An Exploration Of The Association Between Lower Urinary Tract Symptoms And Falls In Older People

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Abstract

Falls and urinary incontinence are both highly prevalent in older people, and are both associated with significant impact on health, impairment of quality of life, increased healthcare resource use and costs. There is a well recognised but unexplained association between lower urinary tract symptoms (LUTS), including urgency, urgency incontinence, and nocturia, and falls in older people. Despite calls from the research community, the causes of this association are unknown and little attention has been paid to the potential underlying reasons for the association. There is evidence that the sensation of a strong desire to void (SDV) can influence cognitive function in younger people, and there is a strong association between the prevalence of LUTS in older adults and cognitive dysfunction. This thesis examines the hypothesis that urinary urgency acts as a source of diverted attention, the concept where performing two cognitively demanding tasks leads to impairment in one or both of those tasks. This concept is explored by using cognitive testing and gait analysis in people with and without overactive bladder (OAB) when they are experiencing an urgent need to void, when they are distracted by a validated source of diverted attention, the n back test, and when neither condition is the case. The underlying literature and theory is outlined in Chapters One and Two.

In Chapter Three, healthy volunteers without LUTS performed the Trail Making B (TMT-B) test and a test of simple reaction time (SRT) under the three conditions. The SRT increased significantly with both SDV and distraction, from 371ms to 421ms and 582ms respectively ($p=0.018$ and $p<0.001$), but performance on TMT-B was unaffected. In Chapter Four a similar experiment in adults over the age of 65 without LUTS demonstrated the same effect, with SRT increasing from 451ms to 515ms with SDV and 885ms with distraction ($p<0.001$ for both).

In Chapter Five the performance on cognitive testing when undistracted and with an empty bladder of older adults with and without OAB was undertaken. In this trial older adults with OAB took significantly longer to complete the TMT-B, (103s vs 77s, $p=0.003$), suggesting that those with OAB had demonstrable impairment of executive function.

Chapter Six describes a pilot study of a novel experimental approach to assessing gait in older women with LUTS, using 3 dimensional instrumented gait analysis in women aged over 65 with OAB when they were at baseline and when experiencing urinary urgency.

This study confirmed the feasibility and safety of the method, which was used in Chapter Seven to perform gait analysis in adults age over 65 with OAB walking with urgency, when distracted by the n back test, and with an empty bladder. This study demonstrated significant reduction in gait velocity (from $1.1ms^{-1}$ at baseline to $1.0\ ms^{-1}$ with urgency and $0.8\ ms^{-1}$ with distraction, $p=0.008$ and $p<0.001$ respectively), as well as a shortened stride length, suggesting that the sensation of urgency acts as a source of diverted attention to induce gait changes in older adults with OAB.

Taken together these results suggest that older adults with OAB may have impaired executive function compared to their continent peers, and that in adults of all ages with or without OAB, the sensation of SDV can act as a source of diverted attention. In older adults with OAB this effect is sufficiently powerful to induce gait changes which are associated with an increased falls risk. Future research should investigate the possibility and efficacy of dual-task training in older adults with OAB to control urgency and therefore reduce falls risk.

Preface

This thesis comprises original research by William Robert Gibson (WRG), as a result of collaborations with co-authors, examining the influence of both physiological sensations from the lower urinary tract and lower urinary tract symptoms (LUTS) on cognitive function, with the overall aim of exploring the known association LUTS such as urinary urgency and urgency incontinence and falls in older adults. The thesis comprises eight chapters described below.

Chapter One: Introduction.

This chapter provides a detailed outline of the thesis, the background literature, and the underlying physiology, epidemiology, and pathology of LUTS, falls, and the association between them.

Chapter Two: The association between lower urinary tract symptoms and falls: Forming a theoretical model for a research agenda.

This chapter forms a position paper, published in *Neurourology and Urodynamics.* This paper outlines the current state of the evidence regarding falls and LUTS and suggested explanations for the association, and suggests the concept of diverted attention as a potential avenue to be explored. WRG completed the literature search, wrote the manuscript, and created the figures. Co-authors Kathleen F. Hunter (KFH), Richard Camicioli (RC), Joanne Booth (JB) Dawn A. Skelton (DAS), Chantale Dumoulin (CD), Lorna Paul (LP) and Adrian Wagg (AW) formed the initial expert panel that generated the concept for the paper, provided guidance and expert opinion, and critically analysed and edited the manuscript.

Gibson, W., et al., *The association between lower urinary tract symptoms and falls: Forming a theoretical model for a research agenda.* Neurourol Urodyn, 2018. **37**(1): p. 501 – 509.

Chapter Three: Is the strong desire to void a source of diverted attention in healthy adult volunteers?

This chapter, a paper accepted for publication in *Neurourology and Urodynamics,* is an exploratory study of the impact of SDV on cognitive function in young, healthy volunteers. In this trial, we demonstrated a significant increase in reaction time when experiencing SDV and when distracted by a validated source of distraction. WRG conceived of and designed the study with input from AW and KFH, and was responsible for the application for ethics approval. Participants were recruited, consented, and data collected by a summer student (Rachael Morrison, RM), supervised by WRG. Data were analysed by WRG. WRG wrote the manuscript with input from AW, KFH, and RM. This study received ethics approval from the University of Alberta Health Research Ethics Board, Pro00072171. These data were presented at the 2018 International Continence Society Annual Meeting in Philadelphia, USA.

Chapter Four: Does the strong desire to void act as a source of diverted attention in older adults without lower urinary tract symptoms?

This chapter describes a study of cognitively intact older adults with LUTS. Similar to Chapter 2, we compared two tests of cognition; the simple reaction time (SRT) and time to complete the Trail Making B (TMT-B) test under three conditions; with an empty bladder and no distraction, when distracted, and when experiencing SDV. In this study we again demonstrated a significant increase in reaction time with both distraction and SDV.

WRG conceived and designed the study and obtained ethics approval, with input from AW and KFH. Recruitment, consent, and data collection were performed by a summer student (Asad Makhani, AM) and research assistant (Amy Weinberg, ARW) under the supervision of WRG. WRG performed the data analysis and wrote the manuscript with input from AW, AM, and KFH. This study received ethics approval from the University of Alberta Health Research Ethics Board, Pro00081048, and will be presented at the 2019 International Continence Society Annual Meeting, Gothenburg, Sweden.

Chapter Five: Do older adults with OAB demonstrate impaired executive function compared to their peers without OAB?

This chapter describes a comparison of performance in a test of executive function, the TMT-B, and SRT in community-dwelling older adults without subjective cognitive impairment. We compared these tests between two groups, those without LUTS and those with a clinical diagnosis of overactive bladder (OAB). We demonstrated that those with OAB had significantly slower times to complete the TMT-B, suggesting that they had impaired executive function compared to the control group.

WRG conceived and designed the study and obtained ethics approval, with input from AW and KFH. Recruitment, consent, and data collection were performed by a summer student (AM) and research assistant (ARW) under the supervision of WRG. WRG performed the data analysis and wrote the manuscript with input from AW, AM, and KFH. This study received ethics approval from the University of Alberta Health Research Ethics Board, Pro00079683, and was funded by the Canadian Geriatrics Society Pfizer Continence Research Grant. These data were presented at the 2019 Canadian Geriatrics Society Annual Meeting in Halifax, NS.

Chapter Six: Measuring gait variables using motion capture in older women with urinary urgency: a pilot study.

This chapter comprises a paper describing a pilot study of utilising 3-Dimensional Instrumental Gait Analysis (3D IGA) in 10 older women with OAB when they experience urinary urgency, and comparing their gait to the bladder empty condition, with each individual as their own control. We demonstrated that 3D IGA is a feasible experimental method for investigating gait parameters in older adults experiencing urinary urgency. The results also demonstrated a decrease in gait velocity with urgency, and established that, at least in this small sample, the intra-participant variability in gait patterns precluded meaningful comparison of kinematic data.

KFH, AW conceived the study, with advice from a gait analyst, Justin Lewicke (JL) and a physiotherapist, Vickie Buttar (VB). KFH obtained ethics approval, recruited the participants, and collected the data with the assistance of the gait analyst. WRG analysed the data and wrote the manuscript with input from KFH, AW, and Allyson Jones (AJ). This study received ethics approval from the University of Alberta Health Research Ethics Board, Pro00022975, and the findings were presented at the 2017 International Continence Society Annual Meeting, Florence, Italy.

Chapter Seven: Urinary urgency acts as a source of diverted attention leading to changes in gait in older adults with overactive bladder.

This chapter describes a study using 3D IGA to compare the gait of 27 older people with OAB under three conditions; bladder empty, urinary urgency, and when distracted. We demonstrated that gait velocity and stride length are both reduced by urgency and distraction, suggesting that urgency may be acting as a source of diverted attention and that this is, at least in part, the reason for the association between falls and LUTS in older people. We also found a small increase in forward lean with urgency but not distraction, which may relate to contraction of the pelvic floor during walking. A subgroup analysis found no evidence that presence or absence of a detrusor overactivity diagnosis influenced the effects observed.

KFH and AW conceived the study. The study was designed initially by KFH and AW based on the pilot and refined by WRG. WRG obtained ethics approval and recruited participants and collected data with the input of a research assistant (ARW) and gait analyst (JL). WRG analysed the data and wrote the manuscript with input from KFH, AW and AJ. This study received ethics approval from the University of Alberta Health Research Ethics Board, Pro00054370, The findings were presented at the 2019 Canadian Urological Association Annual Meeting in Québec City, Québec, and were presented at the 2019 International Continence Society Annual Meeting, Gothenburg, Sweden. The study was funded by the 2015 Canadian Urological Association Astellas Research Fellowship.

Chapter Eight: Conclusions and future research

This chapter summarises the findings of the overall research program; that SDV has similar deleterious cognitive effects as distraction in older and younger people without LUTS, that older adults with OAB have demonstrable executive dysfunction compared to a similar group without LUTS, and that, in older adults with OAB, urinary urgency induces changes in gait which are similar to those induced by distraction, and are associated with increased falls risk. These data enable us to adapt the conceptual diagram of links between LUTS and falls outlined in Chapter Two.

