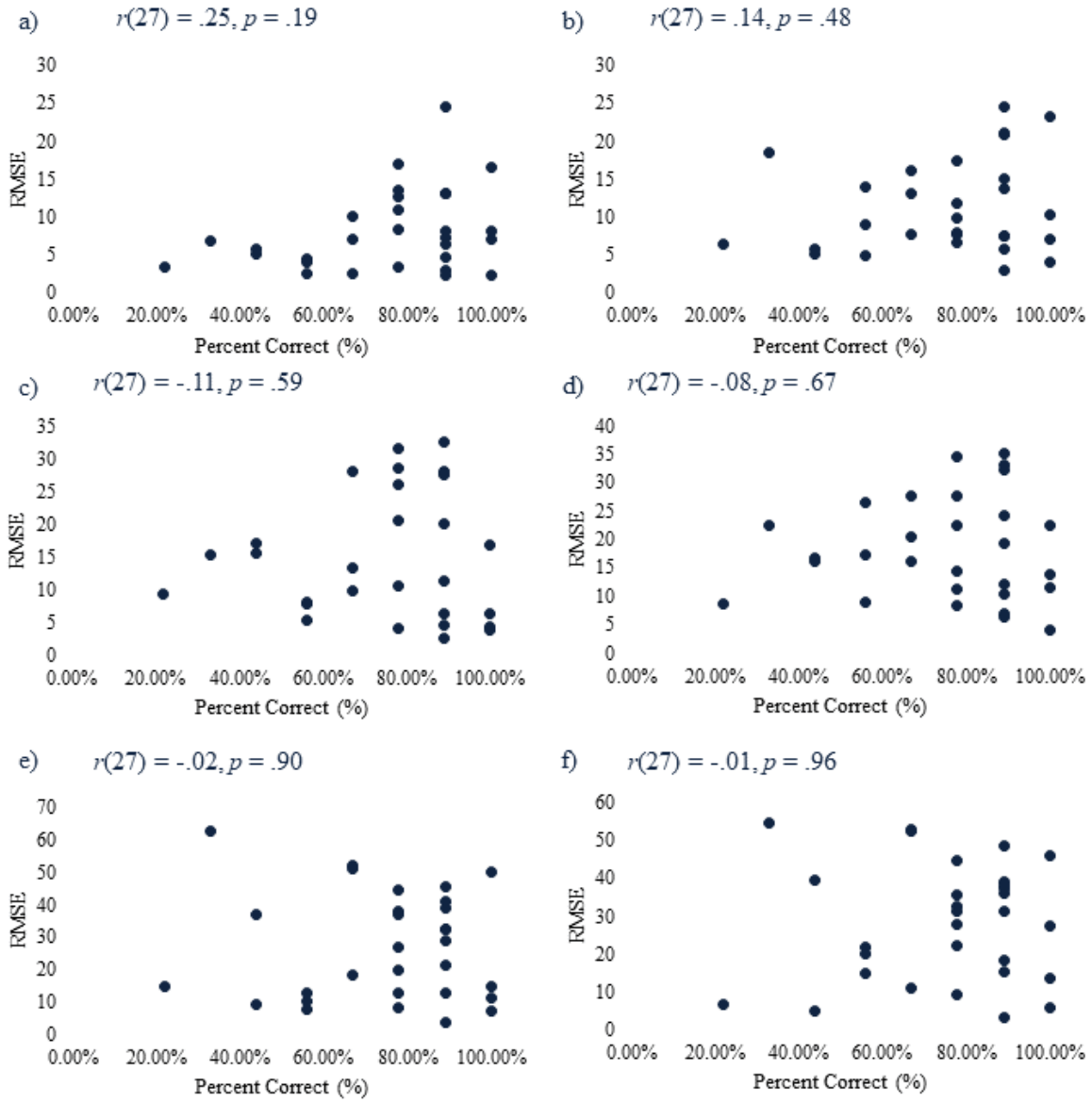

Figure 4.10 Association between accuracy in the force-matching task and accuracy in the passive elongation task; a) 25% with visual feedback, b) 25% without visual feedback, c) 50% with visual feedback, d) 50% without visual feedback, e) 75% with visual feedback,

4.6 Discussion

A novel IVD protocol was developed to assess LAM proprioception through a passive elongation task and a LAM force-matching task. Participants exhibited a wide range of accuracy in detecting changes in LAM length, and while no floor effects were noted, four of the 30 participants were 100% accurate. We recommend adding IVD opening diameters at ±2.5mm above and below the reference diameter to address the potential ceiling effect in accuracy.

Based on the findings in objective 2a, we recommend assessing force-matching accuracy with RMSE computed over a window length of 0.25s or 0.50s located between 1.00s and 1.50s from the first force peak along the force-time curve; these window lengths and this location represent the most stable portion of the force-time curves at the 25% and 50% of the MVC targets. Given the significant impact that window length and location along the force-time curve over which the RMSE is computed have on force-matching outcomes, researchers should clearly report their methods and consider standardizing data processing methods so that valid comparisons can be made across studies.

Through computing RMSE using a 0.50s window between 1.00 and 1.50s after the first force peak, both target force and feedback type independently influenced participant accuracy on the force-matching task. It is therefore recommended that force-matching accuracy be evaluated at different target forces and with and without visual feedback on force production in studies aimed at evaluating differences in force accuracy. The inclusion of trials with visual feedback allows for an assessment of the individual's relative reliance on their proprioceptive and visual systems for task performance; where better performance with visual feedback may indicate a lack of proprioceptive awareness and no difference based on feedback may suggest strong proprioceptive awareness. While our findings suggest an overall improvement in accuracy on

this task with visual feedback, there was no difference between the visual and no visual feedback conditions across the force targets. This may suggest that reliance on the visual system is similar across the different contraction intensities on the LAM force-matching task.

4.6.1 Passive elongation task

The passive elongation task was adapted from joint position tasks used to assess limb proprioception in peripheral muscles[36,37]. We chose to assess the ability to detect changes in muscle length through an elongation comparison task to see if women were aware of these changes in their LAMs in the mid-sagittal plane, which reflects the line of action of the pubovisceral component. There was wide variability in the ability to detect changes in muscle length observed among women in this sample, and performance was not associated with age or parity.

In contrast, using an air-inflated catheter to record the first sensation of intravaginal stretch using the methods of limits, Mahoney et al.[30] found that genital stretch perception thresholds increased with age. They reported that this assessment targeted the Aα and Aβ nerve fibers that transmit sensations of vaginal tone and stretch[30], and determined this test to be clinically feasible, valid, and reproducible. However, the method of limits has been criticized for being influenced by participant reaction time and concentration[32,47] which may have biased their results. The testing method developed for the protocol presented here follows a method of levels approach, which is less influenced by reaction time[32] and did not demonstrate any association with age. Similar to the findings of the current study, Mahoney et al[30] found no impact of parity on stretch perception thresholds, which suggests that vaginal delivery may have no long-term effects on the sensory function of Aα and Aβ nerve fibers[30]. In a subsequent study using the same technique, Mahoney

et al.[29] found only an initial deterioration of stretch perception thresholds that returned to antenatal levels at 6 months post-partum. In this study, we specifically recruited participants who were not within a 6-month postpartum period, and we only recorded the self-report of delivery method and history of perineal injury, which may be important factors to consider if this protocol is to be used on clinical populations.

We found no evidence of floor effects on accuracy in detecting LAM elongation in the sample. However, 4 of 30 participants achieved 100% accuracy. Further refinement of this protocol may be needed to reduce the potential for ceiling effects, such as including increments of ±2.5mm diameter. Repeatability testing is another important next step in the development of this assessment protocol.

4.6.2 Force-matching task

To our knowledge, this is the first study to have systematically evaluated measurement strategies to determine the accuracy of force-matching by the LAMs. We assessed differences in RMSE from the target using three different window lengths and across the force-time curve. RMSE computed using all three window lengths followed the same trend, increasing over time after the first peak of the contraction to 2.5s afterwards; implying that all of the three window lengths tested are appropriate for assessing force-matching accuracy using RMSE. The findings further suggest that maintaining a steady LAM contraction is difficult for untrained individuals, even at contraction intensities that are well below maximum voluntary contractile efforts. Morin et al.[7] reported reductions and large fluctuations in force when women attempted to sustain maximal LAM contraction efforts over a 90s period. In this study, women displayed difficulty with

maintaining a steady contraction even during low-intensity contractile efforts (25%, 50% MVC) sustained for a short time (2.5s).

Periods of stability in the RMSE were observed across the force-time curve at the 25% and 50% MVC target forces. The plateaus in RMSE observed when smaller windows were used to compute it suggests that force may be more stable between 1.00 and 1.50s after the initial force peak; this may be the best time-point at which to assess accuracy in a force-matching task in the LAMs. A similar assessment for a force-matching task in the index finger demonstrated a plateau in RMSE beginning between 2.5-3.0s after the initiation of the contraction, however in that case, the plateau was maintained until the end of the task. Based on the results of the current study, individuals appear to have less capacity to generate stable contraction output of the LAMs compared to hand muscles[40]. This is not surprising given that the muscle architecture in the hand is optimized for fine motor control[48], which is not the case for the LAMs.

In the only previous study[31] reporting on LAM proprioception using a force-matching task, no description of force steadiness or error in the force-time curve was provided, and as such, the results cannot be compared with those of the current study. Based on the findings of this study, we recommend assessing the accuracy of LAM force-matching using a window length of 0.25s or 0.50s located between 1.00 and 1.50s after the first force peak of the force-time curve. Future studies should employ a standard signal processing method to allow for valid comparisons in results.

Participants were more accurate in matching the target force when they had visual feedback on the LAM force-matching task. Similar findings have been reported at the shoulder using comparable methods[41,49]. Without visual feedback, the body must rely on sensory input from

muscle spindles and Golgi tendon organs to estimate the amount of contractile force being produced by the muscle and to correct it. These mechanoreceptors are present in the LAMs[50], though mechanoreceptors in the vaginal mucosa[51,52] may also detect the force applied by the IVD arms. Significant improvements in force-matching accuracy when visual feedback is provided, compared to no visual feedback, could indicate deficits in the transmission of afferent mechanoreceptor information to the brainstem and central nervous system and could impact control of the LAMs. Interestingly, while visual feedback may improve force accuracy, as observed in this study, it does not appear to improve maximum force generation capacity in the LAMs[53]. This is in contrast to some literature on grip strength, where there is a small improvement in strength with the addition of visual feedback[54,55]. The findings of this study support the inclusion of force-matching trials with and without visual feedback.

While visual feedback is incorporated into the day-to-day function of the limbs, women do not receive and use visual information on their LAM length or force output during daily tasks. The impact of visual feedback on LAM function may be useful in assessing and potentially training proprioceptive function in the LAMs. Indeed, biofeedback in the form of electromyography or ultrasound imaging is used by some physiotherapists and continence nurse specialists to help women improve their awareness and function of their LAMs; however, there is currently insufficient data to support the use of biofeedback for training the LAMs[56]. Moreover, personal home pelvic floor muscle training devices have recently emerged with mobile apps that provide visual feedback on force production during tasks (e.g. The Elvie Trainer[57], Perifit, KegelSmart, etc.). The impact of providing visual feedback on contractile forces generated by the LAMs on training outcomes and functional outcomes is not known.

Women were also more accurate when attempting to match the lowest target force (25% MVC) with a LAM contraction, much like the findings reported for the spine[58] and finger musculature[39]. Indeed, the resolution of the proprioceptive system may be impacted by contractile force. At higher contraction intensities, with more motor units firing and a significant amount of sensory information already being provided, the proprioceptive system may not be able to provide feedback on minor changes in force. Though we did not observe an interaction between feedback and target force in our assessment of force accuracy within the LAMs, past research has noted that the additional information provided by the visual system may improve accuracy at higher-intensity force targets by supplying the information necessary to make minor changes in force[39,49]. As we found that the accuracy at reaching each force target was different, we propose that future protocols involving force-matching tasks should include all three target forces, as each may provide unique information to the assessment.

Interestingly, the difference between the no visual and visual feedback conditions was found to be similar across all three target forces. While there was evidence of the independent effects of feedback and target force, the lack of difference between the feedback conditions across target forces may suggest that reliance on the visual system to improve task performance is similar at each contraction intensity. This is in contrast to previous work at the finger[39] and shoulder[49], where visual feedback improved participant performance on a force-matching task at higher contraction intensities but not at lower ones. Unlike the hand and shoulder, the LAMs do not typically receive visual feedback on their task performance and as such, visual information may be incorporated into task performance differently from other parts of the body. More research is needed to understand what the role of visual feedback might be on LAM sense of force.

Peak force from MVCs were used to create the target forces for this task and may have influenced performance on the force-matching task as it is typically a rapid spike in the force-time curve, which could have made the higher force targets more difficult. However, it is frequently seen on force-time curves of LAM MVCs that participants demonstrate significant difficulty with sustaining a maximal effort contraction, so using an estimate of a participant's maximal effort over an extended time period may not have been as meaningful for creating the force targets. Moreover, our correlations indicated that LAM MVC peak force was not associated with accuracy measured during the force-matching task. Additionally, the lack of association between age and parity and RMSE suggests that LAM contraction awareness and control are likely not impacted by these factors. However, a larger and more diverse sample of participants is needed to confirm these findings.

4.6.3 Association between force-matching and elongation testing outcomes

There were no associations between findings on the active force-matching task (RMSE) and the passive elongation task (% correct), indicating that these tests assess different aspects of LAM proprioception. Similarly, a study assessing joint position and force sense at the ankle also found no association between comparable outcomes[59]. As such, we recommend using both tests when assessing LAM proprioception with an IVD.

4.6.4 Limitations and Future directions

This study represents an essential step in the generation of a standardized set of assessment protocols to evaluate LAM proprioception and builds on a previously reported force-matching task protocol[31] and an intravaginal sensation protocol[30] reported in the literature. The force-matching protocol described here includes an evaluation of real-time visual force feedback which

may be important for evaluating proprioceptive function, and this study provides a robust assessment of signal processing methods to establish a standardized approach. The passive elongation task employs a method of levels instead of the method of limits to determine changes in LAM length since the latter has been criticized in the literature[32].

We aimed to recruit a diverse sample of participants in terms of age, parity, and continence function, however, the resulting sample was not ethnically diverse, as the majority of the sample was Caucasian. Future research should consider the evaluation of proprioception in a more diverse sample that is age- and parity-matched. Moreover, a more detailed history of vaginal delivery interventions and the nature of any perineal tear or episiotomies may be considered in future research, as they could influence the function of local mechanoreceptors.

Future protocols may also consider exploring the influence of different instructions to reach specific targets, such as contracting slowly or quickly[41], as we did not provide participants with specific instructions on how to reach the targets in the force-matching task other than to reach but not exceed the target. It is also important to note that the IVD in this study assessed LAM force production only in the sagittal plane due to its anteroposterior alignment. Given the multiplanar anatomy of the LAMs[60], there may be other components of LAM proprioception in the other planes of movement that may be important for future research to consider.

4.7 Conclusions

Through this study, we created novel methods for assessing LAM proprioception using a mechatronic IVD. We developed two tasks to assess different aspects of proprioception: a passive elongation task to assess the ability to detect changes in LAM length and a force-matching task to assess LAM active tension sense. These assessments demonstrated that they

indeed assess different aspects of LAM proprioception and that there is a wide variety in LAM awareness among women. Furthermore, accuracy during the force-matching task was better at lower target forces (25% MVC) than higher target forces (75%MVC) and the use of visual feedback improved accuracy.

Based on the findings of this study, RMSE computed over a 0.25s or 0.50s window appear to provide stable estimates of force-matching accuracy, when computed between 1.00 to 1.50s after the initial force peak. Indeed, measures of RMSE acquired over different points of the force-time curve may be important, as RMSE tends to increase over time. However, given the impact of window length and location along the force-time curve over which the RMSE is computed, researchers should clearly report their methods and consider standardizing data processing methods so that valid comparisons can be made across studies.

This study represents an essential step in the development of a standard assessment for LAM proprioception. The next steps are to determine the repeatability of the proprioceptive outcome measures described here and to determine whether a ceiling effect may hinder group comparisons. The information gained from LAM proprioceptive assessments could improve our understanding of the role of the LAMs in pelvic floor disorders and may be used to refine current treatment strategies to include proprioceptive training.

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Chapter 5: Levator ani passive force, strength, power, motor control, and proprioception in women with and without stress urinary incontinence: a cross-sectional, observational study

Authors: Kaylee Brooks and Linda McLean

5.1 Abstract

Aims: The aims of this study were to determine (1) whether there are differences in levator ani muscle (LAM) passive force, strength, power, motor control, or proprioception between women with and without SUI, while concurrently considering parity, and (2) the feasibility of detecting an impact of LAM proprioception, passive forces and/or motor function on physiotherapy outcomes among women with SUI. **Methods:** Adult women naïve to LAM exercises were recruited from the local community into continent and SUI groups. In a supine position with an intravaginal dynamometer (IVD) in situ, participants were instructed to perform three maximal voluntary contractions (MVCs) followed by a series of as many quick repeated contractions as they could generate within 15s. LAM proprioception was evaluated using a passive muscle elongation task and a force-matching task performed with and without visual feedback. Women with SUI underwent a 12-week physiotherapy program and then completed a follow-up questionnaire to record their SUI symptoms. Between-group comparisons were made using analysis of variance (ANOVA) models, independent samples t-tests, or Mann-Whitney U tests as appropriate. **Results:** Thirty women (16 with SUI and 14 without) participated. No significant differences were found between women with and without SUI on any IVD outcome measures. Parous participants generated less force during a voluntary contraction (η^2 = .14), contracted (η^2 = .12) and relaxed (η^2 = .10) their LAMs more slowly than nulliparous participants. Accuracy among parous participants was less influenced by the provision of visual feedback on the force-

matching task than nulliparous participants (η^2 = .16). There was no impact of continence status or parity on the ability to detect changes in LAM length on the passive elongation task. Women with SUI who were cured with physiotherapy did not demonstrate differences in LAM passive or active force assessed prior to the intervention compared to those who were not cured. However, the effect sizes from these measures suggest that they may generate (d = .84) and release (r = .35) force more slowly during MVCs, perform more quick repeated contractions (d = 1.14) in 15s and be less accurate at force-matching (η^2 = .23) before treatment compared to those who are not cured. **Conclusion:** While women with SUI did not demonstrate impairments in LAM force-generating capacity or proprioception, parity appeared to impact these outcomes and should be investigated further, as parity is a risk factor for the development of pelvic floor disorders. The results also suggest that those with SUI who are cured with a physiotherapy intervention may be those who demonstrate lower LAM power and higher error in proprioceptive measures compared to those who are not cured. Further investigation is warranted.

5.2 Introduction

Stress urinary incontinence (SUI) affects 25% of women in Canada[1], yet despite its high prevalence and knowledge of risk factors such as parity[2,3], its pathophysiology remains unclear. Among theories of SUI pathophysiology, weakness of the levator ani muscles (LAMs)—which help to prevent urine leakage by lifting the bladder and compressing the urethra[4–6]—is thought to contribute to SUI pathophysiology[6]. While training the LAMs does cure and reduce SUI symptoms in up to 70% of SUI cases[7], empirical evidence is lacking to support the assumption that LAM weakness is a contributor to SUI[8–10]. Indeed, some reports suggest that women with SUI demonstrate lower LAM strength[11–16] compared to continent women, while others have found no differences in LAM strength between women with and without SUI[8–10]. However,

methods used to assess LAM strength have varied, with some studies[11,14] relying on manual palpation assessment which is not reliable[17].

More recent research has incorporated intravaginal dynamometry in LAM function assessments[9,18], and this approach has quickly become the criterion standard for the objective assessment of passive (stiffness) and active (strength/power/endurance) LAM characteristics[6,18,19]. Using an intravaginal dynamometer (IVD), Morin et al. [9] found that passive forces while the LAMs were at rest were significantly higher in women with SUI compared to their continent counterparts but there was no difference in LAM strength between the groups. They also found that women with SUI generated force more slowly during voluntary contractions and produced fewer quick contractions within 15s than their continent counterparts; all participants were parous individuals. This finding was consistent with previous work by Madill et al.[20] who reported that during coughing, women with SUI generated closure force more slowly than those without SUI, when using pressure sensors embedded in the anterior and posterior walls of an intravaginal probe. As such, IVD assessments that go beyond LAM strength alone may reflect the functional changes that contribute to SUI pathophysiology and further functional tests should be considered.

LAM functional testing may include examinations of different aspects of active and passive force generating capacity and proprioception, as is done in peripheral muscle assessments[21]. Proprioception, defined as the perception of joint/limb position, force generation, and joint/limb movement[22,23], has a demonstrated impact on motor function in peripheral limbs[23,24] and on rehabilitation outcomes[24,25]. Indeed, injured individuals often exhibit changes in the proprioception of injured joint/limb compared to the uninjured limb and to uninjured individuals[25,26]. Proprioception may therefore also be of importance to SUI pathophysiology[27] as

changes in LAM motor control have been identified as a potential contributing factor, including altered muscular activation patterns compared to continent women during voluntary contractions[8], coughing[20], and postural perturbations[28], asymmetry during LAM contractions[29], and a slower relaxation of the LAMs after a quick contraction[30]. Additionally, there are anecdotal reports from physiotherapists that some women with SUI demonstrate difficulties with LAM relaxation, but there are no reports in the literature of similar measures being evaluated with an IVD.

Measuring LAM function and proprioception may also improve our understanding of the mechanism through which physiotherapy enhances urinary continence. While pelvic floor muscle training is effective for SUI symptom reduction as stated above, it only offers a complete cure to 56% of the those that complete it[7]. Several models predictive of women's success with physiotherapy for SUI have indicated that objectively measured LAM strength is not a significant contributor to symptom reduction[31,32]. Moreover, a recent report concluded that the extent of changes in LAM strength induced by physiotherapy were not associated with a proportional improvement in SUI symptoms[33]. As such, different aspects of LAM function (such as motor control and proprioception) may improve our understanding of both the pathophysiology of SUI and the mechanisms through which exercise-based treatments improve these symptoms.

The aim of this study was to use intravaginal dynamometry to compare LAM motor and proprioceptive function between women with and without SUI, and to identify candidate variables derived through dynamometry that may be relevant to the success of physiotherapy intervention for SUI.

The primary objectives were to:

a) Compare women with and without SUI on dynamometry-based active and passive measures of LAM function recorded during a maximal voluntary contraction (MVC) and a series of quick contractions, while considering parity as a potentially confounding variable.
b) Compare women with and without SUI on measures of LAM proprioception, including accuracy on a passive muscle elongation task and performance on a force-matching task, while considering parity as a potentially confounding variable.

The secondary objective was to perform a feasibility analysis to determine whether the aspects of LAM function and/or proprioception measured above might be relevant to physiotherapy outcomes. The measures of interest were:

a) Recruitment rate.
b) Protocol completion/ data loss.
c) Effect sizes for the passive and active dynamometry measures from objectives 1 and 2.

5.3 Methods

5.3.1 Participants

This study was approved by the Health Sciences and Sciences Research Ethics Board of the University of Ottawa for compliance with the ethical conduct of human research (H-07-20-5945) and COVID-19 safety precautions (Appendix A). See Chapter 3 for a description of the sample and recruitment.

5.3.2 Intravaginal dynamometer

The custom mechatronic IVD has been described previously[34] and demonstrates valid load measurement and speed control during bench testing, and reliable *in vivo* measurements of active and passive LAM forces [35]. The device was interfaced with a PowerLab data acquisition system (LabChart 8, ADInstruments, Colorado Springs, CO) and controlled using a custom computer program run through MATLAB™ (R2022a, Mathworks, Natick, MA). Prior to each participant's visit, a new set of IVD arms was 3D printed (Ultimaker S5, Ultimaker B.V., Geldermalsen, Netherlands) in biocompatible plastic. IVD arms were single-participant use. They were washed in soap and water, air dried, and then covered with a separate condom on each arm before use. Data processing was conducted off-line using custom scripts written in MATLAB (R2022a, Mathworks, Natick, MA) for all dynamometric variables. Each raw force-time curve was smoothed using a Butterworth filter (2nd order, dual pass, low pass, 5 Hz cut-off).

5.3.3 Procedure

See Chapter 3 for a description of the initial assessment and recording of demographic information. The researcher received >20 hours of hands-on training on the manual assessment of LAM function and on the use of the IVD from an academic pelvic health physiotherapist (10+ years of experience) who had used the device in research for over 2 years and was deemed to be competent at these skills.

The researcher provided instruction and feedback on proper LAM contraction through visual inspection and digital palpation to ensure that the contraction was performed correctly before collecting data with the IVD. A correct contraction was defined as a palpable attempt (at least a

flicker of muscle contraction, i.e., Modified Oxford Scale score of at least 1/5) to close the levator hiatus and lift the perineum with minimal use of accessory muscle contractions in the hip/gluteal region without bearing down or breath-holding. Following confirmation of a correct LAM contraction, the dynamometric assessment began. The IVD was first calibrated, then lubricant was applied to the condom-covered arms of the IVD, which were inserted into the participant's vagina, either self-guided or inserted by the researcher at the participant's request. The researcher confirmed the correct device positioning and participant comfort.

5.3.4 Maximal voluntary contraction task

The arms of the IVD were opened to 35mm at a speed of 20mm/s and the researcher monitored the forces on the computer to ensure that the stress relaxation response had stabilized before cuing the participant to contract. The participant was then instructed, upon the researcher's cue, to contract their LAMs as hard and as fast as they could over a 3s period. Standardized encouragement was used: "Breathe in, breathe out, and Squeeze, Squeeze, SQUEEZE, HARD, HARD, HARD!" and then "Relax, let the contraction go." MVCs were repeated 3 times with a minimum of 60s provided between trials to mitigate any effects of fatigue.

5.3.5 Fast contraction task

Next, the participant was instructed to contract their LAMs as hard and as fast as they could, relaxing their LAMs after each contraction, and repeating the contraction as many times as possible within a 15s period. This was done without coaching or encouragement, which could influence the number of force peaks recorded. When the participant was ready, the arms of the IVD were opened at 20mm/s to a 35mm diameter, and once the passive forces had stabilized, the researcher instructed the participant to begin performing as many fast, strong contractions as they

could. After 15s, the researcher signalled the participant to stop the contractions, relax their LAMs and wait for the IVD arms to close. This task was performed only once.

5.3.6 Proprioception tasks

Methods for evaluating the detection of changes in LAM length and force-matching accuracy were implemented based on the findings of Chapter 4. With the IVD in place, the reference diameter was identified as the opening diameter that produced a passive force between 1.4-1.5N, from which 2 more diameters were calculated, one that was 5mm larger and one that was 5mm smaller. For this test, the arms of the dynamometer were opened first to the reference diameter and then closed. Within 30s, the arms were opened again to the required test diameter, and the participant was asked to identify whether the test diameter was the same, larger or smaller than the reference diameter. Three trials of each test diameter were completed in a random order.

For the force-matching task, participants were asked to perform PFM contractions to reach but not exceed personalized force targets. Personalized targets were calculated as a percentage (25%, 50%, and 75%) of the participants' maximum contractile force as per formula 3.1. Three trials with visual feedback and three trials without visual feedback were performed at each target force.

Participants with SUI underwent a 12-week pelvic floor physiotherapy intervention at the clinic they had planned on attending *a priori*. See Chapter 3 for a description of the physiotherapy intervention and outcomes.

5.3.7 Sample size

To the best of the authors' knowledge, there were no reports in the literature comparing LAM proprioception between women with and without SUI at the time of protocol development. As such, the sample size estimate was based on effect sizes from a study by Morin et al. [7] where dynamometric outcomes of PFM function were compared between women with (n = 59) and without SUI (n = 30). Measures of passive forces (d = .86) with the LAMs at rest, RFD (d = .75), and number of quick contractions in 15s (d = .54) demonstrated moderate to large effect sizes. However, measures of LAM strength on voluntary contraction were non-significant in this study with no effect (d = .10). Using G*Power (version 3.1.9.7) and α=0.05; β=0.80, to detect large effect sizes, we estimated that a total of 52 participants would be required to meet the primary objective (n = 26 per group. To account for potential data loss, we increased the sample size per group to 30 participants.

A study by Dumoulin et al.[30] (cured n = 42; not cured n = 15) was considered for the sample size estimate, however, not enough information was reported to estimate an effect size for the sample size calculation. As such, we aimed to use the sample of 30 women with SUI recruited to address the primary objective to estimate the sample size required to detect group differences for the same outcomes in women with SUI who were or were not cured of SUI with a physiotherapy intervention.

5.4 Data processing and analysis

Data processing for the MVC task force-time curves was conducted using custom MATLAB (R2022a, Mathworks, Natick, MA) programs. Each raw force-time curve was smoothed using a 2nd order, dual pass, low pass (5 Hz 3dB cut-off) Butterworth filter. Outcome measures of interest from the MVC task included the stress-relaxation coefficient after initial arm-opening,

baseline force prior to the MVC, peak force, relative peak force, and RFD during the MVC, and RFR and baseline force after the MVC. All outcomes were calculated as previously described[35]. RFR is a new variable and was calculated as the slope of the curve (similar to the RFD) between a visually selected point at the end of the contraction and a second point visually selected as the return to baseline (See Figure 5.1). The outcomes of interest from the fast contraction task included the number of contractions in 15s and RFD of the first contraction. For the proprioception measures, outcomes included the percentage of correctly identified IVD diameters, the root mean square error (RMSE) from the target, and a difference measure between the no visual and visual feedback conditions; all proprioception outcomes were calculated as per the description in Chapter 4, Section 4.3.6.

All statistical tests were performed using IBM SPSS Statistical Software Version 25 (IBM Corp; Armonk, NY, USA). Descriptive and questionnaire data were assessed using Mann-Whitney U tests and Chi-Square analyses. All IVD outcomes were compared between women with and without SUI using two-way analysis of variance (ANOVAs) models, which included parity (coded as nulliparous/parous) as a between-subjects variable. The active LAM measures including peak force, relative peak force, RFD, and RFR were non-normal, however, because analyses of variance (ANOVAs) are known to be robust to normality violations[36,37], ANOVA models were used. Pairwise comparisons were used to assess any main effects and effect sizes were reported as partial eta squared. A mixed model ANOVA was used to assess the outcomes of the force-matching task with feedback type, target force, continence status, and parity as factors in the model; simple effects analysis was used to assess interactions, with partial eta-squared effect sizes. A second mixed model ANOVA was used to assess the impact of target force, continence status, and parity on the difference measure, calculated as the difference

between the two feedback conditions. Cure with physiotherapy intervention was defined as individuals that had scores of ≤4 on the ICIQ-FLUTS. A comparison between women with SUI who completed their planned physiotherapy intervention and were cured vs not cured was performed using independent t-tests or Mann-Whitney U tests depending on normality. Cohen's d or r effect sizes reported depending on which statistical test was performed. Lastly, a mixed model ANOVA was used to assess the impact of feedback conditions, target force, and cure status on accuracy during the force-matching task, and a second ANOVA was used to assess the impact of target force and cure status on the difference between the feedback conditions. Partial eta squared effect sizes were reported these models. P-values were not corrected as this study was exploratory and effect sizes were more relevant to informing future work.

Due to the conflicting findings of PFM function in women with and without SUI reported in the literature[6-14], we planned a preliminary analysis after reaching half of our estimated sample size (n = 30). At this checkpoint, the effect sizes for the differences between women with and without SUI were computed. If the effect sizes were moderate to large, recruitment would continue to the planned 60 individuals; if the effect sizes were nil to small, we planned to stop recruitment due to a low probability of detecting the expected differences.

5.5 Results

5.5.1 Sample characteristics

Thirty women participated (See Figure 5.2): n = 14 were continent and n = 16 reported symptoms consistent with SUI. The SUI group was older than the controls (49 ± 11 years vs. 38 ± 13 years; p=.01) but there was no significant difference in parity (control parous n = 6, SUI parous n = 12, p = .14) between groups (See Table 5.1). No participant in the sample smoked and

groups only differed on the urinary incontinence and filling subscale scores of the ICIQ-FLUTS (see Table 5.2).

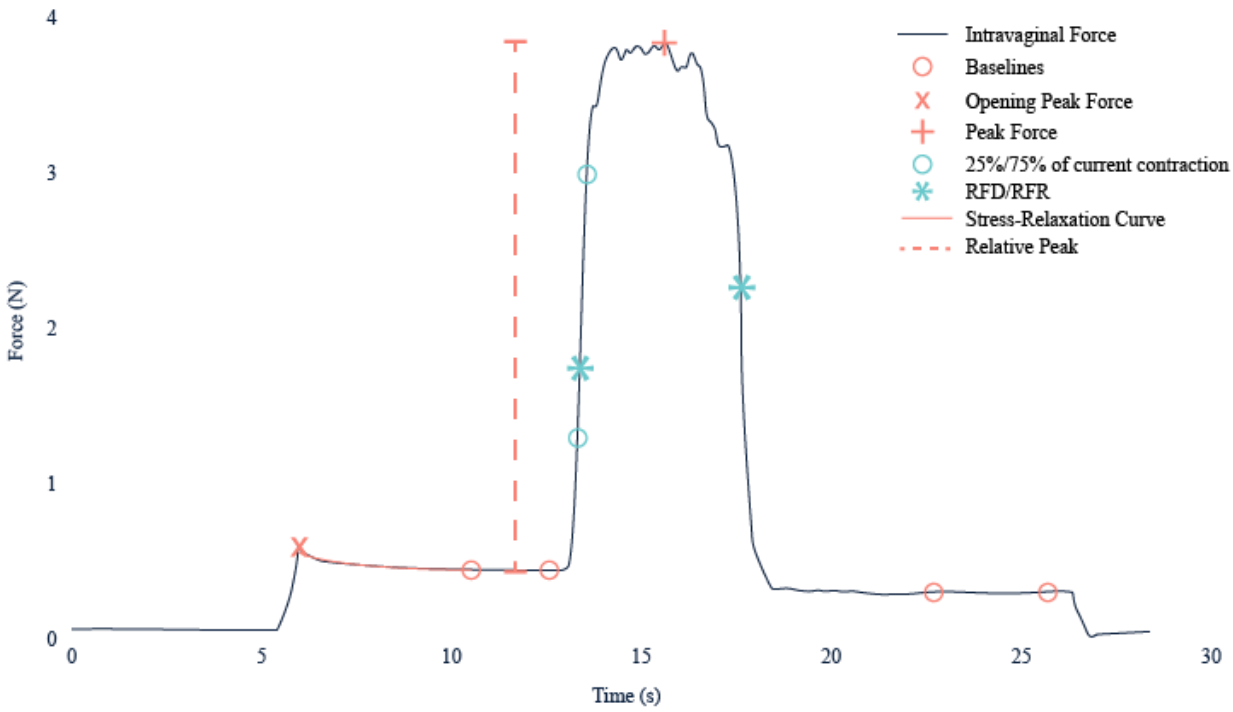

Figure 5.1 Raw force-time curve of a levator ani muscle maximal voluntary contraction displaying the outcomes of interest. Abbreviations: rate of force development (RFD); rate of force relaxation (RFR).

5.5.2 Recruitment rates and data loss

Participant recruitment began in December 2021 averaging one participant per month for the control group and two individuals per month for the SUI group. As of February 2022, recruitment for women with SUI reached a steady rate of 2-3 participants per month until June 2022, at which point recruitment stopped to ensure that they would have time to complete their physiotherapy treatment prior to the preliminary analysis in September 2022. All participants completed the dynamometric assessment apart from one individual for whom there are no force-

matching task outcomes due to equipment failure. No participants reported discomfort with the testing protocols.

Twelve of the 16 women with SUI attended physiotherapy as originally planned. One participant decided not to attend physiotherapy due to a lack of financial support, and two reported a lack of time/desire to partake in the treatment after the laboratory-based assessment. One further participant who underwent the physiotherapy intervention did not respond to the ICIQ-FLUTS questionnaire after their physiotherapy intervention and was therefore excluded from the analysis; the attrition rate was 25%. Women with SUI who were cured (n = 5) of their symptoms demonstrated lower scores on the ICIQ-FLUTS urinary incontinence subscale (i.e. mild SUI symptoms) prior to the physiotherapy intervention compared to women who were not cured (n = 7; p = .00, see Table 5.3), but did not differ on any other characteristics assessed by the questionnaires. While all participants did PFMT in their physiotherapy intervention, only nine women provided further details on the types of exercises performed in treatment: one participant stated that she was taught "The Knack", two participants reported performing PFM contractions in different positions and exercises, and five participants reported instruction on breathing and the pelvic floor.

5.5.3 Differences in maximal voluntary contraction characteristics between women with and without stress urinary incontinence

Women with SUI did not differ from continent women on measures of passive force at baseline prior to the MVC ($F(1, 26) = .11$, $p = .74$; $\eta^2 = .00$), nor after the MVC ($F(1, 26) = .23$, $p = .63$, $\eta^2 = .01$; See Figure 5.3). The stress-relaxation coefficient was not different between groups

($F(1, 26) = .54$, $p = .46$, $\eta^2 = .02$), and parity did not affect any of the passive force variables ($p > .05$).

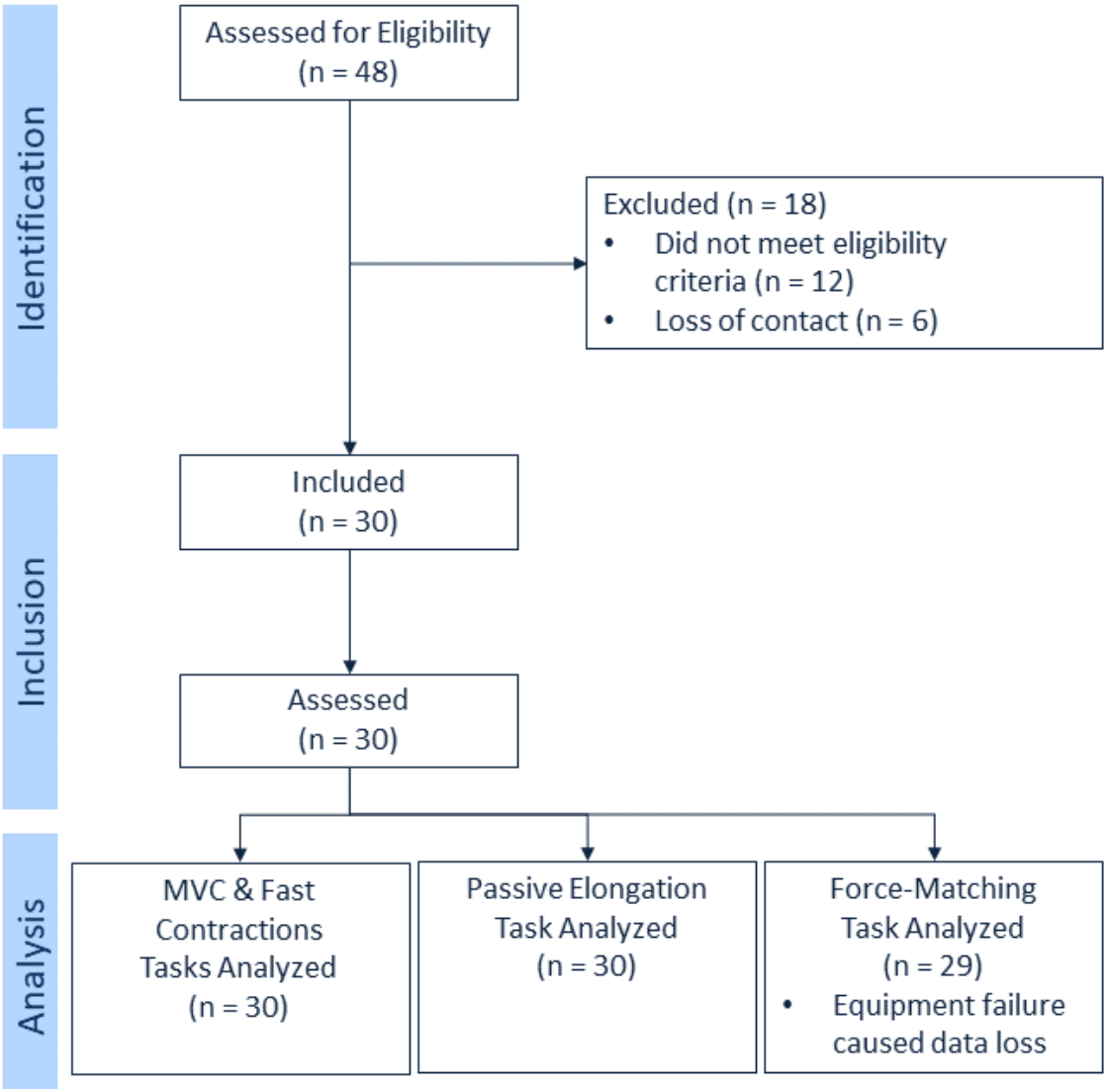

Figure 5.2 Flowchart participant recruitment and analysis

Table 5.1 Sample characteristics and demographic information

Demographics	Stress Urinary Incontinence Group (mean ±SD or n)	Control Group (mean ±SD or n)
Height (m)	1.66 ± .06	1.66 ± .05
Weight (kg)	72.33 ± 17.13	64.35 ± 14.56
Body Mass Index (kg/m^2)	26.39 ± 6.41	23.39 ± 5.49
Wasit-Hip Ratio (cm)	0.79 ± .07	0.79 ± .06
Parity		
0	4	6
1	1	2
2	6	4
>2	5	2
Menopause		
Yes	8	4
No	8	10
Ethnicity		
White	14	11
Middle Eastern	0	1
East/Southeast Asian	1	0
Mixed (Mediterranean/White)	0	1
Mixed (Indigenous/White)	1	0
Mixed (Black/White/French Canadian)	0	1
Highest Level of Education		
High School	1	1

College	0	1
Bachelors	9	7
Masters	5	4
Doctorate (MD or PhD)	1	1
Contraceptive Use		
Yes	1	4
No	15	10
Hormone Replacement Therapy Use		
Yes	2	1
No	14	13
Phase of Cycle During Testing		
Menstrual Cycle Days 1 – 14	1	5
Menstrual Cycle Days 15 – 28	7	5
No Cycle	8	4

Table 5.2 Questionnaire results of women with and without stress urinary incontinence.