A future program of research and clinical recommendations is then outlined. Specifically, further investigative avenues are identified with functional brain imaging, the utility of including frailty and measures of frailty within the model, research in healthy volunteers to assess the influence of pelvic floor contraction on gait, and intervention trials using pharmacotherapy or dual-task physiotherapy to assess the impact of these treatments on the influence of urgency on gait and cognitive function.

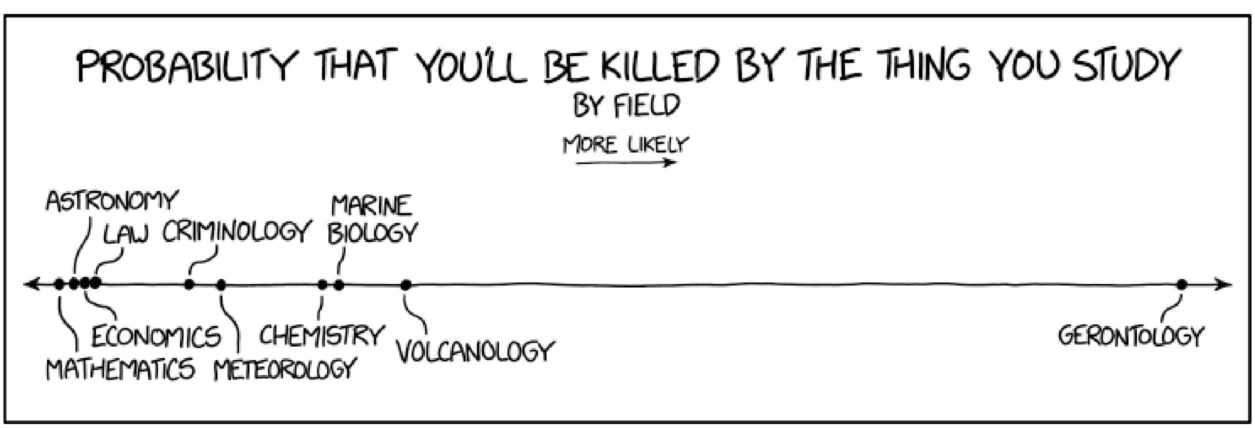
Acknowledgements

Many researchers consider that they are standing on the shoulders of giants, and in my case it is more true than most. I am endlessly grateful to my supervisors and mentors, the very tall Adrian Wagg and the not so tall Kathleen Hunter, for their unfailing guidance, patience, and mentorship over the course of producing this thesis, to Allyson Jones for her physiotherapy expertise, and to my external examiners Professor Mary Palmer and Dr Suzette Brémault-Phillips. Thanks are due to Susie Orme for getting me interested in continence in the first place, and to the clinical colleagues too numerous to mention for their support in my development as a geriatrician and gerontologist. I am grateful to my summer students, Rachael Morrison and Asad Makhani, for their interest in the field and for their hard work, to my research assistant Amy Weinberg for the assistance with data collection, and to Justin Lewicke in the gait lab for his expertise and help with the gait analysis. I am also grateful to the staff in the Division of Geriatric Medicine, particularly Joan Kravic and Deepika Jadhav.

I am lucky beyond measure to have a supportive and loving family; thanks to my mother, Pam Stanier and father Frank Gibson, for a wonderful childhood and endless support in adult life, and for the support of family and friends across the world.

Above all, thanks to my wonderful, creative, fabulous wife Clare, whose infinite support and love, energy and enthusiasm, creativity and silliness has kept me going for many years. She remains out of my league.

Finally, thanks to everyone who has given me that sad, sympathetic look when I've met them at a party and told them I research why incontinent old people fall over. This is for you.



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Contents

List of Tables

List of Figures

Chapter One

Introduction

Background

There is a well-recognised but unexplained association between falls and lower urinary tract symptoms (LUTS) including nocturia [1-4], urgency [5, 6], and urgency urinary incontinence (UUI) [5, 7]. In Australian men, the presence of urgency incontinence, defined as weekly episodes of UUI, was associated with a higher incidence of falls (OR 2.57 95%CI 1.51 – 4.3) [5]. In women, Brown *et al.* found that those with weekly urgency incontinence had higher odds of falling, with odd ratios of 1.26 (95%CI 1.14 – 1.4) between those with UUI weekly and those without. Chiarelli *et al.* performed a meta-analysis of the available trials in 2009, finding the odds of falling were 1.45 (95%CI 1.36 – 1.54) in the presence of any incontinence and 1.54 (95%CI 1.14 – 1.69) with urgency incontinence [8]. More recently, in 2018, a systematic review of 15 trials reported a 1.3 to 2.3 fold increase in risk for those with overactive bladder (OAB), compared to those without [9].

Although variously explained as being due to rushing to get to the toilet [8, 10] or due to slipping in their own urine following an episode of incontinence [11], there is no published evidence which supports these explanations. There are few data suggesting a temporal relationship between falls and LUTS [12, 13], and the response to a strong desire to void (SDV) in middle-aged, continent women is to reduce gait speed [14].

There are, however, reasons to suspect that urinary urgency may influence gait via cognitive processes. Lewis *et al.* demonstrated a reduction in performance on tests of detection, visual attention, and working memory in young adults experiencing SDV [15], and urinary urge, the physiological desire to urinate, was associated with a reduced ability to resist impulsive choices and in performance in the colour naming Stroop test in healthy volunteers [16].

Lower Urinary Tract Symptoms

LUTS are defined as being *storage*, experienced during the storage phase of the bladder, *voiding*, those experienced the voiding phase, and *post micturition*, those experienced immediately after voiding [17-19].

Storage LUTS	
Urgency	The sudden compelling desire to pass urine that is difficult to defer
Frequency	The complaint of voiding too frequently
Nocturia	The number of times urine is passed during the main sleep period. Having woken to pass urine for the first time, each urination must be followed by sleep or the intention to sleep.
Urinary Incontinence (UI)	The complaint of any involuntary leakage of urine
Urgency Urinary Incontinence (UUI)	Urinary incontinence preceded by urgency
Stress Urinary Incontinence	The complaint of the involuntary leakage of urine on effort or exertion, or on sneezing or coughing
Voiding LUTS	
Hesitancy	Difficulty in initiating micturition resulting in a delay in the onset of voiding
Straining	The muscular effort used to either initiate, maintain, or improve the urinary stream

Intermittency	Urine flow which stops and starts
Slow stream	The perception of reduced urine flow, usually compared to previous performance or in comparison to others
Splitting/Spraying	Complaint that the urine passage is a spray or split rather than a single directional stream
Terminal Dribble	Complaint that during the final part of voiding there is noticeable slowing of the flow to drops or a trickling stream
Post Micturition Symptoms	
Feeling of incomplete emptying	The sensation that the bladder has not emptied fully after voiding
Post-voiding incontinence	Complaint of a further involuntary passage (incontinence) of urine or dribbling following the completion of voiding

Storage LUTS, including urgency, frequency, nocturia and urinary incontinence, are prevalent in the general population and become increasingly common in association with increasing age. In the EpinCONT study [20], a cohort study of 27,936 community-dwelling Norwegian women, investigators reported a prevalence of urinary incontinence of 10% (95%CI 9.0 – 11.7) among women 20–24 years of age, rising to 40% (95%CI 27.6 – 51.1) in those ≥90 years of age. Similarly, in the multinational EPidemiology of InContinence (EPIC) study, which surveyed approximately 19,000 adults by telephone, over 60% of those ≥40 years of age reported at least one LUTS, the commonest of which was nocturia [21]. The prevalence of all LUTS rose in association with increasing age, with 37.6% (95%CI 36.0 – 39.2) of men and 42% (95%CI 40.4 – 43.6) of women <40 years of age reporting at least one LUTS, compared with 62.9% (95%CI 61 – 64.9) and 58.7%

(95%CI 57 – 60.5), respectively, of those aged >60 years. A similar age-associated rise was observed in the prevalence of urinary urgency, from 7.1% (95%CI 6.3 – 8.0) in men and 9.7% (95%CI 8.8 – 10.7) in women <40 years of age to 19.1% (95%CI 17.5 – 20.7) and 18.3% (95%CI 16.9 – 19.6), respectively, in those ≥60 years of age. The prevalence of incontinence (of any cause) increased from 2.4% (95%CI 1.9 – 2.9) and 7.3% (95%CI 6.5 – 8.1) in men and women <40 years of age to 5.4% (95%CI 4.9 – 5.9) and 19.5% (95%CI 18.7 – 20.3) in those >60 years of age. Both studies included only community dwelling older people and therefore excluded those in long term care, a group reported to have even higher rates of LUTS and incontinence [22]. The prevalence of LUTS by age and type (from EPIC) is shown in Figure 1.1.

Falls

Falls, defined as an unexpected event in which an individual comes to rest on the ground, floor, or lower level [23] are also common in older adults. Up to one third of people aged over 65 years, and half of those over 80 years old, will fall in any given year [24]. Falls in older adults have significant consequences to individuals and result in high costs to the healthcare system. In the Newcastle 85+ Cohort study which studied 816 community-dwelling older adults in the UK, over 38% had fallen in the previous year, 30% had attended hospital, and 12.8% required admission to hospital. A quarter of those who fell reported "going out less often" as a result and 40% felt they had lost confidence [25]. In the USA, analysis of the National Vital Statistics System and the Web-based Injury Statistics Query and Reporting System found that the total cost of falls in older adults in 2015 was US$50 billion [26]. In 2012, there were 3.2 million falls requiring medical attention in the US and 24,190 fatalities [27]. In Canada, falls were responsible for 7.3% of all hospital admissions of older people in 2004 with annual direct costs of falls estimated at C$2 billion [28].

Cognitive Factors

Both walking and continence are seemingly automatic processes that, despite having a degree of automaticity [29, 30] require some active cognitive input to achieve and are skills learned in early life. Continence – the ability to pass urine at a time and place of one's choosing – depends on the appropriate signalling by the lower urinary tract to the brain, the processing of those signals, and the ability to hold the bladder in storage mode until the individual can get to appropriate toileting facilities. As the kidneys maintain homeostasis, urine is produced as a waste product and stored in the bladder, which acts as both an organ of storage and expulsion [31]. As the bladder fills, stretch receptors in the detrusor and urothelium transmit sensory information via Aδ and C fibres in the pelvic, hypogastric, and pudendal nerves via the sacral plexus and spinal cord to multiple areas of the brain including the periaqueductal grey matter (PAG), the frontal and prefrontal cortices, the supplemental motor area, and the paraventricular nucleus [30, 31]. These higher centres in turn feed into the pontine micturition centre (PMC) which acts as a physiological switch, switching the bladder from storage to voiding phase. During bladder filling, when voiding and the sensation of urge is being suppressed, the parasympathetic efferent pathways and the PMC are held in the "off" state [32], causing the urethral sphincter to contract and the detrusor to relax, holding the bladder in storage mode and thereby maintaining continence [30].

Similarly, although largely an automatic process, maintaining balance and successful ambulation relies on the processing of sensory information from proprioceptors in the limbs and trunk, the vestibulocochlear system, and the visual system. Walking is a particularly demanding task, requiring coordinated adjustments in posture and limb positioning from step to step to avoid falling [33, 34]. Whereas the use of functional brain imaging when experiencing bladder sensation can be performed relatively easily [35], functional brain imaging during standing is a technically difficult task. However, Ouchi and colleagues utilised a mobile gantry PET system, finding that standing with feet together activated the cerebellar anterior lobe and the right visual cortex and standing in tandem was accompanied by activation within the visual association cortex, the anterior and posterior cerebellar vermis as well as within the midbrain [36].

As such, continence, gait and balance are processes requiring active, although unconscious, cognitive input, and the performance of these tasks may be impaired by processes which cause cognitive dysfunction.

Executive Function and Diverted Attention

A key aspect of both maintaining continence and balance is executive function (EF), the cognitive domain involved in "volition, planning, purposive action, and action monitoring" [37]. Women with impaired executive function are more likely to have urinary urgency than those with intact EF [38], and impaired EF is associated with increased falls risk [39-41]. In addition, those with intact EF have higher self-selected gait speed [42]. EF is also involved in the ability to perform two or more cognitively demanding tasks simultaneously – the concept of dual tasking, also referred to as distraction or diverted attention. Dual tasking leads to a decline in the performance of one or both tasks [43], and is the rationale for the widespread prohibition of using cellular telephones when driving [44]. Diverted attention influences gait in older people, leading to a reduction in gait speed and increased in gait variability [40, 45-47]. The inability to walk when distracted has also been shown to predict falls risk [48].

Conclusions

LUTS are associated with an increased risk of falls in older people. The sensation of both urinary urge and urgency induce impaired cognitive performance and changes in gait. Impaired executive function and diverted attention are both associated with increased risk of falls.

This thesis therefore aims to investigate the potential links and underlying causes of the association between LUTS and falls in older people, with a focus on the bidirectional relationship between cognitive function and the lower urinary tract, and the notion of urge or urgency acting as a source of diverted attention examined. Specifically, it addresses the following research questions:

- What is known about the association between LUTS and falls?
- Does SDV induce changes in cognitive performance in young, healthy volunteers?
    - If so, are those changes similar to those induced by a source of distraction?
- Is this effect also seen in older people without LUTS?
- Are there demonstrable differences in executive function between older adults with and without OAB?
- Can 3D instrumented gait analysis be effectively used to capture gait data in older people when they are experiencing urinary urgency?
- Does urinary urgency induce changes in gait in older people with OAB?
    - If so, are those gait changes similar to those induced by a source of distraction?

This thesis describes a series of experiments to test these questions in turn, addressing the underlying hypothesis that the sensation of urinary urge or urgency acts a source of diverted attention, and that this is part of the explanation for the known association between falls and LUTS in older people.

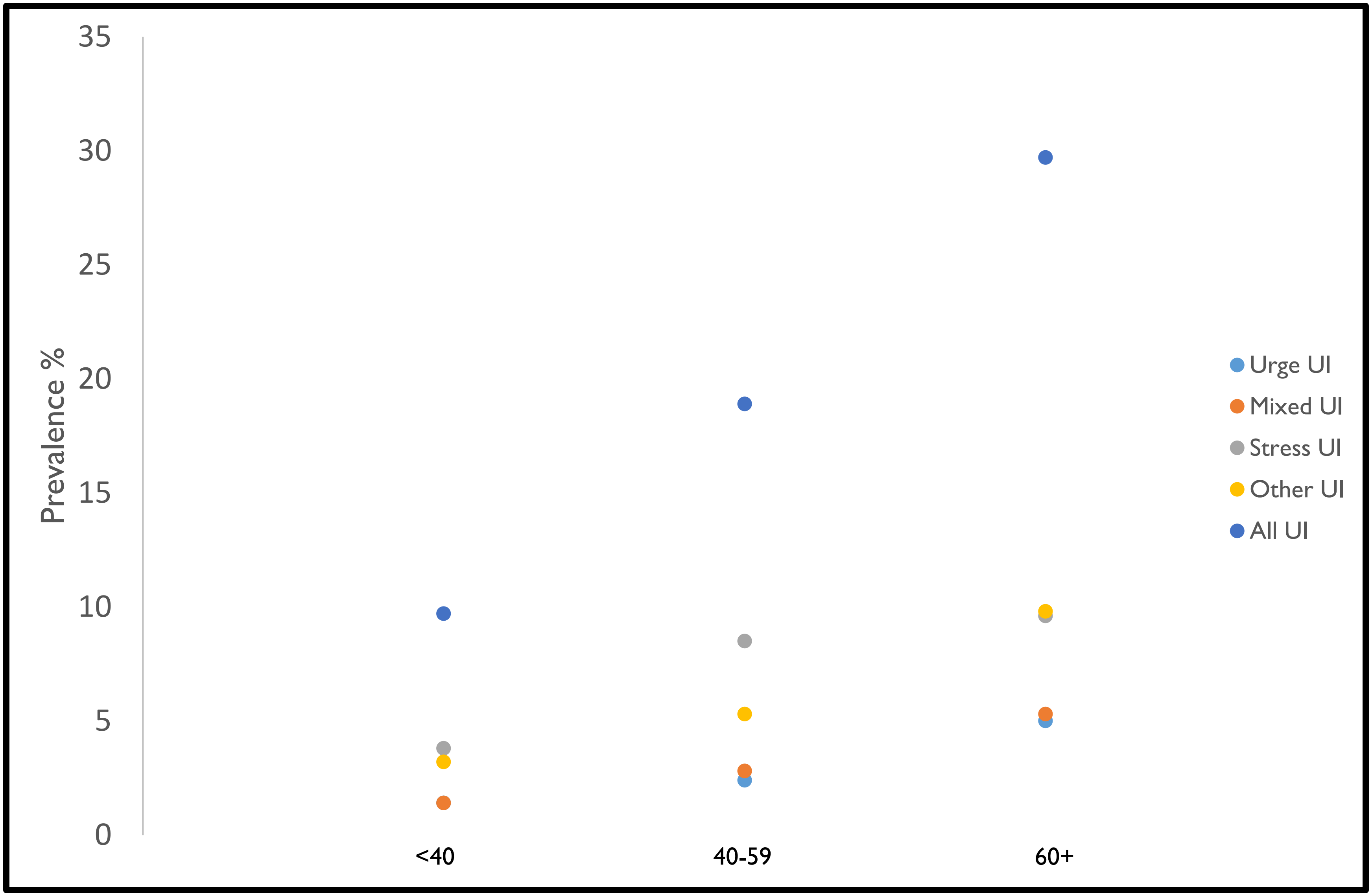

Figure 1.1: Prevalence of LUTS by age group (from EPIC)

Chapter Two

The association between lower urinary tract symptoms and falls: Forming a theoretical model for a research agenda

Gibson W, Hunter KF, Camicioli R, Booth J, Skelton DA, Dumoulin C, Paul L, Wagg A. The association between lower urinary tract symptoms and falls: Forming a theoretical model for a research agenda. Neurourology and Urodynamics. 2018;37(1):501-9

Abstract

There is a well-recognised association between falls and lower urinary tract symptoms (LUTS) in older adults, with estimates of odd ratios for falls in the presence of LUTS ranging between 1.5 and 2.3. Falls and LUTS are both highly prevalent among older people and both are markers of frailty, with significant associated morbidity, mortality, and healthcare resource cost. Despite the recognition of this association, there has been little research to examine its potential causes, and no intervention trial has established if reducing LUTS or urinary incontinence can reduce the risk of falls. In this paper, stemming from a meeting of experts in the field, the current evidence base and hypothesised causal linkages for this association are reviewed and an outline for a potential research agenda to advance the science in the area is forwarded.

Introduction

Urinary incontinence (UI) and lower urinary tract symptoms (LUTS), including urinary urgency, frequency, and nocturia are highly prevalent amongst the general population; this prevalence rises in association with increasing age [1, 2]. LUTS and UI are stigmatising conditions [3], which are often under-reported and under-treated, particularly in older individuals [4, 5]. The most common form of UI in older people is urgency urinary incontinence (UUI), urine loss associated with urinary urgency; a sudden, overwhelming desire to void that is difficult to defer [6].

Frequency, urgency and nocturia, the most common LUTS, which are also components of overactive bladder syndrome (OAB) [6], are extremely common in later life; with up to 50% of men and 60% of women aged over 70 years old describing at least one lower urinary tract symptom [1]. The diagnosis of OAB requires the individual to report urinary urgency.

Up to one third of people aged over 65 years, and half of those over 80 years old, will fall in any given year [7]. Falls, defined by the World Health Organisation as "an event which results in a person coming to rest inadvertently on the ground or floor or other lower level" [8] are often recurrent, with around half of people who fall experiencing another within 12 months [9]. Falls negatively affect quality of life, cause individual pain and suffering, lead to functional decline, and are associated with significant healthcare resource use. In the UK, 38% of the 816 participants in the Newcastle 85+ Cohort Study had fallen in the previous year, with 10% of those having fallen suffering a fracture at an average cost of £2000 per person (2007 prices) [10]. In the USA, there were approximately 24,190 fatal and 3.2 million non-fatal falls among older adults, at a total cost of over US$30 billion in 2015 [11]. In Canada, by 2031, the annual direct healthcare costs attributable to falls is predicted to reach C$4.4 billion, and in 2004, falls were responsible for 7.3% of all hospital admissions of older people. The annual direct cost of fall-related injuries was estimated at C$2 billion [12].