Questionnaire	Stress Urinary Incontinence Group (mean ±SD or n)	Control Group (mean ±SD or n)	P value
ICIQ-FLUTS			
Urinary Incontinence (0 – 20)	**8.06 ± 3.70**	**1.36 ± 1.01**	**.00***
Filling (0 - 16)	**3.88 ± 2.36**	**1.93 ± 1.44**	**.03***
Voiding (0 - 12)	1.38 ± 1.78	0.79 ± 1.12	.50
ICIQ-VS			
Total (0 - 53)	4.81 ± 4.71	4.07 ± 3.67	.76
Sexual Matters (0 - 58)	7.38 ± 10.56	5.29 ± 7.87	.73
Quality of Life (0 - 10)	1.50 ± 2.19	0.29 ± 0.83	.09
ICIQ-B			
Bowel Pattern (1 – 21)	5.13 ± 1.55	5.64 ± 2.06	.48
Bowel Control (0 - 28)	1.67 ± 1.50	1.64 ± 1.15	.81
Quality of Life (0 - 26)	1.53 ± 2.72	0.79 ± 1.67	.45
FSFI[+]			
Total (2 - 36)	25.76 ± 4.79	24.46 ± 5.87	.76

Bolded* values are significant at the $p < .05$ level. [+]the total score does not include the three individuals who reported no sexual activity within that last 4 weeks. Abbreviations: International Consultation on Incontinence Questionnaire (ICIQ) - Female Lower Urinary Tract Symptoms (ICIQ-FLUTS); ICIQ-Vaginal Symptoms (ICIQ-VS); ICIQ-Bowel (ICIQ-B); Female Sexual Function Index (FSFI); stress urinary incontinence (SUI).

Table 5.3 Questionnaire results of women with SUI who were cured or not after a physiotherapy intervention.

Questionnaire	**Cured (mean ±SD)**	**Not Cured (mean ±SD)**	**P value**
ICIQ-FLUTS Before Physiotherapy			
Urinary Incontinence (0 – 20)	**6.20 ± 1.30**	**11.14 ± 2.97**	**.01***
Filling (0 - 16)	2.20 ± 1.30	4.86 ± 2.67	.08
Voiding (0 - 12)	2.00 ± 2.35	1.14 ± 1.86	.54
ICIQ-VS			
Total (0 - 53)	4.80 ± 3.03	4.29 ± 4.79	.56
Sexual Matters (0 - 58)	13.80 ± 13.79	4.29 ± 7.52	.17
Quality of Life (0 - 10)	2.80 ± 2.95	1.14 ± 1.86	.20
ICIQ-B			
Bowel Pattern (1 – 21)	5.40 ± 1.34	4.67 ± 1.51	.45
Bowel Control (0 - 28)	1.80 ± 1.64	1.33 ± 1.03	.70
Quality of Life (0 - 26)	2.00 ± 1.87	0.17 ± 0.41	.09
FSFI[+]			
Total (2 - 36)	24.96 ± 5.87	26.80 ± 3.64	.54
ICIQ-FLUTS After Physiotherapy			
Urinary Incontinence (0 – 20)	**3.40 ± 0.55**	**9.14 ± 3.39**	**.00***
Filling (0 - 16)	1.40 ± 0.89	3.29 ± 2.06	.11
Voiding (0 - 12)	1.20 ± 1.30	0.86 ± 1.46	.64
Global Rating of Patient Satisfaction and Perception of Improvement Questionnaire			
Q1. Patient satisfaction with progress. (*n*)			

Completely	3	3	-
Somewhat	2	4	-
Not at all	0	0	-
Q2. How patient feels overall (*n*)			-
Much Better	2	1	-
Better	3	4	-
About the Same	0	2	-
Worse	0	0	-
Much Worse	0	0	-
Patient Estimated Percent Improved	66.60 ± 28.06	43.57 ± 22.55	-

Bolded* values are significant at the $p < .05$ level. [+]the total score does not include the three individuals who reported no sexual activity within that last 4 weeks. Abbreviations: International Consultation on Incontinence Questionnaire (ICIQ) - Female Lower Urinary Tract Symptoms (ICIQ-FLUTS); ICIQ-Vaginal Symptoms (ICIQ-VS); ICIQ-Bowel (ICIQ-B); Female Sexual Function Index (FSFI); stress urinary incontinence (SUI); stress urinary incontinence (SUI); pelvic floor muscle training (PFMT).

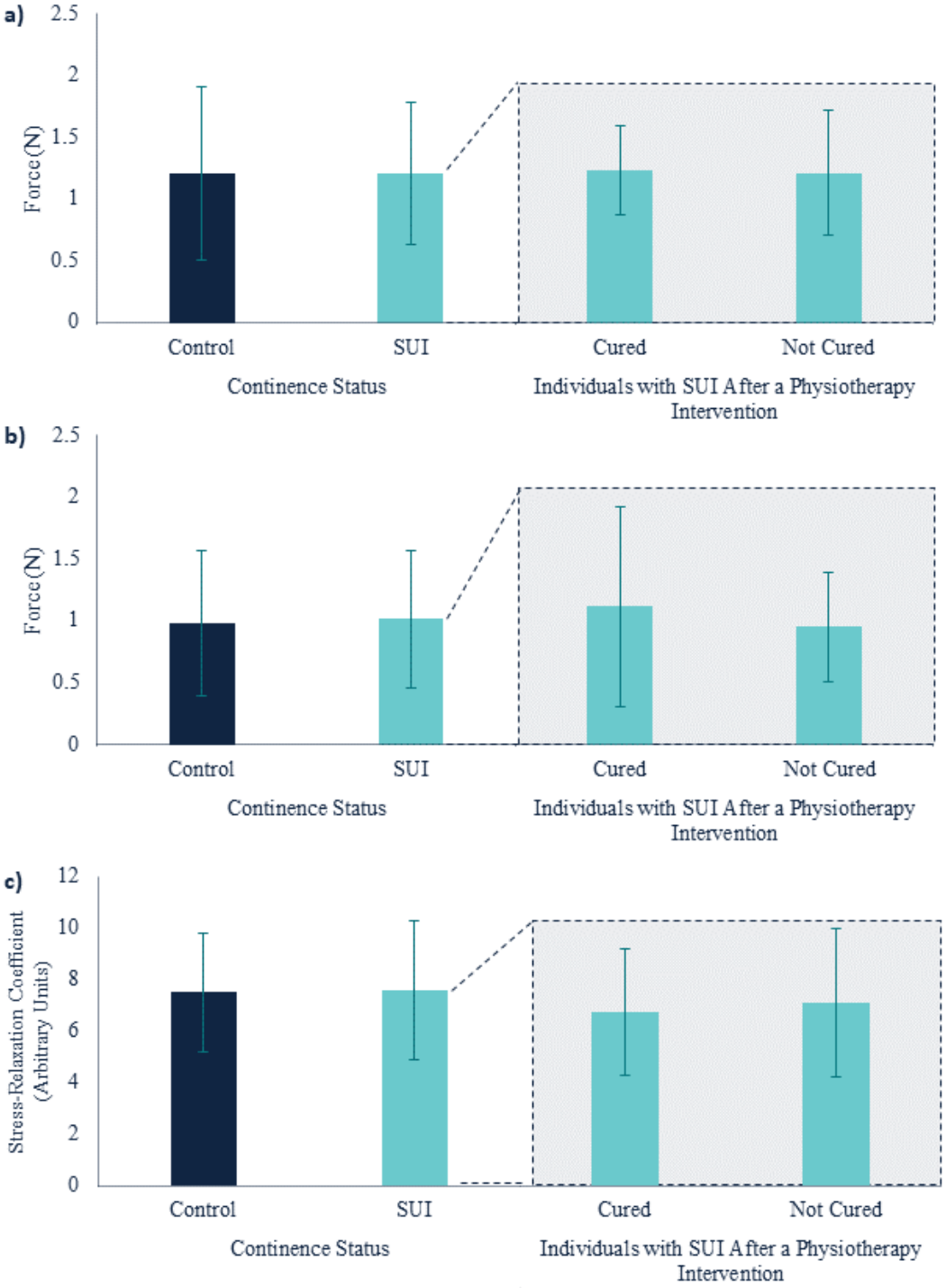

Figure 5.3 Passive LAM characteristics of women with and without stress urinary incontinence and the characteristics of those women with SUI after a physiotherapy intervention; a) Baseline force before an MVC, b) Baseline force after an MVC, c) Stress-relaxation coefficient prior to an MVC. Error bars are standard deviations; Cured and Not Cured are women from the SUI group who completed 12 weeks of physiotherapy. Abbreviations: stress urinary incontinence (SUI); maximal voluntary contraction (MVC); levator ani muscle (LAM).

Women with SUI did not differ from those without SUI in terms of peak force ($F(1, 26) = .05$, $p = .83$, $\eta^2 = .00$) or relative peak force reached during the MVC ($F(1, 26) = .16$, $p = .69$, $\eta^2 = .01$; Figure 5.4); however, parity was trending towards significance in both models with moderate effect sizes that nearly reach the cut-off for large effects ($\eta^2 = .14$), suggesting that parous women reached lower peak forces (2.88N ± 1.82; $F(1, 26) = 3.60$, $p = .07$, $\eta^2 = .12$) and relative peak forces (1.82N ± 1.49; $F(1, 26) = 3.16$, $p = .07$, $\eta^2 = .12$) during the MVC compared to nulliparous women (peak 4.59N ± 2.50, relative peak 3.17N ± 1.85; See Figure 5.5). Controls and women with SUI also did not differ significantly on RFD ($F(1, 26) = .31$, $p = .58$, $\eta^2 = .01$) of the MVC nor the RFR ($F(1, 26) = .15$, $p = .70$, $\eta^2 = .01$) after the MVC. Parity was again trending toward significance in the models with moderate effect sizes that nearly reach the cut-off for large effects ($\eta^2 = .14$), suggesting that parous women demonstrated slower RFD (4.35N/s ± 3.44; $F(1, 26) = 3.43$, $p = .08$, $\eta^2 = .12$) and slower RFR (2.96N/s ± 3.87; $F(1, 26) = 2.88$, $p = .10$, $\eta^2 = .10$) than nulliparous women (RFD 7.23 ± 3.62; RFR 5.22N/s ± 3.87).

5.5.4 Differences in the number of fast repeated contractions performed in 15 seconds between women with and without stress urinary incontinence

Women with SUI (8.69 ± 3.22) did not differ from the continent women (9.69 ± 4.09) in the number of contractions produced during the 15s time interval ($F(1, 26) = .60$, $p = .45$, $\eta^2 = .02$). RFD of the first contraction in the series of repeated contractions was log-transformed due to skewness in the data. Controls and those with SUI did not differ on the RFD of the first contraction of the series ($F(1, 26) = .09$, $p = .77$; $\eta^2 = .00$; See Figure 5.6).

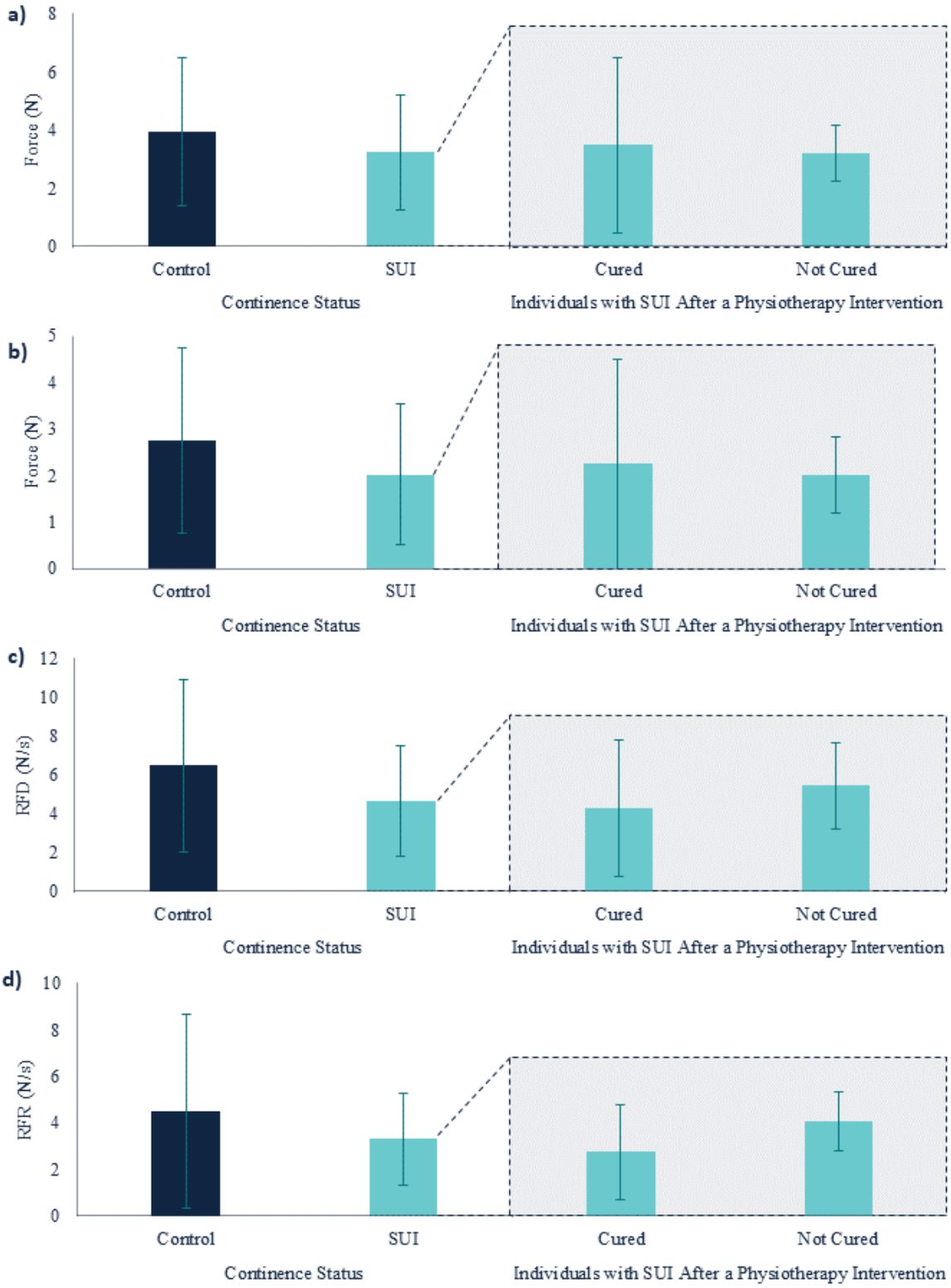

Figure 5.4 Active LAM characteristics of women with and without SUI and the characteristics of those women with SUI after a physiotherapy intervention a) Peak force during an MVC, b) Relative peak force during an MVC, c) RFD during an MVC, d) RFR after an MVC. Values reported are raw values not log transformed; Error bars are standard deviations; Cured and Not

Cured are women from the SUI group who completed 12 weeks of physiotherapy; stress urinary incontinence (SUI); rate of force development (RFD); rate of force relaxation(RFR); maximal voluntary contraction (MVC); levator ani muscle (LAM).

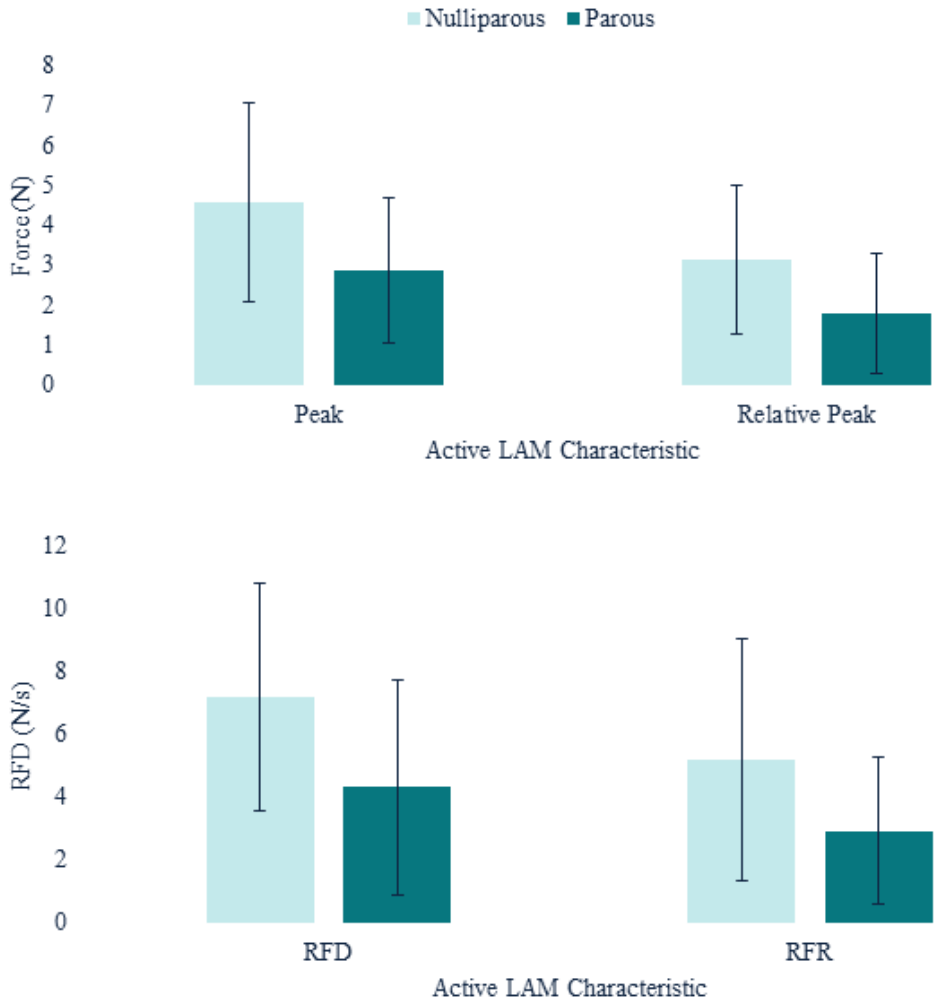

Figure 5.5 The impact of parity on active levator ani muscle characteristics regardless of continence status. error bars are standard deviations; rate of force development (RFD); rate of force relaxation (RFR); levator ani muscle (LAM).

An interaction between group and parity, while not significant, demonstrated a moderate effect size ($F(1, 26) = 2.69$, $p = .11$; $\eta^2 = .10$), suggesting that women with SUI who are parous may generate force more slowly ($p = .03$) than women with SUI who are nulliparous on the first contraction in a series of quick contractions (See Figure 5.6).

5.5.5 Differences in levator ani muscle proprioception between women with and without stress urinary incontinence

The passive elongation task did not suggest that women with SUI differ from continent women in their ability to detect changes in LAM length ($F(1, 26) = .01$, $p = .91$, $\eta^2 = .00$), and parity did not influence performance on this task ($F(1, 26) = .32$, $p = .58$, $\eta^2 = .01$).

There was also no difference in performance on the force-matching task between women with and without SUI. There were main effects of feedback (sphericity assumed, $F(1, 25) = 10.86$, $p = .00$, $\eta^2 = .30$) and target force (Greenhouse-Geisser, $F(12, 50) = 33.35$, $p = .00$, $\eta^2 = .57$), indicating that women were more accurate in reaching their intended force target when visual feedback was provided and lower target forces were used, regardless of continence status.

There was an interaction between feedback and parity (sphericity assumed, $F(1, 25) = 4.87$, $p = .04$, $\eta^2 = .16$), suggesting that visual feedback may not influence accuracy among parous women, but that it may improve accuracy among nulliparous women (See Figures 5.7), with a large effect size.

There was no difference between target forces (25%, 50%, 75% of MVC) on the difference measure between the no visual and visual feedback conditions on the force-matching task ($F(2, 50) = .47$, $p = .63$, $\eta^2 = .02$). Nor was there an interaction between group (SUI or control) and target force ($F(2, 50) = .09$, $p = .92$, $\eta^2 = .00$). While not significant, there was a moderate effect size for an interaction between parity (parous/nulliparous) and target force ($F(2, 50) = 1.57$, $p = .22$, $\eta^2 = .06$), suggesting that parous women had smaller difference values than nulliparous women at higher target forces (50% and 75%) compared to the lower force target (25%; $F(1, 25) = 3.02$, $p = .10$, $\eta^2 = .11$).

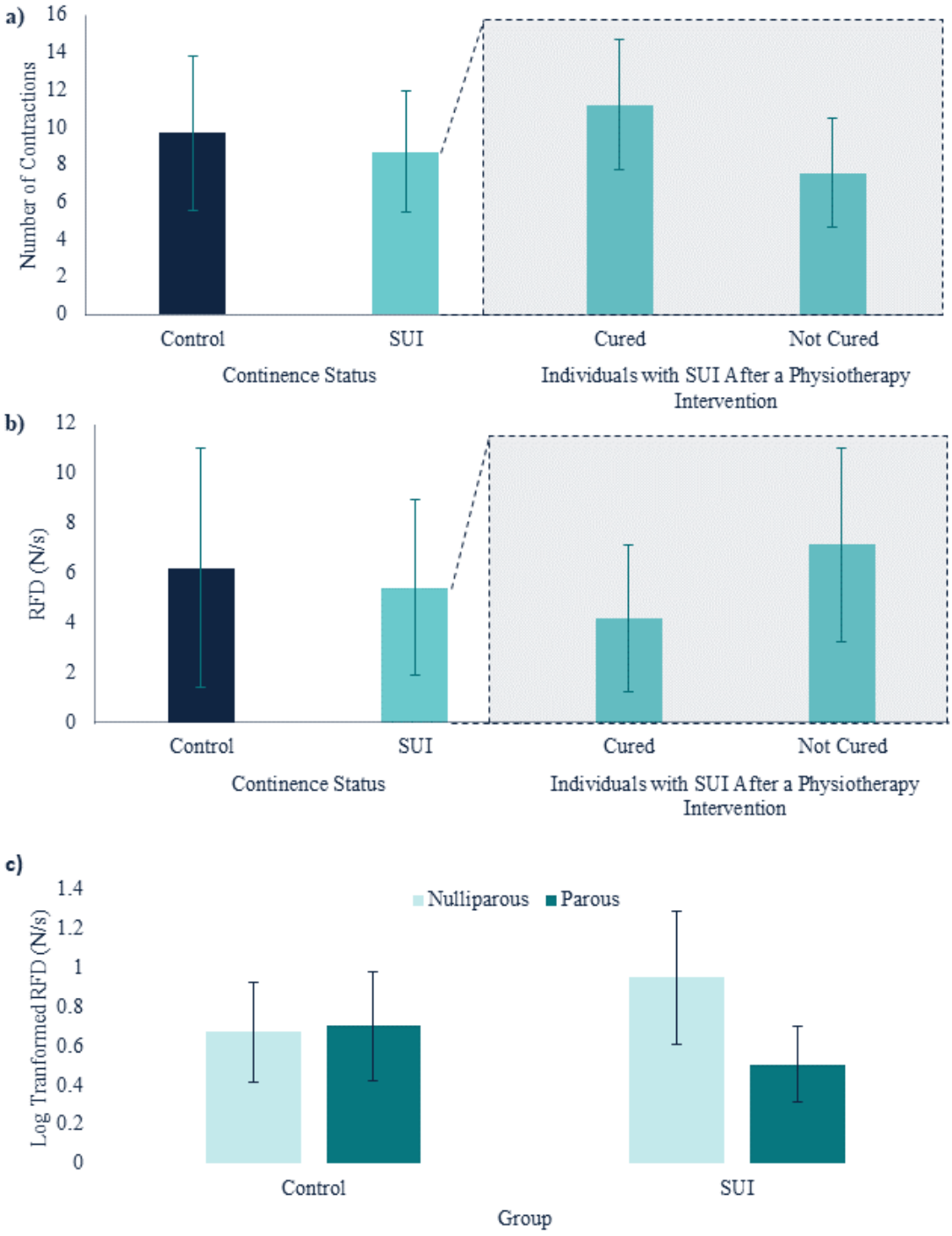

Figure 5.6 Number of LAM contractions and the RFD of the first contraction during a fast repeated contractions task between women with and without SUI as well as women with SUI who were cured or not; a) number of fast repeated contractions in 15 seconds, b) RFD of the first contraction, c) Interaction of continence status and parity on the rate of force development of the first contraction in a quick repeated contractions task. Error bars are standard deviations; Cured and Not Cured are women from the SUI group who completed 12 weeks of physiotherapist-supervised PFMT; stress urinary incontinence (SUI); rate of force development (RFD).

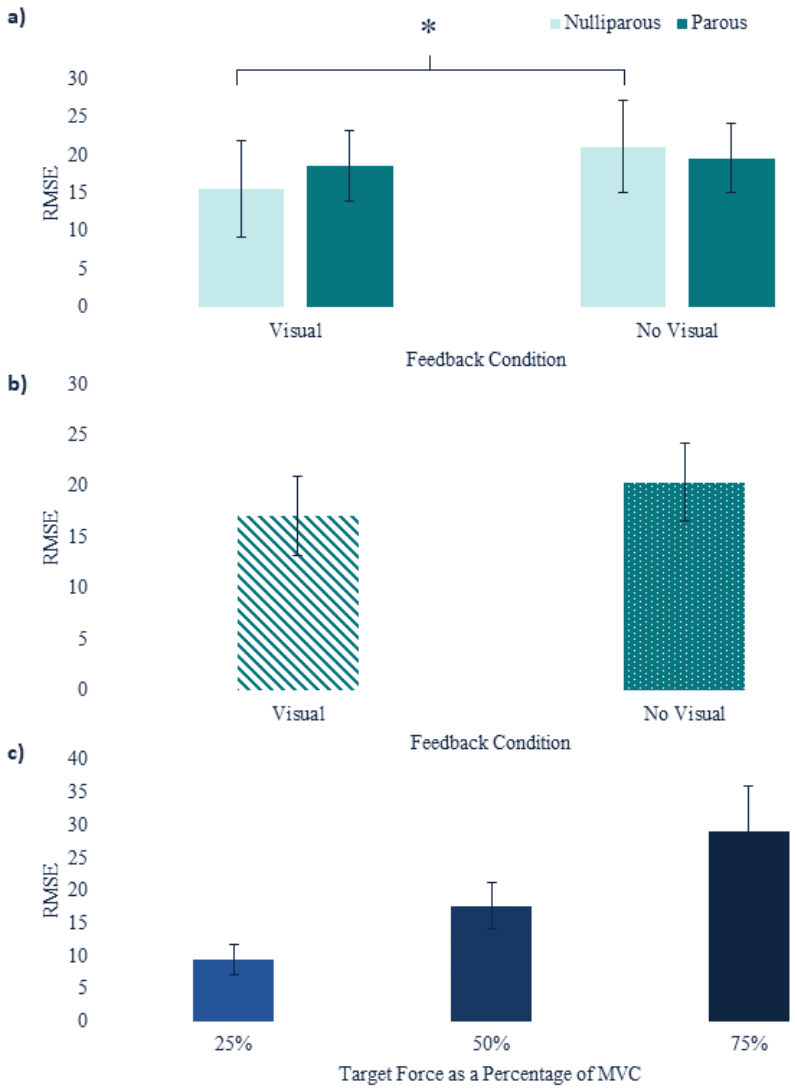

Figure 5.7 Factors influencing accuracy of force-matching by the levator ani muscles; A) Interaction of feedback condition (visual or no visual) and parity on accuracy, B) Main effect of feedback on accuracy, C) Main effect of target force on accuracy. * Denotes significance at $p < .05$; presented values are the estimated marginal means from the ANOVA; error bars are 95% confidence intervals; root mean square error (RMSE); levator ani muscle (LAM).

The between-subjects factor of the mixed model ANOVA found no differences in force-matching accuracy between those with and without SUI ($F(1, 25) = .00$, $p = .96$, $\eta^2 = .00$), but there was a significant difference based on parity ($F(1, 25) = 4.87$, $p = .04$, $\eta^2 = .16$). The difference measure was smaller among parous women (estimated marginal mean = 1.84, 95% CI

[-1.36, 3.52]) compared to nulliparous women (estimated marginal mean = 5.48, 95% CI [2.18, 8.79]).

5.5.6 Differences in levator ani muscle function and proprioception between women with stress urinary incontinence who were cured or not with physiotherapy

Those with SUI who were cured with physiotherapy did not differ significantly from those who were not cured on passive forces measured during dynamometer arm opening ($t(10) = -.06$, $p = .95$, $d = .03$), passive forces after an MVC ($t(10) = -.45$, $p = .67$, $d = .26$), and stress-relaxation coefficients ($t(10) = .24$, $p = .82$, $d = .14$); all measures had nil to small effect sizes. There was also no difference between those who were and were not cured of their symptoms in terms of LAM force-generating characteristics (non-normal data), including peak force ($U = 14.00$, $p = .64$, $r = .16$), relative peak force ($U = 13.00$, $p = .53$, $r = .21$), RFD ($U = 11.00$, $p = .34$, $r = .30$), and RFR ($U = 10.00$, $p = .27$, $r = .35$) with small to moderate effect sizes. However, those with SUI who were cured after the intervention tended to generate more quick contractions over a 15s interval (11.20 ± 3.49, $t(10) = -1.96$, $p = .08$) than those who were not cured (7.57 ± 2.94); this outcome had a large effect size, d = 1.14. RFD on the first contraction in the series of fast contractions was not different between groups (Cured 4.15N/s ± 2.94; Not Cured 7.13N/s ± 3.89; $t(10) = -1.96$, $p = .08$, d = .84; See Figures 4.3 and 4.4) but also had a large effect.

In terms of proprioception, women who were cured of their SUI symptoms (0.78 ± 0.21, $t(10) = -.17$, $p = .87$, $d = .01$) did not differ in their accuracy at detecting changes in muscle length from women who were not cured of SUI (0.79 ± 0.12). On the force-matching task, there was a trend for an interaction between cure status and target force (sphericity assumed, $F(2, 18) = 2.71$, $p = .09$, $\eta^2 = .23$), where the error was higher at the 75% target ($F(1, 9) = 5.45$, $p = .04$, $\eta^2 = .38$)

among women who were cured with physiotherapy (estimated marginal mean = 31.20, 95% CI [19.96, 42.43]) compared to those who were not cured (estimated marginal mean = 22.90, 95% CI [12.64, 33.15]; See Figure 4.8). At the lower force targets (25% and 50%), accuracy was comparable between the groups, $F(1, 9) = .43$, $p = .53$, $\eta^2 = .05$. Considering the entire sample, there was a significant main effect of target force (sphericity assumed, $F(2, 18) = 26.77$, $p = .00$, $\eta^2 = .75$), where accuracy was lower at higher target force levels, but there was no impact of feedback (sphericity assumed, $F(1, 9) = .25$, $p = .63$, $\eta^2 = .03$).

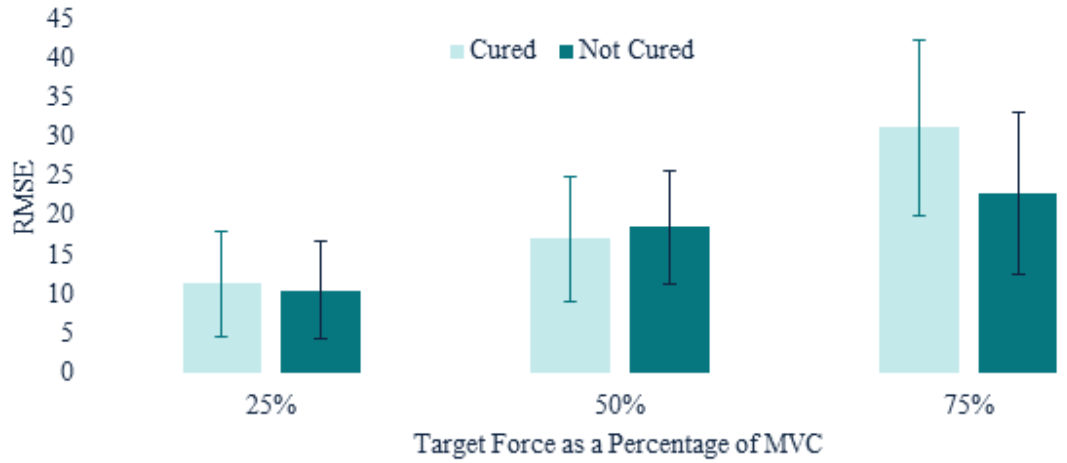

Figure 5.8 Displaying the trend between cure status and force matching accuracy at the different target forces among women with SUI who were and were not cured after 12-weeks of physiotherapy intervention. Values are the estimated marginal means from the analysis of variance model. Abbreviations: root mean square error (RMSE); maximal voluntary contraction (MVC).

The mixed model ANOVA for the difference measure (no visual – visual feedback) found no difference between target forces (25%, 50%, 75% of MVC) on the force-matching task ($F(2, 18) = .28$, $p = .76$, $\eta^2 = .03$). While not significant, there was a moderate effect size for an interaction between cure status (cured and not cured) and target force ($F(2, 18) = .64$, $p = .54$, $\eta^2 = .06$), suggesting that women who were cured displayed positive difference values at all target forces, while women who were not cured had negative difference values at the 50% and 75% force

targets, ($F(1, 9) = 1.02$, $p = .34$, $\eta^2 = .10$). This may suggest that while visual feedback improved performance on the task at all target forces for women who were cured, it did not improve performance for those who were not cured at the higher target force levels. The between-subjects factor of the mixed model ANOVA found no differences between those who were and were not cured with a physiotherapy intervention ($F(1, 9) = .09$, $p = .78$, $\eta^2 = .01$).

5.6 Discussion

The stopping criteria were reached at the planned preliminary analysis point (i.e. n = 30 participants completed the protocol), for between-group differences in measures of LAM passive and active forces, and proprioceptive function. The findings of this preliminary analysis did not indicate that LAM passive forces, strength, motor control, or proprioception were different between those with and without SUI. Parous women, however, demonstrated less force-generating capacity than nulliparous women, and, unlike nulliparous women, their accuracy on the force-matching task was not improved when visual feedback was provided. Of the 16 women who completed the protocol, 12 continued to the 12-week physiotherapy intervention as planned, while 4 (25%) did not. Of the 12 participants who completed the intervention, five were considered cured. The analysis indicated that differences in some IVD measures were feasible for future studies focused on predicting participant success with a physiotherapy intervention. Specifically, the effect sizes suggested that women who were cured of their SUI symptoms tended to generate more quick contractions over a 15-second time interval, were less accurate when attempting to reach the 75% MVC target force level and relied more on visual feedback to improve proprioception, and demonstrated slower RFD and RFR than those who were not cured.

5.6.1 Recruitment and sample characteristics

The study achieved a steady participant recruitment rate but was initially slow to start due to repeated closures related to the COVID-19 pandemic (including a completed laboratory shutdown for 8 months). These restrictions delayed the start date of recruitment and likely influenced participant retention in the physiotherapy intervention, which was low, despite recruiting women with SUI directly from physiotherapy clinics. The study sample included many individuals with children, which may have affected participant retention with recurring school closures and unpredictability in the availability of childcare for both data collection and/or physiotherapy treatment sessions. Recruitment and retention rates may be improved by offering childcare during data collection and physiotherapy treatment sessions, providing physiotherapy sessions at no charge and/or providing participants with compensation, and recruiting more clinical partners.

After reaching half of the intended sample size, the planned preliminary analysis suggested that the majority of effect sizes were nil to small for differences in LAM function between women with and without SUI. A previous study[9] with a sample size similar to the intended sample size found moderate to large effect sizes on all measures, apart from LAM strength, between women with and without SUI. As our sample at half the size only indicated no to small effects on all measures, further recruitment of participants was unlikely to change the findings.

Among women with SUI who were and were not cured of their symptoms through a physiotherapy intervention, future studies may plan to recruit approximately 64 individuals per group to adequately power a study aiming for the moderate to large effect sizes found in this study; this estimate may be increased to 80 individuals per group to account for the 25% attrition rate. This sample size estimation was calculated using G*Power (version 3.1.9.7) with α=0.05

and β=0.80 for moderate effect sizes. Given the rate of recruitment in this study, the recruitment period should be open for 2 to 3 years to achieve this sample size.

5.6.2 Objective 1: Differences in passive and active levator ani forces between women with and without stress urinary incontinence

5.6.2.1 Passive force outcomes

Through using an IVD to measure force at rest and in response to tissue elongation, no differences in passive forces before and after an MVC, and no differences in stress-relaxation responses were observed between women with and without SUI. These results corroborate the findings of other studies in which an IVD was used to assess passive tissue properties and found no association with continence status[15,16]. Conversely, Morin et al.[9] found that young, parous women with SUI demonstrated significantly lower passive forces than young, parous continent controls (ages ranged from 21-44 years). However, information on how recently these women had given birth was not reported, the AP diameters of the IVD were smaller than those used in the current study, and the measurement of passive force was not clearly reported. AP diameter and opening speed on IVDs are known to influence passive forces[38], though it is odd that differences between groups were found at the smaller AP diameters used by Morin et al.[9] and not the larger diameters used in the current study. The current sample included both parous and nulliparous women and had a larger age range (19 – 67 years), which may have contributed to the differences in results. Additionally, the study did not mention what section of the 15s recorded signal they used in the calculation of passive force. Further research into the passive characteristics of the LAMs and paravaginal tissues is needed to better understand the role they may play in SUI pathophysiology.

5.6.2.2 Active force outcomes

In this study, those with SUI did not demonstrate weakness of their LAMs relative to continent women. This finding is similar to that of Morin et al.[9] but is in contrast to the findings of Chamochumbi et al.[15], who found that women with SUI produced lower LAM forces than controls using an IVD. These differences may be related to variations in strength testing protocols, recruitment bias, or detection bias. Indeed, there has been a lot of contradictory research regarding the association between LAM strength and SUI[8–10,13–16], and no previous study reported that the investigators were blinded to continence status.

To mitigate urine leakage during tasks that challenge the continence mechanism, it is logical to expect that the PFMs must contract quickly enough to meet the demands imposed by the rapid rise in intra-abdominal pressure. RFD reflects muscle fibre type, contractile efficiency, and motor control[39], which are thought to be impaired among women with SUI[8,9,20,28,29,40]. The current sample demonstrated no differences in the ability of women with SUI to generate voluntary force rapidly when compared to their continent counterparts. The lack of standardization of measurement tools[9,20] and methods[39–41] makes it difficult to compare studies. For example, when calculating RFD, Morin et al.[9] did not disclose the method used for calculating slope (e.g. overall slope, average instantaneous slope, or slope over a given region of the force-time curve). The RFD calculation used in this thesis was chosen to ensure that the measure was representative of the linear portion of the curve to reduce the influence of acceleration or deceleration on the outcome[38]. Measurement tools, protocols, and analysis techniques require more standardization and better reporting to allow for comparisons of RFD across studies and to ultimately determine its impact on SUI pathophysiology.

The literature suggests that PFM recruitment and activation may present differently in individuals with severe and mild SUI symptom severity. Research into the automatic recruitment of the LAMs during a cough suggests that individuals with more severe SUI symptoms (n = 8) may display a slower rate of pressure generation compared to more mild cases (n = 8)[20]. Similarly, Smith et al.[28] reported higher PFM activation among women with mild SUI (n = 7) compared to those with moderate to severe SUI (n = 9) during challenges to postural stability in standing. Similar trends in voluntary recruitment of the LAMs have yet to be reported. While our sample had a range of symptom severity reported through the ICIQ-FLUTS urinary incontinence subscale (3 - 16), the sample was not designed to evaluate the impact of SUI severity on the outcomes. Further research is needed to better understand the mechanisms associated with SUI.

The number of quick contractions performed within 15s did not differ based on continence status alone. This contrasts with the findings of Morin et al.[9], who reported fewer contractions within the time limit and slower RFD on the first contraction in the series among women with SUI; findings which they suggested were reflective of poor LAM motor control. In the current study, only a tendency for parous women with SUI to generate force more slowly than nulliparous women with SUI on the first contraction in the series was found (η^2 = .10), which is similar to Morin et al.[9]. This observed trend may reflect the multifactorial pathophysiology of SUI[6], where LAM function may play a role in SUI pathophysiology for parous individuals, but not for nulliparae. However, this task may be influenced by the peak contraction forces reached in the 15s period, as those who generated lower forces may be able to perform more quick contractions than those who reached higher forces. Moreover, passive forces (baseline values at rest) before and after these quick contractions could have also influenced the number of contractions, as it was observed in testing that some women did not fully relax their PFMs between contractions.

These factors may have played a role in the differences between our findings and those of Morin et al.[9]; further research is needed to better understand the importance of being able to generate LAM contractile force rapidly, and the relative importance of voluntary contractions compared to automatic activation.

RFR was included as an outcome in this study due to anecdotal reports from pelvic floor physiotherapists that women with SUI often have difficulty relaxing their LAMs after contraction. However, there was no evidence of this in the current study. Only one previous study has investigated LAM relaxation among women with SUI, finding that, compared to continent women, those with SUI took longer to return to their baseline EMG activity levels after performing a fast contraction[30]. Relaxation is often defined as the ability to control muscle activity, such that muscles not currently being used for a task are quiet[42]. A reduced ability to relax the LAMs may reflect impaired motor control and/or higher excitability of corticomotor pathways. While there is evidence of altered LAM motor control in those with SUI[8,9,20,28,29,40], there is currently no description of the role of corticomotor excitability in this population. Further research is needed to explore measurements of pelvic floor relaxation as it may still play a role in SUI pathophysiology.

5.6.2.3 Proprioception outcomes

In this study, there was no difference in proprioception noted between women with and without SUI. This contrasts the findings of Kharaji et al.[43] who reported that women with SUI demonstrated better accuracy on a force-matching task than continent women. However, the methods reported by Kharaji et al.[43] lacked detail on processes for target force randomization and signal processing methods; particularly concerning the section of the force-time curve used to assess participant accuracy, which can be influenced by the high variance during the first second

of the task[44]. It was unclear how visual feedback may have been used in this study as the methods seemed to imply that visual feedback may have been included as a biofeedback training tool. However, an analysis of the impact of visual feedback on the force-matching task was not performed.