There is a well-recognised association between falls and LUTS in older adults [13-20]. Older people with urinary urgency or UUI are significantly more likely to fall and sustain injury compared to age-matched controls, with estimates of the odds ratio (OR) for falls ranging from 1.5 to 2.3 [14, 21, 22]. However, the reasons for this association are neither understood nor well-studied. This paper is the result of a meeting of health professionals and researchers with expertise in LUTS in older people, exercise physiology, cognitive processing, rehabilitation and bladder physiology. Here, the current state of the research evidence is reviewed, a theoretical framework to explain the association is proposed, and a research agenda to better explain this phenomenon outlined.

What is known about the association between falls and LUTS?

Brown and colleagues [13] performed a secondary analysis of data from an osteoporosis cohort study, examining a group of 6049 community-dwelling older women using regular self-completed questionnaires sent to all participants every four months. In this cohort, followed for an average of three years, those with at least one weekly UUI episode were more likely to fall (OR 1.26, 95%CI 1.14 – 1.40) than those without. Weekly UUI was also associated with higher odds of sustaining a non-spinal fracture (hazard ratio 1.34 95%CI 1.06 – 1.69). In this study, stress incontinence was not associated with higher odds of falling (OR 1.06, 95%CI 0.95 – 1.19) or sustaining a fracture (relative hazard 0.98, 95%CI 0.75 –1.28). Analysis of the Concord Health and Ageing in Men Project, a longitudinal study of community-dwelling men in Australia followed 1090 men over a period of 2 years. Here, the presence of urgency incontinence, defined as weekly episodes of UUI, was associated with a higher incidence of falls (OR 2.57 95%CI 1.51 – 4.3) and men with a higher International Prostate Symptom Score storage sub-score, defined as a score of 19 and above, had a higher incident rate of falls (incident rate ratio 1.72 (95%CI 1.24 – 2.38) [23]. A Japanese study of patients with Parkinson's disease found that increased micturition frequency either by day or night was not associated with falls, but that the presence of urinary urgency was strongly associated with a large increase in the odds of falling (OR 5.14 95%CI 1.51 – 17.48). Only 14% of the falls reported in this study occurred on the way to or from the toilet [24].

A recent systematic review of the association between falls and LUTS in community-dwelling men aged 60 years and over identified six cross-sectional studies and three prospective cohort studies. The identified data were only suitable for qualitative synthesis but urinary incontinence and storage LUTS were consistently shown to have a weak to moderate association with an increased likelihood of falls. None of the identified studies examined potential causes for these associations; the categorisation of continence or not and degree of accounting for confounding variables was inconsistent across the included studies [25]. A small cross-sectional analysis of community dwelling women aged 65 and over in the US examined the association between nocturia, nocturnal enuresis and falls. Neither severity of UI nor severity of nocturia was associated with an increased risk of falls, but there was a statistically significant association between nocturnal enuresis and impairment of physical function and the presence of frailty. However, in the multivariable regression model, which included age, physical function, and the frequency of nocturnal enuresis episodes, only physical function remained as significant risk factor for falls [26]. One study, a prospective cohort study of older men in the USA, identified a statistically significant association between straining to void and falls, with a 60% increase in falls risk for those reporting the need to push or strain to initiate urination at least half the time [27]

The use of sedative medications has been identified as a potential risk factor for falls in those with LUTS. In long-term users of benzodiazepines, urinary incontinence and LUTS were an independent risk factor for falls in older adults, irrespective of the degree of exposure to these drugs. An exposure-response relationship was observed between the frequency of incontinence and falls, with falls occurring in 17% of participants with incontinence only once weekly, 25% of those with incontinence two to three times per week, 60% of those with incontinence daily, and 58% of those with incontinence more than once per day [28].

There is, therefore, evidence for a reasonably strong association between falls and LUTS/UI in older adults, but the mechanism underlying this is unexplained. Little research has addressed this and additionally, despite calls for such work to be undertaken, no intervention trial has yet been performed to examine if treating LUTS can reduce the risk of falls [29, 30].

Potential links and avenues for further study

Rushing to the toilet or slipping in urine

The idea that the reason that people with incontinence are more likely to fall is due to rushing to get to the toilet or by slipping in their own urine following an episode of incontinence has been cited in previous publications as an explanation of the association between LUTS and falls [14, 31] without either evidence or clarification. These were reviews and cited no data relevant to this claim. A case-control study in the UK found no temporal association between getting to the toilet and falling, suggesting that a simplistic explanation such as rushing is unlikely to be the underlying link between the two entities [32]. In this study only 6% of participants identified a temporal relationship between their fall and experience of urgency. This is similar to the finding of Sakushima *et al.* [24], which reported 14% of falls related to getting to or from the toilet, but did not examine whether or not those people perceived themselves to be ”rushing”. In addition, there is evidence from continent, middle aged women that the response to SDV is to slow down, not to speed up or rush [33]. The idea that “rushing” explains the association between urgency and falls should therefore be viewed with caution until evidence supporting this intuitive hypothesis is produced. At present, there is no evidence to support rushing as a link between urgency and falls, and the limited evidence available suggests that rushing is not implicated in the association.

Activity restriction

Lower levels of physical activity have been associated with increased falls and there is evidence that fear of falling is associated with decreased activity in older adults [34, 35]. For some people there is consequent avoidance of activity resulting from the fear of falling, which in turn further impairs physical ability and increases the risk of future falls [36]. Women with incontinence will often limit their participation in physical activity and sport as a result of their incontinence, and recent work found that older women with UI had worse performance on tests of balance and reported more falls than continent, age-matched controls [37]. There is evidence that the presence of urinary incontinence is associated with limitations in activities of daily living, and that incontinence in older adults is associated with deconditioning, the development of obesity and a decline in general health [38]. However, some studies have only found reduced levels of physical activity associated with stress, but not urgency incontinence [39]. For example, a French cohort study of 1942 community-dwelling women aged between 75 and 85 used a panel of balance assessments and the International Consultation on Incontinence Questionnaire–Short Form questionnaire (ICIQ-SF) to assess the associations between physical limitation and LUTS. The authors reported a significant deterioration in all the standard mobility and balance test results according to the severity of UI, including timed up and go, standing balance, walking balance, and single leg stand time [40].

Given that deconditioning and reduced physical fitness is associated with an increase in falls risk, responding to urinary urgency in a deconditioned older person may, in itself, increase the risk of a subsequent fall. Exercise interventions have been demonstrated to be effective in reducing the frequency of incontinence episodes in nursing home residents [41] and community-dwelling older women [42]. A short-term (8-week) intervention of physiotherapy-delivered training in mobility and toileting skills in non-demented older women living in a care facility resulted in a 37% reduction in the daily urine loss [43]. Likewise there is good evidence that increasing physical activity can decrease falls in older adults living in the community [44], in institutions [45] and in individuals with dementia [46]. A systematic review of cost-effectiveness of falls studies concluded that physical activity, specifically the Otago Exercise programme in those 80 years and older, was one of three cost saving falls prevention strategies [47].

Current evidence tentatively supports a bi-directional relationship between urinary incontinence and activity restriction, with those experiencing incontinence reducing their trips outside the home and those with limited mobility experiencing more incontinence.

Frailty, multimorbidity, and polypharmacy

It is undeniable that urinary incontinence, and in particular urgency incontinence, can be considered as a geriatric syndrome and a marker of frailty and, furthermore, frailty is strongly associated with falls [48, 49]. Frailty, defined by Fried as "a biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiological systems, and causing vulnerability to adverse outcomes" [50] is not synonymous with multimorbidity, or disability, but rather describes a state of increased vulnerability to adverse outcome. Many tools exist for quantifying and diagnosing frailty [51-53], a detailed discussion of which is beyond the scope of this review.

It is conceivable that no causal link exists between falls and incontinence or LUTS, and that these are both markers of frailty. UI and UUI have been associated with musculoskeletal conditions including low back pain and osteoarthritis in a cross-sectional study of older women in Japan [54]. A retrospective cross sectional study of older patients admitted to hospital in Germany with a fracture found that those with UI were frailer, more dependent, and had higher levels of physical and cognitive impairment than those without UI [55]. Both frailty and LUTS are strongly associated with multimorbidity and polypharmacy, which in turn are influenced by the presence of vascular risk factors [56] and chronic inflammation [57]. A retrospective analysis of drug dispensing data in a Japanese cohort found that polypharmacy was associated with the use of medications known to contribute to urgency [58]. Similarly, a Canadian cross-sectional study identified a strong association (OR 4.9, 95%CI 3.1 – 7.9) between polypharmacy, defined as 5 or more medications, and the prescription of a medication known to cause LUTS [59]. However, there is little evidence that polypharmacy in the absence of drugs that cause incontinence has an impact on the lower urinary tract, and it is likely that the association between polypharmacy and urgency relates to the fact that the more drugs an individual is prescribed, the higher the odds that one of them will be a drug known to induce urgency.

Several other specific comorbidities are associated with both LUTS and falls. For example, as well as being associated with arterial disease, diabetes mellitus has well documented effects on the lower urinary tract and is associated with impaired bladder emptying and urgency [60], and can cause neuropathies that may predispose to falls including peripheral neuropathy causing gait disturbance and autonomic neuropathy causing postural hypotension [61]. Likewise, Parkinson's disease is commonly associated with both LUTS [62] and falls [63]. There are, therefore, many illnesses and conditions which cause both LUTS and falls, and future epidemiological research should ensure that these potential confounders are accurately accounted for in the analysis.

These relationships are summarised in Figure 2.1. The observed association between falls and LUTS in older adults may therefore be due to the confounding effect of their multiple common causes. However, given that the epidemiological evidence for this association is overwhelmingly from community-based studies, the majority of available data come from non-frail individuals. Brown *et al.* identified 20% of their cohort as being frail (defined by the investigators based being "weak, unsteady, and fragile") at baseline, and Noguchi *et al.*, although not specifically identifying frailty as a measure at enrolment, described a cohort in which 97% of participants were mobile without the use of a walking aid [23]. A case-control study of nursing home residents in the USA found that those with UI or OAB exhibited higher rates of cognitive impairment, mobility impairment, and higher numbers of comorbidities than those without [64]. It is, therefore, reasonable to suggest that although frailty is a common cause of both falls and LUTS/UI, there are other complex contributors to the association, including the role of cognitive influences and potentially other, as yet unknown, links. The paucity of evidence from frail or institutionalised older people limits the applicability of the current evidence base to this population.