Across the entire sample, women were more accurate when visual feedback was provided and when contractile intensity was lower (25, 50% MVC vs 75% MVC). Better accuracy when visual feedback is provided may reflect deficits in proprioceptive feedback from the mechanoreceptors and surrounding tissues. Additionally, the reduction in accuracy with higher target forces may reflect a limited resolution of the proprioceptive system that may be impacted by contractile force; where the system may not be able to provide feedback on minor changes in force when there is already a significant amount of sensory information being provided during contraction. Interestingly, while there was no effect of SUI on force-matching accuracy, there was a significant interaction between feedback and parity on the force-matching task. The provision of visual feedback improved accuracy among nulliparous women but not among parous women. This finding was repeated in the difference measure between the feedback conditions which found that parous women demonstrated smaller differences than nulliparous women. This lack of improvement in accuracy among parous women when visual feedback is provided on a LAM force-matching task cannot be explained by impairments in LAM proprioception. Alternatively, these findings may suggest a reduced ability to integrate sensorimotor information among parous women, which warrants further research. Overall, this study provides no evidence that women with SUI have impaired LAM proprioception, though more research is needed to better understand the role of LAM proprioception in LAM function and the development of pelvic floor disorders.

5.6.3 Parity and levator ani function

Among all variables associated with active force generation, parity demonstrated moderate to large effect sizes. This suggested that nulliparous women were stronger, could generate force more quickly, and could relax faster than parous women. Similar findings have been reported when strength was measured by palpation and perinometry[45,46]. These findings suggest that pregnancy and vaginal delivery may alter LAM function. This is not surprising given the pelvic floor loading incurred during pregnancy, which may strain pelvic floor muscles, nerves, and connective tissues, as well as the increased risk for traumatic injury to these structures during vaginal delivery. Indeed, a recent cadaver study found evidence of greater muscle fibre length in the PFMs of parous women, which they suggested may result in reduced force production[47]. The findings of this study also indicated that there may be an interaction between parity and continence status on the RFD of the first contraction in a series of quick, repeated contractions, where parous women with SUI may demonstrate slower force generation than nulliparous individuals with SUI, though a similar interaction was not found in the RFD on an MVC. This trend may lend support to the theory that SUI is multifactorial[6] and that parity may be involved in a set of particular changes in structure and function that lead to the development of SUI symptoms in some individuals. More research is needed to further explore the role of parity on LAM function, and its impact on SUI pathophysiology and treatment outcomes.

5.6.4 Objective 2: Differences between women with stress urinary incontinence who are cured or not cured after a physiotherapy intervention

Predictive models of success with physiotherapy interventions for women with SUI have reported conflicting findings, where in some, low LAM function before treatment was associated with greater improvement[32,48], and others found that high LAM function before treatment was

associated with greater improvement[49]. One study also suggested that there is no association between SUI symptom improvement and aspects of LAM function measured prospectively through the PERFECT Scheme (which assesses LAM strength and aspects of motor control through palpation[50]), despite the finding that both SUI symptoms and PERFECT scheme scores improve after a physiotherapy intervention[33]. As has been found in other studies, women who were cured also demonstrated milder symptoms than those who were not cured[7], and LAM strength measured before the intervention was not different between groups[31,32].

The effect sizes found in this study suggested that women with SUI who were cured with a physiotherapy intervention displayed lower RFD (r = .30) and RFR (r = .35) during a maximum effort contraction, as well as decreased accuracy and more reliance on visual feedback at higher force targets on the proprioception task. Together, these findings suggest that physiotherapy interventions for women with mild to moderate SUI may have a greater impact when LAM power and relaxation are slower, and proprioception is reduced. This could suggest that to experience a cure with physiotherapy, one may need to have the capacity to increase force generation abilities and improve LAM proprioception; where individuals who are already able to quickly build and release force or are already accurate in sensing contractile force efforts may not experience symptom improvement with physiotherapy. However, more research is needed to understand the factors that are associated with a cure for SUI with physiotherapy interventions. The findings of this work indicate that assessments of particular aspects of LAM function using an IVD are feasible to perform in future work assessing characteristics that are predictive of cure with a physiotherapy intervention.

5.6.5 Strengths and limitations

The methodology chosen for this study was a strength, as it was designed to reduce bias in the results. To accomplish this, individuals naïve to PFM training were recruited, the assessor was blinded to the continence status of the participants, IVD arm diameters and target forces were randomized, and a careful assessment of specific regions along the force-time curve (as described in Chapter 4) were used. Moreover, the investigation of the impact of the visual system on force-matching task accuracy to examine proprioceptive acuity was a novel component of the protocol that, to the best of the authors' knowledge, has not been reported in previous research on similar tasks.

The lack of control over the physiotherapy interventions delivered in this study may be seen as a limitation, however, this was deliberate as the intent was to generate externally valid findings. In this way, the physiotherapy programs were individualized, and the methods of instruction and exercise parameters varied, which makes the findings more generalizable to current physiotherapy practices. However, the variability in the number of treatment sessions attended, adherence to the treatment, and the variety of exercises reported by participants may have influenced our cure rate. That said, stronger reporting protocols for the tracking of participant exercise programs and adherence to the training may further improve generalizability.

The cure criteria used in this study depended on the recall of leakage over the past 4-weeks using the ICIQ-FLUTS. This questionnaire was selected based on its strong measurement properties[51] and recommendation by the International Continence Society[52]. The criteria for a cure, ≤4 on the ICIQ-FLUTS UI subscale, was based on previous research[53,54] and allows for comparison across studies. Using this criterion, the cure rate observed in this study was 42%, which is in line with previous research[31,32,48,55,56]. Given the multifactorial nature of SUI, the use of a single

questionnaire may limit the extent of change noted in symptom reduction[52], however, based on the cure rate in this study, the cure criteria appear to be feasible.

As much of this work is exploratory, the effect sizes can be used to inform and power future studies investigating LAM function and proprioception, with a particular focus on women with SUI who are and are not cured with a physiotherapy intervention and parous and nulliparous women.

5.7 Conclusions

No differences were observed in the passive, active or proprioceptive function of the LAMs when women with SUI were compared to continent women. However, parity independently affected LAM force-generating characteristics. The lower maximum contractile force, slower force generation and relaxation, and lack of visual feedback influence on proprioception measures observed among parous women compared to nulliparae should be further investigated to see what role these differences may play in the development of pelvic floor disorders. Based on moderate effect sizes, women whose SUI symptoms were effectively cured through a physiotherapy intervention may demonstrate deficits in LAM power (RFD), motor control (RFR), and proprioception. As such, objective assessments of muscle power and motor control should be considered in future models aiming to predict success with a physiotherapy intervention, which may help us to understand the optimal patient characteristics and LAM training parameters for successful conservative management of SUI in women.

5.8 References

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Chapter 6: The relationship between light touch sensation at genital sites innervated by the pudendal nerve and stress urinary incontinence in women.

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6.1 Abstract

Background: Although research suggests that damage to the motor components of the pudendal nerve may be implicated in the pathophysiology of stress urinary incontinence (SUI) in women, the role of sensory impairment in the distribution of the pudendal nerve is largely unknown and has not been investigated using rigorous methodology.

Aim: The aim of this study was to investigate differences in light touch sensation thresholds within the sensory distribution of the pudendal nerve between women with and without SUI.

Methods: Thirty women, 16 with SUI and 14 healthy controls, underwent light touch sensation threshold testing at three locations normally innervated by the pudendal nerve: the posterior aspect of the urethral meatus, the middle of the perineum, and the external anal sphincter (EAS) on the right side. Two control sites were also tested, one at the right anterior third of the labia majora (innervated by the genitofemoral nerve) and one at the right ankle (innervated by a branch of the femoral nerve). Descriptive data were used to identify potential cases of sensory nerve impairment at each test site, based on sensation perception thresholds >3 standard deviations above the mean. Multiple linear regression models were used to assess the relationship between continence status and light touch sensation thresholds while accounting for age and parity.

Results: Four participants demonstrated outlier sensory thresholds each at only one genital site. Overall, incontinent women had higher sensation thresholds than continent women at the EAS

(R^2 = .29, p = .04) site but not at the urethral meatus (R^2 = .08, p = .58). The mid-perineal site (R^2 = .24, p = .08) and the labia majora site (R2 = .25, p = .07), though not significant, demonstrated a tendency to have higher light touch sensation thresholds among those with SUI compared to continent controls; the effect was mediated at the labia majora by age, and was significant only after an outlier was removed. Continence status had no effect on sensory thresholds at the ankle site (R^2 = .03, p = .86), and there was also no effect of age or parity.

Discussion: Light touch sensation thresholds in the pudendal nerve may be higher in women with SUI, however the models explained a minority of variance at each site and therefore other factors may be relevant. Those participants (n = 4) who demonstrated high sensation thresholds (>3SD) did so at only one site, suggesting that nerve impairments, when present, are localized to individual branches and/or receptor sites. Further research is needed to understand the causes and implications of the higher light touch sensation thresholds at the EAS among women with SUI.

6.2 Introduction

Stress urinary incontinence (SUI) is common among women[1], generally leading to embarrassing symptoms and impairing quality of life[2]. Despite its prevalence, the pathophysiology of SUI in women remains unclear; however, urethral and bladder neck structure and support, functional impairments of the urethral rhabdosphincter (UR) and levator ani muscles (LAMs), and changes in nerve function are thought to contribute[3].

The female-typical lower urinary tract, external genitalia, and the skin of the perineum are innervated by the pudendal nerve and its branches, which contain both motor and sensory fibers[4]. There is evidence of pudendal nerve damage and subsequent reinnervation among those with SUI, based on prolonged pudendal nerve terminal motor latency (PNTML) relative to controls at

the external anal sphincter (EAS) and/or circumvaginal musculature[5–9]. In clinical EMG assessments performed using concentric needle electrodes, women with SUI demonstrate higher fibre density at the EAS[7,10], lower turns-to-amplitude ratios and fewer turns per second in the UR[11], EAS, and LAMs[12], and slower motor unit recruitment of the UR[11] when compared to continent women. However, other studies have reported no differences in PNTMLs between women with and without SUI[7,13,14]. As there is no consensus on the impact of nerve damage and/or reinnervation processes on urinary continence, it is difficult to determine the extent of the involvement of nerve damage in the pathophysiology of SUI; especially given the likely variability in the presence, nature, and severity of pudendal nerve damage incurred due to life events such as pregnancy, parturition, and aging.

As there is some evidence of motor nerve damage in women with SUI, it is logical to expect to find changes in sensation in regions innervated by sensory fibers that travel along the same nerves. However, genital sensation has not been specifically evaluated in this population. The few published studies on genital sensation among women with SUI have included a variety of assessment approaches, and findings have been variable. Two studies involving quantitative sensory testing (QST) reported contrasting findings. The first study revealed that among women with self-reported sexual dysfunction, those with SUI had higher thermal and vibratory sensation thresholds in the genital region compared to continent women[15]. The other study found no difference between women with SUI and age-matched controls on vibratory sensory acuity[16] at the clitoris. However, sensation at the clitoris may not be representative of pudendal nerve sensory function because it has multiple innervations[17]. Two other studies assessed sensory acuity at skin sites innervated by the pudendal nerve using current perception threshold (CPT) testing. One study found no sensory differences among women with SUI, urgency urinary

incontinence, and mixed urinary incontinence[18] yet none of these groups were compared to continent women. The second study found that women with SUI had higher CPTs at the clitoris and urethra than continent controls[19]. However, CPT may not be a reliable method of sensory testing and does not represent real-world sensory inputs in comparison to QST methods[20]. It therefore remains unclear whether women with SUI experience sensory changes in the pudendal nerve distribution.

Current diagnostic tools for assessing sensation often include graded vibratory or thermal stimuli. However, a more affordable and accessible option is a set of monofilaments, such as the commercially available Semmes-Weinstein or Von Frey filaments. These filaments are commonly used to assess skin sensation changes found in carpal tunnel syndrome,[21] diabetic neuropathy[22], and nerve regeneration after breast surgery[23]. A previous study by Romanzi et al.[24] examined the use of monofilaments to assess genital skin sensation, finding that it demonstrated good test-retest reliability and that it was valid in determining the presence of sensory impairment within a small group of women with known impairments. The authors used the same sample of 32 participants to describe normative values, yet the sample included women with urinary incontinence (n=7), previous vaginal surgery (n=2), and previous abdominal-pelvic surgery (n=6) which may have influenced their findings. Further, information on incontinence subtype or surgical approach was not provided[24].

The aim of this study was to determine, using QST, if women with SUI demonstrate differences in light touch sensation thresholds in the areas of genital skin innervated by branches of the pudendal nerve compared to those without SUI.

6.3 Materials and methods

This study was approved by the Health Sciences and Sciences Research Ethics Board of the University of Ottawa for compliance with ethical conduct of human research and COVID-19 safety precautions (H-07-20-5945; Appendix A).

6.3.1 Participants

Women over the age of 18 years were recruited from the community and local pelvic health physiotherapy clinics. See Chapter 3 for a description of the data collection process and sample recruitment.

6.3.2 Monofilaments

The monofilaments used for QST were made from sterile suture material (Prolene, Ethicon Inc.; Surgilene, Davis and Geck) that varied in both length and diameter according to previously published protocols[25,26]. These monofilaments were designed to mimic the lower range of commercial Von Fey filaments, which include 14 filaments used to deliver forces from 0.0045g to 11.749g, with three additional filaments to exert even lower force levels from 0.0015g to 0.0035g. Each filament was clamped at the appropriate length using hemostatic forceps. A new set of filaments was used for each participant.

6.3.3 Procedure

Informed consent was acquired (Appendix G) and then the participants attended a 2-hour QST assessment in a laboratory setting. This assessment was the second visit embedded within a larger study protocol which included other assessments not relevant to the current study. The researcher performing the data collection was blinded to the continence status of the participant

for the duration of the study. Demographic information was recorded using standardized methods (Appendix H) and a basic genital inspection was performed by the researcher to ensure that there was no evidence of infection, mass(es), or fissure(s) that would make the assessment uncomfortable for the participant and/or alter sensation which would have resulted in exclusion (no participants were excluded for this reason). During the QST assessment, the participant was in the lithotomy position with the lower legs supported. The room temperature was held constant at 23 degrees Celsius.

Light touch thresholds were assessed using a 2-down-one-up staircase method which requires two positive responses (e.g. 'Yes, I felt something') to the same stimulus before moving to the next lower force, while only one negative response (e.g. 'No I didn't feel anything') is required to move up to the next higher force[27]. Filaments were applied perpendicularly to the skin surface and the assessor manually applied force to bend the filament to form a semi-circle (See Figure 6.1). Filaments were held in place for approximately 1.5s and the inter-stimulus interval was approximately 5s. A custom computer program was used to generate the sequence of application of filaments, randomly embedding blank trials 20% of the time, during which a filament was picked up and held near the participant but did not touch them. Each assessment began with the smallest filament (Filament #1) and, to reduce testing time, every third filament was applied until the participant provided two positive responses to the same stimulus. After this, the computer program prompted the researcher to apply the next thinner filament until a 'No' response was reached, then the computer prompted for the next thicker filament until two 'yes' responses were obtained, and so on. The computer program stopped after 5 reversals and the last 4 reversals in filament size were averaged to determine the tactile threshold. At the first 'Yes' response, the participant was also asked to choose an adjective from a list to describe the sensation (e.g.

ticklish, mild, prickling, tingling, brushing, dull) which was recorded. These adjectives were selected based on previous research in a sample of women with vulvar pain which used the same assessment technique[25].

6.3.4 Sensation testing sites

The testing sites included one control site at the right ankle approximately 2cm above the medial malleolus, which is innervated by the medial saphenous nerve (a cutaneous branch of the femoral nerve, including contributions from L3-L4 nerve roots), and a genital control site located on the anterior third of the right side of the labia majora, which is innervated by the genitofemoral nerve (including contributions from L1-L2 nerve roots). The three pudendal nerve sites (nerve roots S2-S4) included the 6 o'clock position of the urethral meatus, the middle of the perineum, and approximately 2cm to the right of the EAS (Figure 6.2). A surgical marker was used to mark the test sites to ensure sensation was assessed at the same location each time, and the protocol was repeated three times at each site.

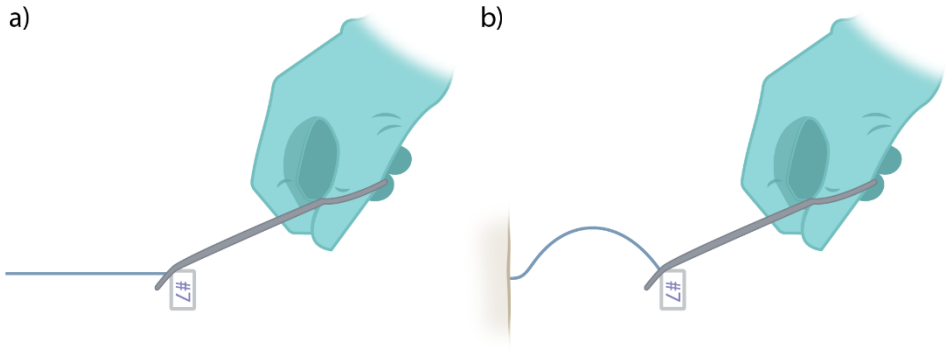

Figure 6.1 Application of monofilaments to the skin surface for quantitative sensation testing of light touch sensory thresholds. a) Displaying the filament and forceps b) Displaying the curvature of the filament with gentle force applied.

6.3.5 Sample size

A previous report of genital sensation[15] in women with SUI showed moderate to large effect sizes. Genital sensation thresholds for warm, cold, and vibratory stimuli between women with a self-reported sexual dysfunction with and without SUI, as reported by Lowenstein et al.[15], all showed large (≥0.8) Cohen's d effect sizes. In particular, the clitoral stimulation sites reported group differences in warm (Continent women n = 114 [38.5ºC ±0.19], women with SUI n = 63 [41.3ºC±0.36]) and vibratory (Continent women [1.8µm ±0.8], women with SUI [5.8µm±0.2]) sensation thresholds. Using G*Power (version 3.1.9.7) and α=0.05; β=0.80, to detect moderate effect sizes for genital sensation thresholds a sample of 14 women per group was needed. As such, we aimed to recruit a total of 15 participants per group to account for possible data loss.

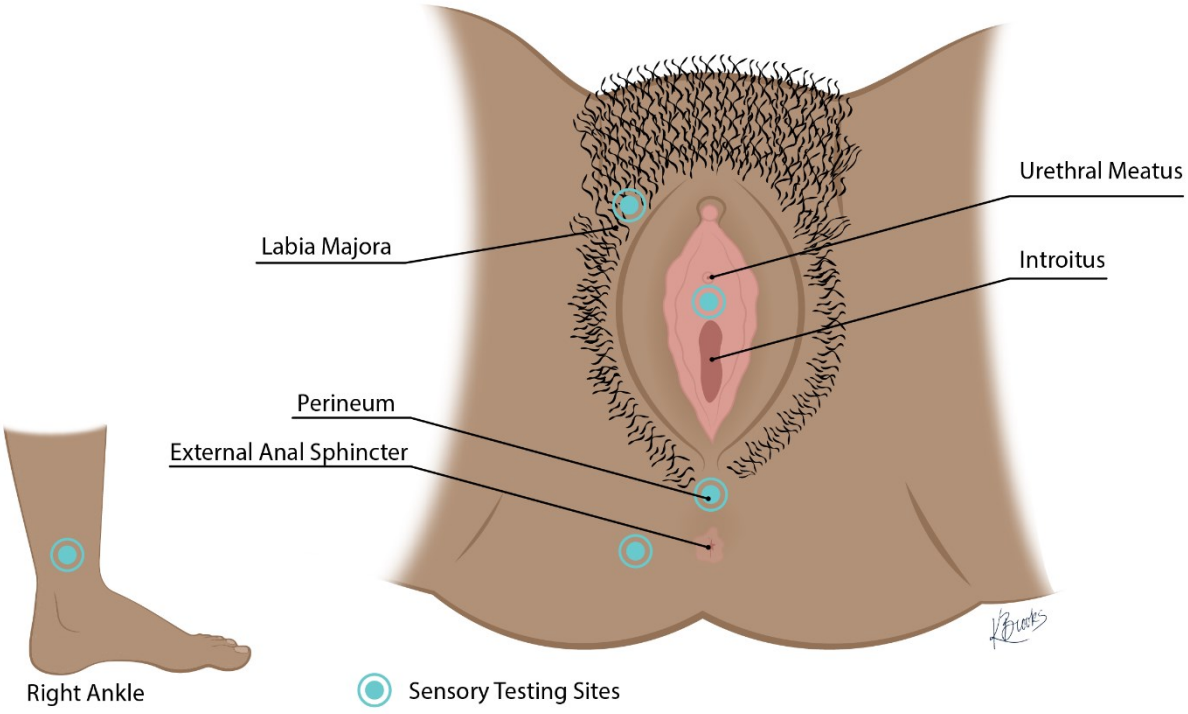

Figure 6.2 Light touch sensation testing sites at the right labia majora, posterior aspect of the urethral meatus, middle of the perineum, right of the external anal sphincter, and right ankle.

6.4 Data Analysis

Demographic and questionnaire data were compared between the control and SUI groups using Mann-Whitney U tests, while categorical data were compared using Chi-Square tests. For sensory thresholds, an average of the 3 trials was retained (in mN) as the outcome at each site. Histograms were generated for each group and outliers were identified as thresholds that were > 3 standard deviations (SD) from the mean. A mixed model analysis of covariance (ANCOVA) was planned to compare sensation thresholds between groups across all sites, while including age and parity as covariates. However, the data violated the assumptions of ANCOVA and as such were analyzed using linear regression models to account for the potential mediating effects of age and parity while assessing the relationship between sensation thresholds and continence status (continent or SUI). As the data were not normally distributed, each model was bootstrapped using the bias-corrected and accelerated method based on 1000 samples[28]. As outliers can influence regression models, two models were created if outlier(s) (>3SD from the mean) were present: one including the outlier(s) and one without the outlier(s) to investigate the impact of outliers on the model. Data were reported as means and SD unless otherwise specified. Word choices were displayed in pie charts as the percentage of usage in each group. Alpha level was set at .05.

6.5 Results

Forty-eight women were screened for eligibility. Among those, 30 were eligible, provided informed consent to participate, and completed the assessment (See Figure 6.3). Data from one participant were subsequently excluded from the analysis due to the participant having reported the use of over-the-counter pain medication prior to testing, thus the analysis was based on a sample of n = 29: 16 with SUI and 13 continent women.

6.5.1 Sample characteristics

The participants with SUI were significantly older (median (interquartile range) = 51 (16) years; p = .03) than those in the control group (35 (24) years), however, there was no difference in parity between the groups (p = .14). Table 6.1 presents sample characteristics. Women with SUI did not differ from continent women on measures of vaginal and bowel symptoms or sexual function based on the questionnaire data, but they had significantly higher scores on the ICIQ-FLUTS urinary incontinence and filling symptoms subscales compared to continent controls (See Table 6.2).

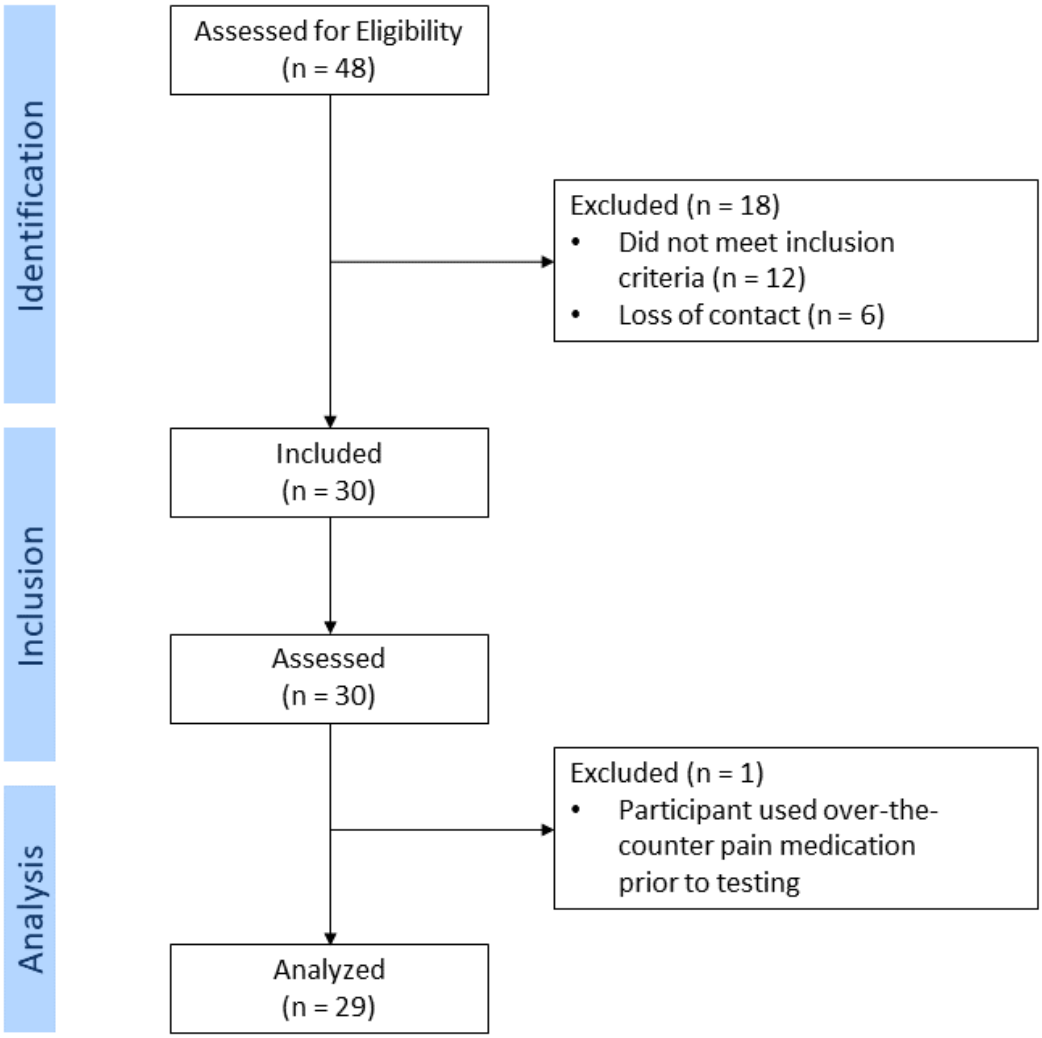

Figure 6.3 Flowchart participant recruitment and analysis.

Table 6.1 Sample characteristics and demographic information reported as medians and interquartile ranges or frequency of cases.

Demographics	Control	Stress Urinary Incontinence
Age (Years)	35 (24)	51 (16)
Height (m)	1.68 (0.08)	1.64 (0.08)
Weight (kg)	62.60 (26.08)	70.31 (22.34)
Body Mass Index (kg/m^2)	22.37 (9.30)	24.51 (9.02)
Wasit-Hip Ratio (cm)	0.79 (0.07)	0.77 (0.08)
Parity (n)		
0	5	4
1	2	1
2	4	6
>2	2	5
Menopause		
Yes	4	8
No	9	8
Ethnicity (n)		
White	10	14
Middle Eastern	1	0
East/Southeast Asian	0	1
Mixed (Mediterranean/White)	1	0
Mixed (Indigenous/White)	0	1
Mixed (Black/White/French Canadian)	1	0
Highest Level of Education (n)		

High School	1	1
College	1	0
Bachelors	6	9
Masters	4	5
Doctorate (MD or PhD)	1	1
Contraceptive Use (n)		
Yes	3	1
No	10	15
Hormone Replacement Therapy Use (n)		
Yes	1	2
No	12	14
Phase of Cycle During Testing (n)		
Menstrual Cycle Days 1 – 14	4	1
Menstrual Cycle Days 15 – 28	5	7
No Cycle	4	8

Table 6.2 Questionnaire results between women with and without stress urinary incontinence reported as means and standard deviations.

Questionnaire	Control	Stress Urinary Incontinence	P value
ICIQ-FLUTS			
Urinary Incontinence (0 – 20)	1.46 ± 0.97	8.06 ± 3.70	**.00***
Filling (0 – 16)	1.85 ± 1.46	3.88 ± 2.36	**.02***
Voiding (0 - 12)	0.69 ± 1.11	1.38 ± 1.78	.34
ICIQ-VS			
Total (0 – 53)	4.38 ± 3.62	4.81 ± 4.71	.97
Sexual Matters (0 - 58)	5.69 ± 8.04	7.38 ± 10.56	.79
Quality of Life (0 - 10)	0.31 ± 0.86	1.50 ± 2.19	.06
ICIQ-B			
Bowel Pattern (1 – 21)	5.54 ± 2.11	5.13 ± 1.55	.64
Bowel Control (0 - 28)	1.54 ± 1.13	1.67 ± 2.24	.98
Quality of Life (0 - 26)	0.69 ± 1.70	1.53 ± 2.72	.26
FSFI^{+}			
Total (2 - 36)	24.46 ± 5.81	25.76 ± 4.79	.76

Bolded* indicates significance at the .05 level. $^{+}$the total score does not include the three individuals who reported no sexual activity within that last 4 weeks. Abbreviations: International Consultation on Incontinence Questionnaire (ICIQ) - Female Lower Urinary Tract Symptoms (ICIQ-FLUTS); ICIQ-Vaginal Symptoms (ICIQ-VS); ICIQ-Bowel (ICIQ-B); Female Sexual Function Index (FSFI); stress urinary incontinence (SUI); Higher scores on the ICIQ-FLUTS, ICIQ-VS, and ICIQ-B indicate poor functioning in their respective domains; higher scores on the FSFI indicate better sexual functioning/being currently active in sexual activities.

6.5.2 Light touch sensory threshold models

The light touch sensory thresholds at each site are presented in Table 6.3. The multiple linear regression models for the sensory threshold at the right labia majora, urethra, perineum, and EAS each contained one outlier, which may have influenced the models to a greater extent than the other thresholds indicated by the casewise diagnostics for bias in the model (Cook's distance >

0.14, Standardized DFFIT >1, and Covariance ratio < 0.59). The outliers identified at each site were recorded from a different participant in each case, and each outlier had a higher threshold compared to the rest of the sample. As these outliers could be meaningful, a sensitivity analysis was performed. Two regression models were generated for each site: Model 1 with the outlier included and Model 2 with the outlier removed. Both models were considered in the interpretation of the findings.

Table 6.3 Light touch sensation thresholds (mN) at genital sites between women with and without stress urinary incontinence.

	Overall (n = 29) Mean ± SD	Control (n = 13) Mean ± SD	SUI (n = 16) Mean ± SD
Right Ankle (Medial Saphenous Nerve)	4.43 ± 2.27	4.57 ± 2.43	4.33 ± 2.21
Right Labia Majora (Genitofemoral Nerve)	1.53 ± 1.69	0.79 ± 0.77	2.12 ± 2.01
Urethral Meatus (Perineal Branch of Pudendal Nerve)	14.64 ± 26.83	13.40 ± 23.75	15.57 ± 29.67
Perineum (Perineal Branch of Pudendal Nerve)	1.24 ± 1.04	1.12 ± 1.26	1.34 ± 0.85
Right of the External Anal Sphincter (Inferior Rectal Nerve Branch of Pudendal Nerve)	2.83 ± 6.14	1.04 ± 0.84	4.29 ± 8.04

Stress urinary incontinence (SUI).

6.5.3 Right ankle site

At the right ankle (control) site, there was no association between light touch sensation and continence status (R^2 = .00, p = .79). The addition of age and parity in the second step of the model indicated no influence of these factors on light touch sensation threshold (R^2 = .03, p = .86) and adding these factors did not change the relationship between continence status and light touch sensation (*Step 2* F_{Change} = 0.34, p = .72). See Appendix J for the Regression Models.

6.5.4 Right labia majora site

One outlier was identified, a participant belonging to the SUI group (age = 48 years, parous), whose sensory threshold of 7.99mN resulted in a z-score of 3.82. Model 1 (including the outlier, n = 29) was significant with only continence status included as a factor (R^2 = .16, p = .03). Participants with SUI tended to demonstrate higher sensation thresholds than continent individuals (p = .09). The addition of age and parity did not account for significant variance in the model (*Step 2* F_{Change} = 0.78, p = .47) and rendered it non-significant (R^2 = .21, p = .12).

Model 2 (outlier removed, n = 28) was significant with only continence status included (R^2 = .16, p = .03). With age and parity added as factors, the model was again no longer significant (R^2 = .25, p = .07). See Appendix K for the Regression Models.

6.5.5 Urethral site

Data from one participant were excluded for the urethral site, as blank trials were correctly identified less than 75% of the time, therefore the sample size for this analysis was n = 28. In addition, an outlier was identified within the SUI group (age = 52 years, parous), whose sensory threshold of 115.22mN resulted in a z-score of 3.75. Model 1 (outlier included n = 28) was not significant when only continence status was entered (R^2 = .00, p = .84), and remained non-

significant (R^2 = .08, p = .58) with the addition of age and parity (*Step 2* F_{Change} = 0.97, p = .39)). With the outlier removed, the model remained non-significant. See Appendix L for the regression models.

6.5.6 Perineal site

An outlier was identified within the control group (age = 56 years, parous), whose sensation threshold of 4.95mN resulted in a z-score of 3.56. Model 1 (outlier included n = 29) was not significant with only continence status included (R^2 = .01, p = .58). The addition of age and parity did not change the model significantly (F_{Change} = 0.01, p = .99), which remained non-significant (R^2 = .01, p = .96).

Model 2 (outlier removed, n = 28) was not significant with only continence status included (R^2 = .12, p = .07) but approached significance. With age and parity added to the model, it remained non-significant (R^2 = .24, p = .08), and this step did not produce a significant change in the F statistic (*Step 2* F_{Change} = 1.83, p = .18). Continence status was a significant model coefficient in the first step (p = .05) and it remained significant (p = .02) with the addition of age and parity. See Appendix M for a full summary of the regression models.

6.5.7 External anal sphincter light touch sensation thresholds regression model

An outlier was identified within the SUI group (age = 51 years, parous) who demonstrated a sensory threshold of 33.93mN resulting in a z-score of 5.07. Model 1 (outlier included n = 29) was not significant with only continence status included (R^2 = .07, p = .16). The addition of age and parity did not change the model significantly (*Step 2* F_{Change} = 0.34, p = .71) and the overall model remained non-significant (R^2 = .10, p = .46).

Model 2 (outlier removed, $n = 28$), was significant with only continence status included ($R^2 = .21$, $p = .01$). With the addition of age and parity, the model remained significant ($R^2 = .29$, $p = .04$), though this step did not produce a significant change in the F statistic (*Step 2* $F_{Change} = 1.26$, $p = .30$). Continence status was a significant model coefficient in the first step ($p = .03$) and remained significant ($p = .04$) with the addition of age and parity, indicating that the presence of SUI is associated with an increase in EAS light touch sensation. See Appendix N for a full summary of the regression models.

6.5.8 Outliers with high light touch sensation thresholds

The outliers identified in light touch sensation thresholds at the right labia majora, urethra, perineum, and EAS are described in Table 6.4; all outliers were parous. The first case was a woman with SUI (age = 48 years) who demonstrated a higher light touch sensory threshold at the right labia majora site (z = 3.82). She did not demonstrate high thresholds at the perineal (z = 1.04), urethral (z = -0.53), or EAS (z = -0.29) sites. The second case was a woman with SUI (age = 52 years) who demonstrated a high urethral light touch sensation threshold (z = 3.75) but did not demonstrate high sensory thresholds at the other sites (right labia majora z = 0.08, perineum z = -0.73, EAS z = -0.27). The third case was a continent woman (age = 56 years) who displayed a high light touch sensation threshold at the perineum (z = 3.56) but did not demonstrate any other elevated thresholds at the genital sites (-0.29<z<-0.52). The fourth case was a woman with SUI (age = 51 years) who presented with a high light touch sensation threshold at the EAS site (z = 5.07) but did not demonstrate high thresholds at the other genital sites (0.01<z<0.31; Table 5.4).

6.5.9 Word choices

Descriptors associated with the sensation test were similar between groups at the right ankle, however at the genital sites, women with SUI tended to use “prickling” and “mild” more often than continent controls. Controls tended to say the filaments were “mild” and/or “ticklish” more often than women with SUI. All participants felt that the urethral site was prickling more often than other descriptors (see Figure 6.4).

6.6 Discussion

To the best of our knowledge, this is the first study to assess the presence of light touch sensory thresholds among women with SUI, as a means of detecting potential pudendal nerve involvement in SUI pathophysiology. Higher sensory thresholds were detected among women with SUI compared to continent women at the EAS but not at the other sites innervated by the pudendal nerve (mid-perineum and urethral meatus). Thus, it is unlikely that SUI is associated with sensory impairment of the pudendal nerve. These findings are more likely to be related to focal disruption of the terminal branches of the pudendal nerve or to the nerve endings. Consistent with this, through evaluating outliers, no individual demonstrated consistent sensory impairment across all sites innervated by the pudendal nerve.

In all models, continence status explained very little of the variance in the data. This indicates that there may be other important factors involved in the impairment of light touch sensation at genital sites[24,29,30] that were not investigated here. These may include scar tissue from perineal tears or episiotomies and damaged skin from repeated or prolonged exposure to urine.

Table 6.4 Light touch sensation thresholds at genital sites among women who had a threshold above three standard deviations from the mean. Data presented as thresholds in mN with z-scores in brackets.

						Sensory Thresholds in mN (z-score)				
Participant	Group	Age (Years)	Number of Births	Perineal Injury	ICIQ-FLUTS UI Score (0 – 20)	Right Ankle	Right Labia Majora	Urethra	Perineum	External Anal Sphincter
1	SUI	48	2	Perineal Tear x2	8	2.55 (-0.83)	**7.99 (3.82)**	0.51 (-0.53)	2.33 (1.04)	1.03 (-0.29)
2	SUI	52	2	Episiotomy x1	11	**7.71 (1.44)**	1.65 (0.08)	**115.22 (3.75)**	0.47 (-0.73)	1.17 (-0.27)
3	Control	56	2	Episiotomy x1 Perineal Tear x1	3	2.63 (-0.79)	0.78 (-0.44)	0.67 (-0.52)	**4.95 (3.56)**	1.07 (-0.29)
4	SUI	51	2	No Injury	5	**8.14 (1.63)**	1.54 (0.01)	23.06 (0.31)	1.46 (0.21)	**33.93 (5.07)**

Values are bolded if they are more than three standard deviations away from the mean (based on z-scores); Abbreviations: Stress urinary incontinence (SUI).

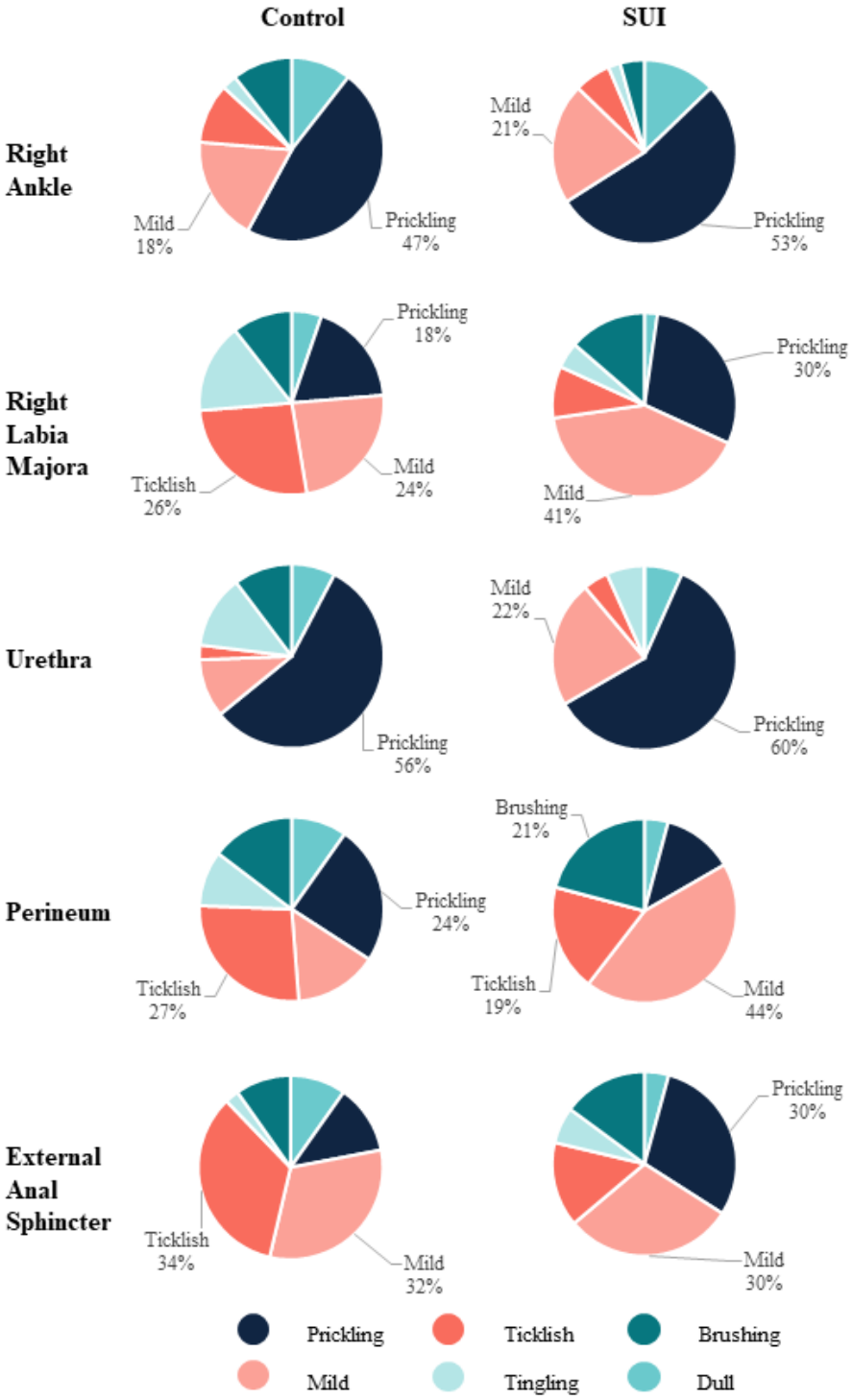

Figure 6.4 Frequency of adjective used to describe the first monofilament participants could feel displayed in percentages. SUI denotes stress urinary incontinence.

Abbreviations: stress urinary incontinence (SUI).

Changes in sensory thresholds are known to increase with age, typically presenting at 60 years of age and over[31]. Our sample contained only 4 individuals over the age of 60 years (61 – 67 years), all of whom experienced SUI. Indeed, there was a significant difference in age between the continent and incontinent groups; thus, multiple linear regression models were used to account for the influence of age on statistical outcomes. We also included a control site (right ankle) to determine whether any differences in sensory thresholds observed in the pudendal nerve distribution might be the result of overall differences in sensation related to age or some other external factor. At the right ankle site, there was no association between continence status and light touch sensation thresholds, nor was there a change in this relationship when age was included in the model.

Parity was also included in the models, as pregnancy and vaginal delivery may result in pudendal nerve injury or injury to branches of the pudendal nerve, and this has been proposed as a contributing factor in SUI pathophysiology[3]. There was no association between parity and light touch genital sensation thresholds in this sample. However, this result should be interpreted with caution as the study may have been underpowered to detect any effects of parity on sensation thresholds given the wide variability in the location and extent of nerve injury that may occur during vaginal childbirth. Instead, we controlled for parity in the linear regression models to look more closely at the association between continence status and genital light touch sensation. Interestingly, all outliers were parous women.

The main finding of this study was that SUI was associated with a higher light touch sensation threshold at the EAS. Reduced sensation at this site may indicate damage to the pudendal nerve or its inferior rectal branch that provides sensory innervation to the inferior part of the anal canal and skin surrounding the anal sphincter as well as motor innervation to the EAS[32,33]. Of note,

there is significant variability in the pathway of the inferior rectal nerve[34,35] and individuals displaying high EAS sensory thresholds may have inferior rectal nerve variations that are more prone to injury. However, the regression model accounted for only a small amount of variance in the data, therefore other factors may play an important part in the higher sensory thresholds at the EAS among women with SUI. A prospective study is needed to better understand the mechanisms underlying the reduction in light touch sensation among women with SUI at the perianal skin.

At the mid-perineum site, while continence status was a significant model coefficient, the overall model was not significant and explained very little of the variance in the data. The exploratory nature of the analysis, which generated multiple linear regression models, may have resulted in Type 1 error. Yet, sensory impairment at this location may indicate damage to the pudendal nerve or its perineal branch that provides sensory innervation to the skin of the perineum, vulvar vestibule, and posterior portion of the labia[32,33]. Indeed, the branches of the perineal nerve are located superficially, and thus a perineal tear or episiotomy may also compromise perineal sensation[4]. While detailed records on the presence and extent of perineal damage incurred during childbirth were not available, this information was collected through participant interviews. The participant in the control group whose perineal sensation threshold was an outlier at this site had a history of 2 vaginal deliveries: one where she experienced a perineal tear (grade unknown) and one where an episiotomy was performed. She described sensation at this site as brushing and ticklish, which is more similar to the description of perineal sensation from the women with SUI. Her sensation thresholds at the other genital sites were less than one standard deviation away from the sample mean, which suggests that she may have sustained focal damage to a superficial branch of the perineal nerve innervating her perineum.

The finding that women with SUI had higher light touch sensation thresholds at the right labia majora compared to those without SUI was an unexpected result. The anterior third of the labia majora is typically innervated by the genitofemoral nerve (L1-L2) and was included as a control site to be used as a basis for comparison to sites innervated by the pudendal nerve. While the age range in the sample was too small to determine any meaningful effect of age on labia majora light touch sensation thresholds, controlling for age in the model reduced the strength of the association between continence status and sensory thresholds, rendering it non-significant. It is possible that a sample with a larger age range may reveal an association between age and light touch sensation thresholds at the labia majora[24,29], however the very small amount of variance in the data explained by the model (<25%), and the fact that including age in the model resulted in a weaker model suggested that age does not likely influence light touch sensation at this site. Sensory changes at the anterior third of the labia majora could also reflect genitofemoral nerve injury incurred due to compression or entrapment during pregnancy and/or delivery[36,37], though this has not been reported in the literature, and, like age, is unlikely because the addition of parity into the model rendered it non-significant. The outlier at this test site was a parous woman with SUI who did not demonstrate elevated sensory thresholds at sites innervated by the pudendal nerve. As such, she may have experienced genitofemoral nerve compression during her pregnancy and/or vaginal delivery (2 deliveries).

Despite the association between sensory thresholds and continence status at the other genital sites, none was observed at the urethral meatus site. The urethral thresholds found in this study were significantly higher than those reported by Connell et al.[30] who also assessed urethral light touch sensation thresholds using monofilaments. However, the QST methods differed between studies. In this study, we used the staircase method of threshold testing proposed by Cornsweet[27]

rather than the ascending method of monofilament testing utilized by Connell et al.[30] Moreover, the exact positioning of the test site for the urethra was not reported by Connell et al.[30] and may have differed from the current study.

There was a trend suggesting that parity may be associated with changes in light touch sensation at the urethral meatus, which should be explored further. Previous research has indicated that pregnancy and delivery are implicated in changes to stretch and vibration[38] sensory thresholds within the urethra, so these factors may play a role in changes to light touch sensation as well. In this study, one participant from the SUI group reported not being able to feel any of the filaments at the urethral site (outlier case), while 2 others (one from the SUI group and the other a parous control) experienced at least one trial where they did not feel the largest filament. These findings suggest that injury to the perineal branch of the pudendal nerve may occur in some cases and may be associated with parity. While light touch sensation at the urethral meatus does not reflect sensation within the urethra itself [4], it may provide valuable information about the functioning of the perineal nerve and its branches to the labia minora, vaginal vestibule, inferior portion of the vaginal canal, and posterior aspect of the labia majora. Future studies should consider assessing sensation both at the urethral meatus (through light touch) and at the urethral mucosa (through pressure) to investigate the relationship between these testing sites.

In the event of sensory nerve injury and subsequent reinnervation, there is a lack of target specificity when the nerve regrows, such that a different area or mechanoreceptor could be innervated by axonal sprouts[39]. Depending on the pathway of the nerve, the severity of the peripheral nerve injury, and the accuracy in reinnervating the appropriate targets[40], the relationship between light touch sensation thresholds and continence status may be blurred. Individual variation in innervation is also common and dermatome maps of the human body are

not always accurate[41,42]; thus, in some individuals, locations like the anterior aspect of the labia majora, may be innervated by a different nerve such as the pudendal nerve, which may have impacted findings at the genital control site. Current knowledge of the genitofemoral and pudendal nerves come from small cadaver studies[34,35,43–48] which have indicated that there is variation in the branching and pathways of the nerves[34,46]. Future work should consider monitoring sensation thresholds prior to and during pregnancy, as well as more detailed reporting around the duration of labour/delivery and the location and extent of any perineal tearing during delivery.

The study findings are limited in generalizability by the sample of predominantly Caucasian women. The significant difference in the age of the women with and without SUI was handled by the inclusion of age in the regression models to improve the interpretability of the associations found. That said, the age range of the sample was too small to investigate the concurrent impact of age on sensation thresholds.

The method used to determine light touch sensory thresholds is considered a strength[49], particularly when considering that previous studies have only employed the method of limits[24,30]. The chosen assessment sites thoughtfully explored the various sensory branches of the pudendal nerve and did not include a clitoral site as this region is thought to receive innervation from multiple nerves[17] and thus may not be reflective of pudendal nerve integrity. Future studies should consider evaluating aspects of sensation at the perineum, the EAS and the urethra using different modalities (vibration, temperature, etc.) concurrently with the QST methods used in this study, ensuring samples are matched by age and parity, recruiting a larger sample size, and stratifying the sample by the type and extent of perineal injury sustained during childbirth in order to better understand any alterations in sensation among women with SUI. Further,

combining methods to evaluate both sensory and motor nerve function to determine the prevalence of pudendal nerve injury among women with SUI and its impact on lower urinary tract functioning would help us to better understand neural involvement in SUI pathophysiology.

6.7 Conclusions

The findings of this study support the idea that changes in sensory nerve function may be associated with SUI, yet the observed reductions in sensory function appear to be associated with focal disruption of sensory branches at the perineum and EAS and not the pudendal nerve as a whole. While these associations do not provide any evidence of causation, changes in EAS sensation should be investigated further among women with SUI to determine whether they influence symptom severity or treatment outcomes.

6.8 References

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Chapter 7: An investigation of voluntary and involuntary pelvic floor muscle activation between women with and without stress urinary incontinence: a feasibility study

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7.1 Abstract

Aims: The primary aim of this study was to determine whether there are differences in voluntary and/or evoked muscle activation of the levator ani muscles (LAMs), urethral rhabdosphincter (UR), bulbospongiosus (BSM), and external anal sphincter (EAS) between women with and without SUI. The secondary aim was to determine the feasibility of using peripheral nerve conduction studies and/or voluntary activation to evaluate differences in pudendal nerve function between women with SUI who were and were not cured with a physiotherapy intervention.

Methods: Adult women naïve to PFM training were recruited into continent and SUI groups. Differential electrodes were placed intravaginally over the mid-urethra (UR), the LAMs, and the EAS on the right side. A St. Marks electrode was used to stimulate the pudendal nerve intravaginally and to record resultant evoked potentials from the BSM. Participants performed three maximum voluntary contractions (MVCs) and then relaxed while the pudendal nerve was stimulated intravaginally, and ten compound muscle action potentials (CMAPs) were recorded from all muscle sites. Women with SUI then attended a physiotherapy intervention for 12 weeks, after which they completed a questionnaire to determine whether or not they were cured. Women with SUI were grouped into cured (score ≤ 4) and not cured (score >4) and effect sizes were used to explore group differences. Recruitment rate, data loss and attrition were described. Group comparisons (SUI vs control; cured vs not cured) were explored using analysis of variance models with parity considered as a factor and Mann-Whitney U tests as appropriate to compare

CMAP onset latencies, MVC peak amplitudes, and amplitude rise times during MVC; effect sizes were computed. **Results:** Thirty women (16 with SUI and 14 controls) participated. Recruitment was approximately three participants per month over ten months. Seven participants reported discomfort during testing based on the intravaginal electrodes and subsequently had the LAM (n = 2) or UR (n = 1) or both (n = 4) electrodes removed. CMAP onset latency to all PFMs was not different based on continence status or parity and the effect sizes were small. During MVC, BSM peak amplitude was lower among those with SUI compared to controls ($F(1, 22) = 6.44$, $p = .02$; $\eta^2 = .23$). The amplitude rise time of EMG activation did not differ by continence status or parity and had a small effect size. Women with SUI who were cured after a physiotherapy intervention were not different in any outcomes from those who were not cured, and effect sizes were small, except for the CMAP onset latency to the LAMs which demonstrated a large effect size ($r = .62$). This finding suggested that women who were cured demonstrated longer CMAP latencies to the LAMs than those who were not cured. **Conclusion:** The findings of this study do not support the hypothesis that there are differences in voluntary and evoked PFM activation between women with and without SUI and suggest that pudendal motor neuropathy may not play a role in mild SUI pathology. The findings also suggest that voluntary and evoked EMG signals may not be useful in predicting the success of physiotherapy treatment for SUI.

7.2 Introduction

Stress urinary incontinence (SUI) affects 25% of women in Canada[1]. Despite this high prevalence, the pathophysiology of SUI remains unclear. Previous research suggests that SUI pathophysiology may involve urethral and bladder neck structure and support and functional impairments of the urethral rhabdosphincter (UR) and levator ani muscles (LAMs); with

potential implication of neuropathic changes to the motor innervation of the striated pelvic floor muscles (PFMs)[2].

The pelvic floor is predominantly innervated by the pudendal nerve[3] which branches to provide motor innervation to the superficial PFMs (external anal sphincter (EAS), bulbospongiosus (BSM), ischiocavernosus, and superficial transverse perineal muscle), UR, and sensory innervation to perineum[4,5]. In some cases, the pudendal nerve is also believed to provide input to the LAMs[3,6,7]. Vaginal delivery may cause injury to the various branches of the pudendal nerve, and this may contribute to SUI pathophysiology[8,9]. Indeed, electromyography (EMG) studies have found that women with SUI demonstrate markers of denervation and subsequent reinnervation of orphaned motor units (e.g., prolonged pudendal nerve terminal motor latencies (PNTMLs) to the EAS[10–12] and UR[10–14], increased fibre density within the EAS[13,15], lower turns per amplitude and turns per second in the UR[16], EAS, and LAMs[17], and slower motor unit potential recruitment of the UR[16]). However, other studies have reported no differences in markers of denervation between women with and without SUI (e.g. PNTMLs to the EAS[13] or the circumvaginal musculature[18,19]). There is currently no consensus on the impact of pudendal neuropathy, as measured through nerve conduction time, on continence status, nor its potential impact on treatment outcomes.

Changes in voluntary PFM activation have also been found between women with and without SUI, and the results are similarly mixed. Some research supports lower EMG activity of the LAMs during contraction[20] and maximal voluntary contractions (MVCs)[21], while others report higher EMG activity during MVCs[22] and static holds[23]. Research has also found no differences in peak EMG amplitudes between women with SUI and their continent counterparts on fast voluntary contractions, though this study did find that women with SUI took longer than controls

to relax their PFMs back to baseline activity levels after contraction[24]. On intravaginal dynamometry measures of PFM function, women with SUI have demonstrated slower rates of force development than continent women during voluntary contractions[25]; however, when a similar measure was performed on the rate of activation with EMG, there was no difference between groups based on continence status[24]. Like the measures of nerve conduction time, there is no consensus on the involvement of voluntary PFM activation on SUI pathophysiology, nor its influence on treatment outcomes.

The recommended first line of treatment for women with SUI is physiotherapist-supervised PFM training, which, while effective, cures only 50% of those who complete it[26]. Models predicting success in symptom reduction with PFM training have included variables such as demographic information (e.g. parity, body mass index[27,28]), LAM function assessed digitally[27–29] and through intravaginal dynamometry[30], symptom severity[28,29], and pelvic morphology[28,31]. Only one study has investigated the role of pudendal nerve function and corticomotor control of the PFMs, finding that peripheral innervation was not different between those with SUI who were cured and those who were not cured after a PFM training intervention[19]. The study indicated that after the intervention, the women who were cured demonstrated higher corticomotor excitability to the EAS and circumvaginal muscles compared to those who were not cured. However, the study was not prospective, and thus the impact of voluntary and evoked activation on physiotherapy treatment outcomes among women with SUI remains unknown.

The first objective was to investigate differences in voluntary and evoked activation of the PFMs between women with and without SUI. The primary outcomes were compound muscle action potential (CMAP) onset latency, maximum voluntary activation amplitude and amplitude rise

time of four different PFMs (the LAMs, UR, BSM, and EAS) while considering parity as a potentially confounding factor.

The second objective was to determine the feasibility of using peripheral nerve conduction studies to evaluate differences in pudendal nerve conduction between women with SUI who were cured with physiotherapist-supervised PFM training and those who were not. The outcomes were:

1. Recruitment rate
2. Protocol completion rate /data loss
3. Effect sizes for:
    i. CMAP onset latency to the LAMs, UR, BSM, or EAS.
    ii. Maximum voluntary activation amplitude and amplitude rise time of the LAMs, UR, BSM, and EAS.

7.3 Methods

This cross-sectional, observational, prospective cohort study was approved by the Health Sciences and Sciences Research Ethics Board of the University of Ottawa as complying with National standards for the ethical conduct of human research (H-07-20-5945) and COVID-19 safety precautions (Appendix A).

7.3.1 Participants

Women over the age of 18 years were recruited from the community through posters and social media posts, and from local physiotherapy clinics through flyers and referrals by pelvic health physiotherapists. See Chapter 3 for a description of the data collection process and participant recruitment.

7.3.2 Sample size

Sample size estimates were based on previous studies assessing PNTMLs[12–14,18] and MVCs measured through surface EMG[32] and were computed with G*Power (version 3.1.9.7) using α=0.05; β=0.80. Sample size calculations for the amplitude rise time for women with and without SUI could not be performed based on the limited information reported in the only study found to report this measure in women with SUI[24].

Most studies found medium to large effect sizes when comparing PNTMLs between women with and without SUI (Snooks et al.[13] control n = 31, SUI n = 12, d = 3.35; Smith et al.[12] control n = 42 SUI n = 34, d = 0.80; Meyer et al.[14] control n = 7, SUI with low-pressure urethra n = 38, d = 0.68) except for Cavalcanti et al.[18] who found no significant difference (effect size = n/a) between continent (n = 19) and incontinent women (n = 33). Based on a large effect size, the required sample size was 28 per group (i.e. 28 continent women and 28 with SUI).

Another study reported a large effect size (d=1.51) for EMG amplitude recorded during MVC between groups of women with (n=20) and without SUI (n=20)[32]. Again, based on this large effect size, the required sample size was 28 per group. As such, we aimed to recruit 30 women per group to account for any data loss.

Only Gunnarsson et al.[19] (cured n = 9, not cured n = 9, control n = 12) was considered for the sample size estimate to detect differences in the outcome measures obtained for each muscle (i.e. BSM, LAMs, UR, EAS) between women with SUI who were and were not cured with the physiotherapy intervention. However, this study did not report enough information to estimate effect size. As such, we aimed to use the sample of 30 women with SUI recruited to address the

first objective to estimate the sample size required to detect group differences for these outcomes in this population for the second objective.

7.3.3 Equipment

7.2.2.1 Intravaginal Differential Suction Electrode (DSE)

Intravaginal EMG data collection with a DSE has previously been described (See Figure 7.1)[33,34]. EMG signals recorded using the DSE demonstrate excellent between-trial reliability[33], and are less susceptible to motion artifact[33] and crosstalk[34] from hip adductors/rotators compared to signals recorded from other commercially available probes (e.g. Femiscan™). Prior to each participant's visit, new DSEs were printed (Ultimaker 2+/Ultimaker S5, Ultimaker B.V., Geldermalsen, Netherlands) in biocompatible plastic (PLA), assembled, and cleaned.

7.3.2.2 EMG System

EMG electrodes were interfaced with Delsys™ D.E.2.1. preamplifiers, which in turn were interfaced with a Delsys Bagnoli™ 16 EMG amplification system (CMRR=90dB at 60Hz, bandwidth 20–450Hz). An overall gain of X1000 was set for all EMG channels. Amplified EMG data were digitized [16bit National Instruments analog to digital converter (AD Instruments Ltd., CO, USA set to a ±5V input range)] and acquired at 1000Hz through PowerLab data acquisition software (LabChart 8, ADInstruments, Colorado Springs, CO). The stimulating electrodes on the St. Marks electrode were interfaced with a Digitimer Isolated Stimulator DS7 (Welwyn Garden City, Hertfordshire, England).

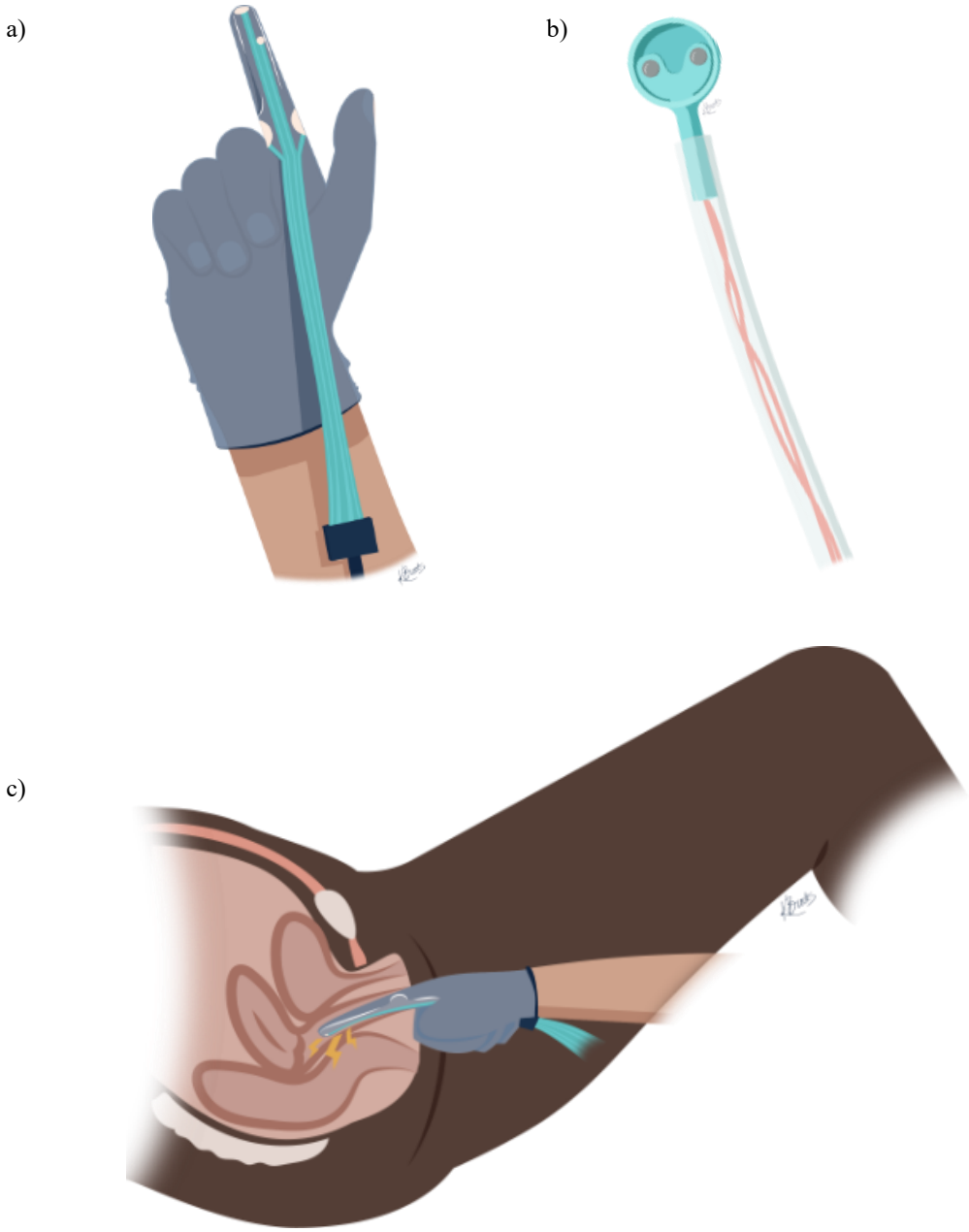

Figure 7.1 Illustration of the electrodes and pudendal nerve stimulation techniques used in this study, a) St. Marks electrode, b) Differential suction electrode closeup, c) Intravaginal pudendal nerve stimulation technique.

7.3.4 Procedure

The researcher performing the examinations received competency-based training on the evaluation and teaching of PFM contractions from a pelvic health physiotherapist with 10+ years

of experience and received specialized training in acquiring PFM EMG data from a pelvic health physiotherapist with 3+ years of EMG research experience, overseen by the thesis supervisor, who had over 20 years of experience with PFM EMG.

The researcher remained blinded to the participant's continence status and acquired informed consent from the participant (Appendix G). Assessment sessions took place in a private examination room. Demographic information (e.g., age, menopausal status, parity) was collected through self-report and anthropometric data (e.g., height, weight) were collected using standardized techniques (Appendix H). Next, with the participant in supine on an examination plinth, a genital inspection was performed to ensure that there were no obvious signs of infection, dermatological conditions, or pelvic mass(es) that could make the assessment uncomfortable or might interfere with data collection; no participants were excluded for these reasons. The participant was then instructed on how to perform a proper PFM contraction, with feedback provided through both visual inspection and digital palpation. The researcher confirmed that there was closure of the levator hiatus and a lift of the perineum with minimal use of accessory muscle contractions in the hip/gluteal region, and without bearing down or breath-holding; no participants were excluded for being unable to contract their PFMs. The protocol was paused for breaks or to use the nearby toilet facilities as needed.

A single-use, pre-gelled adhesive common reference electrode (Kendall H49P, 30mm x 30mm, Cardinal Health) was placed on the skin overlying the right anterior superior iliac spine after preparing the site by abrading it with an alcohol swab. Two pre-gelled, bipolar adhesive surface electrodes (Kendall H49P, 30mm x 30mm, Cardinal Health) were trimmed to a 15mm diameter circle and placed on the skin overlying the right side of the EAS with an interelectrode distance of 5mm. Medical tape was placed over the electrodes to ensure that they maintained contact with

the skin throughout the protocol. Next, a DSE was prepared by placing electrode gel over the contact surfaces and lubricant on the outside surface of the electrode. With a gloved and lubricated digit, the researcher gently guided her finger into the participant's vagina and palpated the anterior vaginal wall for the approximate location of the mid-urethra. Once confirmed, the researcher guided the DSE into the participant's vagina and placed the electrode at the level of the mid-urethra. A research assistant withdrew 0.3ml of air from the DSE tubing using a syringe apparatus to generate a gentle suction force to keep the electrode in place. A second DSE was prepared, along with a St. Marks electrode (Cephalon, Sundsholmen, Nörresundby, Denmark; see Figure 7.1). Both electrodes were guided into the participant's vagina. The DSE was fixed to the right side of the vaginal wall at the level of the LAMs—correct positioning was confirmed by palpating the muscle during a contraction. The St. Marks electrode was situated such that the fingertip with the stimulating electrode pair palpated the ischial spine on the right side and the recording electrode pair was located at the vaginal introitus (at the BSM).

All EMG signals were inspected for quality before beginning the study tasks. This was done by continuously recording the signals while the participant submaximally contracted and relaxed their LAMs. If the participant reported discomfort during the contractions at the site of the intravaginal electrodes, the electrode causing the discomfort was removed. Typically, only one of the intravaginal electrodes was removed, but some cases required both DSEs to be removed for participant comfort.

7.2.3.1 Maximal Voluntary Contractions (MVCs)

Three MVCs were performed by the participant while EMG signals were recorded from all channels. The participant was instructed to contract their PFMs as quickly and as strongly as they could, and to hold the contraction for 5s using the following cues: "Breathe in, breathe out, and

Squeeze, Squeeze, SQUEEZE, HARD, HARD, HARD!" and then to relax their PFMs using the cues: "Relax, let the contraction go." There was one minute of rest between repeated contractions.

7.2.3.2 Pudendal Nerve Stimulation

With all electrodes in place, the researcher began pudendal nerve stimulation with a low intensity (15mA) square wave pulse of 0.1ms duration which was triggered by a computer through the LabChart 8.0 software (AD Instruments Ltd., CO, USA). The stimulation intensity was increased incrementally until there was no concordant increase in the amplitude of the evoked EMG signal recorded from all channels. Once this intensity was reached, the stimulus intensity was increased by 20% and ten stimuli were delivered with 30-second rests between trials. The resultant evoked potentials were recorded synchronously from all channels. During this task, the participant remained in a relaxed supine position. If the patient reported discomfort with the stimulation, the task was discontinued. This concluded the data collection session.

After their assessment, women with SUI consulted the local pelvic health physiotherapist that they had previously selected and attended a 12-week physiotherapy intervention. While all physiotherapists recommended PFM training (PFMT) and prescribed a home exercise plan, the exercise prescription and number of visits were not standardized across participants. After 12 weeks, participants were asked to complete the ICIQ-FLUTS, the Global Rating of Patient Satisfaction, and the Global Perception of Improvement Questionnaires (Appendix I). They were also asked to share details of their PFMT via email (e.g. number of sessions attended, assigned exercises, and an estimate of how many days per week the participant performed the exercises at home). Participants were considered cured after the physiotherapy intervention if they had a score of ≤4 on the ICIQ-FLUTS urinary incontinence subscale.

7.3.5 Data processing and analysis

All EMG signals were processed using custom MATLAB software (R2022a, Mathworks, Natick, MA). The ten CMAPs generated through pudendal nerve stimulation were ensemble averaged. CMAP onset latency was determined using visual inspection of the ensemble averaged CMAPs.

MVC signals were detrended to remove DC offset, notch filtered at 60 Hz to remove line interference, full wave rectified, then low pass filtered using a 6^{th} order Butterworth filter with a 6 Hz cut-off. The peak of the smoothed EMG signal was determined for each MVC trial and channel. The rise time for EMG amplitude was calculated as the time in milliseconds for the signal to increase from 10% to 90% of the peak.

All statistical analyses were performed using IBM SPSS Statistical Software Version 25 (IBM Corp; Armonk, NY, USA). Descriptive and questionnaire data were assessed using Mann-Whitney U and Chi-Square tests. Normality testing using the Shapiro-Wilk test and visual inspection of histograms found a mix of normal and non-normal distributions across the data, however, analyses of variance (ANOVAs) are known to be robust to normality violations[35,36] so ANOVA models were used with sensitivity analyses performed when there were outliers. Homogeneity of variance was assessed using Levene's Test. A repeated measures ANOVA was used to assess the impact of continence status and parity (yes/no) on CMAP onset latencies across muscle sites (BSM, LAMs, UR, EAS). Outliers were identified as onset latencies that were three standard deviations above the mean. Separate ANOVA models were used to assess the peak amplitude reached during an MVC and the amplitude rise time at each muscle site, including continence status and parity (yes/no) as factors. As this was an exploratory analysis, alpha was not adjusted to account for multiple comparisons. Lastly, independent t-tests or Mann-

Whitney U tests were used as appropriate to explore the differences in CMAP onset latency, peak MVC amplitude, and rise time during the MVC between women with SUI who were cured and not cured with their physiotherapy intervention. Effect sizes are reported as partial eta squared or *r* based on the statistical test performed. Partial eta squared were interpreted as 0.01 is a small effect, 0.06 is a moderate effect, and 0.14 is a large effect. The *r* effect sizes were interpreted as 0.1 is a small effect, 0.3 is a moderate effect, and 0.5 is a large effect.

Due to the conflicting findings of prolonged PNTMLs reported in the literature[12,13,18], we planned a preliminary analysis after reaching half of our target sample size (n = 30). At this time, the effect sizes for the differences between women with and without SUI were computed, and a revised sample size estimate was determined. If the effect sizes were moderate to large, recruitment would continue to the planned 60 individuals; if the effect sizes were nil to small, we planned to stop recruitment given the low probability of detecting the expected differences.

7.4 Results

7.4.1 Sample characteristics

Out of 48 women screened for eligibility between December 2021 and September 2022, 30 were included (*n* = 16 in the SUI group and *n* = 14 in the control group; see Figure 7.2). The SUI group (49 ± 11 years, *p* = .01) was older than the controls (38 ± 13 years), but there was no difference in parity (control parous *n* = 6, SUI parous *n* = 12, *p* = .14). No participant smoked and the groups only differed on urinary incontinence and filling subscale scores of the ICIQ-FLUTS. See Table 7.1 for demographic data and Table 7.2 for questionnaire results.

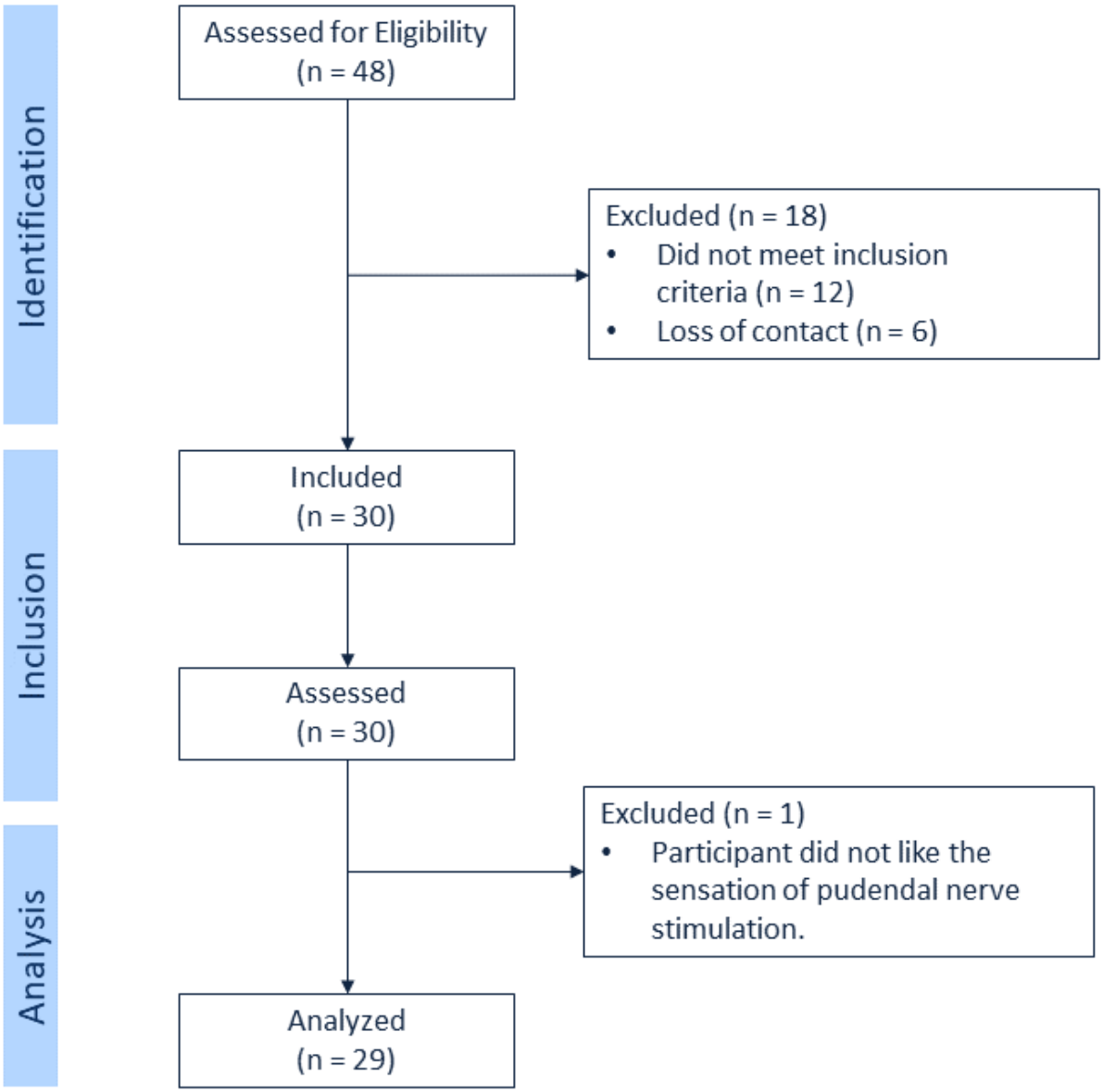

Figure 7.2 Flowchart participant recruitment and analysis.

Among the 12 women who attended physiotherapy, 5 were cured and 7 were not cured after the 12-week intervention (42% cure rate). Women who were not cured of their SUI symptoms were older (median[interquartile range]; age = 53[10] years vs 46[4] years, p = .01) and had smaller waist-to-hip ratios (W/H ratio = 0.74[0.03] vs 0.79[0.10], p = .02) compared to those who were cured. Women with SUI who were cured of their symptoms had lower ICIQ-FLUTS subscale

scores prior to their physiotherapy intervention compared to women who were not cured (p = .00, see Table 7.3), but did not differ on any other characteristics assessed by the questionnaires.

Table 7.1 Sample characteristics and demographic information

Demographics	**Stress Urinary Incontinence Group (mean ±SD or n)**	**Control Group (mean ±SD or n)**
Height (m)	1.66 ± .06	1.66 ± .05
Weight (kg)	72.33 ± 17.13	64.35 ± 14.56
Body Mass Index (kg/m^2)	26.39 ± 6.41	23.39 ± 5.49
Wasit-Hip Ratio (cm)	0.79 ± .07	0.79 ± .06
Parity		
0	4	6
1	1	2
2	6	4
>2	5	2
Menopause		
Yes	8	4
No	8	10
Ethnicity		
White	14	11
Middle Eastern	0	1
East/Southeast Asian	1	0
Mixed (Mediterranean/White)	0	1
Mixed (Indigenous/White)	1	0
Mixed (Black/White/French Canadian)	0	1

Highest Level of Education		
High School	1	1
College	0	1
Bachelors	9	7
Masters	5	4
Doctorate (MD or PhD)	1	1
Contraceptive Use		
Yes	1	4
No	15	10
Hormone Replacement Therapy Use		
Yes	2	1
No	14	13
Phase of Cycle During Testing		
Menstrual Cycle Days 1 – 14	1	5
Menstrual Cycle Days 15 – 28	7	5
No Cycle	8	4

Abbreviations: Standard deviation (SD).

Table 7.2 Questionnaire results of women with and without stress urinary incontinence.

Questionnaire	Stress Urinary Incontinence Group (mean ±SD or n)	Control Group (mean ±SD or n)	P value
ICIQ-FLUTS			
Urinary Incontinence (0 – 20)	**8.06 ± 3.70**	**1.36 ± 1.01**	**.00***
Filling (0 - 16)	**3.88 ± 2.36**	**1.93 ± 1.44**	**.03***
Voiding (0 - 12)	1.38 ± 1.78	0.79 ± 1.12	.50
ICIQ-VS			
Total (0 - 53)	4.81 ± 4.71	4.07 ± 3.67	.76
Sexual Matters (0 - 58)	7.38 ± 10.56	5.29 ± 7.87	.73
Quality of Life (0 - 10)	1.50 ± 2.19	0.29 ± 0.83	.09
ICIQ-B			
Bowel Pattern (1 – 21)	5.13 ± 1.55	5.64 ± 2.06	.48
Bowel Control (0 - 28)	1.67 ± 1.50	1.64 ± 1.15	.81
Quality of Life (0 - 26)	1.53 ± 2.72	0.79 ± 1.67	.45
FSFI (2 - 36)$^{+}$	25.76 ± 4.79	24.46 ± 5.81	.79

Bolded* values are significant at the $p < .05$ level. $^{+}$the total score does not include the three individuals who reported no sexual activity within that last 4 weeks. Abbreviations: International Consultation on Incontinence Questionnaire (ICIQ) - Female Lower Urinary Tract Symptoms (ICIQ-FLUTS); ICIQ-Vaginal Symptoms (ICIQ-VS); ICIQ-Bowel (ICIQ-B); Female Sexual Function Index (FSFI); stress urinary incontinence (SUI).

Table 7.3 Questionnaire results of women with stress urinary incontinence who were cured or not after a physiotherapy intervention.

Questionnaire	**Cured (mean ±SD)**	**Not Cured (mean ±SD)**	**P value**
ICIQ-FLUTS Before Physiotherapy			
Urinary Incontinence (0 – 20)	**6.20 ± 1.30**	**11.14 ± 2.97**	**.01***
Filling (0 - 16)	2.20 ± 1.30	4.86 ± 2.67	.08
Voiding (0 - 12)	2.00 ± 2.35	1.14 ± 1.86	.54
ICIQ-VS			
Total (0 - 53)	4.80 ± 3.03	4.29 ± 4.79	.56
Sexual Matters (0 - 58)	13.80 ± 13.79	4.29 ± 7.52	.17
Quality of Life (0 - 10)	2.80 ± 2.95	1.14 ± 1.86	.20
ICIQ-B			
Bowel Pattern (1 – 21)	5.40 ± 1.34	4.67 ± 1.51	.45
Bowel Control (0 - 28)	1.80 ± 1.64	1.33 ± 1.03	.70
Quality of Life (0 - 26)	2.00 ± 1.87	0.17 ± 0.41	.09
FSFI^{+}			
Total (2 - 36)	24.96 ± 5.87	26.80 ± 3.64	.54
ICIQ-FLUTS After Physiotherapy			
Urinary Incontinence (0 – 20)	**3.40 ± 0.55**	**9.14 ± 3.39**	**.00***
Filling (0 - 16)	1.40 ± 0.89	3.29 ± 2.06	.11
Voiding (0 - 12)	1.20 ± 1.30	0.86 ± 1.46	.64
Global Rating of Patient Satisfaction and Perception of Improvement Questionnaire			

Q1. Patient satisfaction with progress. (*n*)			
Completely	3	3	-
Somewhat	2	4	-
Not at all	0	0	-
Q2. How patient feels overall (*n*)			-
Much Better	2	1	-
Better	3	4	-
About the Same	0	2	-
Worse	0	0	-
Much Worse	0	0	-
Patient Estimated Percent Improved	66.60 ± 28.06	43.57 ± 22.55	-

Bolded* values are significant at the $p < .05$ level. [+]the total score does not include the three individuals who reported no sexual activity within that last 4 weeks. Abbreviations: International Consultation on Incontinence Questionnaire (ICIQ) - Female Lower Urinary Tract Symptoms (ICIQ-FLUTS); ICIQ-Vaginal Symptoms (ICIQ-VS); ICIQ-Bowel (ICIQ-B); Female Sexual Function Index (FSFI); stress urinary incontinence (SUI); stress urinary incontinence (SUI); pelvic floor muscle training (PFMT).

7.4.2 Recruitment rates and data loss

Initial participant recruitment began (December 2021) slowly for each group and averaged one participant per month for the control group and two individuals per month for the SUI group. By February 2022, recruitment for women with SUI reached a steady rate of 2-3 women per month until June 2022. After that date, recruitment was closed to women with SUI to ensure that they would have time to complete their physiotherapy treatment before the scheduled preliminary analysis in September 2022. All participants completed the study session, however, one

participant reported discomfort with the stimulation and as such this aspect of the protocol was discontinued.

Of the 16 women with SUI, only 12 participated in their planned physiotherapy treatment. One participant decided not to attend physiotherapy due to a lack of financial support, and two reported a lack of time/desire to attend after completing the laboratory-based assessment. One further participant who underwent the physiotherapy intervention did not respond to the ICIQ-FLUTS questionnaire after their physiotherapy intervention and was therefore excluded from the analysis; the attrition rate was 25%. While all participants did PFMT in their physiotherapy intervention, nine women provided further details on the types of exercises performed in treatment: one participant stated that she was taught "The Knack", two participants reported performing PFM contractions in different positions and exercises, and five participants reported instruction on breathing and the pelvic floor.

During data collection, seven participants reported discomfort with multiple electrodes in the vaginal canal and subsequently had one or both removed: LAM (n = 2), UR (n = 1), and both (n = 4). While optimizing the position of the St. Marks electrode, 5 participants had their LAM electrode dislodged from the vaginal wall, while the UR electrode was dislodged in 2 participants. The overall dataset included CMAPs recorded from the LAMs (n = 16), UR (n = 20), BSM (n = 27), and EAS (n = 27), and MVC signals recorded from the LAMs (n = 21), UR (n = 19), BSM (n = 26), and EAS (n = 27). However, there were no detectable CMAPs in 4 participants; two demonstrated no detectable CMAPs at the BSM [one continent (40 years, nulliparous) and one with SUI (51 years, parous)], but both demonstrated clear CMAPs on the other channels. One participant (continent, 47 years, parous) demonstrated no CMAP at the

LAMs but had clear CMAPs across all other channels. Lastly, one participant (SUI, 36 years, nulliparous) demonstrated no CMAP at the UR, but all other signals were visible.