Central control and cognitive factors

The maintenance of continence is not an innate ability; much like walking, it is a learned skill developed in the early years of life, and once attained, continence is under conscious control [65]. Numerous areas of the brain are involved in the maintenance of continence, with research techniques including brain imaging, functional brain imaging, and evidence from disease-specific studies being used to delineate the complex relationships between them [66]. Functional positron emission scanning in young people shows that the periaqueductal grey matter, pons, and ventral and dorsal portions of the pontine tegmentum are active during bladder filling [67]. Functional magnetic resonance imaging studies in older people suggest that failure of activation in areas of the brain relating to continence, such as the orbitofrontal regions and the insula may lessen the ability to suppress urgency [68]. There is a known association between vascular risk factors and LUTS [56], and the presence of white matter hyperintensities (WMH) within periventricular and subcortical regions of the brain is associated with functional and cognitive impairment, an increased incidence of urinary urgency and detrusor overactivity on cystometry and a difficulty in maintaining continence [69, 70]. It has been suggested that changes in the ageing brain, such as the accumulation of white matter hyperintensities, lead to a failure to suppress the physiological sensation of bladder filling, leading to urgency and urgency incontinence [71]. Older adults with vascular dementia are more likely to have LUTS, specifically urgency and UUI, than those with Alzheimer's disease [72]. Those with high WMH burden in the frontal lobes are more likely to have incontinence, more severe incontinence, and higher symptom bother [69]. Likewise, the presence of WMH is associated with other geriatric syndromes including cognitive impairment [73] and falls, with data from cross-sectional studies demonstrating that the burden of WMH correlates with frequency of falls [74], and longitudinal data suggesting that the progression of WMH is associated with an increase in the risk of falls in older people over time [75].

The role of executive function in gait and continence

Executive function (EF) can be defined as "a variety of cognitive processes that use and modify information from many cortical sensory systems in the anterior and posterior brain regions to modulate and produce behaviour" [76]. EF covers a broad range of cognitive tasks, divided by Lezak into "volition, planning, purposive action, and action monitoring" [77]. The areas identified by functional brain imaging as being important in the maintenance of continence and the suppression of urgency are also those involved in handling executive function, and a study in community-dwelling women aged ≥60 found that those with impaired executive function, tested with 5 separate tests, were more likely to have urgency incontinence than other LUTS [78].

Likewise, intact executive function is a necessary component of safe walking [76]. Walking and the avoidance of falling are not automatic tasks; they require continuous cognitive input and control [79, 80]. In particular, "successful walking", defined as the ability to get from point to point without falling or fearing falling through instability, is dependent on executive function [76]. Impairment of executive function has been shown to have a negative effect on gait, with associated increased risk of falls; the InCHIANTI study found that cognitively intact older adults who performed poorly on the trail making test, a validated test of executive function, had a lower self-selected gait speed when walking over an obstacle course [81].

A key aspect of EF is the ability to dual task, that is, to manage simultaneous tasks which divert attention. Diverted attention is the condition in which performing two tasks simultaneously leads to deterioration in performance of one or both tasks, referred to by some as dual task costs [82]. There are three main categories of explanation proposed for this phenomenon; capacity sharing, a model which suggests that the brain has a finite capacity for global function, and if simultaneous tasks exceed this threshold, performance declines; the bottleneck (or task-switching) model which suggests that individual brain areas can only perform one function at a time, so if competing tasks require the same pathway, a bottleneck occurs, slowing processing and the cross-talk model, which suggests that simultaneous tasks are more difficult if they both require similar sensory input [82]. EF is felt to be predominantly a function of the frontal and prefrontal cortices, those areas involved in the maintenance of continence, but other areas of the brain, including the limbic system and parietal lobes are also involved [76].

There is evidence from continent, middle-aged women that the sensation of SDV induces changes in gait, including an increase in stride-time variability and reduction in gait velocity [33], changes which are associated with increased falls risk [83]. Performance of a distraction task while attempting voluntary contraction of the urethral and anal sphincters causes a reduction in the strength of the contraction as measured with sphincter electromyography [84]. A Japanese study found that, in a cohort of women attending a clinic with menopausal symptoms, those with UUI had greater reaction times, as measured with a ruler-drop test, than women with other subtypes of incontinence, although no conclusion can be drawn on the direction of effect for this association. Even in healthy, continent young people SDV has deleterious effects on cognition; a small study using SDV as a model for pain found that healthy volunteers who were asked to drink fluid until they experienced an "intense urge" to void had significantly worse cognitive performance on tests of detection, visual attention, and working memory compared to both baseline and post-voiding states [85]. In older adults with incontinence, a multicomponent intervention comprising pelvic floor training and video game dancing improved dual-task performance in women aged over 65, with subgroup analysis suggesting that the largest improvement on the n back test, a measure of dual task ability, was in women with incontinence [86]. In a focus group based study of adults aged 70 years and older, the women involved identified the desire to void as a source of distraction that may affect the performance of other tasks [87].

It can be hypothesised that the sensation of urinary urgency, or SDV, acts as a source of diverted attention, and that other simultaneous cognitive tasks require dual tasking (at cognitive cost) to complete. Given that dual tasking is a well-recognised cause of gait changes and increased falls risk, it may be that this is one underlying mechanism linking urinary urgency and falls. If urinary urgency is a source of attentional demand, then given that that dual-task training can reduce falls risk under dual task conditions there is the potential for novel interventions to address the urgency and linked falls risk.

A model for future research

The oft-quoted explanation that urinary urgency causes falls due to rushing to the toilet is an intuitive response, but not supported by the evidence. The temporal relationship between falls and LUTS is far from well-established, and the response to a desire to void appears to be to slow down, not speed up [33]. The "rushing" hypothesis has not been subjected to systematic examination and should, therefore, no longer be accepted until there is evidence to support this.

There is good evidence that older adults with LUTS are more likely to have lower levels of physical activity, and that people with lower levels of physical activity are more likely to have LUTS, but the direction of this association is unclear. Further research, both epidemiological and interventional, should be considered to delineate and investigate the role of activity restriction on LUTS and the maintenance of continence in older adults and the role of LUTS and incontinence on activity restriction.

Potential relationships and linkages between LUTS and falls risk factors are outlined in Figure 2.2. There are currently many unexplained steps in the relationship between falls and LUTS with a rich research agenda to be explored. The potential role of urgency as a source of attentional demand can be investigated by comparing the performance of various tasks, such as walking or cognitive tests under conditions of no distraction, urinary urgency, and a validated source of diverted attention such as the n back test. There is a need for further high-quality epidemiological work to disentangle the influences of frailty, multimorbidity and other factors in LUTS and falls, and it remains unknown if current treatments for OAB, including conservative and pharmacological treatments, either reduce or increase the risk of falling in older people [88]. The development of functional brain imaging may provide increasingly sophisticated understanding of the central control of continence, and as our understanding of the underlying physiology of OAB and other LUTS improves, further avenues of study will become apparent. It is clear that WMH are an important common cause of both LUTS and falls, and as such including MRI in studies examining the links between falls and LUTS would be valuable to exclude this factor from analysis.

Despite having a high prevalence of both falls and LUTS, frail and institutionalised older adults are often excluded from research. It is important that researchers consider the needs of this population and include them, where possible, in future research.

As Donald Rumsfeld famously told us, the investigation of unknown unknowns is challenging. Clearer data regarding the circumstances of falls in those with LUTS, preferably through robust, prospective data collection, would allow the identification of other potential avenues for study.

There is a rich and unexplored research agenda, and we encourage the development of research projects and programmes to explore these potential links. Does gait change in response to urgency? What changes are observable? Is there a reliable way to induce "urgency" in a gait lab? What underlies this change? Are cognitive factors involved? Are there observable changes to the pelvic floor when walking with and without urgency? Can we ameliorate the associated risk of falls by treating urgency? This is by its nature a multidisciplinary problem and the opportunities for cross-professional collaboration, by researchers and those who fund research, are large.

Conclusions

There is a clear association between LUTS, in particular nocturia, urinary urgency and urgency incontinence, and falls in older adults, with significant associated morbidity, mortality, and healthcare resource use. It is not clear, however, to what extent this relationship is due to falls and LUTS having a common cause, and how much is due to factors such as dual tasking, activity restriction, and other, as yet unrecognised, mechanisms. There is little evidence supporting the commonly-held belief that this relationship can be explained through rushing to get to a toilet, and there is evidence to support there being at least an element of "common cause"; that both LUTS and UI are common in later life and very common among the frail. Moving forward using the model we outline will facilitate a greater sophistication in understanding of how these factors are linked and identification of novel interventions to test.