7.4.3 Compound muscle action potential onset latency between women with and without stress urinary incontinence

No differences in CMAP onset latency were observed at any PFM site between women with SUI and continent women ($F(1, 9) = .39$, $p = .55$; $\eta^2 = .04$), and latency was not affected by parity ($F(1, 9) = .01$, $p = .93$; $\eta^2 = .00$). Onset latencies were not significantly different across the muscle sites (Greenhouse Geisser correction, $F(1, 13.42) = .15$, $p = .81$; $\eta^2 = .02$; See Figure 7.3). Three cases were identified as outliers, all with latencies shorter than the sample mean.

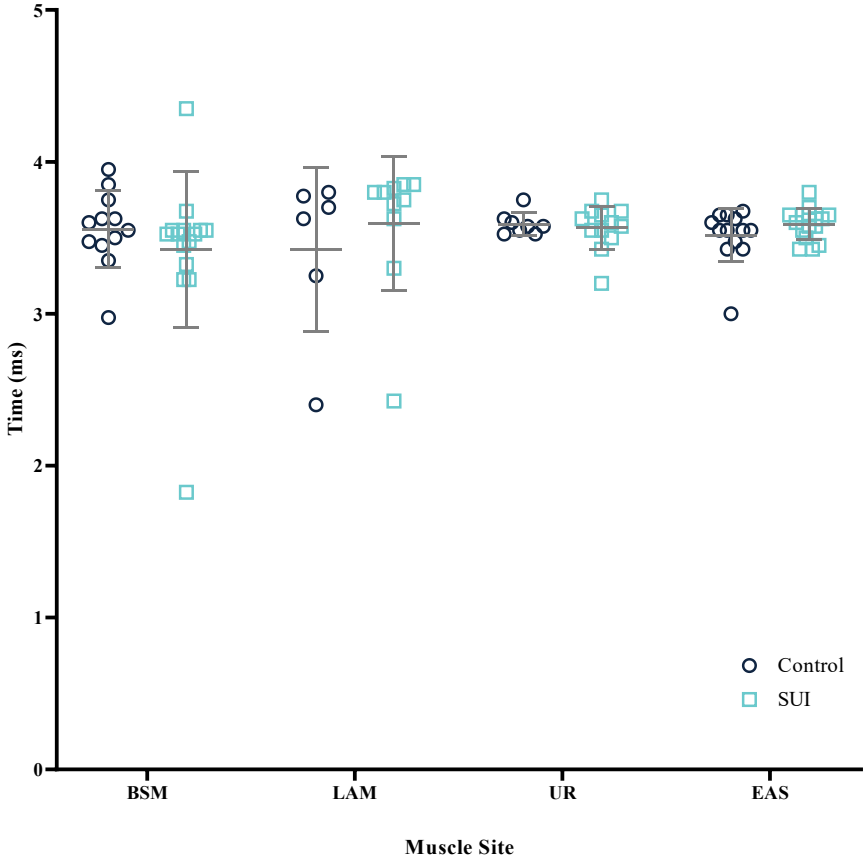

Figure 7.3 Compound Muscle Action Potential (CMAP) onset latencies of women with stress urinary incontinence and continent women across the muscle sites of interest.

Error Bars represent the mean ± one standard deviation; bulbospongiosus (BSM); levator ani muscles (LAM); urethral rhabdosphincter (UR); external anal sphincter (EAS).

7.4.4 Maximal voluntary contraction characteristics among women with and without stress urinary incontinence

No interaction between continence status and parity was observed in the peak amplitude of the EMG signal recorded during PFM MVC. There was a tendency for parity to interact with continence status at the LAMs ($F(1, 16) = .3.54$, $p = .08$; $\eta^2 = .18$), however, this finding was likely driven by a single value that was just below the three standard deviations above the mean. With this participant removed, the trend in the interaction effect was no longer present ($F(1, 15) = .1.06$, $p = .32$; $\eta^2 = .07$). Peak amplitudes during PFM MVC were significantly smaller at the BSM in the women with SUI compared to the continent women (0.02 mV ± 0.01 vs 0.04 mV ± 0.014, $F(1, 22) = 6.44$, $p = .02$; $\eta^2 = .23$), while peak amplitudes at the other muscle sites were not different based on continence status [LAMs $F(1, 16) = 1.45$, $p = .25$; $\eta^2 = .08$, UR $F(1, 15) = .19$, $p = .67$; $\eta^2 = .01$, EAS $F(1, 23) = .32$, $p = .58$; $\eta^2 = .01$; See Figure 7.4] and effect sizes were small. Parity did not affect the peak amplitude of the PFM MVC at any muscle site (BSM $F(1, 22) = .97$, $p = .34$; $\eta^2 = .04$, LAMs $F(1, 16) = .06$, $p = .82$; $\eta^2 = .00$, UR $F(1, 15) = 1.87$, $p = .19$; $\eta^2 = .11$). While the peak amplitude of the EAS tended to be higher among parous compared to nulliparous participants (0.46 mV ± 0.02 vs 0.03 mV ± 0.02, $F(1, 23) = 3.33$, $p = .08$; $\eta^2 = .13$), the effect size was moderate. See Figure 7.5 for an example of the processed EMG signals recorded from all sites simultaneously during an MVC.

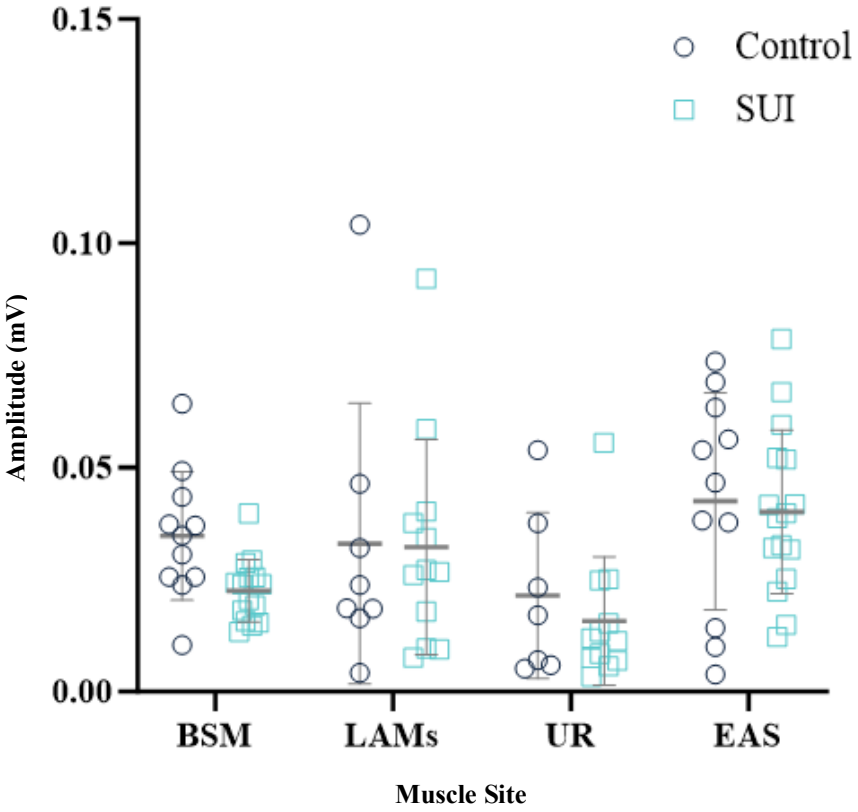

Figure 7.4 Non-normalized peak amplitudes reached during a maximal voluntary contraction between women with and without stress urinary incontinence across muscle sites.
Error Bars represent one standard deviation above and below the mean, which is indicated by the horizontal bar; bulbospongiosus (BSM); levator ani muscles (LAM); urethral rhabdosphincter (UR); external anal sphincter (EAS).

The rise time of the EMG amplitude during MVC was significantly different across muscle sites ($F(1, 33) = 4.56$, $p = .02$; $\eta^2 = .29$), where the BSM reached its maximum peak more slowly than the LAMs (estimate marginal means (95% confidence intervals); 162.96ms (128.47, 197.45) vs 122.91ms (93.20, 152.62), $p = .03$) regardless of continence status ($F(1, 11) = .05$, $p = .82$; $\eta^2 = .01$) or parity ($F(1, 11) = 1.42$, $p = .26$; $\eta^2 = .11$). The rise time of the BSM was not different from the EAS or UR ($p > .05$) based on Bonferroni corrected pairwise comparisons (See Figure 7.6).

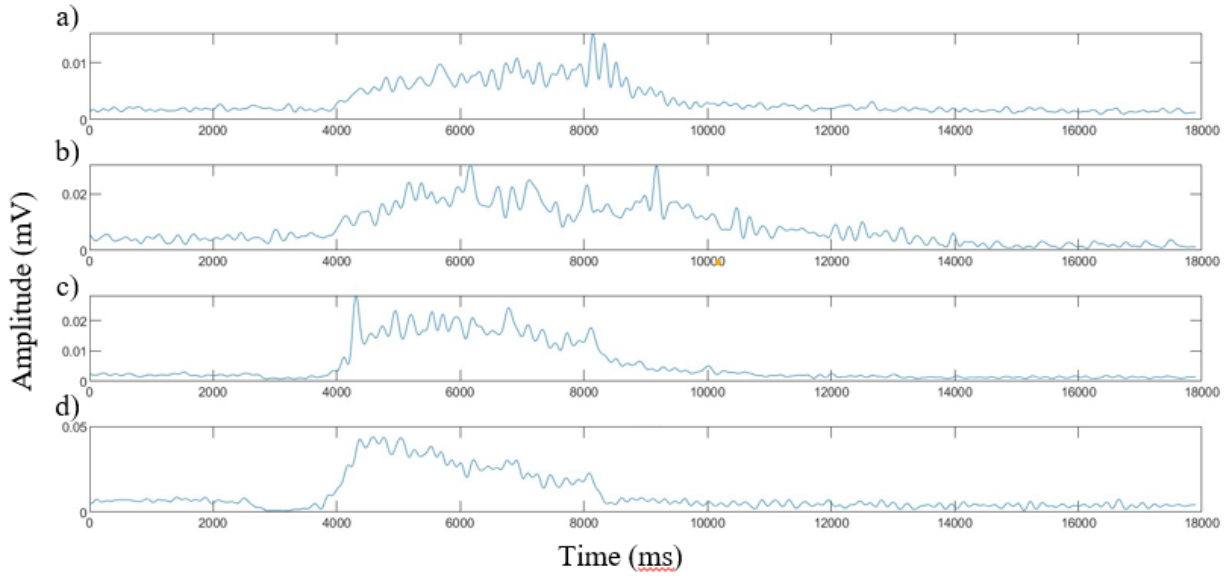

Figure 7.5 Processed electromyographic signals from all muscle of interest recorded during a maximal voluntary contraction, a) bulbospongiosus muscle, b) external anal sphincter, c) urethral rhabdosphincter, d) levator ani muscles. Participant was a parous woman with stress urinary incontinence.

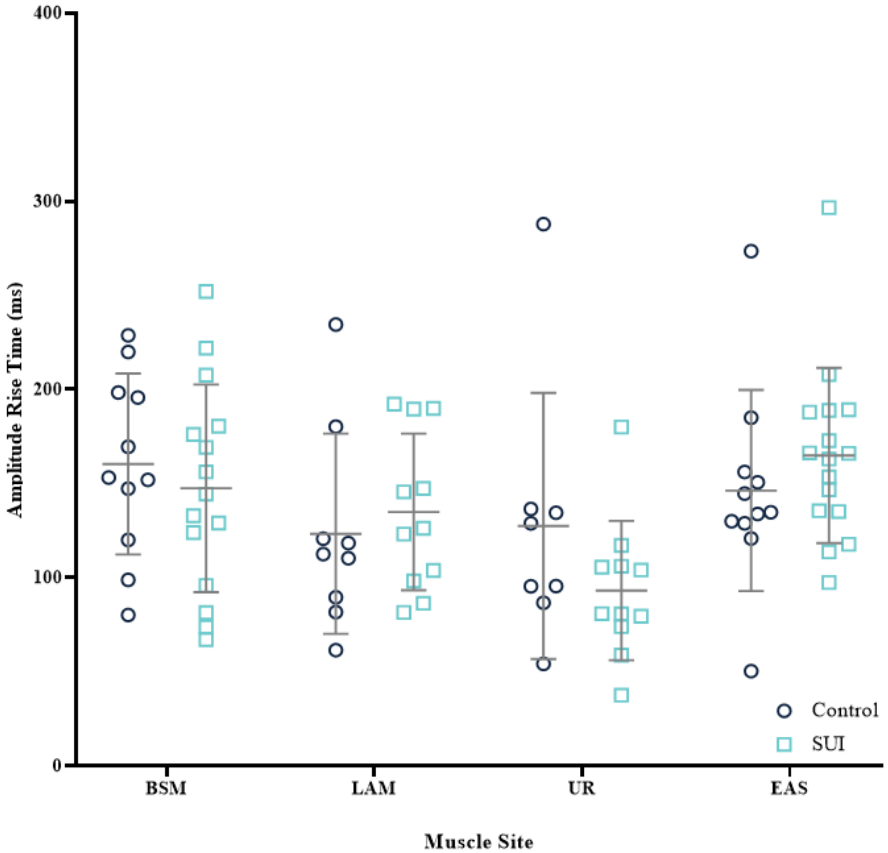

Figure 7.6 Amplitude rise time from 10% to 90% of the peak amplitude reached during a maximal voluntary contraction between women with and without stress urinary incontinence

across muscle sites. Error Bars represent one standard deviation above and below the mean; bulbospongiosus (BSM); levator ani muscles (LAM); urethral rhabdosphincter (UR); external anal sphincter (EAS).

7.4.5 Exploration of differences in compound muscle action potential amplitude and maximal voluntary contraction characteristics between women with stress urinary incontinence who were and were not cured with a physiotherapy intervention

Women with SUI who were cured after the physiotherapy intervention did not differ from women who were not cured in terms of CMAP onset latency to the BSM, LAMs, UR, and EAS; all effect sizes were small except for the CMAPs to the LAMs which had a large effect size.

The peak amplitude of the EMG recorded during MVC and the rise time during the same contraction was not different between those with SUI who were cured and those who were not cured after the intervention, and most had small effect sizes (See Table 7.4).

Table 7.4 Compound muscle action potential onset latencies and maximal voluntary contraction efforts among women with and without stress urinary incontinence who attended a physiotherapy intervention.

Outcome & Muscle Site	**Cured**	**Not Cured**	***P* value**	**Effect Size (*r*)**
CMAP Onset Latency (ms)				
Bulbospongiosus	3.53 (0.05)	3.38 (0.41)	.76	.12
Levator Ani	3.85 (0.04)	3.68 (0.40)	.06	.62
Urethral Rhabdosphincter	3.58 (0.15)	3.63 (0.20)	.44	.25
External Anal Sphincter	3.58 (0.20)	3.60 (0.16)	.34	.31
EMG Amplitude during MVC (μV)				

Bulbospongiosus	20.39 (8.75)	21.74 (16.76)	.58	.17
Levator Ani Muscles	27.09 (11.18)	26.65 (18.09)	.66	.16
Urethral Rhabdosphincter	11.29 (52.92)	14.28 (14.87)	.62	.16
External Anal Sphincter	32.05 (31.88)	38.72 (10.03)	.57	.16
Rise Time (ms)				
Bulbospongiosus	156.17 (125.17)	136.67 (60.29)	.86	.06
Levator Ani Muscles	98.17 (51.75)	123.17 (53.79)	.88	.05
Urethral Rhabdosphincter	79.50 (104.99)	77.38 (61.75)	.72	.11
External Anal Sphincter	163.00 (60.50)	172.67 (71.50)	.37	.26

Compound muscle action potential (CMAP); values are reported as group medians (interquartile range).

7.5 Discussion

At the planned preliminary analysis point for this study (i.e. after n = 30 participants completed the protocol), the stopping criteria were reached. Effect sizes were small for between-group differences in measures of voluntary and evoked neuromuscular activation of the PFMs, suggesting a low probability of detecting group differences between women with and without SUI once the target sample size was reached, which halted the study. Among those women who completed the protocol, there was a significant amount of data loss due to electrodes becoming dislodged and/or participants reporting discomfort with the insertion of multiple DSEs within the vagina along with the St. Mark's electrode. After 16 participants with SUI completed the

laboratory-based protocol, 12 continued with the 12-week physiotherapy intervention as planned, while 4 (25%) did not. Among the 12 participants who completed a physiotherapy intervention, 5 were considered cured. The analysis suggested low feasibility for detecting differences in voluntary or evoked activation of the PFMs between women with SUI who were cured vs those who were not cured after physiotherapy intervention.

7.5.1 Recruitment and sample characteristics

While the study achieved a steady participant recruitment rate, the recruitment start date was delayed due to the COVID-19 pandemic which caused repeated closures (including a complete laboratory shutdown for 8 months) and restrictions during both data collection and physiotherapy intervention sessions. Factors associated with the pandemic may have also influenced our participant retention in the physiotherapy intervention, which was low, despite having recruited women with SUI directly from physiotherapy clinics. As our sample included many individuals who had children, participant retention may have also been affected by school closures and the availability of childcare for data collection and physiotherapy treatment sessions. Participant recruitment rates may be increased by offering childcare during the data collection and/or physiotherapy treatment sessions, providing physiotherapy sessions at no charge, recruiting more clinical partners, and providing participants with compensation.

After reaching half of the intended sample size, the planned preliminary analysis suggested that the majority of the effect sizes were nil to small. Previous studies[12,13] with similar or larger sample sizes (n = 43, n = 45) demonstrated large effect sizes for group differences in PNTML, except for Cavalcanti et al.[18] who found no significant differences in PNTMLs between women

with and without SUI (n=52). Further recruitment of participants was unlikely to alter the findings.

Participant discomfort was reported when two DSEs were used concurrently with a St. Marks electrode, leading to the removal of either the LAM (n = 2) or UR (n = 1) or both (n = 4) electrodes in seven participants. A previous study in which the DSE was used intravaginally had no reports of discomfort[33]. The reported discomfort in the present study may be due to the limited intravaginal space for multiple instruments. Manufacturing DSEs using a softer material, such as silicone, may make the instrumentation more comfortable when multiple DSEs are used in close proximity and/or recording from only one muscle at a time may be preferred.

Due to the large amount of data loss associated with both participant discomfort and the unintended dislodging of the DSEs with the St. Marks electrode while locating the correct stimulation point, it may not be feasible to study PNTMLs through intravaginal stimulation when recording from multiple muscles concurrently. Instead, pudendal nerve stimulation may be best performed anally or through nerve root stimulation to reduce potential discomfort and the chance of dislodging electrodes during testing, despite the reports of preferred comfort with intravaginal stimulation[37].

The study sample is generalizable to predominantly Caucasian women with and without mild to moderate SUI symptoms between the ages of 19 to 67 years. Moreover, the physiotherapy intervention consisted of individualized programs, with varied methods of instruction and exercise parameters; this allowed for more generalizable physiotherapy practices. With this intervention, the cure rate was 42% which is in line with the cure rates reported in studies with more tightly controlled physiotherapy interventions[28,30]. However, regular contact with the

participants for better reporting on their exercise programs, number of visits, and adherence to the program may allow for better comparisons to other studies.

7.5.2 Objective 1: Differences in voluntary and evoked activation between women with and without SUI

7.5.2.1Evoked EMG activation

The CMAP data suggested no evidence of motor neuropathy among women with SUI. While longer PNTMLs to the EAS and BSM have previously been reported among those with SUI compared to continent women[10–14], our results did not corroborate these findings. Prolonged PNTMLs are thought to be associated with trauma to the pudendal nerve incurred during pregnancy and vaginal delivery[8,9], though the relevance of these observed changes has been debated[38]. In addition to the current study, others have reported no difference in PNTMLs to the EAS[13] and circumvaginal musculature[18,19] between those with and without SUI. While PNTML is considered useful for detecting gross nerve damage[39], substantive demyelination is required before the CMAP latency is prolonged[39,40]. As such, prior damage to the myelinated pudendal nerve fibers incurred by participants in this study during vaginal delivery, may not have been severe enough to result in lasting changes in pudendal nerve conduction. Previous research indicates that signs of impaired motor conduction are observed immediately after vaginal delivery, but return to normal ranges within 6 weeks to 6 months postpartum[8,9,41–43]; all participants in the current study were a minimum of 6 months postpartum. Persistent pudendal nerve impairment after vaginal delivery may be rare and the prevalence of these prolonged PNTMLs is estimated to be between 11—21%[9,41] but was based on small samples (n = 14, n = 22)[9,41]. As such, this study may have been underpowered to detect group differences in pudendal

neuropathy based on the low prevalence of the condition but did find a small number of select cases without detectable CMAPs.

Despite the reported good reproducibility of CMAPs from intravaginal stimulation of the pudendal[37], others suggest that it may be poor[18,44]. Indeed, the stimulus artifact in pudendal nerve CMAPs often prevents the quantification of CMAP amplitude, duration, and area, leaving PNTML as the only measure that is reported[45,46]. This was observed in the current study, where CMAPs were most often superimposed on the stimulus artifact (Figure 7.7). As such, CMAP latency was the only parameter that could be reported. Typical PNTMLs to the EAS and BSM have been reported as 2ms, and it has been suggested that latencies greater than 2ms may be reflective of pudendal nerve damage[46]. The mean PNTML observed in the current study was close to 3.5ms, which, while within the range of values reported by others[10,12,13,18] is higher. Based on the distance between the stimulation and recording site on the St. Mark's electrode, an onset latency of 3.5ms represents a conduction velocity of approximately100m/s, which is higher than what would be expected for motor nerves based on normative values reported for the upper (40 to 55m/s) and lower (50 to 70m/s) extremities[45]. The latencies reported here and elsewhere seem unlikely to be the result of stimulating the pudendal nerve itself but are more likely to be the result of stimulating terminal branches of the pudendal and levator ani nerves and/or the muscle fibers directly[46]. As such the validity of PNTMLs from intravaginal or anal stimulation is unclear. While it may help to rule out complete peripheral nerve lesions in some cases[46], it may not be useful for detecting incomplete lesions or demyelination.

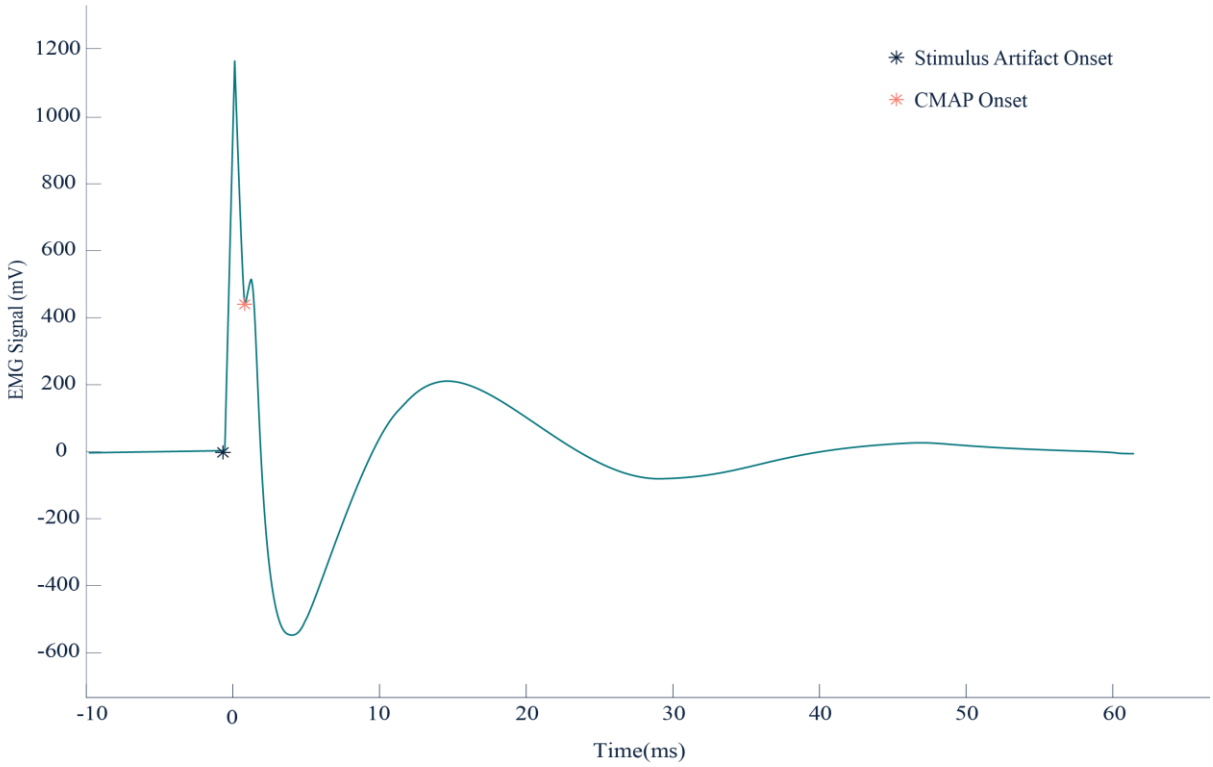

Figure 7.7 Compound muscle action potential (CMAP) from the external anal sphincter depicting the point selected as the stimulus artifact onset and the CMAP onset.

There were four cases in which a CMAP was not detected: two at the BSM, one at the LAMs, and one at the UR. While this could indicate severe nerve damage, as a lack of CMAPs may suggest neuropathy, no participant demonstrated signs of impairment along more than one branch of the pudendal nerve. This may indicate that the impairment is isolated to terminal branches and not the pudendal nerve as a whole. However, the presence of voluntary muscle activation recorded from all participants at these PFM sites, even when it was not possible to evoke a CMAP, suggests that these participants may exhibit variation in innervation of the PFMs[6,45,47].

7.5.2.2 Voluntary EMG activation

EMG activation amplitudes recorded from the LAMs, UR, and EAS during PFM MVC were not affected by continence status nor parity; however, the BSM peak amplitude was lower among those with SUI compared to continent individuals. While this result may indicate impaired neuromuscular activation of the BSM[21], this finding should be interpreted with caution as the alpha level of statistical testing was not corrected for multiple comparisons due to the exploratory nature of this study; this finding may therefore be spurious.

Additionally, the amplitudes of the PFM EMG signals recorded during this study were not normalized. EMG normalization is typically recommended when comparing muscle activation during functional tasks among individuals and between groups[48], however common practice in these cases often involves normalizing to MVC. Indeed, normalization to maximal contraction may be instructive to study motor control during functional tasks and the findings of this study suggest that normalization to PFM MVC is feasible since activation amplitude was not found to be different between those with and without SUI. While some research reports that women with mild SUI demonstrate higher LAM activation during postural perturbations[49] or static holds[23] when compared to continent women, other studies report lower LAM activation amplitude during MVC in women with SUI compared to continent women using both normalized[21] and non-normalized EMG signal amplitude[20,32,50,51]. Despite these conflicting results, the current findings do not support the presence of differences in PFM EMG activation between those with and without SUI, except at the BSM. However, SUI symptom severity may impact EMG activation amplitude[21,52]. Though the sample in the current study presented with a wide range of symptom severity (ICIQ-FLUTS UI subscale scores ranging from 3 - 16), the sample was

underpowered to investigate the effect of incontinence severity on EMG outcomes, which may be why we found no group differences.

Similar to the rate of activation measure in the study by Leitner et al. [24], the current study found no difference in the amplitude rise time of the LAMs based on continence status. However, others have found that women with SUI generate force more slowly compared to continent controls using dynamometry[25] and pressure sensors[52]. These conflicting findings may be explained by a delay between excitation (EMG activation) and contraction (force generation) and should be investigated further. This study also indicated that the BSM took longer to reach its peak amplitude than the LAMs, which may reflect differences in muscle function. The LAMs are required to produce short, quick bursts of activity (e.g., during coughs) as well as tonic activity to support the pelvic organs[53]. While the BSM is thought to play a role in sexual function through vaginal closure and compression of vestibular glands during the erection of clitoral structures[54], which may require a slower amplitude rise time.

7.5.3 Objective 2: Differences between women with stress urinary incontinence who are cured vs not cured after a physiotherapy intervention

Effect sizes for the CMAP latencies were small, indicating no differences between women with SUI who were cured of their symptoms with a physiotherapy intervention and those who were not cured. Only the CMAP at the LAMs displayed a large effect size, suggesting that individuals who were cured with a physiotherapy intervention may have prolonged PNTMLs to the LAMs compared to those who were not cured. However, it seems odd that individuals displaying potential signs of nerve impairment would experience a cure with physiotherapy, as one would expect that individuals without nerve impairment would do better with an exercise-based

intervention. Moreover, the magnitude of this difference was relatively small (0.17ms) which may not be clinically relevant, though criteria for clinically relevant cut-offs of the pudendal nerve have not been established. Swash et al.[55] have suggested that PNTMLs of more than 2.5ms indicate nerve injury in women with incontinence, but this would suggest that all of the study participants had nerve impairment and this cut-off value has not been validated by further research.

Previous work by Gunnarsson et al.[19] also reported no differences in peripheral nerve function between women with SUI who were (n = 9) and were not cured (n = 9) of their symptoms when evaluated after a physiotherapy intervention. Similarly, no group differences in CMAP latencies were observed, though there was an individual who had no detectable CMAP at the UR. While this may indicate localized damage to the perineal branch of the pudendal nerve, the participant demonstrated voluntary activation at all recorded sites, which may instead reflect alternative innervation of the UR. Moreover, this participant was nulliparous, so it is unlikely that the lack of CMAP would be the result of nerve damage incurred through vaginal delivery.

The effect sizes for group differences in MVC peak amplitude and rise time were small between those who were and were not cured of their SUI symptoms after a physiotherapy intervention, suggesting no differences in voluntary activation between these groups. As such, it seems unlikely that the success of a physiotherapy intervention for SUI is associated with voluntary and evoked PFM activation.

7.5.4 Strengths and limitations

Researcher blinding was a strength of this study and is not explicitly reported by the other studies[12–14,18] investigating PNTMLs in women with SUI. Moreover, the use of the DSEs was

also a strength of the study as these electrodes have demonstrated excellent between-trial reliability[33] and are less susceptible to motion artifact[33] and crosstalk[34] from the hip adductors/rotators in comparison to commercially available intravaginal probe electrodes.

The cure criteria used in this study relied on the self-reported leakage events over a 4-week period[56,57]. We chose a cure criterion cut-off (≤4 on the ICIQ-FLUTS UI subscale) to be consistent with previous research[58,59] thus allowing for comparisons across studies. Using this criterion, 5 women were considered cured of their symptoms and 7 were not, resulting in a cure rate of 42%, which is in line with past research[27–31]. However, using only the ICIQ-FLUTS questionnaire to assess cure may limit the extent of change noted in symptom reduction[57], as it has been recommended by the International Continence Society to use both subjective and objective outcomes when evaluating treatment outcomes[57]. Despite this recommendation, the use of the ICIQ-FLUTS UI subscale for cure criteria seems feasible based on the cure rate obtained.

While the DSE has not been specifically validated for EMG recordings from the UR, there were observable differences in CMAP latency recorded from the UR and LAM sites which suggests that the signals measured by the urethral electrode were not significantly impacted by volume conduction from the LAMs. Future research should validate the DSE for urethral EMG, as it is less invasive than urethral EMG techniques currently used, such as concentric needle EMG[60] or electrodes mounted on a catheter[61].

Future research may not find measurements of pudendal nerve conduction through intravaginal stimulation relevant to the study of SUI pathophysiology for those with mild to moderate cases. Instead, future research may choose to focus on neuromuscular activation measured through needle EMG. Previous research has indicated that there are signs of denervation-related motor

unit loss in the levator ani[17] and EAS[13] of women with SUI compared to controls, which is suggestive of neuropathic changes in these muscles. Determining whether these neuropathic changes result in concurrent alterations in muscle function through dynamometric assessments of contractile force, motor control, and proprioception may be warranted in this population.

7.6 Conclusions

At the planned preliminary analysis point for the study (n = 30), the stopping criteria were reached as the effect sizes for between-group differences were small, suggesting a low probability of detecting these differences after reaching the target sample size (n = 60). The findings of this study do not support the presence of differences in evoked potentials and voluntary activation recorded from the PFMs between women with and without SUI. There was also a substantive amount of data loss from electrodes becoming dislodged during testing and some participants reported discomfort with multiple intravaginal electrodes being used concurrently. Thus, changes to the protocol would be needed to improve participant comfort and reduce data loss prior to any further research. Moreover, the feasibility of detecting group differences in voluntary and evoked potentials between women with SUI who were and were not cured of their symptoms with a physiotherapy intervention was also low. As such, the findings additionally suggest that measures of voluntary and evoked potentials may not be useful in predicting the success of physiotherapy treatments for women with SUI.

7.7 References

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Chapter 8: General discussion

Although there is a growing body of literature on the sensorimotor correlates of stress urinary incontinence (SUI) in women, they are not yet well understood. More clarity on the role of nerve and muscle dysfunction is needed to improve our understanding of SUI as well as to understand the factors that impact the success of conservative interventions. Previous research has reported on motor and sensory nerve function of the pudendal nerve among women with SUI[63,170], but to the best of the author's knowledge, no previous studies have reported on a comprehensive sensorimotor assessment like the one presented in this dissertation. The aim of this thesis was to begin to address gaps in knowledge around the potential involvement of motor and sensory neuropathy in SUI, as well as the potential impact of impairments in motor and sensory nerve function on the outcome of physiotherapy interventions for SUI. The findings from this thesis identify areas of focus for future research on sensorimotor impairments in SUI that may be relevant to both scientists and clinicians. Additionally, the dynamometry-based proprioceptive protocol developed through this thesis may be used in future research to better understand normative proprioceptive function in the female-typical pelvic floor and to determine if impaired proprioceptive function may play a role in SUI and other pelvic floor disorders.

8.1 Review of chapters

This dissertation presents four chapters describing the development of proprioceptive testing methods and a comprehensive sensorimotor assessment individually exploring differences in muscle function and proprioception, light touch sensation, and motor nerve function in a sample of women with and without SUI.

Chapter 4 describes the development of a novel pelvic floor muscle (PFM) proprioception testing protocol that was modelled after tests of limb proprioception and was designed to examine the

participant's ability to detect passive changes in PFM length and sense of PFM contractile force. Through this study, we established robust data collection and data processing techniques. Using these techniques, we found that accuracy in detecting changes in PFM length and sense of PFM force output have wide variance and that force-matching performance is influenced by both the provision of visual feedback and the target contraction intensity. Participants were better able to control their PFM contraction with visual feedback and at lower contractile intensities. Information generated from using this protocol in different populations may improve our knowledge of normative PFM proprioception and its role in the pathophysiology of SUI and other pelvic floor disorders.

The findings reported in Chapter 5 suggest that PFM motor function does not differ between women with and without SUI. At the planned preliminary analysis point for the study (n = 30), the trial-stopping criteria were reached as the effect sizes for between-group differences in LAM passive, active, and proprioceptive function were small, suggesting a low probability of detecting group differences once the target sample size was reached (control n = 30, SUI n = 30). However, the effect sizes indicated that participants with SUI who had more room for improvement in PFM power, control, and proprioception tended to be more successful with physiotherapy interventions. As has been reported previously[241,242], women who were cured with a physiotherapy intervention also demonstrated milder SUI symptoms while those who were not cured had more severe symptoms when measured by the International Consultation on Incontinence Questionnaire—Female Lower Urinary Tract Symptoms (ICIQ-FLUTS). These findings may indicate that PFM power, control, and proprioception may be predictive of a cure with physiotherapy interventions for women with SUI and warrant further investigation.

Additionally, the findings reported in this chapter suggest that parity may affect PFM function, motor control, and proprioception. Parous women demonstrated lower PFM force-generating capacity but were not influenced by visual feedback on the proprioception force-matching task. The observed differences in PFM function with parity may be relevant to the pathophysiology of SUI and other pelvic floor disorders[243].

In Chapter 6, the regression models of genital light touch sensation thresholds indicated that SUI was associated with higher sensory thresholds when tested on the perianal skin. Though not significant, sensory thresholds at the perineum and labia majora tended to be higher in women with SUI compared to continent controls as well. The examination of outlier cases with elevated sensory thresholds found that each case had an impairment at only one site; suggesting that each outlier may have had a focal sensory impairment rather than impairment of the pudendal nerve as a whole. The findings of this study suggest that using monofilaments to assess genital light touch sensation may inform only on focal sensory disruptions rather than the pudendal nerve as a whole.

The final experiment presented in Chapter 7 investigated differences in voluntary and evoked PFM activation between women with and without SUI. At the planned preliminary analysis point for the study (n = 30), the trial-stopping criteria were reached as the effect sizes for between-group differences in both voluntary and evoked potentials were small, suggesting a low probability of detecting group differences once the target sample size was reached (control n = 30, SUI n = 30). There was also substantive data loss from electrodes becoming dislodged during testing and some participants reported discomfort when multiple intravaginal electrodes were used concurrently.

The small effect sizes for this analysis, suggest that pudendal neuropathy may not be relevant to mild SUI pathophysiology, at least for the individuals who participated in this study. Among the overall sample (n = 29), there were four individuals who did not demonstrate detectable CMAPs, each only at one site (bulbospongiosus [BSM] n = 2; LAMs n = 1; urethral rhabdosphincter [UR] n = 1). While this finding may indicate the presence of nerve damage, CMAPs were present in the other recorded sites and voluntary activation was present at all sites, which suggests that these individuals may have variation in their innervation.

The secondary objective was to assess the feasibility of detecting differences in voluntary and evoked PFM activation of the BSM, UR, LAMs, and EAS in women with SUI who were and were not cured with a physiotherapy intervention. Twelve of 16 women with SUI completed a physiotherapy intervention after attending the laboratory-based assessment protocol. Of these participants, five were considered cured (42% cure rate) after the intervention. The effect sizes for this analysis were small and suggested low feasibility for detecting differences in this sample. As such, voluntary and evoked PFM activation may not be useful in predicting the success of physiotherapy treatment for SUI.

8.2 Sensorimotor impairment in stress urinary incontinence

Despite evidence in the literature supporting a role for sensorimotor impairment in SUI pathophysiology[55,57,58,60,63,76,169,170,200], the research in this dissertation suggests that there was no evidence of group differences in sensorimotor function between women with and without SUI. That said, there were individual cases of outlying values indicating potential motor nerve impairment (n = 4) and light touch genital sensory loss (n = 4). However, only one case presented as an outlier in both the motor nerve and sensory testing.

This case displayed no detectable CMAP at the BSM and demonstrated an extremely high sensory threshold at the perianal skin. The participant was 51 years old, parous with two vaginal deliveries, and had mild SUI symptoms. Both the BSM and perianal skin receive innervation from the pudendal nerve[104], however, the BSM receives motor input through the perineal branch while the perianal skin receives sensory innervation from the inferior rectal branch [244,245]. Thus, the nerve testing may have uncovered some evidence of focal impairments rather than impairments to the nerve as a whole. If the pudendal nerve had been damaged as a whole, one would expect to see both motor and sensory changes across more of the nerve branches (i.e impacting the UR, EAS, and BSM) and higher sensory thresholds at more than one stimulation site (i.e. external urethral meatus, perianal skin, and perineum) with concurrent motor and sensory nerve impairment along the same nerve branches. Alternatively, as the individual was parous, she may have experienced more diffuse nerve damage immediately after childbirth (i.e. damage to multiple branches of the pudendal nerve) and then recovered to antepartum levels of nerve function[208,210], leaving only the more severely damaged branches with lasting signs of impairment.

The observed changes in motor and sensory nerve function in the outlier case did not appear to translate into detectable impairments in PFM proprioception. The participant demonstrated a similar score to the sample average in performance on the passive elongation task and had values on the force-matching task that were within the 95% confidence intervals for each target and feedback condition. However, the nerve impairments may have influenced outcomes from the dynamometry assessment, where this individual demonstrated a rate of relaxation that was outside of the bounds of the 95% confidence interval for both continent and incontinent women, indicating a decreased ability to relax their PFMs post-contraction. This could suggest impaired

motor control and/or higher excitability of corticomotor pathways. That said, the branches demonstrating nerve impairment were the perineal and inferior rectal branches, which are not thought to be involved with the deeper layer of the PFMs (LAMs)[244,245], though variation in innervation does exist across individuals[246]. It seems unlikely that damage to these specific branches of the pudendal nerve was involved in the slowed relaxation of the PFMs post-contraction. Unfortunately, this participant's electrode to the LAMs became dislodged during testing and the recorded signals were not useable to determine if there may be motor nerve impairment detected through pudendal nerve stimulation. Further testing would be required to better understand this particular case.

The remaining outlier cases for the motor nerve assessment did not demonstrate concurrent signs of sensory impairment. However, one outlier had no detectable CMAP at the LAMs, a poor ability to detect changes in PFM length, and difficulty in performing a series of quick PFM contractions in 15 seconds. In contrast to the expectation that the outlier cases would only be present in those with SUI, this participant was continent, parous (1 Caesarean and 3 vaginal deliveries), and 47 years old. While the lack of detectable CMAP at the LAMs may indicate nerve damage, this participant did demonstrate LAM activation on EMG and contractile force on the IVD during voluntary contractions, which may instead suggest that they had no pudendal innervation to the LAMs. This participant also displayed a poor ability to discern changes in PFM length during the passive elongation task (i.e. performance was below the lower bound of the 95% confidence interval) which suggests that there may be some proprioceptive impairment, though there was no evidence of this on the force-matching task. Moreover, the number of contractions performed by this participant on the fast contractions task was low and outside of the lower bound of the 95% confidence interval, which is suggestive of poor motor control.

Together, these findings may reflect impairment of the levator ani nerve, however, an assessment of levator ani nerve function was beyond the scope of this thesis.

The remaining participants who demonstrated outliers in sensory thresholds did not demonstrate concurrent signs of motor nerve or proprioceptive impairments. However, one individual (52 years old, parous with two vaginal deliveries, and moderate SUI symptoms) who had a high sensory threshold at the UR displayed poor motor control on the fast contractions task (i.e. outside of the lower bound of the 95% confidence interval). The UR is innervated by the perineal branch of the pudendal nerve, which is not known to innervate the LAMs. As such, it is unlikely that the sensory nerve impairment to the UR played a role in LAM motor control during the quick contractions task. This participant's symptoms were improved but not cured after a 12-week physiotherapy intervention.

While the prevalence of pudendal and levator ani nerve injuries is currently unknown, it appears that the prevalence of nerve impairment incurred through natural life events (e.g. pregnancy, vaginal delivery, aging, etc.) is low[247]. Therefore, it was unlikely that group differences in motor nerve conduction or genital sensation thresholds would be observed in our sample. Instead, it was more likely that we would find a small percentage of individual cases of nerve impairment. Moreover, the lack of consistent changes in PFM function and proprioception in the outlier cases demonstrating nerve impairment suggests that sensorimotor function may not play a role in mild SUI pathophysiology.

Lastly, among women with SUI who were and were not cured with a physiotherapy intervention, there were no group differences in motor nerve function; however, the effect sizes from the IVD outcomes did indicate that to see improvement with physiotherapy, room for improvement in

PFM function and proprioception may be needed. This suggests that while sensorimotor function may not be important to mild SUI pathophysiology, some aspects of muscle function may be relevant to predicting the likelihood of success with conservative treatment and should be investigated further.

8.3 Parity and evidence of sensorimotor impairment

The sensorimotor assessment of the PFMs demonstrated no group differences in motor nerve conduction or genital sensation based on parity. However, seven outlier cases were identified from these assessments and the majority of these cases were found in parous women. Though the evidence of nerve impairments did not always correspond to concurrent changes in PFM function and proprioception, group differences in these outcomes were found based on parity. Parous women demonstrated a reduced ability to generate and release force during maximum effort contractions and their sense of PFM contractile force did not depend on the presence of visual feedback. These group differences in muscle function warrant further investigation to determine their potential involvement in pelvic floor disorders.

It is possible that the motor or sensory nerve impairments observed in the outlier cases were the result of damage incurred during childbirth, as the pudendal and levator ani nerves are thought to be prone to damage during pregnancy[212,248] and vaginal delivery[207–210,249]. Initial signs of impairment in motor conduction, such as prolonged pudendal nerve terminal motor latencies (PNTMLs)[207–210], increased turns per amplitude[51,144], and increased sensory thresholds have been observed immediately after vaginal delivery[248], but appear to return to normal ranges within 6 weeks or 6 months postpartum[51,144,207,208,210,248]. Interestingly, small subsets of women have demonstrated persistent signs of nerve impairment beyond this recovery period, which has been associated with the onset of SUI symptoms in some cases[208,210]. In one longitudinal study, 5

women (21%) of 24 participants with prolonged PNTMLs in the early postpartum period reported SUI symptoms at a 5-year follow-up assessment[208]. Similarly, Sultan et al.[210] found that 12 women (11%) of 105 demonstrated persistent prolonged PNTMLs at 6 weeks postpartum, but only one participant reported urinary incontinence symptoms (subtype not specified). At a 6-month follow-up in the same sample, only 4 women (18%) demonstrated persistent prolonged PNTML but there were no reports of urinary incontinence. However, both studies assessed PNTMLs at the EAS rather than motor and sensory innervation across multiple branches of the pudendal nerve, so we lack comparable research showing patterns of impairment across the branches of the pudendal nerve. The recovery of motor and sensory nerve function by 6 months postpartum for the majority of women in these samples may suggest that one would be unlikely to find group differences in motor and sensory nerve function, but instead find a small percentage of women with persistent signs of nerve impairment.

The nerve impairments identified in these outlier cases did not consistently translate to concurrent changes in PFM function and proprioception. That said, some of the cases displayed a reduced ability to relax the PFMs after a maximum effort contraction, poor proprioception on the PFM elongation task, and a decreased ability to generate quick PFM contractions within a time limit. However, the affected nerves were not branches that specifically innervated the LAMs, so it is unlikely that the individual cases of motor or sensory nerve impairment were related to the observed changes in PFM function and proprioception.

The group differences in PFM function and proprioception based on parity suggest that these aspects of function are changed with pregnancy and vaginal delivery. Compared to nulliparous women, parous women demonstrated a reduced ability to generate force and relax their pelvic floor after a maximum effort contraction. These findings build on previous work that has

suggested that parous women demonstrate increased LAM muscle fibre length[250] and neuropathic changes in the urethra [212] and LAMs[51,144], which may be associated with functional changes in the pelvic floor.

For parous women, accuracy on the force-matching task did not depend on the availability of visual feedback, which significantly improved the performance of nulliparous women. While there was no evidence of proprioceptive impairments among the parous women, the findings may point to a reduced ability to integrate sensory and motor information. Further research is needed to better understand the impact of parity on motor control and proprioception in the PFMs, which may improve our understanding of the role of parity in pelvic floor disorders.

8.4 Novel pelvic floor muscle proprioception assessment

At the time that the proprioception testing protocol was developed for this thesis, there were no published studies in the literature which objectively examined PFM proprioception. While some authors have suggested that proprioception may be important to PFM contributions to continence control[72,75,77,200,204,206], very little is known about it. Our goal was to develop a standardized, objective assessment of PFM proprioception using an IVD. The protocol presented here is a novel contribution to pelvic floor assessment techniques that has the potential to inform on the proprioceptive function of the female-typical pelvic floor. The outcomes generated through this approach may help to improve our understanding of rehabilitation outcomes and enhance current rehabilitation protocols.

Proprioception is a key component of motor control[251]. Past research has found that women often require further instruction and/or feedback through palpation to develop the ability to perform a proper voluntary PFM contraction[252–256] and have reported impairments in PFM coordination

between those with and without pelvic floor disorders [35–39]. Since the creation of this protocol, one research group has published a PFM proprioception test to evaluate sense of force output[72] and another research group has assessed intravaginal stretch sensation, but not among women with SUI[257]. Kharaji et al.[72] developed a PFM force-matching task with an IVD, comparing the sense of force output between women with (n = 23) and without SUI (n = 18). They found that at both IVD apertures, women with SUI demonstrated less error on the force-matching task with moderate effect sizes (d = .67, d = .46) than continent women. However, the details of data processing were not described despite the influence that signal processing can have on the results of a proprioception protocol[258], nor was researcher blinding stated.

A study by Mahoney et al.[257]described an intravaginal stretch perception protocol using the method of limits, whereby, a catheter was inflated within the vagina until the participant indicated the first sensation of an intravaginal stretch. They found that this protocol was repeatable[257] and used it in a subsequent study on antenatal and postnatal intravaginal stretch sensation, finding that women with uncomplicated vaginal deliveries recovered antepartum levels of intravaginal stretch sensation at 6-months postpartum[248]. However, their protocol uses the method of limits, which can be influenced by participant reaction time and can therefore elevate thresholds[259]. Additionally, intravaginal stretch sensation may not be comparable to changes in muscle length as intravaginal sensation would be more focused on mechanoreceptors in the vaginal mucosa rather than proprioceptive information from the PFMs. The protocols developed and presented in this thesis address the research gaps left by the two previous studies, by thoroughly describing the data collection and processing protocols, following standards from proprioception tests for the limbs, and reducing the impact of reaction time on threshold measurements by using a method of levels-style testing[259].

Though we did not find differences between those with and without SUI, these proprioceptive outcomes may uncover proprioception impairments in other pelvic floor disorders. Future work should include reliability testing and evaluate the application of proprioceptive testing in other pelvic floor disorders. The development and refinement of the proprioception testing protocol described in this dissertation makes a substantive contribution to PFM research, which has the potential to advance our knowledge of normative function and dysfunction in the PFMs.

8.5 Strengths and Limitations

A strength of the research presented in this doctoral thesis was the comprehensive assessment of the sensorimotor function of the pelvic floor. As the sensorimotor system is complex, performing a wide array of tests on a small sample of women allowed us to do two things: 1) integrate our findings across assessments to build a more thorough picture of how any potential impairments may co-occur, and 2) to identify areas of focus for future research on women with SUI. Promising avenues of study from this dissertation may include:

- Investigate the influence of age and parity on genital sensation at the anterior labia majora, as we found that increased sensation was associated with SUI but mediated by age and parity.
- Investigate the role of parity on PFM function and proprioception measured with an IVD and what implications there are for pelvic floor disorders. In our study, we found that pelvic floor function and proprioception were different based on parity but not continence status.
- Explore the influence of instruction on how to contract the PFMs on participant accuracy during a PFM force-matching task. Instructions on how to reach a target force could influence the strategies that people employ to accomplish the task. The researcher

performing the data collection observed people using three different strategies to hit the target forces: contract slowly and smoothly to the target and try to maintain the sub-maximal squeeze, contract in a stepwise manner until they reached the target, and contract to 100% then relaxing the contraction until the force-time curve reached the target.

- Determine if sensorimotor impairments play a role in severe SUI symptoms, as this study does not indicate that it plays a role in mild SUI cases. Some research indicates that SUI symptom severity may influence involuntary pelvic floor activation patterns[204,205], yet it has not been thoroughly investigated.
- Investigate the comfort of differential suction electrodes (DSEs) made from a softer material, like a medical grade silicone, for assessing LAM and UR activation simultaneously. Participants in our study found multiple DSEs uncomfortable during testing and improved participant comfort may reduce data loss in EMG studies involving intravaginal suction electrodes.

Another strength of the research presented in this thesis is the careful selection of investigations to improve objectivity and reliability in the evaluation of the various aspects of sensorimotor function in the female-typical pelvic floor. For example, we selected monofilaments for our assessment of genital sensation and St. Mark's electrodes with vaginal stimulation for the motor nerve protocol because they had previously demonstrated good reliability[78,260]. Additionally, we used an IVD for PFM function and proprioceptive assessments, as this is currently the most objective way to assess the pelvic floor. This also helped with maintaining researcher blinding, as group assignments may be unblinded in palpation assessments[77,261,262]. Both the sensory and motor nerve protocols were comprehensive, including several nerve branches relevant to lower

urinary tract function. For example, in the sensation testing protocol, we studied areas of the genital skin innervated by three branches of the pudendal nerve, rather than just one nerve branch or the clitoris, which is thought to be innervated by more than just the pudendal nerve[64]. By examining all three sites, we created a more comprehensive assessment which had the potential to pinpoint the branches of the pudendal nerve that demonstrated impairment. Lastly, the assessor in this study was blinded to group assignment, which was a strength, as blinding has not been reported in many of the studies referenced throughout this dissertation.

Though the comprehensive sensorimotor assessment was a strength, it was also a limitation. The protocol was long (2 sessions x 2 hours) and involved testing techniques of a sensitive nature, which may have been a factor in participant recruitment. As data collection also took place during the COVID-19 pandemic, we had to comply with constantly changing public health policy and university rules and regulations for safety, including a complete laboratory shutdown for 8 months, which limited recruitment. An alternative to the comprehensive sensorimotor assessment could have been to focus on only one aspect of the assessment (e.g. only motor nerve, sensory thresholds, or proprioception), and potentially recruit a larger sample. However, given the low feasibility of recruitment during the pandemic, we opted to recruit a small sample and, knowing that the study may be underpowered, use these data to generate hypotheses for future research.

While previous groups had already performed investigations of motor and sensory nerve function of the pudendal nerve[63,170], to the best of the author's knowledge, no previous studies have reported on a comprehensive sensorimotor assessment like the one presented here. Though each aspect of the assessment is presented separately in this dissertation, the results converge; taken together, the findings do not support the presence of sensorimotor impairment among women

with mild SUI. If there had been evidence of sensorimotor impairment in our sample, we would have expected to see evidence of nerve impairments with corresponding changes in muscle function (e.g. slower contractions or changes in proprioception).

The comprehensive assessment performed for this thesis did highlight changes in sensorimotor function based on parity. In the IVD assessment of PFM function and proprioception, parous women demonstrated deficits in force generation and motor control, but better LAM proprioception in the force-matching task than nulliparous women on the IVD protocol. These findings warrant further research to determine the role of parity in PFM function and motor control.

The low generalizability of this sample is a limitation of this dissertation, as the recruitment techniques created a biased sample. Women included in this study were able to take a significant amount of time off of work, and access childcare for both the data collection times and physiotherapy appointments if they attended the intervention portion of the study. Moreover, the waitlists of the physiotherapy clinics would have only had women that could afford treatment and had knowledge of such treatment availabilities. As such this sample is only generalizable to women in higher socioeconomic statuses and should be interpreted within these limits

8.6 Rehabilitation implications

This dissertation research was based on a biomedical model, involving basic sciences in the assessment of function and dysfunction of sensorimotor aspects of the urinary continence system. This model simplifies illnesses/conditions to impairment in structure or function[263] and is limited in generalizability and applicability to real-world situations, as it does not account for psychological, social, or environmental contexts. As the specific focus of this thesis was on the

physiological differences between continent and incontinent individuals, the biomedical model was important for objectively organizing the information to direct the study. It also allowed us to objectively define the presence or absence of SUI for the classification of the study groups and to establish criteria to describe a cure with treatment.

The research presented in this dissertation contributes to the body of literature in the rehabilitation sciences in two important ways. First, the development of a novel PFM proprioception protocol may enhance our understanding of normal pelvic floor function and proprioceptive impairment and has the potential to inform on the role of PFM proprioceptive impairment in pathology and rehabilitation. The protocol developed for this purpose builds on previously developed assessments of the peripheral limbs and adapts these techniques to the PFMs. At the time of study conception, no proprioceptive testing protocol for the pelvic floor had been published in the literature. Despite another protocol being published while this research was underway, the protocol developed through this dissertation has undergone robust testing of the role of visual feedback and signal processing methods and advances a standardized approach to testing PFM proprioception for future research.

Second, this dissertation highlights that sensorimotor impairment is unlikely to be a substantive contributing factor to individuals with mild SUI symptoms. As our effect sizes ranged from no effect to small, it suggests that rehabilitation strategies for this group of patients may not need to be re-evaluated or consider additional sensorimotor rehabilitation techniques. That said, our sample was not large enough to assess whether sensorimotor impairments may be a component of more severe SUI symptom pathophysiology. Some studies have noted that involuntary PFM activation is different between mild and severe SUI cases[204,205], which may suggest that sensorimotor impairments could play a role in more severe cases but aren't relevant to mild SUI

pathophysiology. In predictive models aimed at determining which women with SUI will benefit from a physiotherapy intervention, mild SUI symptoms were associated with a cure while more severe symptoms are associated with no cure[241,242]. This could suggest that severe SUI symptoms may be associated with injuries to the PFMs and surrounding tissues that are beyond the capacity of physiotherapy interventions to cure, or that additional treatment techniques (e.g. sensorimotor rehabilitation techniques) may enhance rehabilitation outcomes among women with more severe symptoms. As SUI is multifactorial, each case may be unique in the factors that have contributed to the development of symptoms. More research is needed to understand how physiotherapist-supervised PFM training through physiotherapy interventions improves continence function as the mechanism through which this treatment works is not yet clearly understood [203].

8.7 Conclusions

This dissertation explores the sensorimotor correlates of SUI in women through a biomedical lens. The goal of this was to advance our knowledge of impairment at the most basic levels of structure and function. This work can be used to focus future research on the specific aspects of function that demonstrate the most promise for improving our knowledge of SUI pathophysiology and to generate hypotheses for future studies to address those that hold the most promise for understanding pelvic floor disorders. Ultimately, this dissertation is part of the foundation upon which future research aimed at understanding the pathophysiology of pelvic floor disorders can build to accelerate advancement in this field.

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Appendix A: Ethics Approval

15/02/2022

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-07-20-5945
Titre du projet / Project Title	Sensory and motor correlates of stress urinary incontinence in women and their influence on pelvic floor muscle training outcomes.
Type de projet / Project Type	Thèse de doctorat / Doctoral thesis
Statut du projet / Project Status	Renouvelé / Renewed
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	15/03/2021
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	14/03/2023

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Kaylee BROOKS	École des sciences de la réadaptation / School of Rehabilitation Sciences	Chercheur Principal / Principal Investigator
Linda MCLEAN	École des sciences de la réadaptation / School of Rehabilitation Sciences	Superviseur / Supervisor
Duane HICKLING	Département de chirurgie / Department of Surgery	Co-chercheur / Co-investigator
Silvia SARAIVA	École des sciences de l'activité physique / School of Human Kinetics	Coordonnateur de recherche / Research Coordinator

Conditions spéciales ou commentaires / Special conditions or comments

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Appendix B: Telephone Interview

Telephone Interview

Hello, my name is _____ and I am the Recruitment Officer at the Motor Function Measurement Laboratory run by Dr. Linda McLean at the University of Ottawa.

Thank you for your interest in our study entitled, "Sensory and motor correlates of stress urinary incontinence in women and their influence on pelvic floor muscle training outcomes"

I would like to tell you about the study, and the details of what your participation would entail if you are eligible and choose to participate. If, after I describe the study to you, you are still interested in participating, then I will ask you a few questions to determine your eligibility for the study. This description will take approximately 15 minutes. Is now an appropriate time to complete the interview?

[If not a convenient time, set a day and time for a call to discuss the study].
[If it is a convenient time, continue]

Please feel free to interrupt me at any time if you have questions.

You are being invited to participate in this study because,

[Select the reason that applies to the participant]

1) You have contacted us directly with interest in the study and you do not currently have any pelvic floor disorders
2) You are planning to receive pelvic floor physiotherapy to treat your SUI symptoms.

3) You have already received pelvic floor physiotherapy to treat SUI symptoms.

Is my information correct?

[If yes—continue below.]

[If no—seek clarification and affirm interest in participating before continuing.]

I will start by telling you a bit about the reasons for why we are doing this study.

Many women experience daily urine leakage which is also referred to as urinary incontinence and the most common among women is stress urinary incontinence, which is defined as the involuntary loss of urine during an exertion, cough, or sneeze. Pelvic floor muscle exercises supervised by a pelvic floor physiotherapist can improve the symptoms of stress urinary incontinence, however, only half of the women who complete the intervention are cured. One of the key goals of the research in our laboratory is to better understand why some women's symptoms improve more than others with pelvic floor muscle exercises. While we know that the sensory and motor nerves can be strained during childbirth and that there is some evidence of this damage in women who suffer from stress urinary incontinence, these injuries have not been studied very much. In particular, there has been very little research on the role of motor and sensory nerve impairments in this exercise-based intervention.

As such, through this study we plan to assess the presence of motor and sensory nerve impairments in women with stress urinary incontinence, and to determine if sensory or motor impairments may be responsible for the failure of pelvic floor exercises to alleviate symptoms of incontinence in some women.

The University of Ottawa Health Sciences and Sciences Research Ethics Board has reviewed the ethical components of this study and has found it to be in compliance with national standards.

Do you have any questions so far?

[If yes, pause to answer questions.]

[If no, continue below.]

Should you choose to participate, your participation in the study would be limited to two visits to the Motor Function Measurement Laboratory at the University of Ottawa Lees Avenue campus. Each visit will take approximately 2 to 2.5 hours. Are you still interested in hearing more?

[If no, ask if there is a better time to discuss the study further, and note this day and time down on the telephone log sheet. If not interested in participating, ask why and record response on a log sheet. Thank her for her time.]

[If yes, continue below]

If you agree to participate, you will receive access to online questionnaires through an e-mail link, which we will ask you to complete before your laboratory assessment. Should you prefer, you may receive paper copies of the questionnaires, and a female research assistant will help you fill them out if you request assistance.

[If they have been referred from a physiotherapist use (1), if they have contacted us directly (Control) use (2), if they have already finished physiotherapy use (3)]

1) You will receive two invitations to complete questionnaires. The first invitation will ask you to complete a series of four questionnaires that should take you no more than 30-minutes total to complete. They will ask you about your (1) lower urinary tract symptoms—including urine leakage, (2) bowel control and patterns, (3) vaginal symptoms and associated sexual matters, and (4) quality of life. You will be asked to fill out the questionnaires as soon as possible as your answers might change after you begin physiotherapy. We also ask that you complete these questionnaires before attending the first laboratory session. The second e-mail invitation will be sent to you 12-weeks after

your first physiotherapy visit and will consist of two questionnaires which will ask you about your urinary tract symptoms as well as your feelings of improvement with physiotherapy; these questionnaires should take you no more than 10-minutes to complete.

2) You will receive an e-mail invitation with links to four questionnaires that should take you no more than 30-minutes in total to complete. These questionnaires will ask you about your (1) lower urinary tract symptoms—including urine leakage, (2) bowel control and patterns, (3) vaginal symptoms and associated sexual matters, and (4) quality of life. You will be asked to fill out the questionnaires before attending the laboratory session.

3) You will receive an e-mail invitation with links to five questionnaires that should take you no more than 30-minutes in total to complete. These questionnaires will ask you about your (1) lower urinary tract symptoms—including urine leakage, (2) bowel control and patterns, (3) vaginal symptoms and associated sexual matters, (4) quality of life, and (5) your feelings of improvement with physiotherapy. You will be asked to fill out the questionnaires before attending the laboratory session.

The first laboratory session will take approximately two and a half hours. We ask that for both laboratory assessments you wear a surgical or cloth mask and provide verbal confirmation of two COVID-19 vaccinations. We ask that you bring a copy of your vaccinations with you to the laboratory assessment in the event that university personnel request to see it, and we will provide you with a surgical mask if you do not have one. You also have the option of bringing in a friend or family member to the testing sessions, if that makes you feel more comfortable. They will also be required to wear a mask while in the building and have proof of vaccination on their person while in university buildings. If you would like to have an additional person in the room during your examination session but do not wish to bring a friend or family member, I will be available during the testing session to be in the room with you. Ms. Brooks and her assistant will wear a surgical mask and full personal protective equipment during this assessment.

At the first visit you will be asked to sign a study information and consent form, which Ms. Kaylee Brooks—a research assistant and doctoral candidate working under the direct supervision of Dr. McLean—will go over with you to ensure you fully understand what the study entails. Before signing this form, you should make sure that all of your questions and concerns have been adequately addressed. If you do not consent to participate, we will ask you whether or not we can retain your contact information and contact you to see if you are interested in future studies in our laboratory. If you do not wish us to contact you in the future, we will permanently delete your contact information from our database.

If you agree to participate, you will be shown into an examination room for an assessment completed by Ms. Brooks. First, she will measure and record your height, weight, and waist and hip circumference. Then Ms. Brooks will leave you in the examination room to undress from the waist down and cover yourself with a gown and sheet that will be provided for you. When you are ready, you will be asked to call Ms. Brooks and her research assistant, who will help to prepare instrumentation and operate the computers used to collect data, back into the room. While wearing gloves, Ms. Brooks will perform a quick genital examination to ensure that there is no evidence of

factors such as infection that might interfere with your ability to participate, and that there are no health concerns or risks that you might cause you to experience discomfort during the protocol. Once this screening has been completed, you will be shown the automated intravaginal dynamometer (IVD), which is a device that will be used for some of the testing. Ms. Brooks will provide you with the thumb switch for the IVD which will stop the device during testing at any time. She will then explain the protocol for the first assessment, which will examine your ability to feel your pelvic floor muscles move. Ms. Brooks will instruct you to relax while the IVD arms—which are coved in latex-free condoms—open to specific diameters. First, she will determine your reference diameter for the test, which is the diameter at which the arms open to produce approximately 1.4-1.5N of force while at rest. During the testing, you will be provided with this reference first and then a second diameter will be presented to you immediately after and you will compare the reference to the new diameter and decide if it is larger, smaller, or the same as the reference. The testing session will include 3 trials with diameters that are 5mm larger than the reference, 3 trials with diameters that are 5mm smaller than the reference, and 3 trials with diameters that are the same as the reference. Once you understand how the testing session will work, you will be instructed to lie on the examination table while you guide the IVD arms your vagina. Once you are comfortable, the testing will begin.

Next, using the same IVD, the arms will be opened slightly, and you will be instructed by Ms. Brooks to contract your pelvic floor muscles with maximal effort. This task will be repeated three times. Then she will ask you to contract your pelvic floor muscles as hard and as fast as you can repeatedly over a 15s time period. Next, you will be provided with different target forces to contract your pelvic floor muscles to based on how much force you generated during the maximal contractions. You will be asked to contract to these level both while watching your contraction force displayed on a computer screen and then without being able to see the

computer screen. You will have an opportunity to practice each force level with and without visual feedback 1-3 times before starting the testing session. During testing, you will repeat contractions at each of 3 force levels 3 times with a 1-minute break after each contraction to limit muscle fatigue. The IVD will then be removed.

Ms. Brooks will next prepare you for the assessments of motor nerve function. She will wear examination gloves and will insert a small sensor (electrode) into your vagina using a finger to guide its placement on the anterior vaginal wall. While Ms. Brooks holds the electrode in place, you will be asked to pull the stopper back on an air-filled syringe, which will cause a small suction force to hold the electrode in place during testing. A sticky electrode will also be pressed on the skin beside your anus and a second sticky electrode will be placed on the skin over your right hip. Then Ms. Brooks will put on a new glove that has a specialized electrode attached to it and prepare a second small sensor to be inserted into your vagina. She will feel inside your vagina to make sure that she has the sensor positioned correctly over your pelvic floor muscles and then you will be asked to pull the stopper back on an air-filled syringe, like the previous sensor, to suction it in place. Then, Ms. Brooks will gently shift her finger passed the sensor to locate your nerve and position it correctly to stimulate the motor nerve. Once she has the electrode in the correct position, Ms. Brooks will ask the research assistant to slowly increase the intensity of an electrical impulse that will stimulate the nerve. You will feel your pelvic floor muscles twitch in response to the stimulus. While it may cause some discomfort, it should not be painful. If it is too uncomfortable or extremely painful, please let Ms. Brooks know and she will adjust the electrode and stimulation as needed. When a suitable signal from the electrodes has been found, Ms. Brooks will stimulate your pudendal nerve 10 times. Then you will be asked to contract your pelvic floor muscles voluntarily three times will all of the sensors still in place.

Ms. Brooks will remove all of the electrodes and then both Ms. Brooks and her assistant will leave the room so that you may change back into your clothes. This will conclude the first laboratory assessment.

The second laboratory assessment will be completed within 10 days after the first assessment and will focus on your sensation and ultrasound imaging. It should take approximately two hours. The same research assistant, Ms. Brooks, will greet you when you arrive. Again, you will be required to wear a surgical or cloth mask during the assessment. Ms. Brooks and her assistant will wear a surgical mask and full personal protective equipment during this assessment. Ms. Brooks will review the goals and the protocols of the second assessment with you and answer any questions you have. You will be asked to undress from the waist down in the examination room and cover yourself with a gown and a sheet as you did in the first session. When you are ready, you will invite Ms. Brooks and her assistant into the assessment room. You will be asked to lie down on an examination table with your head supported by a pillow.

This session will start with a sensation test. For each test, Ms. Brooks will instruct you to state yes or no to whether you feel a light touch sensation (touch) after it has been applied to your skin. Five sites will be assessed including your right ankle and four sites in your genital area. These specific sites will be marked with a non-permanent surgical marker to ensure that Ms. Brooks tests the same site each time. The stimulus will be demonstrated first on your forearm so that you can feel what it feels like, and then Ms. Brooks will test each of the study sites, beginning with the ankle before moving to the genital sites. We are looking to record the smallest stimulus that you can feel with each of these sensations, so there should be no discomfort whatsoever associated with the testing. Touch sensation will be tested using small wires that are about as thick as a human hair. Prior to applying a stimulus to any site, Ms. Brooks

will direct your attention to that site by gently touching it with a cotton swab. Each site will be tested three times with each stimulus.

Next, Ms. Brooks will show you the ultrasound probe. In the same position as before, the probe will be placed on your perineum and the image will be optimized to view your pelvic floor muscles. Ms. Brooks will instruct you to contract your pelvic floor muscles maximally 3 times, then she will ask you to stand in front of the exam table and will place the probe in the same place as before. She will instruct you to remain relaxed while three images are collected of your pelvic floor muscles at rest. Ms. Brooks will remove the probe and both her and her assistant will then leave the room so that you can change into your clothes. This will conclude the data collection of the study.

I realize that this is a lot of information. Do you have any questions?

[If yes, respond to questions. If no, continue.]

Are you interested in seeing if you are eligible for participating in the study?

[If yes, continue. If no, ask what the reason is a record on a telephone log. Thank them for their time and tell them to feel free to call back if they change their mind. Ask for consent to keep contact information in our database to future studies. If no consent, delete the contact information from our database]

OK great! Please note that data collected through the eligibility screening process from participants who are not eligible for the study will be destroyed.

Date:_____(yyyy-mm-dd) **Time:_____**

[Part 1: Exclusion Criteria:]

How old are you? _____

Are you currently pregnant?
Yes: _____No: _____
Have you delivered a baby within the past six months?

Yes: _____ No: _____

Do you know if you have a nerve disorder such as a stroke or multiple sclerosis?
If yes: _____

Do you know if you might have a metabolic disorder such as diabetes?
If yes: _____

Do you know if you have a connective tissue disease?

If yes: _____

Do you have any psychologic or psychiatric disorder that you believe might result in the testing procedures causing you anxiety or stress?
If yes: _____

Do you experience pain during sexual intercourse or tampon insertion?
If yes: _____

Have you had a pelvic surgery?
If yes: _____

Do you know if you have a pelvic organ prolapse?
If yes: _____

Do you experience problems controlling your bowels?
If yes: _____

Are you currently taking any medications?
If yes: _____

Do you have any metal implants or piercings in your pelvic region? (Write down piercing location and let Kaylee know as location may affect sensory testing. Ask participant to remove the piercing prior to assessment if they are eligible otherwise)
If yes: _____

Do you have any tattoos near or on your genitals? (Must be at least 6-months after tattoo session and must not have experienced any dysesthesia (e.g. abnormal sensations of burning or aching feeling beyond typical discomfort related to tattooing) with the tattoo)
If yes: _____

Do you currently have hemorrhoids? (May not be eligible if severe)
If yes: _____

[If eligible, continue. If not, thank the participants for her interest in the study and explain why she is not eligible. Ask permission to retain her contact information for future studies.]

Verbal consent: Yes_____ No: _____ Interviewer Signature: _____

[Part 2: Contact Information]

Tel:_____ Leave messages at this number? [Y] [N]

E-mail:_____

Recruitment Source:

a) Physiotherapist Referral Clinic Name:_____
   Start Date: _____

b) Posters in the Community
c) Social Media Advertisement
d) Word of Mouth
e) Previously Participated in an MFM Lab Study & Gave Consent to be Contacted for New Studies

What language would you prefer to communicate in? English or French

[Part 3: Group Assignment]

Do you currently experience any urine leakage on a regular basis? [Y] [N]

If no, do they meet the criteria for the Control group? Move to Group Assignment.

If yes:

1) How often?
    a. Per Day: _____
    b. Per Week: _____
    c. Per Month: _____

2) What types of activities trigger your urine leakage?

- Coughing
- Laughing
- Lifting
- Running
- Jumping
- Sneezing
- Standing from a sitting position
- Sexual Situations
- Putting the key in the door
- Other: _____

3) Approximately when did you start having symptoms? _____
4) Do you experience a sense of urgency before your leakages occur, such that you cannot make it to the toilet before you experience urine leakage?

---

5) If any, what treatments have you tried?

- Changing Voiding Habits
- Prescription Medication
- Pessary
- Alternative Medicine
- Hormone Creams
- Collagen Injection
- Surgery
- Physiotherapy
- Other: _____

If you have undergone physiotherapy for urinary leakage prior to the treatment you are currently undergoing (if referred by a physiotherapist), please describe where your treatment took place,

when this occurred, how many sessions you attended, if you still perform pelvic floor muscle exercises now (include how often and which exercises), and if you experienced a change in your symptoms.

_____

_____

_____

_____

_____

[Part 4: Decision for Study Participation]

[Is this person eligible for the study? [Y] [N]]

[If no, thank them for their time and direct them to the MFM Lab website www.mfmlab.ca for a list of local resources if they would like them.]

[If yes, explain that you will send out the questionnaires that are to be completed before their laboratory assessment. If they meet Control group criteria, send all 4 questionnaires and if it is convenient, book their first and/or second assessment(s). If they have been referred from a physiotherapist, explain that you will be emailing 4 questionnaire that should be completed at the beginning of their treatment (remind them in 7 days if they have not completed it already). If it is convenient at this time, book their first and/or second laboratory assessment(s). Follow-up with the participant enrolled in physiotherapy in 12-weeks and send them the final questionnaire.]

IMPORTANT! Book lab assessments 48-hours post wax or shave near sensory test sites.

Ask if the participant if they are currently menstruating regularly, if yes, ask participant for date of last period to standardize participants' menstrual cycles for testing.

Date of last period: _____

Other notes: _____

_____

Group Assignment (Control or Physiotherapy SUI): _____

_____

If enrolled in the Physiotherapy Group ask for:

Date they had their first Appointment:_____

Physiotherapy Clinic Name: _____

[Date of Reminder for Questionnaire Set 1: _____]

[End of Physiotherapy Date (12-weeks from start date): _____]

End of Telephone Interview

Appendix C: ICIQ-FLUTS

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1.

* Please enter your study ID starting provided in the email that was sent by the researcher (ex: RUN_94; SED_43, Hypo_21)

Study ID

2. F-Score

* 2a: During the night, how many times do you have to get up to urinate, on average?

- ◯ None
- ◯ One
- ◯ Two
- ◯ Three
- ◯ Four or more

* 2b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 3a: Do you have a sudden need to rush to the toilet to urinate?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time
- ◯ All of the time

* 3b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 4a: Do you have pain in your bladder?

- Never
- Occasionally
- Sometimes
- Most of the time
- All of the time

* 4b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 5a: How often do you pass urine during the day?

- 1 to 6 times
- 7 to 8 times
- 9 to 10 times
- 11 to 12 times 13 or more times

* 5b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

3. V-Score

* 6a: Is there a delay before you can start to urinate?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 6b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 7a: Do you have to strain to urinate?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 7b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 8a: Do you stop and start more than once while you urinate?

- Never
- Occasionally
- Sometimes
- Most of the time
- All of the time

* 8b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

4. I-Score

* 9a: Does urine leak before you can get to the toilet?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 9b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 10a: How often do you leak urine?

- ◯ Never
- ◯ Once or less per week
- ◯ Two or three times per week
- ◯ Once per day
- ◯ Several times per day

* 10b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 11a: Does urine leak when you are physically active, exert yourself, cough or sneeze?

- Never
- Occasionally
- Sometimes
- Most of the time All of the time

* 11b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 12a: Do you ever leak urine for no obvious reason and without feeling that you want to go?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time
- ◯

* 12b. How much does this bother you?
Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 13a: Do you leak urine when you are asleep?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time
- ◯

* 13b. How much does this bother you?
Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

1.

* S'il vous plaît, entrez votre ID d'étude de départ fourni dans l'e-mail qui a été envoyé par le chercheur (ex: RUN_94; SED_43; Hypo_21)

Study ID

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2. F-Score

Nous allons essayer de déterminer dans quelle mesure vos troubles urinaires sont un problème pour vous. Nous vous serions reconnaissants de bien vouloir nous aider en remplissant ce questionnaire.

Lorsque vous répondrez aux questions, pensez aux symptômes que vous avez eus au cours des 4 DERNIERES SEMAINES.

* 2a: Pendant la nuit, combien de fois devez-vous vous lever pour uriner, en moyenne?

- 0 fois
- 1 fois
- 2 fois
- 3 fois
- 4 fois ou plus

* 2b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
○	○	○	○	○	○	○	○	○	○	○

* 3a: Devez-vous vous précipiter aux toilettes pour uriner?

- Jamais
- Rarement

Quelquefois

La plupart du temps Tout le temps

* 3b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 4a: Avez-vous des douleurs dans la vessie?

Jamais

Rarement

Quelquefois

La plupart du temps Tout le temps

* 4b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
○	○	○	○	○	○	○	○	○	○	○

* 5a: Pendant la journée, combien de fois urinez-vous, en moyenne?

- ○ 1 à 6 fois
- ○ 7 ou 8 fois
- ○ 9 ou 10 fois
- ○ 11 ou 12 fois
- 13 fois ou plus

* 5b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
○	○	○	○	○	○	○	○	○	○	○

3. V-Score

* 6a: Y a-t-il un moment d'attente avant que vous puissiez commencer à uriner?

- ◯ Jamais
- ◯ Rarement
- ◯ Quelquefois
- ◯ La plupart du temps
- ◯ Tout le temps

* 6b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 7a: Devez-vous faire un effort pour arriver à uriner?

- ◯ Jamais
- ◯ Rarement
- ◯ Quelquefois
- ◯ La plupart du temps
- ◯ Tout le temps

* 7b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 8a: Pendant que vous urinez, votre jet d'urine s'arrête-t-il plus d'une fois, sans que vous le vouliez?

◯

- ◯ Jamais
- ◯ Rarement
- ◯ Quelquefois
- ◯ La plupart du temps
- ◯ Tout le temps

4. I-Score

* 9a: Avez-vous des fuites d'urine avant de pouvoir arriver aux toilettes?

- ◯ Jamais
- ◯ Rarement
- ◯ Quelquefois
- ◯ La plupart du temps
- ◯ Tout le temps

* 9b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 10a: Avez-vous souvent des fuites d'urine?

- ◯ Jamais
- ◯ Environ une fois par semaine
- ◯ 2 ou 3 fois par semaine
- ◯ Une fois par jour
- ◯ Plusieurs fois par jour

* 10b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 11a: Avez-vous des fuites d'urine au cours de vos activités physiques, quand

vous faites un effort, quand vous toussez ou éternuez?

- ◯ Jamais
- ◯ Rarement
- ◯ Quelquefois
- ◯ La plupart du temps
- ◯ Tout le temps

* 13b. Est-ce un problème pour vous?

Entourez un chiffre entre 0 (Ce n'est pas un problème) et 10 (C'est un gros problème)

0 (Ce n'est pas un problème)	1	2	3	4	5	6	7	8	9	10 (C'est un gros problème)
○	○	○	○	○	○	○	○	○	○	○

Appendix D: ICIQ-VS

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ICIQ-VS

* Please enter your study ID provided in the email that was sent by the researcher (ex: RUN_94; SED_43; Hypo_21)

Study ID

Vaginal Symptoms

Many people experience vaginal symptoms some of the time. We are trying to find out how many people experience vaginal symptoms, and how much they bother them. We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the **PAST FOUR WEEKS.**

* 1a: Are you aware of dragging pain in your lower abdomen?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 1b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 2a: Are you aware of soreness in your vagina?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 2b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a

great deal)

* 3a: Do you feel that you have reduced sensation or feeling in or around your vagina?

- Not at all
- A little
- Somewhat
- A lot

* 3b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Prolapse is a common condition affecting the normal support of the pelvic organs, which results in descent or 'dropping down' of the vaginal walls and/or the pelvic organs themselves. This can include the bladder, the bowel and the womb. Symptoms are usually worse on standing up and straining (e.g. lifting, coughing or exercising) and usually better when lying down and relaxing.

Prolapse may cause a variety of problems. We are trying to find out how many people experience prolapse, and how much this bothers them. We would be grateful if you could answer the following questions, thinking about how you have been, on average, **over the PAST FOUR WEEKS.**

* 4a: Do you feel that your vagina is too loose or lax?

- ○ Not at all
- ○ A little
- ○ Somewhat
- ○ A lot

* 4b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 5a: Are you aware of a lump or bulge coming down in your vagina?

- ○ Never
- ○ Occasionally
- ○ Sometimes
- ○ Most of the time All of the time

* 5b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 6a: Do you feel a lump or bulge come out of your vagina, so that you can feel it on the outside or see it on the outside?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 6b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 7a: Do you feel that your vagina is too dry?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 7b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 8a: Do you have to insert a finger into your vagina to help empty your bowels?

- ◯ Never
- ◯ Occasionally
- ◯ Sometimes
- ◯ Most of the time All of the time

* 8b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 9a: Do you feel that your vagina is too tight?

◯ Never

◯ Occasionally

◯ Sometimes

◯ Most of the time All of the time

* 9b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Sexual matters

We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the PAST FOUR WEEKS.

* 10. Do you have a sex life at present?

- ◯ Yes
- ◯ No, because of my vaginal symptoms No,
- ◯ because of other reasons

ICIQ-VS

* 11a: Do worries about your vagina interfere with your sex life?

- ◯ Not at all
- ◯ A little
- ◯ Somewhat
- ◯ A lot

* 11b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 12a: Do you feel that your relationship with your partner is affected by vaginal symptoms?

- ◯ Not at all
- ◯ A little
- ◯ Somewhat
- ◯ A lot

* 12b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 13. How much do you feel that your sex life has been spoilt by vaginal symptoms?

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Quality of life

* 14. Overall, how much do vaginal symptoms interfere with your everyday life?

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Appendix E: ICIQ-B

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ICIQ-B

* Please enter your study ID provided in the email that was sent by the researcher (ex: RUN_94; SED_43)

Study ID

Bowel pattern

Many people experience bowel accidents or bowel leakages. We are trying to find out how many people experience these symptoms and how much this bothers them. We would be grateful if you could answer the following questions, thinking about how you have been over the <u>PAST THREE MONTHS.</u>

* 3a. On average how many times do you open your bowels in 24 hours? **<u>(usual)</u>**

◯ Less than once

◯ One to three times ◯

Three to ten times ◯ Ten or more times

* 3b. On average how many times do you open your bowels in 24 hours? **<u>(at worst)</u>**

◯ Less than once

◯ One to three times ◯

Three to ten times Ten or more times

◯

* 3c. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 4a: How often do you open your bowels during the night from going to bed to sleep until you get up in the morning?

◯ Never

◯ Once

◯ Twice

◯ Three times

◯ Four or more times

* 4b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 5a: Do you have to rush to the toilet when you need to open your bowels?

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- ◯ Always

* 5b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 6a: Do you use medications (tablets or liquids) to stop you opening your bowels?

- ◯ Never
- ◯ Less than once a month
- ◯ Less than once a week
- ◯ Less than once a day
- ◯ About once a day
- ◯ Several times a day

* 6b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 7a: Do you experience pain/soreness around your back passage?

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- ◯ Always

* 7b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Bowel control

* 8a: Do you experience any staining of your underwear or need to wear pads because of your bowels?

- ◯ Never
- ◯ Less than once a month Less than once a week
- ◯ than once a week
- ◯ Less than once a day
- ◯ Everyday

* 8b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 9a: Are you able to control watery or loose stool leaking from your back passage?

- ◯ Always
- ◯ Most of the time
- ◯ Some of the time
- ◯ Rarely
- ◯ Never

* 9b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 10a: Are you able to control accidental loss of formed or solid stool from your back passage?