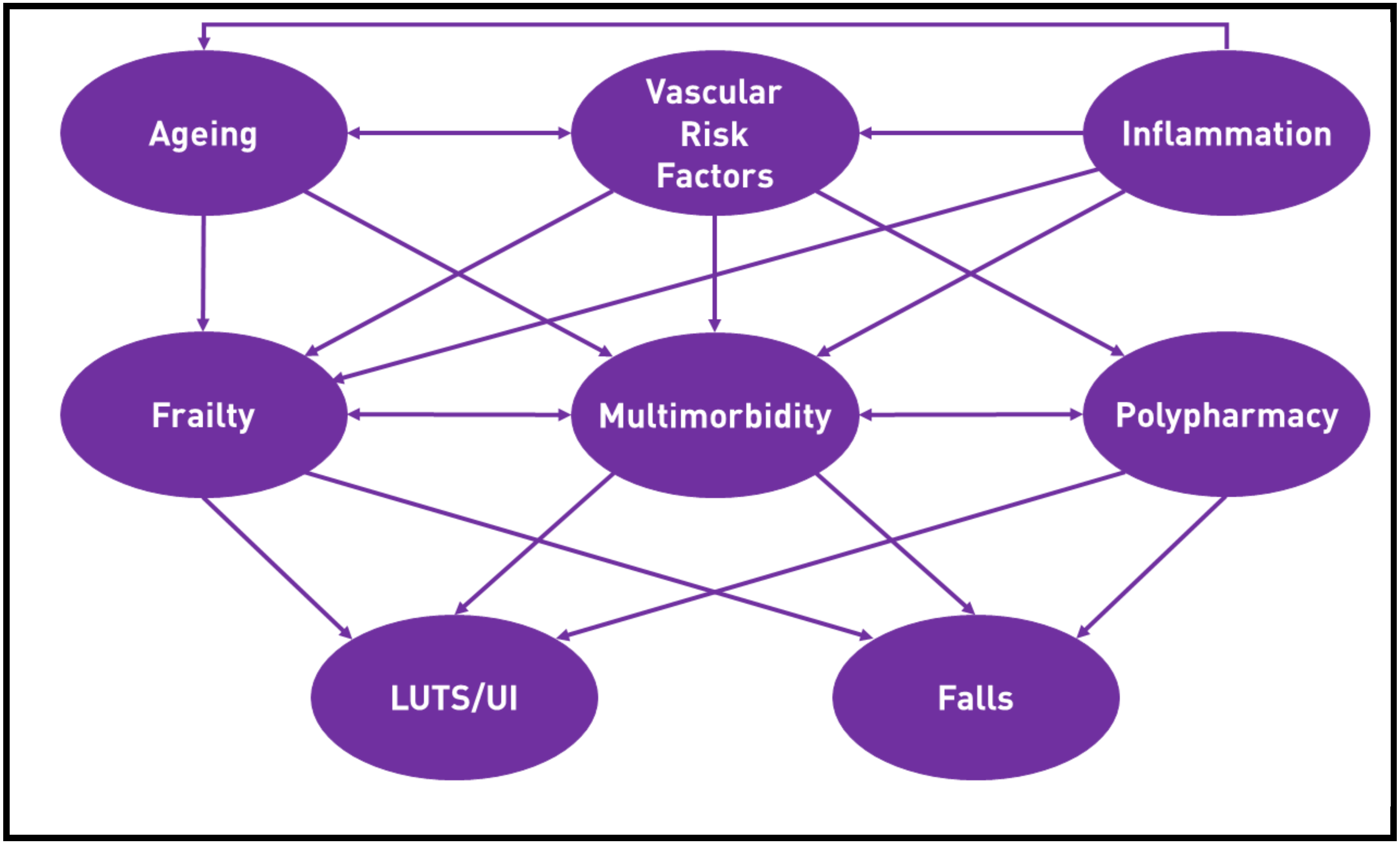

Figure 2.1: Common causes of falls and LUTS in older adults

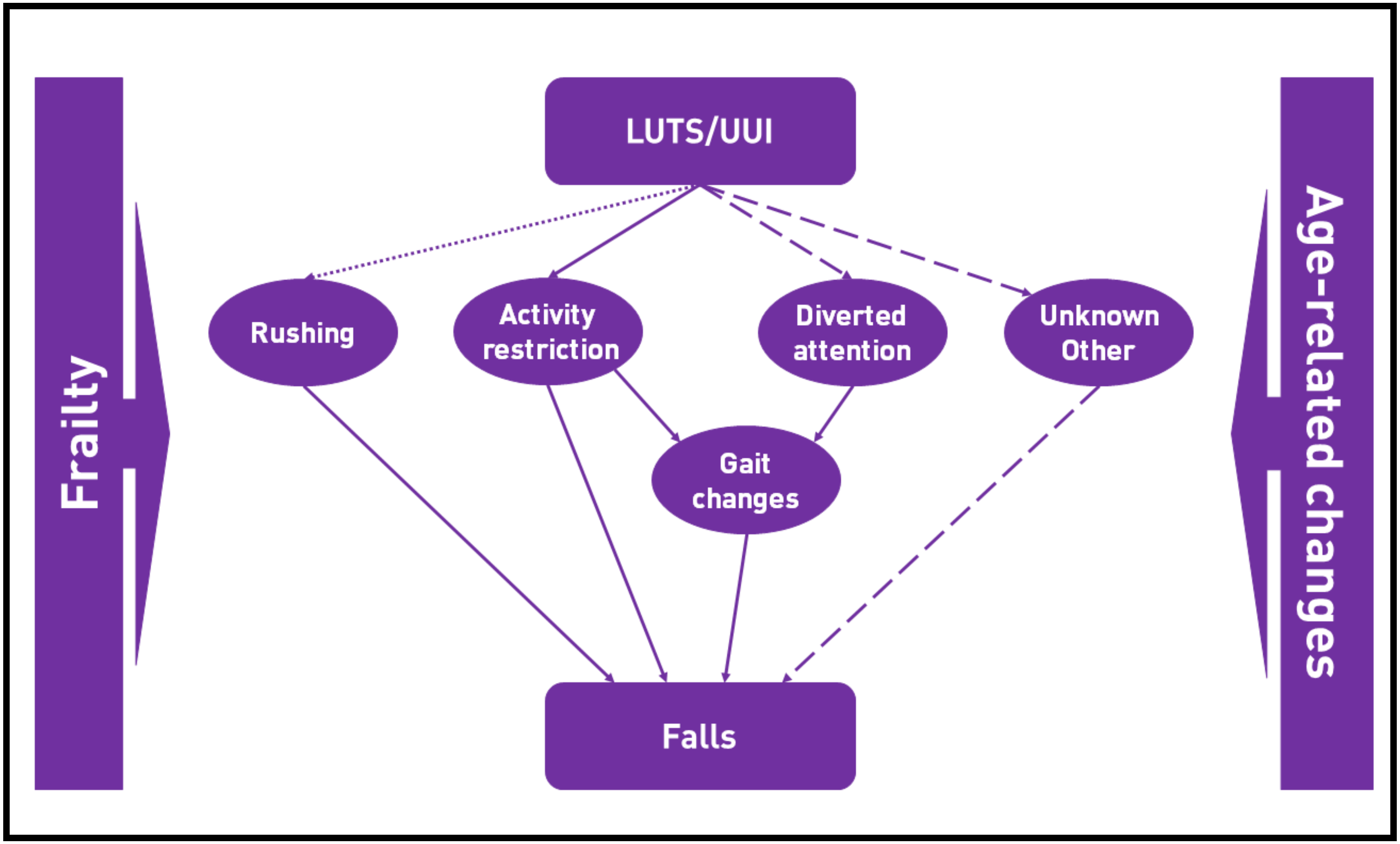

Figure 2.2: Potential (dashed line), known (solid line) and suggested but unsupported (dotted line) links between LUTS and falls.

Chapter 3

Is the strong desire to void a source of diverted attention in healthy adult volunteers?

Abstract

Aims The strong desire to void (SDV) induces changes in both cognition and gait. This may be due to the sensation of urinary urge acting as a source of diverted attention. This exploratory study examined the influence of SDV and a standardised distracting task on the performance of two measures of cognition, a simple reaction time (SRT) test and the Trail Making B test (TMT-B). **Methods** 18 volunteers, 8 male and 10 female, without lower urinary tract symptoms (LUTS) (mean age 22, range 20 – 47), performed a test of SRT and the TMT-B under three conditions; undistracted with an empty bladder, while experiencing SDV, and when performing a simultaneous distracting task, the auditory n back test. **Results** A statistically significant increase in SRT was found when experiencing SDV and when distracted compared to the undistracted, bladder empty condition. The time taken to compete the TMT-B significantly increased with distraction but was not affected by SDV. **Conclusion** SDV induced a similar but smaller change in reaction time when compared to a distracting task, suggesting that SDV may act as a source of diverted attention in continent, healthy volunteers.

Introduction

The maintenance of continence is not an automatic process but rather a learned skill under both conscious and subconscious control [1]. Sensory input from both urothelium and detrusor are transmitted to the central nervous system via the pudendal and hypogastric nerves and these signals are processed by numerous areas of the brain, including the hypothalamus, periaqueductal gray matter (PAG), and the frontal and pre-frontal cortices [2]. Functional positron emission tomography demonstrates that, during bladder filling, the PAG, pons, and ventral and dorsal portions of the pontine tegmentum are active [3], suggesting that the sensation of urge is being actively suppressed. As well as the brain influencing the bladder, the bladder can also influence the brain, and a bidirectional relationship exists. In a study of cognitive performance in young, healthy adults without LUTS [4], Lewis *et al* found a significant decline in the performance on standardised tests of attention and working memory when experiencing a strong desire to void (SDV), which returned to baseline after micturition; psychomotor function was unaffected. SDV also induces gait changes in middle-aged, continent women [5]. Although the mechanism underlying these changes are currently unexplained, it has been suggested that the sensation of urgency may act as a source of diverted attention and lead to gait changes associated with fall risk [6]. We hypothesise that the sensation of urinary urge acts as a distractor, inducing a state of diverted attention. Diverted attention is the situation which occurs when attempting to perform two cognitive tasks simultaneously, leading to a decline in performance in one or both of those tasks [7]. This study therefore examined the hypothesis that SDV acts as a source of diverted attention, leading to a decline in performance on cognitive testing similar to that induced by a validated source of diverted attention, the n back test [8].

Methods

As part of a wider investigative program into the effects of SDV on cognitive performance, younger adults were studied to investigate the effect of SDV on cognitive performance and to compare this effect to the influence of a simultaneous distracting task.

Participants

Participants were recruited via posters placed around the university campus. Study participants were aged 18 or over, had no significant LUTS, defined as a score on the validated Bladder control Self-Assessment Questionnaire (B-SAQ) [9] of less than four, completed on study screening. Exclusion criteria were neurological disease that may affect cognition, significant hearing or visual impairment that would prevent completion of the cognitive task, use of an intermittent or indwelling urinary catheter, and dialysis with anuria. Participants received a small honorarium for their participation in the study. Ethics approval was obtained from the local Research Ethics Office, Pro00072171.

Measures

Two tests of cognitive function were used; an on-line simple reaction time (SRT) test [10], in which participants clicked a mouse as soon as the colour on a computer screen changed from red to green, and the Trail Making B test (TMT-B). SRT is a measure of processing speed and fluid intelligence [11] and is influenced by distraction [12]. The TMT-B (Figure 3.1), in which letters and numbers are alternately connected in ascending order [13], is a validated measure of executive function [14]. The time taken for the participants to complete the TMT-B in each condition was recorded.