- ◯ Always
- ◯ Most of the time
- ◯ Some of the time
- ◯ Rarely
- Never
- ◯

* 10b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 11a: Are you able to control wind (flatus) escaping from your back passage?

- Always
- Most of the time
- Some of the time
- Rarely
- Never

* 11b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 12a: Are you able to control mucus (discharge) leaking from your back passage?

- Always
- Most of the time
- Some of the time
- Rarely
- Never

* 12b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 13a: Do you have bowel accidents when you have no need to open your bowels?

- Never
- Rarely
- Some of the time
- Most of the time
- Always

* 13b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 14a: Are your bowel accidents or leakages unpredictable?

- ○ Never
- ○ Rarely
- ○ Some of the time
- ○ Most of the time
- Always
- ○

* 14b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Other bowel symptoms

* 15. Using the pictures please indicate how your bowel movements are **most** of the time? *(Tick all boxes that apply)*

* 15b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 16a: Do you need to strain to open your bowels? (Tick one box)

○ Never ○ Rarely

Some of the time

Most of the time

Always

* 16b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

* 17a: Is the possibility of having a bowel accident on your mind? (Tick one box)

- ○ Never
- ○ Rarely
- ○ Some of the time
- ○ Most of the time
- ○ Always

* 17b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
○	○	○	○	○	○	○	○	○	○	○

Sexual impact

* 18a: Do you restrict your sexual activities because of your bowels? (Tick one box)

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- Always
- ◯ Not applicable

* 18b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

Quality of life

* 19a: Do your bowels cause you to feel embarrassed? (Tick one box)

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- ◯ Always

* 19b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 20a: Do your bowels cause you to make sure you know where toilets are? (Tick one box)

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- ◯ Always

* 20b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 21a: Do your bowels cause you to make plans according to your bowels?
(Tick one box)

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- ◯ Always

* 21b. How much does this bother you?
Please select a number between 0 (not at all) and 10 (a great deal).

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 22a: Do your bowels cause you to stay home more often than you would like? (Tick one box)

- ◯ Never
- ◯ Rarely
- ◯ Some of the time
- ◯ Most of the time
- ◯ Always

* 22b. How much does this bother you?

Please select a number between 0 (not at all) and 10 (a great deal).

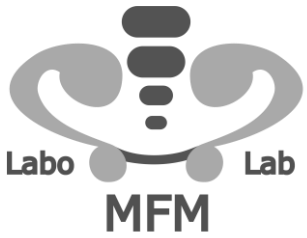
0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

* 23. Overall, how much do your bowels interfere with your everyday life?

0 (not at all)	1	2	3	4	5	6	7	8	9	10 (a great deal)

24. Please use the space below to describe any worries you have about bowel accidents or leakages, what you think may have caused your bowel accidents or leakages, or anything else you think we should know.

Appendix F: FSFI



1. INSTRUCTIONS

These questions ask about your sexual feelings and responses during the past 4 weeks. Please answer the following questions as honestly and clearly as possible. Your responses will be kept completely confidential. In answering these questions the following definitions apply:

- Sexual activity can include caressing, foreplay, masturbation and vaginal intercourse.

- Sexual intercourse is defined as penile penetration (entry) of the vagina.

- Sexual stimulation includes situations like foreplay with a partner, self-stimulation (masturbation) or sexual fantasy.

If there are any questions that does not pertain to you or you do not feel comfortable to answer, skip it and continue the survey.

* 1. Please enter your study ID starting provided in the email that was sent by the researcher (ex: RUN_94; SED_43)

2. Sexual desire or interest is a feeling that includes wanting to have a sexual experience, feeling receptive to a partner's sexual initiation, and thinking or fantasizing about having sex.

Over the past 4 weeks, how often did you feel sexual desire or interest?

- Almost always or always
- Most times (more than half the time)
- Sometimes (about half the time)
- A few times (less than half the time)
- Almost never or never

3. Over the past 4 weeks, how would you rate your level (degree) of sexual desire or interest?

- ◯ Very high
- ◯ High
- ◯ Moderate ◯
- Low
- ◯ Very low or none at all

4. Sexual arousal is a feeling that includes both physical and mental aspects of sexual excitement. It may include feelings of warmth or tingling in the genitals, lubrication (wetness), or muscle contractions.

Over the past 4 weeks, how often did you feel sexually aroused ("turned on") during sexual activity or intercourse?

- ◯ No sexual activity
- ◯ Almost always or always
- ◯ Most times (more than half the time) ◯
- Sometimes (about half the time)
- ◯ A few times (less than half the time) ◯
- Almost never or never

5. Over the past 4 weeks, how would you rate your level of sexual arousal ("turn on") during sexual activity or intercourse?

- ◯ No sexual activity
- ◯ Very high
- ◯ High
- ◯ Moderate
- ◯ Low
- ◯ Very low or none at all

6. Over the past 4 weeks, how confident were you about becoming sexually aroused during sexual activity or intercourse?

- No sexual activity
- Very high confidence
- High confidence
- Moderate confidence
- Low confidence
- Very low or no confidence

7. Over the past 4 weeks, how often have you been satisfied with your arousal (excitement) during sexual activity or intercourse?

- No sexual activity
- Almost always or always
- 4Most times (more than half the time)
- Sometimes (about half the time)
- A few times (less than half the time)
- Almost never or never

8. Over the past 4 weeks, how often did you become lubricated ("wet") during sexual activity or intercourse?

- No sexual activity
- Almost always or always
- Most times (more than half the time)
- Sometimes (about half the time)
- A few times (less than half the time)
- Almost never or never

9. Over the past 4 weeks, how difficult was it to become lubricated ("wet") during sexual activity or intercourse?

- No sexual activity

◯ Extremely difficult or impossible ◯

Very difficult

◯ Difficult

◯ Slightly difficult

◯ Not difficult

10. Over the past 4 weeks, how often did you maintain your lubrication ("wetness") until completion of sexual activity or intercourse?

- ◯ No sexual activity
- ◯ Almost always or always
- ◯ Most times (more than half the time)
- ◯ Sometimes (about half the time)
- ◯ A few times (less than half the time)
- ◯ Almost never or never

11. Over the past 4 weeks, how difficult was it to maintain your lubrication ("wetness") until completion of sexual activity or intercourse?

- ◯ No sexual activity
- ◯ Extremely difficult or impossible
- ◯ Very difficult
- ◯ Difficult
- ◯ Slightly difficult
- ◯ Not difficult

12. Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you reach orgasm (climax)?

- ◯ No sexual activity
- ◯ Almost always or always
- ◯ Most times (more than half the time)
- ◯ Sometimes (about half the time)
- ◯ A few times (less than half the time)
- ◯ Almost never or never

13. Over the past 4 weeks, when you had sexual stimulation or intercourse, how difficult was it for you to reach orgasm (climax)?

◯ No sexual activity

◯ Extremely difficult or impossible ◯

Very difficult

◯ Difficult

◯ Slightly difficult

◯ Not difficult

14. Over the past 4 weeks, how satisfied were you with your ability to reach orgasm (climax) during sexual activity or intercourse?

- ◯ No sexual activity
- ◯ Very satisfied
- ◯ Moderately satisfied
- ◯ About equally satisfied and dissatisfied ◯
- Moderately dissatisfied
- ◯ Very dissatisfied

15. Over the past 4 weeks, how satisfied have you been with the amount of emotional closeness during sexual activity between you and your partner?

- ◯ No sexual activity
- ◯ Very satisfied
- ◯ Moderately satisfied
- ◯ About equally satisfied and dissatisfied ◯
- Moderately dissatisfied
- ◯ Very dissatisfied

16. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?

- ◯ Very satisfied
- ◯ Moderately satisfied
- ◯ About equally satisfied and dissatisfied ◯
- Moderately dissatisfied
- ◯ Very dissatisfied

17. Over the past 4 weeks, how satisfied have you been with your overall sexual life?

◯ Very satisfied

◯ Moderately satisfied

◯ About equally satisfied and dissatisfied ◯

Moderately dissatisfied

◯ Very dissatisfied

18. Over the past 4 weeks, how often did you experience discomfort or pain during vaginal penetration?

- ◯ Did not attempt intercourse ◯
- Almost always or always
- ◯ Most times (more than half the time) ◯
- Sometimes (about half the time)
- ◯ A few times (less than half the time) ◯
- Almost never or never

19. Over the past 4 weeks, how often did you experience discomfort or pain following vaginal penetration?

- ◯ Did not attempt intercourse ◯
- Almost always or always
- ◯ Most times (more than half the time) ◯
- Sometimes (about half the time)
- ◯ A few times (less than half the time) ◯
- Almost never or never

20. Over the past 4 weeks, how would you rate your level (degree) of discomfort or pain during or following vaginal penetration?

- ◯ Did not attempt intercourse ◯
- Very high
- ◯ High
- ◯ Moderate ◯
- Low
- ◯ Very low or none at all

1. INSTRUCTIONS

les questions suivantes portent sur vos sentiments et vos réactions sur le plan sexuel au cours des 4 dernières semaines. Veuillez répondre à ces questions aussi sincèrement que possible. Vos réponses resteront strictement confidentielles.
Lorsque vous répondrez aux questions, tenez compte des définitions suivantes:
-L'activité sexuelle peut comprendre les caresses, les préliminaires, la masturbation, et la pénétration vaginale.
-Le rapport sexuel se définit comme la pénétration (l'introduction) du penis.
-La stimulation sexuelle comprend, par exemple, les préliminaires avec un partenaire, la masturbation et les fantasmes sexuels.

Ne cochez qu'une seule réponse par question
Le désir sexuel est un sentiment qui comprend le désir d'avoir une activite sexuelle, le fait d'être réceptive aux avances sexuelles d'un partenaire et d'avoir des pensées ou des fantasmes à propos de I' acte sexuel.

* 1. S'il vous plaît, entrez votre ID d'étude de départ fourni dans l'e-mail qui a été envoyé par le chercheur (ex: RUN_94; SED_43)

2. Au cours des quatre dernières semaines, avez-vous ressenti un désir sexuel ?

- ◯ Presque toujours ou toujours
- ◯ La plupart du temps (plus de la moitié du temps) ◯
- Parfois (environ la moitié du temps)
- ◯ Rarement (mains de la moitié du temps) ◯
- Presque jamais ou jamais

3. Au cours des 4 dernières semaines, quel a été votre niveau (degré) de désir sexuel ?

- ◯ Très élevé
- ◯ Elevé

- ◯ Moyen
- ◯ Faible
- ◯ Très faible ou inexistant

L'excitation sexuelle est une sensation qui comprend à la fois des aspects physiques et psychologiques. Elle peut comprendre des sensations de chaleur ou de picotement au niveau des organes génitaux, la lubrification (humidité) du vagin ou des contractions musculaires.

4. Au cours des 4 dernières semaines, vous êtes vous sentie excitée sexuellement pendant une activité sexuelle ou un rapport sexuel?

- ◯ Aucune activité sexuelle
- ◯ Presque toujours ou toujours
- ◯ La plupart du temps (plus de la moitié du temps) ◯
- Parfois (environ la moitié du temps)
- ◯ Rarement (mains de la moitié du temps) ◯
- Presque jamais ou jamais

5. Au cours des 4 dernières semaines, quel a été votre niveau (degré) d'excitation sexuelle pendant une activité ou un rapport sexuel?

- ◯ Aucune activité sexuelle ◯
- Très élevé
- ◯ Elevé
- ◯ Moyen
- ◯ Faible
- ◯ Très faible ou inexistant

6. Au cours des 4 dernières semaines, à quel point vous etes-vous sentie sûre de votre capacité à être excitée pendant une activité sexuelle ou un rapport sexuel?

- ◯ Aucune activité sexuelle ◯
- Extrêmement sûre
- ◯ Très sûre

◯ Moyennement sûre ◯

Peu sûre

◯ Très peu sûre ou pas sûre du tout

7. Au cours des 4 dernières semaines, avez-vous été satisfaite de votre degré d'excitation pendant une activité sexuelle ou un rapport sexuel?

- ◯ Aucune activité sexuelle
- ◯ Presque toujours ou toujours
- ◯ La plupart du temps (plus d'une fois sur deux) ◯
- Parfois (environ une fois sur deux)
- ◯ Rarement (moins d'une fois sur deux) ◯
- Presque jamais ou jamais

8. Au cours des 4 dernières semaines, votre vagin était-il lubrifié (humide) pendant une activité sexuelle ou un rapport sexuel?

- ◯ Aucune activité sexuelle
- ◯ Presque toujours ou toujours
- ◯ La plupart du temps (plus d'une fois sur deux) ◯
- Parfois (environ une fois sur deux)
- ◯ Rarement (moins d'une fois sur deux) ◯
- Presque jamais ou jamais

9. Au cours des 4 dernières semaines, à quel point vous a-t-il été difficile d'avoir le vagin lubrifié (humide) pendant une activité sexuelle ou un rapport sexuel?

- ◯ Aucune activité sexuelle
- ◯ Extrêmement difficile ou impossible ◯
- Très difficile
- ◯ Difficile
- ◯ Légèrement difficile ◯
- Pas difficile

10. Au cours des 4 dernières semaines, la lubrification (humidité) de votre vagin a-t-elle duré jusqu'à la fin d'une activité sexuelle ou d'un rapport sexuel?

◯ Aucune activité sexuelle

◯ Presque toujours au toujours

◯ La plupart du temps (plus d'une fois sur deux) ◯

Parfois (environ une fois sur deux)

◯ Rarement (mains d'une fois sur deux) Presque

◯ jamais au jamais

11. Au cours des 4 dernières semaines, à quel point vous a-t-il été difficile de conserver la lubrification (humidité) de votre vagin jusqu'à la fin d'une activité sexuelle ou d'un rapport sexuel?

- ◯ Aucune activité sexuelle
- ◯ Extrêmement difficile au impossible ◯
- Très difficile
- ◯ Difficile
- ◯ Légèrement difficile ◯
- Pas difficile

12. Au cours des 4 dernières semaines, lorsque vous avez été stimulée sexuellement ou que vous avez eu un rapport sexuel, avez-vous atteint l'orgasme?

- ◯ Aucune activité sexuelle
- ◯ Presque toujours au toujours
- ◯ La plupart du temps (plus d'une fois sur deux) ◯
- Parfois (environ une fois sur deux)
- ◯ Rarement (mains d'une fois sur deux} ◯
- Presque jamais au jamais

13. Au cours des 4 dernières semaines, lorsque vous avez eu un rapport sexuel, à quel point vous a-t-il été difficile d'atteindre l'orgasme?

- ◯ Aucune activité sexuelle
- ◯ Extrêmement difficile au impossible ◯
- Très difficile
- ◯ Difficile
- ◯ Légèrement difficile ◯
- Pas difficile

14. Au cours des 4 dernières semaines, à quel point avez-vous été satisfaite de votre

capacité à atteindre l'orgasme pendant une activité sexuelle ou un rapport sexuel ?

◯ Aucune activité sexuelle ◯

Très satisfaite

◯ Moyennement satisfaite ◯

Ni satisfaite, ni insatisfaite ◯

Moyennement insatisfaite

◯ Très insatisfaite

15. Au cours des 4 dernières semaines, à quel point avez-vous été satisfaite de votre relation affective avec votre partenaire pendant une activité sexuelle?

◯ Aucune activité sexuelle ◯

Très satisfaite

◯ Moyennement satisfaite ◯

Ni satisfaite, ni insatisfaite ◯

Moyennement insatisfaite ◯

Très insatisfaite

16. Au cours des 4 dernières semaines, à quel point avez-vous été satisfaite de votre relation avec votre partenaire du point de vue sexuel?

◯ Très satisfaite

◯ Moyennement satisfaite ◯

Ni satisfaite, ni insatisfaite ◯

Moyennement insatisfaite ◯

Très insatisfaite

17. Au cours des 4 dernières semaines, à quel point avez-vous été satisfaite de votre vie sexuelle en général?

◯ Très satisfaite

◯ Moyennement satisfaite ◯

Ni satisfaite, ni insatisfaite ◯

Moyennement insatisfaite ◯

Très insatisfaite

18. Au cours des 4 dernières semaines, avez-vous ressenti une gêne ou de la douleur pendant la pénétration vaginale?

◯ Je n'ai pas eu de rapport sexuel ◯

Presque toujours ou toujours

◯ La plupart du temps (plus d'une fois sur deux) ◯

Parfois (environ une fois sur deux)

◯ Rarement (mains d'une fois sur deux) Presque

◯ jamais ou jamais

19. Au cours des 4 dernières semaines, avez-vous ressenti une gêne ou de la douleur après la pénétration vaginale?

◯ Je n'ai pas eu de rapport sexuel ◯

Presque toujours ou toujours

◯ La plupart du temps (plus d'une fois sur deux) ◯

Parfois (environ une fois sur deux)

◯ Rarement (mains d'une fois sur deux) ◯

Presque jamais ou jamais

20. Au cours des 4 dernières semaines, quel a été votre niveau (degré) de gêne ou de douleur pendant ou après la pénétration vaginale?

◯ Je n'ai pas eu de rapport sexuel ◯

Très élevé

◯ Elevé

◯ Moyen

◯ Faible

◯

Très faible au inexistant

Appendix G: Letter if Information

Letter of Information

Title of Study: Sensory and motor correlates of stress urinary incontinence in women and their influence on pelvic floor muscle training outcomes

Principal Investigator: Linda McLean, Ph.D., Full Professor, School of Rehabilitation Sciences, University of Ottawa. 613-562-5800 ext 2544 and Kaylee Brooks, Ph.D. Candidate, School of Rehabilitation Sciences, University of Ottawa, 613-562-5800 ext 4102.

Funding: This study does not have external funding.

Background Information

Many women experience daily urine leakage which is also referred to as urinary incontinence and the most common among women is stress urinary incontinence, which is defined as the involuntary loss of urine during an exertion, cough, or sneeze. Pelvic floor muscle exercises can improve the symptoms of stress urinary incontinence, however, only half of the women who complete the intervention are cured. One of the key goals of the research in our laboratory is to better understand why some women's symptoms improve more than others with pelvic floor muscle exercises. While we know that the sensory and motor nerves can be strained during childbirth and that there is some evidence of this damage in women who suffer from stress urinary incontinence, these injuries have

not been studied very much. In particular, there has been very little research on the role of motor and sensory nerve impairments in this exercise-based intervention.

As such, through this study we plan to assess the presence of motor and sensory nerve impairments in women with stress urinary incontinence, and to determine if sensory or motor impairments may be responsible for the failure of pelvic floor exercises to alleviate symptoms of incontinence in some women.

The University of Ottawa Health Sciences and Sciences Research Ethics Board has reviewed the ethical components of this study and has found it to be in compliance with national standards. Data from this project will be used for Ms. Brooks' doctoral thesis project at the University of Ottawa.

You will have the option of reading this document on your own, or if you prefer a member of the research team will read this consent form with you and answer any questions you may have. If you choose to participate in the study, you will be required to sign the consent form that follows, indicating your consent to undergo the assessment procedures described here.

We aim to recruit a total of 150 female volunteers in the Ottawa-Gatineau area to participate in this study. We are looking for 30 women without any pelvic floor disorders such as bowel or bladder leakage, pelvic organ prolapse, or pelvic pain. We are also looking for 60 women with stress urinary incontinence who are about to start pelvic floor physiotherapy and will be divided into a cured and not cured group 12-weeks after treatment using the score on a questionnaire about urinary incontinence symptoms. The last group will be 60 women who have already completed PFMT for stress urinary incontinence who will be divided into cured or not cured groups. You are being invited to participate in this study for one of three reasons, (1) you have contacted us directly with interest in the study and you do not currently have any pelvic floor disorders, (2) you were referred by a physiotherapist and are planning to receive pelvic floor physiotherapy to treat

your stress urinary incontinence symptoms, (3) you were referred by a physiotherapist or contacted us directly after having completed treatment and are interested in participating in the study.

The study involves the completion of four online questionnaires, (approximately 30 minutes) and two laboratory evaluation sessions, where visit one will be 2.5 hours and visit 2 will be 2 hours in length.

Participation

Questionnaires

If you are undergoing physiotherapy for stress urinary incontinence symptoms, you will receive two invitations to complete questionnaires. The first invitation will ask you to complete four questionnaires that will ask you about your (1) lower urinary tract symptoms—including urine leakage, (2) bowel control and patterns, (3) vaginal symptoms and associated sexual matters, and (4) quality of life. Each questionnaire should take you no more than 5-minutes to complete with a total of 30-minutes to complete all questionnaires. You will be asked to fill out the questionnaires before attending the first laboratory session and to do so as soon as possible since your answers might change after you begin physiotherapy. The second invitation will be sent to you 12-weeks after your first physiotherapy session and will provide you with a link to two questionnaires that will ask you about your lower urinary tract symptoms—including urine leakage—and if you feel your symptoms improved and were satisfied with the physiotherapy intervention.

If you are NOT receiving physiotherapy, you will receive one e-mail invitation with links to four questionnaires that should take you no more than 30-minutes in total to complete. These questionnaires will ask you about (1) lower urinary tract symptoms—including urine leakage, (2)

bowel control and patterns, (3) vaginal symptoms and associated sexual matters, and (4) quality of life. You will be asked to fill out the questionnaires before attending the laboratory session.

Laboratory Assessments

The two laboratory-based assessments will take place at the Motor Function Measurement Laboratory (Dr. McLean's Laboratory) at the University of Ottawa at 200 Lees Ave. in Room 155D. The sessions will last 2.5 hours for the visit 1 and 2 hours for visit 2, these will be scheduled at your convenience within 10 days of each other. Should you choose to drive to your assessment visits, parking will be provided at no charge through a parking pass. You will be required to bring your own surgical or cloth face mask for these laboratory assessments. If you do not have one, a mask will be provided to you upon entry to the university building.

The study Ph.D. candidate, Kaylee Brooks, under direct the supervision of Dr. McLean, will greet you when you arrive at the laboratory and will be completing your examination. Ms. Brooks has over 5 years of research experience in the field of women's pelvic health and has been trained by local experts on all the evaluation procedures. Ms. Brooks will be assisted by a student research assistant who will help to prepare instrumentation and who will operate the computers used to collect data, but the student will not perform any clinical assessment techniques. As Ms. Brooks is not fluent in French, the student research assistant may act as a translator during the assessment visit if your preferred language is French. Both Ms. Brooks and her research assistant will be wearing full personal protective equipment during your two visits to the laboratory.

After signing this form, you will be asked to provide your age and you will have your height, weight, and waist and hip circumference measured and recorded. You will then be left in a private area to undress from your waist down and to cover yourself with a gown and a sheet. When you

are ready, you will be asked to invite Ms. Brooks and her assistant back into the assessment room. You will be asked to lie down on an examination table with your head supported by a pillow.

While wearing gloves, Ms. Brooks will perform a quick genital examination to ensure that there is no evidence of factors such as infection that might interfere with your ability to participate, and that there are no health concerns or risks that might cause you to experience discomfort during the protocol. Once this screening has been completed, you will be shown the automated intravaginal dynamometer (IVD), which is a device that will be used for some of the testing. Ms. Brooks will provide you with the thumb switch for the IVD which you can press at any time to end the IVD testing. She will then explain the protocol for the first assessment, which will examine your ability to feel your pelvic floor muscles move and decide whether they have been moved to a position that is larger, smaller or the same as compared to a reference position. To do this, the arms of the IVD will be inserted into your vagina, much like the speculum a health care provider uses to perform a PAP test. Ms. Brooks will instruct you to remain relaxed while the IVD arms slowly open to different diameters and you will be asked to identify whether the arms are open to a greater or lesser extent than a reference value.

Next, using the same IVD, the arms will be opened slightly, and you will be instructed by Ms. Brooks to contract your pelvic floor muscles three times as strongly as you can. Then Ms. Brooks will ask you to squeeze your pelvic floor muscles as hard and as fast as you can repeatedly over a 15 second time period. Once completed, you will be presented with three targets on a computer screen, and you will be asked to try to contract your pelvic floor muscles to match the different targets on the screen. You will be given an opportunity to practice until you are comfortable with the task. During testing, you will repeat contractions to try to match each of three force levels, while using the computer monitor for feedback then again without using the computer monitor for feedback.

Ms. Brooks will then prepare you for the assessments of motor nerve function. She will wear examination gloves and will insert a small sensor (electrode) into your vagina using a finger to guide its placement on the anterior vaginal wall. While Ms. Brooks holds the electrode in place, you will be asked to pull the stopper back on an air-filled syringe, which will cause a small suction force to hold the electrode in place during testing. A sticky electrode will also be pressed on the skin beside your anus and a second sticky electrode will be placed on the skin over your

right hip. Then Ms. Brooks will put on a new glove that has a specialized electrode attached to it and prepare a second sensor to be placed in your vagina. She will feel inside your vagina to make sure that she has positioned the sensor correctly over your pelvic floor muscles and then you will be asked to pull the stopper on an air-filled syringe, like the previous sensor, to suction it in place. Then, Ms. Brooks will gently shift her finger with the specialized electrode attached to the glove to locate your nerve and position the electrode correctly to stimulate the motor nerve. Once she has the electrode in the correct position, Ms. Brooks will ask you to contract your pelvic floor muscles as hard as you can for 5 seconds for three trials. Then she will begin the nerve stimulation by asking the research assistant to slowly increase the intensity of an electrical impulse that will stimulate the nerve. You will feel your pelvic floor muscles twitch in response to the stimulus. While the stimulation may cause some discomfort, it should not be painful. If it is too uncomfortable or extremely painful, please let Ms. Brooks know and she can adjust the electrode and stimulation as needed. When a suitable signal has been found, Ms. Brooks will stimulate your pudendal nerve 10 times. Ms. Brooks will then remove all the electrodes. Once removed both Ms. Brooks and her assistant will leave the room so that you may change back into your clothes. This will conclude the first laboratory assessment.

The second laboratory assessment will be completed within 10 days after the first assessment and will focus on your sensation. It should take approximately two hours. The same research assistant, Ms. Brooks, will greet you when you arrive. Again, you will be required to wear a surgical or cloth mask during the assessment. Ms. Brooks and her assistant will wear a surgical mask and full personal protective equipment during this assessment. Ms. Brooks will review the goals and the protocols of the second assessment with you and answer any questions you have. You will be asked to undress from the waist down in the examination room and cover yourself with a gown and a sheet as you did in the first session. When you are ready, you will invite Ms. Brooks and her

assistant into the assessment room. You will be asked to lie down on an examination table with your head supported by a pillow.

This session will involve a sensation test and ultrasound imaging. Ms. Brooks will instruct you to state yes or no to whether you feel certain sensations (light touch) after it has been applied to your skin. Five sites will be assessed including your right ankle and four sites in your genital area. These specific sites will be marked with a non-permanent surgical marker to ensure that Ms. Brooks tests the same site each time. The stimulus will be demonstrated first on your forearm so that you can feel what it feels like, and then Ms. Brooks will test each of the study sites, beginning with the ankle before moving to the genital sites. We are looking to record the smallest stimulus that you can feel with each of these sensations, so there should be no discomfort whatsoever associated with the testing. Touch sensation will be tested using small wires that are about as thick as a human hair. Prior to applying the stimulus to any site, Ms. Brooks will direct your attention to that site by gently touching it with a cotton swab and each site will be tested three times. After the sensation testing, Ms. Brooks will show you an ultrasound probe that will be placed on your perineum to visualize structures in your pelvis. You will be asked to contract your pelvic floor muscles maximally three times while Ms. Brooks captures short ultrasound videos of your muscles. Then, you will be asked to stand in front of the exam table while Ms. Brooks collects three images of your pelvic floor muscles at rest in standing. Ms. Brooks and her assistant will then leave the room so that you can change into your clothes. This will conclude the data collection of the study.

Potential Harms

There are no known risks of infection or inflammation associated with any of the testing procedures used in this study. All the devices, including the electrodes, IVD arms, monofilaments, and examination gloves are used only once and are discarded after use. The devices, and their

wires are disinfected after each use; all sheets, gowns, and pillowcases are laundered after each use.

You may experience some muscle fatigue over the course of the study since you will be asked to repeatedly contract your pelvic floor muscles. To minimize fatigue, resting periods are built into the session, and you may request more rest whenever you like. Feel free to ask to slow down the testing at any time.

Electrical stimulation can generate heat around metal, so please do not volunteer to participate if you have metal implants in your pelvic area and please remove any piercings from your lower body. Do not volunteer to participate if you are pregnant or have a tendency to faint. With respect to electrical stimulation, potential side-effects may include vaginal tenderness which should go away within an hour after the session. You may also take over-the-counter pain relievers such as Tylenol® if you feel this is necessary.

Discomfort

While electrical stimulation of the pelvic floor muscles may not be painful, some people find it unpleasant. The stimulation will cause the pelvic floor muscles, urethra, and anus to contract, this may also be uncomfortable, but it will not cause any harm. Please let Ms. Brooks know if this procedure is too uncomfortable to continue. You may discontinue your participation at any time.

There is a possibility that some women may feel anxious during the testing, and as such, we will make every effort to keep you informed of what is coming next and what it will feel like throughout the protocol in order to minimize your anxiety. Again, you may ask to slow the testing down at any time or discontinue if you so choose.

Inconveniences

Due to the many rest breaks provided during the motor and sensory testing, the protocol is quite lengthy, at approximately 2 hours for each session, which may be inconvenient. You will be able to schedule your assessment outside of regular work hours, during the evening or on weekends if you prefer.

In the event of any research-related injury you will be referred to your regular health care provider to receive appropriate medical treatment/care through your provincial health plan. If urgent care is required, we will contact University of Ottawa Campus security and you will be escorted by the research staff to the Emergency Department of the Ottawa General Hospital to receive care. You are not waiving your legal rights by agreeing to participate in this study.

Benefits

Participation in this study will allow you to learn about your pelvic floor musculature and the role of muscle co-ordination and sensation on pelvic floor muscle training effectiveness. If you are interested in any of the testing procedures or devices, please do not hesitate to ask questions during your assessment. This study does not include a therapeutic intervention. You will be sent an executive summary of the study findings at its completion.

Describe any Relevant Experience Working with this Population or Topic

Our laboratory personnel have tremendous expertise and experience in evaluating pelvic floor muscle structure and function in women and are well-trained in the use and safety of all methods described above.

The Ph.D. candidate, Ms. Brooks, has worked in the Motor Function Measurement Laboratory for over 5 years in women's health research. She has received special training and mentoring from Dr. McLean, the principal investigator of this research, and from Dr. Caroline Pukall, an international expert in human sexuality and genital sensation testing.

Compensation

You will not receive any compensation as a result of your participation in this research.

Withdrawal from the Study

You have the right to withdraw your participation from this study at any time and without providing any reason. If you choose to withdraw from the study, any data provided to that point will be destroyed unless permission to use it is granted.

Confidentiality

You will not be identifiable in any publications, doctoral candidate theses, or presentations resulting from this study. No identifying information will leave the University of Ottawa. There will be one password-protected electronic file, stored on a password secured computer that will remain in the Motor Function Measurement Laboratory. This file will link your name to your participant number. This file will only be accessible by Dr. McLean and her staff and students at The University of Ottawa who have all been instructed on proper procedures for protecting privacy and confidentiality and who have provided signed confidentiality agreements. All electronic records will be stored in a secure database at the University of Ottawa and will be protected by a user password, again only accessible by Dr. McLean and her students and staff. These records will not include your name or other identifying information. All paper records will be stored in a filing cabinet within the Motor Function Measurement Laboratory, which is a restricted access area. All files will be kept for a period of 10 years after the study has been completed. At the end of the retention period, all paper records will be disposed of in confidential waste or shredded, and all electronic records will be permanently deleted from the data server.

Participant Rights

Your participation in this study is voluntary. You may withdraw from this study at any time. You are free to refuse to undergo any aspect of the testing, without giving any reason. The researchers may withdraw you from the study for scientific reasons at any time. In this case, they would give you a clear and valid reason. You have the right to obtain copies of any study forms that contain your personal information.

As a participant in this study, you have the right to an environment that you feel comfortable in. For your safety and for the safety of our team, we will have a third person (female student research assistant) present in the laboratory during all assessment procedures. You may also bring a friend or family member with you to be present in the room if this makes you feel more comfortable.

If at any time, you have further questions or problems you can contact the study investigators:

Linda McLean, PhD at 613-562-5800 ex 2544 or linda.mclean@uottawa.ca

or

Kaylee Brooks, Ph.D. Candidate Rehabilitation Sciences at 613-562-5800 ex 4102 or mfmlab@uottawa.ca

If you have any questions about this study or if you feel that you have experienced a research related injury, please contact Dr. Linda McLean at 613-562-5800 ex 2544 at your earliest convenience.

The University of Ottawa Sciences and Health Sciences Research Ethics Board has reviewed this protocol and has found it to comply with standards for ethical aspects of research studies

involving human participants at The University of Ottawa. If you have any questions about your rights as a research participant, you may contact the Protocol Officer for Ethics in Research at the University of Ottawa, at 613-562-5387 or ethics@uottawa.ca.

Consent to Participate in Research

Title of Study: Sensory and motor correlates of stress urinary incontinence in women and their influence on pelvic floor muscle training outcomes

I understand that I am being asked to participate in a research study and that my participation is voluntary. This study protocol has been explained to me by Ms. Kaylee Brooks, a doctoral researcher.

I have read this 7-page Participant Information Sheet and Consent Form or have had this document read to me. All my questions have been answered to my satisfaction. If I decide at a later stage in the study that I would like to withdraw my consent, I may do so at any time.

I voluntarily agree to participate in this study.

A copy of the Participant Information Sheet and the signed Consent Form will be provided to me for my records.

Signatures

_____

Participant's Name (Please Print)

_____ _____

Participant's Signature Date

Investigator Statement (or Person Explaining the Consent)
I have carefully explained to the research participant the nature of the above research study. To the best of my knowledge, the research participant signing this consent form understands the nature, demands, risks and benefits involved in participating in this study. I acknowledge my responsibility for the care and well-being of the above research participant, to respect the rights and wishes of the research participant, and to conduct the study according to applicable Good Clinical Practice guidelines and regulations.

_____

Name of Investigator/Delegate (Please Print)

_____ _____

Signature of Investigator/Delegate Date

Lettre d'information

Titre de l'étude : Corrélats sensoriels de l'incontinence urinaire à l'effort chez la femme et leur influence sur les résultats de l'entraînement des muscles du plancher pelvien.

Chercheuse principale : Dre. Linda McLean, Ph.D., Professeure titulaire, École des sciences de la réadaptation, l'Université d'Ottawa, 613-562-5800 poste 2544.

Assistante de recherche : Kaylee Brooks, MSc, Candidate au doctorat, École des sciences de la réadaptation, l'Université d'Ottawa, 613-562-5800 poste 4102.

Financement : Cette étude ne bénéficie d'aucun financement externe.

Informations de base :

De nombreuses femmes souffrent au quotidien de fuites urinaires, une pathologie également connue sous le nom d'incontinence urinaire. L'incontinence urinaire à l'effort est sa manifestation la plus courante chez les femmes, et se caractérise par la perte involontaire d'urine pendant un effort physique, lors de toux ou d'éternuements. Bien que l'entrainement des muscles du plancher pelvien puisse améliorer les symptômes de l'incontinence urinaire à l'effort, seule la moitié des femmes qui subissent une telle intervention sont guéries. L'un des principaux objectifs au sein de notre recherche au laboratoire est de mieux comprendre pourquoi les symptômes de certaines femmes s'améliorent plus que d'autres grâce aux entraînements des muscles du plancher pelvien. Alors que nous savons

que les nerfs sensoriels et moteurs peuvent être mis à rude épreuve pendant l'accouchement et qu'il existe des preuves de ce dommage chez les femmes souffrant d'incontinence urinaire à l'effort, ces lésions ont été peu étudiées. En particulier, il y a eu très peu de recherches sur le rôle des troubles des nerfs moteurs et sensoriels dans cette intervention basée sur les efforts physiques.

Par cette étude, nous prévoyons donc d'évaluer la présence de troubles nerveux moteurs et sensoriels chez les femmes souffrant d'incontinence urinaire à l'effort, et de déterminer si ceux-ci peuvent être responsables des insuccès de l'entraînement du plancher pelvien pour soulager les symptômes de l'incontinence chez certaines femmes.

Le comité d'éthique de la recherche en sciences de la santé de l'Université d'Ottawa a examiné les composantes éthiques de cette étude et l'a jugée conforme aux standards nationaux.

Vous aurez la possibilité de lire ce document par vous-même ou, si vous préférez, un membre de l'équipe de recherche vous lira ce formulaire de consentement et répondra à toutes vos questions. Si vous choisissez de participer à l'étude, vous devrez signer le formulaire de consentement qui suit, indiquant votre consentement à vous soumettre aux procédures d'évaluation décrites ci-dessous.

Nous avons pour objectif de recruter un total de 150 participantes volontaires dans la région d'Ottawa-Gatineau pour cette étude. Nous recherchons 30 femmes qui ne souffrent pas de troubles du plancher pelvien (tels que des fuites urinaires ou de selles), qui n'ont aucun prolapsus des organes pelviens et ne souffrent pas des douleurs pelviennes. Nous sommes également à la recherche de 60 femmes souffrant d'incontinence urinaire à l'effort qui vont commencer la physiothérapie. Ces participants seront divisés en un groupe "guéri" et "non guéri" 12 semaines après le traitement, en fonction du score obtenu sur un questionnaire à propos des symptômes de l'incontinence urinaire. Le dernier groupe sera composé de 60 femmes ayant déjà complété la

physiothérapie pour l'incontinence urinaire d'effort qui seront divisées en groupe "guéri" et "non guéri". Vous êtes invitées à participer à cette étude pour l'une des trois raisons suivantes : (1) vous nous avez contactée directement en exprimant votre intérêt pour l'étude et vous ne souffrez pas actuellement de symptômes d'incontinence urinaire à l'effort, (2) vous avez été référé par un physiothérapeute et vous envisagez de suivre la physiothérapie du plancher pelvien pour traiter vos symptômes d'incontinence urinaire d'effort, (3) vous avez été référé par un physiothérapeute ou vous nous avez contacté directement après avoir terminé le traitement de physiothérapie et êtes intéressé à participer dans l'étude.

L'étude consiste à remplir quatre questionnaires en ligne (environ 30 minutes) et deux sessions d'évaluation en laboratoire qui dureront 2,5 heures pour la première visite et 2 heures lors de la seconde.

Participation

Questionnaires

Si vous suivez une physiothérapie pour vos symptômes d'incontinence urinaire à l'effort, vous recevrez deux invitations à remplir des questionnaires. La première invitation vous demandera de remplir quatre questionnaires sur les symptômes des voies urinaires. Ces questionnaires vous interrogeront sur (1) vos symptômes au niveau des voies urinaires inférieures, notamment les fuites urinaires, (2) votre contrôle et vos habitudes intestinales, (3) vos symptômes vaginaux et troubles sexuels et (4) votre qualité de vie. Chaque questionnaire ne devrait pas vous prendre plus de 5 minutes à remplir, avec un total de 30 minutes pour remplir tous les questionnaires. Il vous sera demandé de remplir les questionnaires avant d'assister à la première session de laboratoire et de le faire dès que possible car vos réponses pourraient changer après le début de la physiothérapie. La deuxième invitation vous fournira des liens vers deux questionnaires, que vous recevrez après 12

semaines de physiothérapie. Les questionnaires vous interrogeront sur vos symptômes au niveau du bas appareil urinaire, y compris les fuites urinaires. De plus, il vous demandera d'évaluer votre niveau de satisfaction et si vous pensez que vos symptômes se sont améliorés avec l'intervention physiothérapeutique.

Si vous NE SUIVEZ PAS de physiothérapie, vous recevrez une invitation par courriel avec des liens vers quatre questionnaires qui ne devraient pas vous prendre plus de 30 minutes au total à compléter. Ces questionnaires vous interrogeront sur (1) vos symptômes au niveau des voies urinaires inférieures, notamment les fuites urinaires, (2) votre contrôle et vos habitudes intestinales, (3) vos symptômes vaginaux et troubles sexuels et (4) votre qualité de vie. Il vous sera demandé de remplir ces questionnaires avant d'assister à la séance de laboratoire.

Évaluations en laboratoire

Les deux évaluations en laboratoire se dérouleront au Laboratoire de mesure de la fonction motrice (Laboratoire de la Dre McLean) de l'Université d'Ottawa, 200 avenue Lees, salle 155D. La session 1 durera 2,5 heures et la visite 2 durera 2 heures. Chaque séance sera programmée à votre convenance et dans un délai de 10 jours l'une de l'autre. Si vous choisissez de vous rendre en voiture à ces visites d'évaluation, le stationnement vous sera assuré gratuitement par une place réservée. Vous devrez apporter votre propre masque chirurgical ou en tissu pour ces évaluations en laboratoire. Si vous n'en avez pas, un masque vous sera fourni à l'entrée du bâtiment de l'université.

L'assistante de recherche et candidate au doctorat sous la supervision directe de la Dre McLean, Kaylee Brooks, vous accueillera à votre arrivée au laboratoire et effectuera votre examen. Mlle Brooks a plus de 4 ans d'expérience de recherche dans le domaine de la santé pelvienne des femmes et a été formée par des experts locaux sur toutes les procédures d'évaluation. Mlle Brooks

sera assistée par un stagiaire de recherche qui l'aidera à préparer les instruments et qui fera fonctionner les ordinateurs utilisés pour la collecte des données, mais la stagiaire n'effectuera aucune procédure d'évaluation clinique. Comme Mlle Brooks ne parle pas couramment le français, si votre langue préférée est le français, la stagiaire assistera comme interprète lors de la session d'évaluation. Mlle Brooks et son assistante porteront toutes les deux un masque chirurgical et un équipement de protection individuelle complet lors de vos deux visites au laboratoire.

Après avoir signé ce formulaire, il vous sera demandé de fournir votre âge et ensuite vous serez soumis à la mesure et à l'enregistrement de votre taille, de votre poids et de votre tour de taille et de hanches. Par la suite, vous serez installé dans un espace privé pour vous déshabiller à partir de la taille et vous couvrir d'une blouse et d'un drap. Lorsque vous serez prête, on vous demandera de réinviter Mlle Brooks et son assistante dans la salle d'évaluation. Vous serez invitée à vous allonger sur une table d'examen avec la tête soutenue par un oreiller.

En portant des gants, Mlle Brooks procédera à un bref examen génital pour s'assurer qu'il n'y a aucune présence de d'une infection (ou autres facteurs) qui pourrait interférer avec votre capacité à participer, et vérifier qu'il n'y a pas de risques pour votre santé qui pourraient vous causer un malaise pendant le protocole. Une fois cet examen terminé, on vous montrera un dynamomètre du plancher pelvien, le dynamomètre intra-vaginal automatisé (DIV), qui est un instrument qui sera utilisé lors de certains des évaluations. Mlle Brooks vous fournira l'interrupteur (actionné par le pouce) pour le DIV sur lequel vous pouvez appuyer à tout moment pour mettre fin au test DIV. Par la suite, elle vous expliquera le protocole de la première évaluation, qui examinera votre capacité à sentir les mouvements des muscles de votre plancher pelvien. Elle vous demandera d'identifier si les muscles de votre plancher pelvien ont été déplacés vers une position plus étendue, plus petite ou identique par rapport à une position de référence qui sera déterminé. À cette fin, les bras du DIV seront insérés dans le vagin, comme le fait un professionnel de la santé avec un spéculum lors d'un test Pap. Mlle Brooks vous demandera de rester calme pendant que les bras du DIV s'ouvrent lentement à différents diamètres. Il vous sera ensuite demandé d'identifier si les bras de l'appareil sont plus ou moins écartés en comparaison avec la valeur de référence.

Par la suite, les bras du même DIV seront légèrement écartés et Mlle Brooks vous demandera de contracter les muscles de votre plancher pelvien avec un effort maximal. Cette tâche sera répétée trois fois. Ensuite, Mme Brooks vous demandera de contracter les muscles de votre plancher pelvien aussi fort et aussi vite que possible à plusieurs reprises sur une période de 15 secondes. Une fois terminé, trois cibles vous seront présentées sur un écran d’ordinateur et il vous sera demandé d’essayer de contracter les muscles de votre plancher pelvien pour correspondre aux différentes cibles à l’écran. Vous aurez l'occasion de vous entraîner jusqu'à ce que vous soyez à

l'aise avec cette tâche. L'écran montrera trois niveaux de force à atteindre. Pendant le test, vous effectuerez des contractions pour essayer d'atteindre chacun des trois cibles, tout en consultant l'écran de l'ordinateur. Vous répéterez ensuite l'activité, cette fois sans voir le moniteur de l'ordinateur.

Mlle Brooks vous préparera ensuite pour les évaluations de la fonction motrice des nerfs. Elle portera encore des gants d'examen et insérera un petit capteur (électrode) dans le vagin en utilisant un doigt pour guider le placement sur la paroi vaginale antérieure. Pendant que Mlle Brooks tiendra l'électrode en place, on vous demandera de tirer sur le bouchon d'une seringue remplie d'air, ce qui provoquera une petite force d'aspiration afin de maintenir l'électrode en place pendant la procédure. Une électrode collante sera appliquée sur la peau à côté de l'anus et une deuxième électrode collante sera appliquée sur la peau au-dessus de la hanche droite. Ensuite, Mlle Brooks mettra un nouveau gant équipé d'une électrode spécialisée et préparera une deuxième électrode à placer dans votre vagin. Elle examinera l'intérieur du vagin pour s'assurer que l'électrode est correctement positionnée sur les muscles de vos plancher pelvien, puis il vous sera demandé de tirer sur le bouchon d'une seringue remplie d'air, comme avec l'électrode précédent, pour l'aspirer en place. Ensuite, Mme Brooks déplacera doucement son doigt avec l'électrode spécialisée attachée au gant pour localiser votre nerf et positionner l'électrode correctement pour stimuler le nerf moteur. Une fois qu'elle aura l'électrode dans la bonne position, Mme Brooks vous demandera de contracter les muscles de votre plancher pelvien aussi fort que possible pendant 5 secondes pour trois essais. Puis, elle commencera la stimulation nerveuse et demandera à l'assistante de recherche d'augmenter lentement l'intensité de l'impulsion électrique qui stimulera le nerf. Vous sentirez les muscles de votre plancher pelvien se contracter en réponse au stimulus. Bien que cela puisse causer un certain inconfort, la sensation ne devrait pas être douloureuse. Si la procédure est trop inconfortable ou extrêmement douloureuse, veuillez le faire savoir à Mlle

Brooks afin qu'elle puisse ajuster l'électrode et la stimulation en fonction de vos besoins. Une fois qu'elle a déterminé un signal d'électrode approprié, Mlle Brooks stimulera votre nerf pudendal 10 fois. Elle retirera ensuite toutes les électrodes. Une fois retirées, Mlle Brooks et son assistante quitteront la pièce pour que vous puissiez vous rhabiller. Ceci conclura la première session de laboratoire.

La deuxième évaluation en laboratoire sera effectuée dans les 10 jours suivant la première évaluation et portera sur la sensation. Elle durera environ deux heures. La même assistante de recherche, Mlle Brooks, vous accueillera à votre arrivée. Encore une fois, vous devrez porter un masque chirurgical ou en tissu pendant l'évaluation. Mlle Brooks et la stagiaire porteront toutes les deux un masque chirurgical et un équipement de protection individuelle complet pendant l'évaluation. Mlle Brooks passera en revue avec vous les objectifs et les protocoles de la deuxième évaluation et répondra à toutes vos questions. Vous serez invitée à vous déshabiller dans la salle d'examen et à vous couvrir d'une blouse et d'un drap comme lors de la première session. Lorsque vous serez prête, vous inviterez Mlle Brooks et son assistante à entrer dans la salle d'évaluation. Vous serez invitée à vous allonger sur une table d'examen avec la tête soutenue par un oreiller.

Cette session comprendra une série de tests de sensations et d’échographies. Pour chaque test, Mlle Brooks vous demandera d'indiquer par oui ou par non si vous ressentez certains stimuli (touché léger) après que ceux-ci ont été appliqués sur la peau. Cinq zones seront évaluées, y compris votre cheville droite et quatre zones de votre région génitale. Ces points spécifiques seront marqués avec un marqueur chirurgical non permanent afin d’assurer que Mlle Brooks examine le même point à chaque fois. Chacun des stimuli sera d'abord appliqué sur votre avant-bras pour que vous puissiez percevoir ce que vous ressentirez, puis Mlle Brooks testera chacun des zones, en commençant par la cheville avant de passer aux parties génitales. Puisque nous cherchons à enregistrer le moindre stimulus que vous pouvez ressentir avec chacune de ces

sensations, il ne devrait donc y avoir aucun inconfort associé aux évaluations. La sensation tactile sera testée à l'aide de petits fils qui sont à peu près épais comme un cheveu humain. Avant de procéder à l'application d'un stimulus sur un endroit quelconque, Mlle Brooks fixera votre attention sur cet endroit en le touchant doucement avec un coton-tige et chaque zone sera testée trois fois. Après les tests de sensation, Mlle Brooks vous montrera une sonde d'échographie qui sera placée sur votre périnée pour permettre de visualiser les structures internes de votre pelvis. Il vous sera demandé de contracter vos muscles pelviens à un niveau d'effort maximal trois fois pendant que Mlle Brooks enregistre de courtes vidéos d'échographie de vos muscles. Ensuite, il vous sera demandé de vous placer devant la table d'examen afin que Mlle Brooks puisse prendre trois images de vos muscles du plancher pelviens dans cette position de repos debout. Mlle Brooks et son assistante quitteront ensuite la salle afin que vous puissiez vous rhabiller. Ceci conclura la collecte de données de l'étude.

Risques potentiels

Il n'existe aucun risque connu d'infection ou d'inflammation associé à aucune des procédures utilisées dans cette étude. Tous les équipements, y compris les électrodes, les bras de DIV et les gants d'examen, ne seront utilisés qu'une seule fois et seront jetés après leur utilisation. Les mono-filaments, les instruments et leurs fils sont désinfectés après chaque utilisation. Tous les draps, blouses et taies d'oreiller sont lavés après chaque utilisation.

Il est possible que vous ressentiez une certaine fatigue musculaire au cours de l'étude, puisqu’on vous demandera de contracter les muscles de votre plancher pelvien à plusieurs reprises. Afin de réduire cette fatigue, des périodes de repos sont prévues au cours de chaque séance, et vous pouvez demander à vous reposer plus longtemps si vous le souhaitez. N'hésitez pas à nous demander de ralentir une évaluation à tout moment.

La stimulation électrique peut générer de la chaleur au contact du métal. Ne vous portez donc pas volontaire pour participer si vous avez des implants métalliques dans la région pelvienne et veuillez retirer tout piercing du bas de votre corps. Ne vous portez pas volontaire pour participer si vous êtes enceinte ou si vous avez tendance à vous évanouir. En ce qui concerne la stimulation électrique, les effets secondaires potentiels peuvent inclure une sensibilité vaginale qui devrait disparaître dans l'heure qui suit la séance. Vous pouvez également prendre des analgésiques en vente libre comme le Tylenol® si vous le jugez nécessaire.

Malaises

Bien que la stimulation électrique des muscles du plancher pelvien ne soit pas douloureuse, certaines personnes la trouvent désagréable. La stimulation entraînera une contraction des muscles du plancher pelvien, de l'urètre et de l'anus, ce qui peut également être inconfortable, mais ne causera aucun dommage. Veuillez faire savoir à Mlle Brooks si cette procédure est trop inconfortable pour continuer. Vous pouvez à tout moment cesser de participer.

Il est possible que certaines femmes se sentent nerveuses pendant le déroulement des évaluations et nous ferons donc tout notre possible pour vous tenir informée de la suite des événements et de ce que vous ressentirez tout au long du protocole. Encore une fois, vous pouvez demander à tout moment de ralentir le processus ou de l'interrompre si vous le souhaitez.

Inconvénients

En raison des nombreuses pauses prévues lors des évaluations motrices et sensorielles, le protocole est assez long (environ une heure et demie par séance) ce qui peut être contraignant. Vous aurez la possibilité de programmer votre évaluation en dehors des heures de travail normales, le soir ou le week-end si vous le préférez.

En cas de blessure liée à la recherche, vous serez orientée vers votre prestataire de soins de santé habituel pour recevoir un traitement/des soins médicaux appropriés dans le cadre de votre plan de santé provincial. Si des soins urgents sont nécessaires, nous contacterons la sécurité du campus de l'Université d'Ottawa et vous serez escortée par le personnel de recherche au service d'urgence de l'hôpital général d'Ottawa pour y recevoir des soins. En acceptant de participer à cette étude, vous ne renoncez pas à vos droits légaux.

Avantages

La participation à cette étude vous permettra de vous renseigner sur la musculature de votre plancher pelvien et le rôle de la coordination musculaire et la sensation sur l'efficacité de l'entraînement des muscles du plancher pelvien. Si vous êtes intéressée par l'une des procédures ou l'un des dispositifs des procédures, n'hésitez pas à nous poser des questions lors de votre évaluation. Cette étude ne comprend pas d'intervention thérapeutique. Un résumé des résultats de l'étude vous sera envoyé à sa conclusion.

Description de toute expérience de travail pertinente concernant cette population ou ce sujet

Notre personnel de laboratoire possède une expertise et une expérience exceptionnelles dans l'application des méthodes et de la conduite de la recherche et sont bien formés à l'utilisation et à la sécurité de toutes les méthodes décrites ci-dessus.

L'assistante de recherche et candidate au doctorat, Mlle Brooks, travaille depuis plus de 5 ans au laboratoire de mesure de la fonction motrice dans le domaine de la recherche sur la santé des femmes. Elle a reçu une formation et un mentorat spéciaux de la part de la Dre McLean, la chercheuse principale de cette étude, et de la part de la Dre Caroline Pukall, une experte internationale en matière de sexualité humaine et en évaluation des sensations au niveau des organes génitales.

Compensation

Aucune compensation n’est offerte pour la participation à cette étude.

Désistement de l'étude

Vous avez le droit de vous retirer de cette étude à tout moment, sans besoin de fournir de raisons quelconques. Si vous choisissez de vous désister de l'étude, toutes données que vous nous avez fournies jusqu'à présent seront détruites, sauf si vous nous accordez l'autorisation de les utiliser.

Confidentialité

Vous ne serez pas identifiable dans les publications, thèses de doctorat ou présentations qui résulteront de cette étude. Aucune information permettant de vous identifier ne quittera l'Université d'Ottawa. Il y aura un fichier électronique protégé par un mot de passe, sauvegardé sur un ordinateur protégé par un mot de passe qui restera dans le Laboratoire de mesure de la fonction motrice. Ce fichier reliera votre nom à votre numéro de participant. Ce fichier ne sera accessible que par la Dre McLean, son personnel et les étudiants de l'Université d'Ottawa qui ont tous reçu des instructions sur les procédures à suivre pour protéger la vie privée et la confidentialité et qui ont signé des accords de confidentialité. Tous les dossiers électroniques seront sauvegardés dans une base de données sécurisée à l'Université d'Ottawa et seront protégés par un mot de passe d'utilisateur, également accessible uniquement par la Dre McLean, ses étudiants et son personnel. Ces dossiers ne contiendront pas votre nom ou d'autres informations permettant de vous identifier. Tous les dossiers papier seront conservés dans une armoire de classement au sein du Laboratoire de mesure de la fonction motrice, qui est une zone à accès restreint. Tous les dossiers seront conservés pendant une période de 10 ans après la fin de l'étude. À la fin de la période de conservation, tous les dossiers papier seront jetés dans des déchets confidentiels ou déchiquetés, et tous les dossiers électroniques seront définitivement supprimés du serveur de données.

Droits des participants

Votre participation à cette étude est volontaire. Vous pouvez vous retirer de cette étude à tout moment. Vous êtes libre de refuser de vous soumettre à tout aspect du processus de dépistage, sans en indiquer la raison. Les chercheurs peuvent vous retirer de l'étude pour des raisons scientifiques à tout moment. Dans ce cas, ils vous fourniront une raison claire et valable. Vous avez le droit d'obtenir des copies de tout formulaire d'étude qui contient vos informations personnelles.

En tant que participante à cette étude, vous avez droit à un environnement dans lequel vous vous sentez à l'aise. Pour votre sécurité et celle de notre équipe, une troisième personne (une étudiante assistante de recherche) sera présente dans le laboratoire pendant toutes les procédures d'évaluation. Vous pouvez également amener un.e ami.e ou un membre de votre famille avec vous pour être présent dans la salle si cela vous permet de vous sentir plus confortable.

Si, à tout moment, vous avez d'autres questions ou difficultés, vous pouvez contacter les responsables de l'étude :

Linda McLean, PhD, 613-562-5800 poste 2544 ou linda.mclean@uottawa.ca

Kaylee Brooks, Ph.D. Candidate au doctorat, École des sciences de la réadaptation 613-562-5800 poste 4102 ou mfmlab@uottawa.ca

Si vous avez des questions concernant cette étude ou si vous pensez avoir subi une blessure liée à la recherche, veuillez contacter Dr. Linda McLean at 613-562-5800 poste 2544 à votre convenance.

Les comités d'éthiques de la recherche des sciences et des sciences de la santé à l'Université d'Ottawa ont examiné ce protocole et l'ont jugé en conformité avec les normes nationales pour la conduite éthique de la recherche sur les humains. Si vous avez des questions concernant vos droits comme participante, veuillez contacter le responsable d'éthique en recherche à l'Université d'Ottawa, au 613-562-5387 ou ethics@uottawa.ca.

Consentement à participer à la recherche

Titre de l'étude : Corrélats sensoriels de l'incontinence urinaire à l'effort chez la femme et leur influence sur les résultats de l'entraînement des muscles du plancher pelvien.

Je comprends que l'on me demande de participer à une étude de recherche et que ma participation est volontaire. Ce protocole m'a été expliqué par Mlle. Kaylee Brooks, une chercheuse au doctorat.

J'ai lu cette lettre d'information de huit pages et le formulaire de consentement, ou on m'a lu ces documents. Toutes mes questions ont été répondu à ma satisfaction. Si je décide à un stade ultérieur durant l'étude que je souhaite retirer mon consentement, je peux le faire à tout moment.

J'accepte volontairement de participer à cette étude.

Une copie de la lettre d'information et le formulaire de consentement me seront fournis pour mes dossiers.

Signatures

_____

Nom du participant (Veuillez écrire en lettres d'imprimerie)

_____ _____

Signature du participant Date

Déclaration de l'enquêteur (ou personne expliquant le consentement)

J’ai soigneusement expliqué au participant à la recherche la nature de l’étude décrite ci-dessus. À ma connaissance, le participant à la recherche signant ce document de consentement comprend la nature, les demandes, les risques et les avantages liés à la participation à cette étude. Je reconnais ma responsabilité en ce qui concerne les soins et le bien-être du participant à la recherche susmentionnée et je suis conscient de ma responsabilité de respecter les droits et les souhaits du participant à la recherche et de mener l’étude en conformant aux directives et régulations de bonnes pratiques cliniques applicables.

_____

Nom de l’enquêteur/Délégué (Veuillez écrire en lettres d’imprimerie)

_____ _____

Signature de l’enquêteur/Délégué Date

uOttawa Consent Information Addendum- COVID-19 Risks

Principal Investigator: Linda McLean, Ph.D., Full Professor, School of Rehabilitation Sciences, University of Ottawa. 613-562-5800 ext 2544 and Kaylee Brooks, Ph.D. Candidate, School of Rehabilitation Sciences, University of Ottawa, 613-562-5800 ext 4102.

Study Title: Sensory and motor correlates of stress urinary incontinence in women and their influence on pelvic floor muscle training outcomes

Please read the following statements carefully and feel free to ask questions if anything seems unclear.

We are putting in place safety precautions to reduce exposure to COVID-19, but the risk of exposure can still exist. COVID-19 can result in severe illness, medical expenses, and loss of income and in some cases, death.

If you are considered vulnerable to the effects of COVID-19 (e.g., an older adult; underlying medical conditions or a compromised immune system), please discuss your participation with the research team before consenting to participate.

If you are feeling unwell or experiencing any potential COVID-19 symptoms leading up to the research session, please stay home and notify the research team that you cannot attend. Should you experience symptoms in days following the session, please also notify the research team.

Potential COVID-19 symptoms include new or worsening cough, shortness of breath or difficulty breathing, temperature equal to or over 38C (100.4F), feeling feverish, chills, fatigue or weakness, muscle or body aches, new loss of smell or taste, headache, gastrointestinal symptoms (abdominal pain, diarrhea, vomiting), or feeling very unwell.

To reduce the possibility of COVID-19, we have implemented the following safety procedures:

- Regular handwashing
- Using hand sanitizer when handwashing is not possible
- Wearing of face masks/face coverings
- Physical distancing when possible (as recommended by the local health authority)
- Limiting shared material and documents (pens, paper)
- Sanitizing surfaces and shared equipment
- Waiting 60 minutes between each session
- Using face shields or goggles
- Using lab coats or hospital gowns
- Collecting personal contact information for contact-tracing purposes.

Please advise a researcher if you believe a safety measure is not being taken, or that your safety is at risk.

Considerations for the Participant:

We ask that you:

- Wear a mask or face covering. Masks will be provided by the researcher if you do not have one. If you feel that you are unable to wear a mask, discuss your participation with the research team.
- Complete a screening assessment before each research session.
- Wash or sanitize your hands upon arrival. Hand sanitizer will be provided or a washing station
- will be available.
- Maintain physical distancing to the extent possible during the in-person research activities.

We ask that you follow the health-related directives above for your safety and the safety of the researchers.

Information for Contact Tracing

We are collecting personal contact information for contact-tracing purposes, in the event that you may have been exposed to COVID-19 at the research site.

Your name and contact information:

- Will not be stored with the research data
- Will always be securely stored
- Will only be used if requested by Public Health authorities for COVID-19 contact tracing
- purposes
- Will be held only for the time required by Public Health authorities

Right to Withdraw

You are under no obligation to participate. You can stop participating or withdraw from the study at any time by notifying the researcher using the contact information above.

Thank you for your interest and participation.

Information for Contact Tracing (to be kept separately from research documents)

This information:

- will not be stored with the study data;
- will always be securely stored;
- will be used only if requested by public health to provide this information for COVID-19 contact
- tracing purposes; and

- will be held only for the time required by public health authorities

First Individual

Name (please print): _____(required)

Phone: _____(required)

Email: _____(optional)

Date: _____

Second Individual

Name (please print): _____(required)

Phone: _____(required)

Email: _____(optional)

Date: _____

Appendix H: Data Collection Forms

Sensory and Motor correlates of stress urinary incontinence in women and their influence on pelvic floor muscle training outcomes

First Laboratory Assessment

Study ID: _____

Date: _____(yyyy-mm-dd) **Time: _____**

<u>Part 1: Demographics and Morphological Data</u>

Age: _____ Gender:_____

Number of Pregnancies: _____ Number of Caesareans: _____

Number of Vaginal births: _____ Forceps, suction, episiotomy:_____

Aware of any perineal tears at the time of delivery or diagnosed with levator avulsion:_____

_____

_____

_____

Education Level: _____

If you do not see a category that you feel you identify with, please provide us with your preferred identity and please know that you are not obligated to answer this question if you feel uncomfortable. We ask this question because there is some evidence that more connective tissue damage may happen to people who are of White or Asian descent in comparison to others (Howard et al. 2000, Grodstein et al. 2003, Tennstedt et al., 2008)

Do you identify as:

- White (European descent)
- Black (African, Afro-Caribbean, African Canadian Descent)
- East/Southeast Asian (Chinese, Korean, Japanese, Taiwanese descent or Filipino, Vietnamese, Cambodian, Thai, Indonesian, other Southeast Asian descent)
- Indigenous (First Nations, Metis, Inuit/Inuk descent)
- Latino (Latin American, Hispanic descent)
- Middle Eastern (Arab, Persian, West Asian descent (e.g., Afghan, Egyptian,Iranian, Lebanese, Turkish, Kurdish)
- South Asian (South Asian descent (e.g., East Indian, Pakistani, Bangladeshi, Sri Lankan, Indo-Caribbean)
- Another race category
- Do not know
- Prefer not to answer

_____

_____

Contraceptive Medications: _____

Hormone Replacement Therapy: _____

Do you smoke, if yes #/day and for how long? _____

_____

Other Relevant Information (e.g. Ask is they have red hair, menstrual cycle): _____

_____

_____

Body weight: _____(kg/lbs) Waist: _____(cm)

Height: _____(cm/in) Hips: _____(cm)

BMI: _____(kg/m^2)

Do you have a latex allergy? _____

LOI and consent form completed O Yes O No

Part 2:

Examination of genitals for signs of lesions, infections, or obvious mass(es) that may cause unanticipated discomfort during the assessment.

1 O No visible lesions, infections, or mass(es)

2 O Potential issue: _____

_____

RUN CALIBRATION DYNO FILE IN LABCHART (Save as SM##_calibration)

Part 3: Proprioception Test

Using the intravaginal dynamometer (IVD), participants will be instructed to decide if the IVD diameter is larger, smaller, or the same as their reference diameter. First, to find the participant's reference diameter (diameter at which the IVD arms open to that produces approximately 1.45N), the IVD arms will be opened to 25mm and increased by 5mm until the forces are between 1.4 and 1.5N. The diameter will be increased or decreased by 2mm until the forces are approximately

1.45N. This diameter will be the participant's reference diameter for the duration of the test. The participant will be provided with the reference diameter first followed by a test diameter that is small, larger, or the same as the reference. They will be asked to state their choice which the research assistant will record. Record the order of diameters for each testing session. (Save files determining reference values as passive_#)

IVD Setup:

Opening Distance	Start at 25mm
Standby Time	5s
Hold Open Time	7s
End Time	5s
Opening Speed	20mm/s
Closing Speed	20mm/s

Reference Diameter: _____ 5mm Above: _____ 5mm Below: _____

(Files will be saved as with participant ID and test type/trial number **SM###_P1 or _R1 for reference opening distance**)

	P1	P2	P3	P4	P5	P6	P7	P8	P9
AP Diameter Order (mm)									
Decision on Position									

(S = Same, Lg = Larger, Sm = Smaller)									

Part 4: Kinesthetic Awareness

Explain protocol to participant and instruct to either stare at the ceiling or at the computer screen depending on the visual or non-visual feedback condition.

Part 4a: Instruct participant to squeeze as hard as they can with their pelvic floor muscles when you say "squeeze, squeeze, squeeze as hard as you can, harder, Harder, HARDER" and relax those muscles when you say, "ok now relax, really relax, let go of your pelvic floor".

IVD Setup

Opening Distance	35mm
Standby Time	5s
Hold Open Time	20s
End Time	5s
Opening Speed	20mm/s
Closing Speed	20mm/s

IVD arm diameter is set to 20mm. (Files will be saved as with participant ID and test type/trial number **SM###_MVC#**)

Trial	Baseline (N)	Peak (N)	Relative Peak (N)
1			
2			
3			
4*			

*Trial 4 is a space for a practice MVC trial or extra trial if needed. Only 3 MVCs are required for testing.

Lowest Baseline Force: _____ Highest Relative Peak Force: _____

Fast Contraction Task:

Instruct participant to contract their pelvic floor muscles as hard and as fast as they can with a complete relaxation in between each contraction. Record how many contractions they were able to perform over the course of 15 seconds. Let baseline settle and then have the RA count the participant in for contractions to start at the 16s mark. Then have the RA tell participant to stop after 15s (time = 31s now) the arms will close 4s later (this is a buffer zone of time). One Trial!

IVD Setup

Opening Distance	35mm
Standby Time	5s
Hold Open Time	30s
End Time	5s
Opening Speed	20mm/s

Closing Speed	20mm/s

(Files will be saved as with participant ID and test type/trial number **SM###_fast**)

Trial	Complete (Check off when done)
1	
2*	

*Space for extra trial if there is a mistake and a second trial is needed.

Part 4b:

IVD Setup

Opening Distance	35mm
Standby Time	5s
Hold Open Time	20s
End Time	5s
Opening Speed	20mm/s
Closing Speed	20mm/s

Right click on 100% Force Channel, select arithmetic, input the highest relative peak force and the lowest baseline force into the equation.

Equation: ((Ch11-**Lowest Baseline Force**)/**Highest relative peak force**)*100

Participants will squeeze their pelvic floor muscles to reach but not exceed the force level indicated prior to the opening of the IVD arms and to hold the target for 5 seconds before relaxing. Cue the participant to relax before their contractions and then to squeeze but do NOT coach them to hit the force level. Then cue them to relax after they have held their contraction for 5s. For visual feedback, the participant can look at the computer screen to watch their force in real time. For the non-visual feedback, ask participants to look at the ceiling. 1-minute of rest between contractions.

The order of the force levels will be randomized for each feedback condition. Please write the order in which the force levels will be presented in feedback condition. Leave any notes from testing under the table. The test will begin with 2-3 practice trials for each force level before official testing begins. *Participants can decide the order of trials for practice*.

(Files will be saved as with participant ID and test type/trial number **SM###_P1_%%_V or NV** [feedback type V = Visual and NV = Non-Visual])

PRACTICE	**P1**	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**
Force Level									
Visual Feedback ***(Check when done)***									
Non-Visual Feedback ***(Check when done)***									

Notes:

Get randomized testing order from Excel document in Google Drive in SM Study Folder. Save copy of the randomization in participant's data folder.

(Files will be saved as with participant ID and test type/trial number **SM###_T1_%%_V or NV** [feedback type V = Visual and NV = Non-Visual])

TESTING	**T1**	**T2**	**T3**	**T4**	**T5**	**T6**	**T7**	**T8**	**T9**
Force Level									
Visual Feedback ***(Check when done)***									
Non-Visual Feedback ***(Check when done)***									

Notes:

Part 5: Electrode Placement for Pudendal Nerve Stimulation

- DSE over the mid-urethra (anterior vaginal wall)
- DSE over the LAMs on the right side
- Cloth surface electrodes laterally on the right side of the external anal sphincter
- Skin preparation – clean with rubbing alcohol. Wipe and allow to try. Then place reference electrodes on the anterior superior iliac spine on right side

Check that the EMG channels are working by asking the participant to gently squeeze their pelvic floor muscles.

Attach the St. Mark's electrode to the finger of a new glove and prepare the second DSE for placement on LAM on right side. Explain to the participant the protocol for the nerve stimulation and MVCs and gently guide the finger with the St. Mark's electrode and DSE into the participant's vagina. Palpate for the right LAM and place the DSE (RA will need to plug in the remaining electrodes). Once placed, shift finger with St. Mark's electrode off and past the DSE near where stimulation will occur.

Check that all channels are recording and ask the participant to perform 3 MVCs. Instruct participant to squeeze as hard as they can with their pelvic floor muscles when you say "squeeze, squeeze, squeeze as hard as you can, harder, Harder, HARDER" and relax those muscles when you say, "ok now relax, really relax, let go of your pelvic floor". They will hold the contraction for 5s. (Files saved as **SM###_EMG_MVC#**)

MVC 1	MVC 2	MVC 3

Then gently palpate for the right pudendal nerve without disturbing DSE placement. Stimulate the pudendal nerve with increasing intensity until no further increases in the evoked potential

amplitude. Once ready, increase the stimulus by 20% and stimulate nerve 10x. Make sure to check in with the participant through this process to make sure that they are okay. Watch their face throughout the protocol while the research assistant watches the computer screen for quality control.

(Files will be saved as with participant ID and stimulation intensity **SM###_Stim##** while finding the resting motor threshold. Then save CMAP files as participant ID and stimulation trial number **SM###_##**)

Resting Motor Threshold: _____

Supramaximal Stimulus (*Stimulation Intensity Increased by 20%*): _____

Stimulation 1:_____

Stimulation 2:_____

Stimulation 3:_____

Stimulation 4:_____

Stimulation 5:_____

Stimulation 6:_____

Stimulation 7:_____

Stimulation 8:_____

Stimulation 9:_____

Stimulation 10:_____

*Notes:*_____

_____

_____

_____

_____

Remove the electrodes from the participant.

This ends the first laboratory assessment.

End Time of Assessment: _____

Completed by Print Name: _____ Date: _____

Signature: _____

PI Signature: _____ Date: _____

Scheduled date and time for second assessment: _____

Noted in MFM lab calendar: _____

Research assistant scheduled: _____

Sensory and Motor correlates of stress urinary incontinence in females and their influence on pelvic floor muscle training outcomes

Second Laboratory Assessment

Study ID: _____

Date: _____(yyyy-mm-dd) **Time: _____**

Reaffirmed consent for the second assessment verbally O Yes O No

<u>Part 1: Quantitative Sensation Testing</u>

Explain the protocol to the participant

1) We will be measuring your thresholds for light touch, which is the first instance when you detect sensation.
2) We will mark spots on your ankle, buttocks, and vulva; this will be a one-time use surgical marker that will wash off.
3) I will first touch the spot I am going to test with a cotton swab before we start so that you know to pay attention to it.

4) I will ask you to close your eyes or focus on a spot on the ceiling so that you are not facing me or looking at the testing site, whichever is most comfortable for you. This will prevent any influence of seeing the monofilament applied to the skin surface on the results of the sensation testing.
5) I will ask you if you feel the filament and you will answer with a YES or NO. It may be difficult to tell sometimes, in this case give your best answer.
6) Sometimes there will be no filament applied (a blank trial) just to make sure that we are testing the right thing.

Mark the stimulation sites on the participant.

Part 1a: Monofilaments (Tactile Thresholds)

1) Show the participant the filaments before starting and apply to the forearm.
2) First begin with the ankle site, then move to the randomized genito-pelvic sites.
3) Give clear instruction on when to start looking away/closing eyes, and when they can open them. Touch the site with a cotton swab before applying the first filament.
4) Apply each filament until it bends in a semi-circle, count '*one, one-thousand*'.
5) Repeat trials that were incorrect and immediately inform the RA.
6) Participant must give a Yes/No response.
7) Files will be saved as **TTKBSM## RA#** for Ankle sites and **TTKBSM## T#** for the other trials. The labelling is based on the QST program.

Site	**Trial**		
	1	**2**	**3**
Control: Right Ankle			
Filament # Detected			
Avg grams			
Avg Log Value			
Blank Trial Count			
Correct Blank Trials			

Total Trials Recorded			
Reversal Count			
Pudendal: Posterior Urethra			
Filament # Detected			
Avg grams			
Avg Log Value			
Blank Trial Count			
Correct Blank Trials			
Total Trials Recorded			
Reversal Count			
Pudendal: Perineum			
Filament # Detected			
Avg grams			
Avg Log Value			
Blank Trial Count			
Correct Blank Trials			
Total Trials Recorded			

Reversal Count			
Pudendal: Right EAS			
Filament # Detected			
Avg grams			
Avg Log Value			
Blank Trial Count			
Correct Blank Trials			
Total Trials Recorded			
Reversal Count			
Genito-Femoral: Right Labia Majora			
Filament # Detected			
Avg grams			
Avg Log Value			
Blank Trial Count			
Correct Blank Trials			
Total Trials Recorded			
Reversal Count			

Order of sites Tested: Ankle, _____

(Always start with the ankle, perform all three trials here first then move to genital sites.)

During each trial of each site, when the participant first says they feel the filament, record the first filament they feel, and which adjective they choose that best describes the sensation from the list below.

Adjective List: Ticklish, Mild (light or soft touch), Prickling, Tingling, Brushing, Dull (numb).

Site	Trial 1		Trial 2		Trial 3	
	Filament	Adjective	Filament	Adjective	Filament	Adjective
Ankle						
Right EAS						
Urethra						
Right Labia						
Perineum						

Notes: _____

_____

_____

_____

Part 2: Ultrasound Imaging

Ultrasound assessment using the GE Voluson S6 to assess levator avulsion and bladder neck height during quiet standing. With the participant in supine, collect 3 cineloops in 4D of the

levator hiatus during pelvic floor muscle MVC. Instruct the participant to breathe in, breathe out and squeeze, SQUEEZE, SQUEEZE, HARDER, HARDER, now relax, let the contraction go, really relax your muscles. Then ask the participant to stand with the exam table behind them for support and bend their knees in a small squat to place the probe again. The participant can straighten once the probe is placed. Instruct the participant to relax and record 3 2D cineloops of the urogenital structures at rest.

Supine	**Standing**
MVC1: _____	REST1: _____
MVC2: _____	REST2: _____
MVC3:_____	REST3:_____

Notes:

_____

_____

_____

_____

This ends the second laboratory assessment.

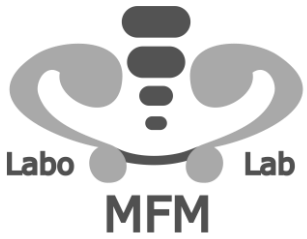
End Time of Assessment: _____

Completed by Print Name: _____ Date: _____

Signature: _____

PI Signature: _____ **Date:** _____

Appendix I: Global Rating of Patient Satisfaction and Perception of Improvement



Global Rating of Patient Satisfaction and Perception of Improvement - KB Patient satisfaction question (PSQ)

* 1. Please enter your study ID starting provided in the email that was sent by the researcher (ex: RUN_94; SED_43)

2. How satisfied are you with your progress in this program?

- Completely
- Somewhat
- Not at all

Labo Lab MFM

Global Rating of Patient Satisfaction and Perception of Improvement - KB Global perception of improvement (GPI)

3. Overall, do you feel that you are: _

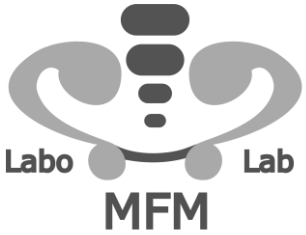
◯ Much better ◯

Better

◯ About the same ◯

Worse

◯ Much worse



Global Rating of Patient Satisfaction and Perception of Improvement - KB Patient estimated percent improvement (EPI)

4. Estimate how much better you are on a scale from 0% (no better) to 100% (completely better).

0% 100%

Appendix J: Regression Model for Ankle

Linear model predictors of right ankle light touch sensation thresholds, with 95% bias corrected and accelerated confidence intervals and standard errors based on 1000 bootstrap samples.

	b (95% CI)	SE	β	p
Model 1				
Step 1				
Constant	4.57 (3.29, 6.03)	0.69		.00
Continence Status	-0.34 (-1.83, 1.25)	0.87	-0.05	.82
Step 2				
Constant	4.76 (1.71, 9.08)	1.67		.01
Continence Status	-0.15 (-1.93, 1.30)	0.91	-0.03	.88
Age	-0.02 (-0.09, 0.07)	0.04	-0.10	.65
Parity	0.80 (-1.26, 2.57)	1.08	0.17	.48

Note. R^2 = .00 for Step 1; R^2 = .03 for Step 2; n = 29 (no large outliers in model); Confidence intervals (CIs) reported in parentheses; standard error of b (SE).

Appendix K: Regression Model for Labia Majora

Linear model predictors of right labia majora light touch sensation thresholds, with 95% bias corrected and accelerated confidence intervals and standard errors based on 1000 bootstrap samples.

	b (95% CI)	SE	β	p
Model 1 – Outlier included				
Step 1				
Constant	0.79 (0.46, 1.16)	0. 21		.01
Continence Status	1.33 (0.40, 2.43)	0.54	.40	.09
Step 2				
Constant	-0.25 (-1.75, 1.11)	0.72		.74
Continence Status	1.05 (0.06, 2.22)	0.58	.32	.12
Age	0.02 (-0.02, 0.05)	0.02	.14	.35
Parity	0.54 (-0.53, 1.76)	0.54	.15	.35
Model 2 – Outlier not included				
Step 1				
Constant	0.79 (0.46, 1.16)	0. 21		.00
Continence Status	0.93 (0.19, 1.78)	0.39	.41	.03
Step 2				
Constant	-0.29 (-1.80, 0.79)	0.73		.68
Continence Status	0.64 (-0.12, 1.36)	0.37	.28	.12
Age	0.02 (-0.01, 0.08)	0.02	.27	.20
Parity	0.25 (-0.63, 1.02)	0.42	.10	.54

Note. Model 1 n = 29, R^2 = .16 for Step 1; R^2 = .21 for Step 2 ; Model 2 n = 28, R^2 = .16 for Step 1; R^2 = .25 for Step 2; Confidence intervals (CIs) reported in parentheses; standard error of b (SE).

Appendix L: Regression Model for Urethra

Linear model predictors of urethral light touch sensation thresholds, with 95% bias corrected and accelerated confidence intervals and standard errors based on 1000 bootstrap samples.

	b (95% CI)	SE	β	p
Model 1 – Outlier Included				
Step 1				
Constant	13.40 (2.82, 28.25)	6.90		.08
Continence Status	2.17 (-15.56, 21.92)	9.89	.04	.84
Step 2				
Constant	-1.47 (-26.92, 16.54)	11.65		.90
Continence Status	-0.78 (-22.19, 21.81)	11.89	-.02	.95
Age	0.15 (-0.60, 1.08)	0.38	.07	.67
Parity	14.23 (2.33, 30.16)	7.36	.24	.09
Model 2 – Outlier not included				
Step 1				
Constant	13.40 (2.92, 27.80)	6.88		.12
Continence Status	-4.48 (-20.90, 8.43)	7.61	-.12	.59
Step 2				
Constant	1.81 (-18.41, 20.83)	9.51		.85
Continence Status	-6.77 (-28.81, 11.21)	11.03	-.19	.56
Age	0.14 (-0.53, 0.88)	0.35	.10	.69
Parity	9.75 (0.61, 20.36)	5.86	.25	.14

Note. Model 1 n = 28, R^2 = .00 for Step 1; R^2 = .08 for Step 2 ; Model 2 n = 27, R^2 = .02 for Step 1; R^2 = .10 for Step 2; Confidence intervals (CIs) reported in parentheses; standard error of b (SE).

Appendix M: Regression Model for Perineum

Linear model predictors of perineal light touch sensation thresholds, with 95% bias corrected and accelerated confidence intervals and standard errors based on 1000 bootstrap samples.

	b (95% CI)	SE	β	p
Model 1 – Outlier included				
Step 1				
Constant	1.12 (0.58, 1.84)	0.34		.01
Continence Status	0.22 (-0.67, 0.94)	0.40	.11	.63
Step 2				
Constant	1.18 (-0.69, 2.61)	0.78		.18
Continence Status	0.24 (-1.07, 1.22)	0.63	.11	.73
Age	-0.00 (-0.04, 0.05)	0.02	-.02	.94
Parity	0.02 (-0.70, 0.77)	0.42	.01	.95
Model 2 – Outlier not included				
Step 1				
Constant	0.79 (0.47, 1.13)	0.15		.00
Continence Status	0.54 (0.05, 1.02)	0.25	.35	.05
Step 2				
Constant	1.67 (0.46, 2.75)	0.57		.01
Continence Status	0.82 (0.20, 1.33)	0.30	.53	.02
Age	-0.02 (-0.05, 0.01)	0.01	-.36	.12
Parity	-0.13 (-0.93, 0.61)	0.33	-.08	.71

Note. Model 1 n = 29, R^2 = .01 for Step 1; R^2 = .01 for Step 2 ; Model 2 n = 28, R^2 = .12 for Step 1; R^2 = .24 for Step 2; Confidence intervals (CIs) reported in parentheses; standard error of b (SE).

Appendix N: Regression Model for External Anal Sphincter

Linear model predictors of external anal sphincter light touch sensation thresholds, with 95% bias corrected and accelerated confidence intervals and standard errors based on 1000 bootstrap samples.

	b (95% CI)	SE	β	p
Model 1 – Outlier included				
Step 1				
Constant	1.04 (0.57, 1.58)	0.24		.14
Continence Status	3.25 (0.71, 6.93)	1.94	.27	.38
Step 2				
Constant	-0.55 (-5.64, 2.21)	1.53		.71
Continence Status	2.88 (0.42, 6.72)	1.92	.24	.39
Age	0.01 (-0.08, 0.11)	0.04	.02	.81
Parity	2.00 (0.09, 4.96)	1.42	.15	.40
Model 2 – Outlier not included				
Step 1				
Constant	1.04 (0.60, 1.55)	0.23		.00
Continence Status	1.27 (0.26, 2.37)	0.46	.46	.03
Step 2				
Constant	0.21 (-1.58, 1.83)	0.86		.81
Continence Status	1.09 (0.10, 1.95)	0.49	.39	.04
Age	0.10 (-0.03, 0.06)	0.02	.10	.64
Parity	0.70 (-0.20, 1.44)	0.43	.24	.10

Note. Model 1 n = 29, R^2 = .07 for Step 1; R^2 = .10 for Step 2 ; Model 2 n = 28, R^2 = .21 for Step 1; R^2 = .29 for Step 2; Confidence intervals (CIs) reported in parentheses; standard error of b (SE).