Study Procedure

Participants completed the two cognitive tasks, SRT and TMT-B, under three conditions; undistracted and with an empty bladder, when experiencing SDV, and when being distracted by the n back test. As the TMT-B has been shown to have a degree of learning effect [15] participants completed two trials of the TMT-B to ensure understanding of the task and to minimise this. The reaction time test was completed five times per condition by each participant with the average of the times used for analysis. The order of the tests and states under which testing was performed was randomised for each person by the blind drawing of identical sealed envelopes containing each of the possible orders of testing made up by staff unconnected with the study.

Distraction was induced by the n back test, in which the researcher reads a list of letters and the participant indicates when the letter read was the same as the letter 2 prior in the sequence (so, in the sequence "C B E F D F A C…" the second occurrence of the letter F would prompt a response). To indicate a response, the participant rang a bell with their non-dominant hand. The n back test is a validated source of diverted attention [16]. All data collection was performed in a quiet room, free from extraneous distraction, and the same computer and internet connection was used for the SRT for all participants.

Both tests were completed in each of the three conditions. In the undistracted condition, the TMT-B and SRT test were done in a quiet non-distracting environment immediately after voiding. In the distracted condition, participants completed both tests while simultaneously performing the auditory n back task. To achieve SDV, participants were asked to drink non-caffeinated, non-alcoholic beverages *ad libitum* until they could no longer delay voiding. A subjective definition of

SDV without quantification was used. Participants were asked to defer voiding for as long as they possibly could. The desired state of SDV was described to the participants as a desire to void so strong that they would leave a movie theatre to go to the toilet during a good movie, an example chosen as a state that would be familiar to the participants, and one under which they would delay voiding as much as possible. Once the participant reached SDV, they conveyed this to researcher and completed the TMT-B and SRT. Participants were then instructed to visit the toilet and empty their bladder. Participants were told that if, during data collection, they were unable to delay any further they could cease the test and go to the toilet, which was located within a few seconds walk of the room. A different form of the n back test and TMT-B were used for each episode of data collection.

Statistical analysis

Analysis was performed using a within-subject repeated measures design. Mean reaction time and time taken to perform the TMT-B were compared between the undistracted state to each of the other conditions using a one-way repeated-measures ANOVA with Bonferroni correction and paired-samples T tests for pairwise comparisons in SPSS v25 (IBM Corp, Armonk, NY). Statistical significance was defined at $p<0.05$. Given the effect size found in similar work by Lewis *et al.* who demonstrated a Cohen's d effect size of >0.8 in a trial investigative the influence of urge on working memory [4], the required sample size was estimated using a conventional Cohen's effect size (d) for a moderate effect (0.5) and a one-tailed paired design for the comparison between undistracted and SDV, giving a required sample size of 17, calculated in G-Power 3 [17].

Results

26 participants were recruited (8 male, 18 female), with a mean age of 22 years (range 20 – 47, SD 6, Median 21). The mean B-SAQ was 1.3 (SD 1.35, range 0 – 3). No participant reported any long-term medical conditions associated with LUTS. All participants were university undergraduates and none were taking medication that may affect cognitive function. All participants successfully completed all portions of the study. There were no episodes of incontinence and all participants reported experiencing SDV whereby they were unable to delay voiding. Participant demographics are given in Table 3.1. Reaction time increased from a baseline of 372ms (SD 58) in the undistracted state to 421ms (SD 83.6) at SDV and 582ms (SD 99.2)

when distracted. Each difference was statistically significant. Although distraction induced a statistically significant increase in the time taken to perform the TMT-B; SDV had no discernible effect, taking an average of 43s (SD 19.0) when undistracted, 44.2s (SD 13.2) at SDV, and 110s (SD 56.4) when distracted ($p>0.99$ and $p<0.001$ repsectively). These data are summarised in Table 3.2. One data point was excluded from the analysis; participant 7 on attempt 4 of the SRT test took 6.3 seconds to react, nearly 5 times the next longest reaction time. At the time of testing the investigator recorded this as an error of a missed response rather than a delayed reaction. The order in which testing occurred did not influence the results for SRT ($p=0.48$) or TMT-B ($p=0.44$), as assessed with a two-way repeated measures ANOVA, suggesting that there were was no significant learning effect.

Data for individuals are shown graphically in Figures 3.2 – 3.5.

Discussion

This study demonstrated a statistically significant increase in reaction time comparing the undistracted state to SVD and between the undistracted to the distracted state in healthy young adults. The impact of SDV was in the same direction but of a lesser magnitude than the distracting task. To put this into perspective, an increase in reaction time observed here with SDV of would add 1.5 metres to the stopping distance of a car at highway speeds (110kph/70mph). Likewise, a 50ms increase in reaction time has been demonstrated after 40 hours of sleep deprivation [18] and is twice the increase in reaction time seen at a blood alcohol concentration of 50g/dl [19]. There was no increase in the time taken to complete the TMT-B at SDV. The TMT-B tests numerous domains of cognition, including attention, visual search and scanning, sequencing and shifting, psychomotor speed, abstraction, flexibility, and the ability to execute and modify a plan of action [20], whereas SRT is a simpler cognitive task, testing perception and response execution. It could be hypothesised that, as there are more cognitive domains involved in the TMT-B, there is more redundancy in the system, allowing cognitive compensation. In addition, the TMT-B is subject to learning effects, although this was effect mitigated by allowing 2 practice attempts and by randomising the order in which the states were tested. Tuk *et al.* [21] examined how the sensation of "urgency", as an inhibitory signal, has spillover effects to an unrelated behavioural domain via inhibitory networks in the brain. It should be noted that, as in this trial, asymptomatic volunteers took part and use of the term "urgency" would not meet the International Continence Society definition [22] This was, in fact, SDV. Here, participants were asked to perform the Stroop verbal reasoning test, in which they had to identify the colour of text which reads a different colour (for example, the word RED in blue ink). They found that SDV impaired performance, suggesting a failure of inhibition. They also found that people experiencing SDV would choose immediate gratification, selecting a small financial reward the next day rather than a larger reward at a later date. Together, these results together provide evidence that as well as being under conscious control, the sensation of needing to void has effects on other cognitive domains.

There are three main proposed models of diverted attention; capacity sharing, a model which suggests that the brain has a finite capacity for global function, and if simultaneous tasks exceed this threshold, performance declines; the bottleneck (or task-switching) model which suggests that individual brain areas can only perform one function at a time, so if competing tasks require the same pathway, a bottleneck occurs, slowing processing, and the cross-talk model, which suggests that simultaneous tasks are more difficult if they both require similar sensory input [7]. The impact of diverted attention on task performance is the reason for the ban on driving while using cellular telephones [23] and there is good evidence in both young [24] and older adults [25-27] that diverted attention induces changes in gait. It has been previously suggested that diverted attention may be the link between LUTS and falls in older adults [6].

Similar to previous work [4], this study demonstrated an impairment in cognitive performance induced by SDV. This is the first study to demonstrate that this effect is similar to, but smaller than, the effect of a distracting task, suggesting that SDV may act as a source of diverted attention in even young, healthy people without LUTS.

Maintaining continence requires the active suppression of SDV. Functional MRI imaging of people actively suppressing urgency has shown increased activity in several areas of the brain, including the periaqueductal grey matter (PAG), anterior cingulate gyrus (ACG), frontal, and pre-frontal cortices [2, 28, 29]. These areas are similar to those involved in inhibition of unwanted thoughts and feelings [30]; this would be consistent with the experience of the urge to void as an unwanted or unpleasant sensation. The ACG, right inferior frontal cortex (rFIC), and dorsolateral prefrontal cortex (DLPFC) are also involved in motor inhibition, with these areas showing increased activation when a desired motor function is being actively suppressed [31, 32]. As such, the motor inhibition required to *not* press the spacebar during the SRT task requires the same areas of the brain which are active during suppression of urgency, fitting with both the bottleneck and capacity sharing models of dual-task theory [7].

This study has several limitations. Although both the TMT-B and SRT are validated tools for measuring cognitive function, they are both relatively straightforward to perform compared to more complex cognitive tests, and may be insensitive for subtle changes in cognitive performance. However, a participant knowing they had to complete a longer cognitive test may be tempted to indicate their SDV earlier than one facing a short test. In addition, we relied on a subjective report of SDV, without reference to the volume in the bladder or any urodynamic parameters, and did not utilise a validated scale such as the Urgency Sensation Scale (USS) [33]. The utility and validity of such scales has been questioned [34, 35], and all participants were given a clear description of the required sensation and all reported they were unable to delay any further without extreme discomfort, equivalent to a 4 on the USS. They were also aware that they could abandon cognitive testing to void, and that the time to complete the tests was short, less than 90 seconds on average. All the participants reported that they could not have delayed voiding any longer. Adding an additional test between achieving SDV and cognitive testing would potentially cause our participants to being testing earlier.

These results demonstrate an influence of SDV on cognition in young, healthy, cognitively intact adults without LUTS. Future research should investigate this effect in other populations; older people, those with LUTS or OAB, and in those with cognitive impairment. In addition, should a similar effect be demonstrated in those with OAB, comparing the effect on and off treatment for OAB would be valuable.

Conclusions

In this small sample of healthy volunteers without LUTS, SDV induced a significant increase in reaction time. A similar but larger effect was induced by the simultaneous performance of a distracting task. These results suggest that SDV may act as a source of diverted attention in young, healthy volunteers.

Table 3.1: Demographics

n	18
Age	
Mean	22 years
Median	21 years
SD	60 years
Range	20 – 47 years
Sex	
Female	18 (70%)
Male	8 (30%)
B-SAQ	
Mean	1.3
Median	1
SD	1.35
Range	0 – 3

Table 3.2: SRT and TMT-B time in three conditions

	Undistracted (Mean (SD)) 95%CI	SDV (Mean (SD)) 95%CI	Distracted (Mean (SD)) 95%CI	Undistracted to SDV Significance Mean Difference (95%CI)	Undistracted to Distracted Significance Mean Difference (95% CI)	SDV to Distracted Significance Mean Difference (95%CI)
Reaction Time (ms)	371.9 (58.0) 345 - 399	421.0 (83.6) 381 - 461	582.5 (99.2) 536 - 628	p=0.018 49 (7.1 - 91.0)	p<0.001 252.9 (134.9 - 370.8)	p=0.001 203.8 (85.5 - 322.2)
Trail-Making B (s)	43.3 (19.0) 34.5 - 52.1	44.3 (13.2) 38.2 - 50.4	110.6 (56.4) 84.5 - 137.0	p>0.99 0.9 (-9.2 - 7.2)	p<0.001 67.4 (40.2 - 94.4)	P<0.001 66.3 (39.7-93.0)

Repeated measures ANOVA with Bonferroni correction

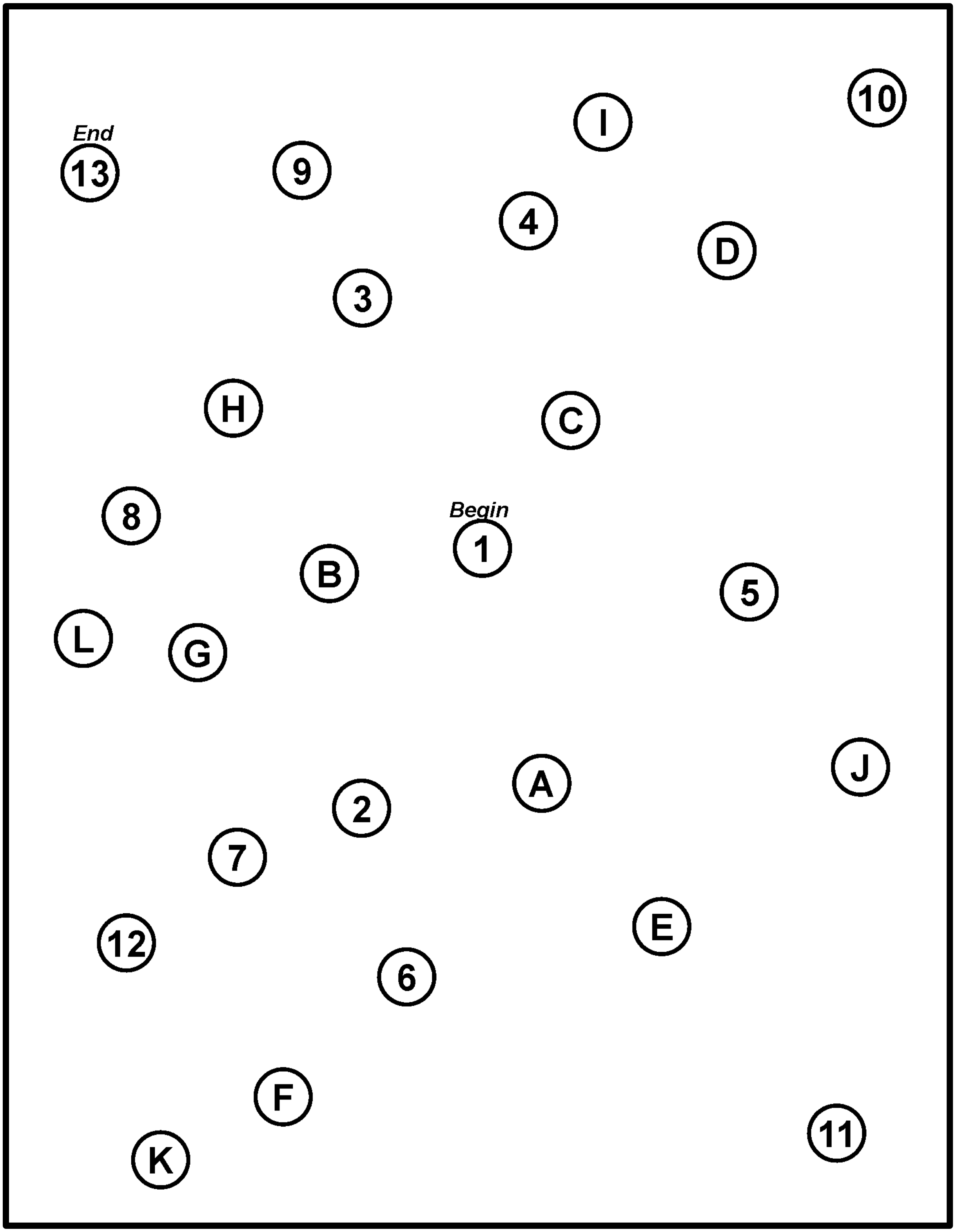

Figure 3.1 Trail Making B Test

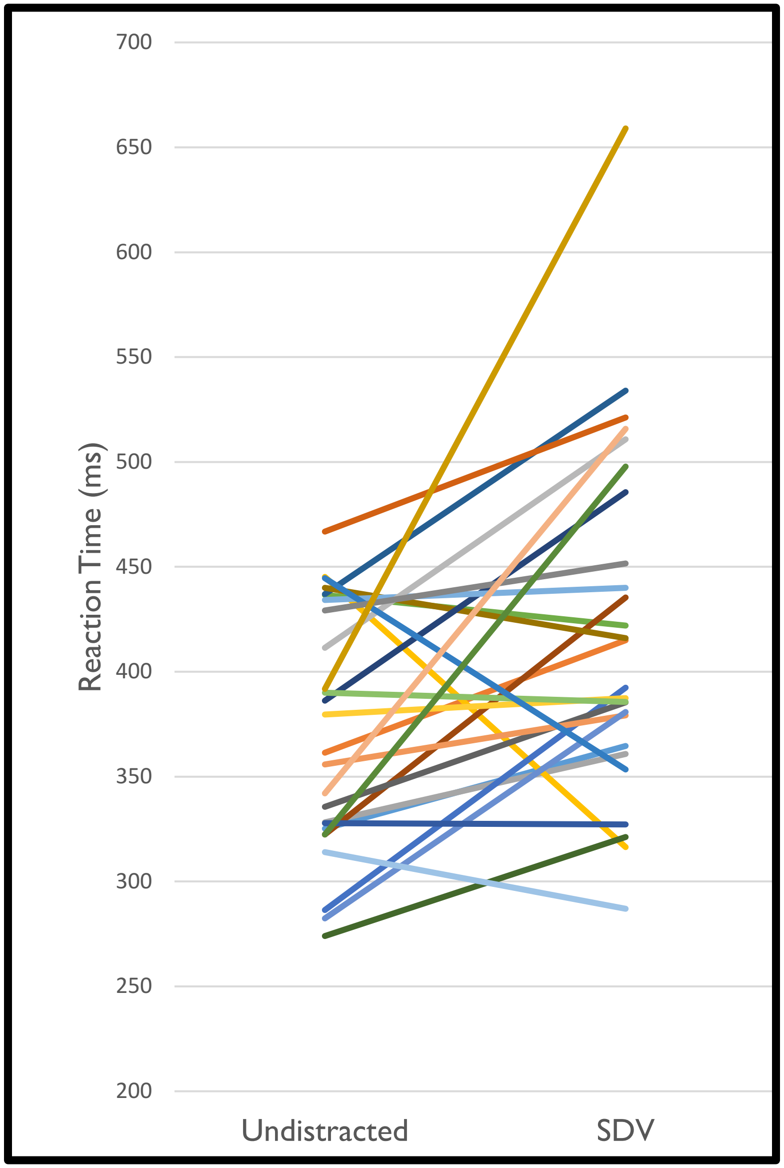

Figure 3.2: SRT Undistracted to SDV

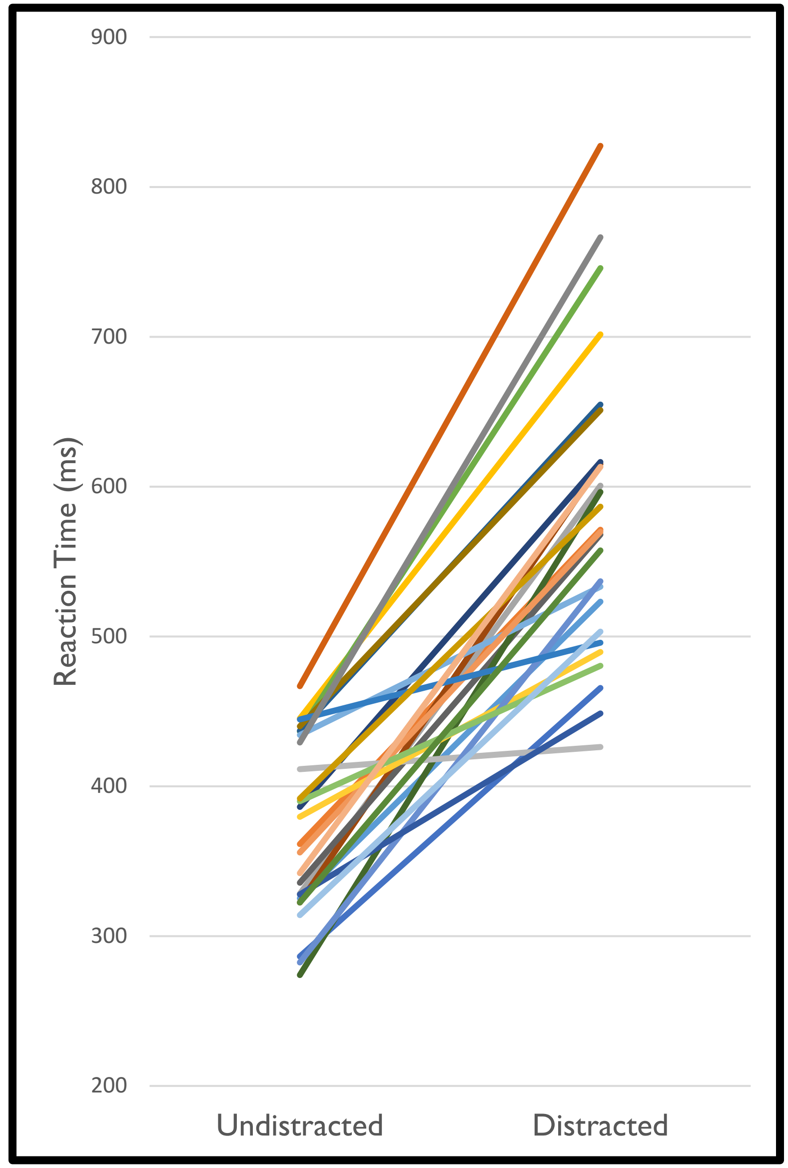

Figure 3.3: SRT Undistracted to Distracted

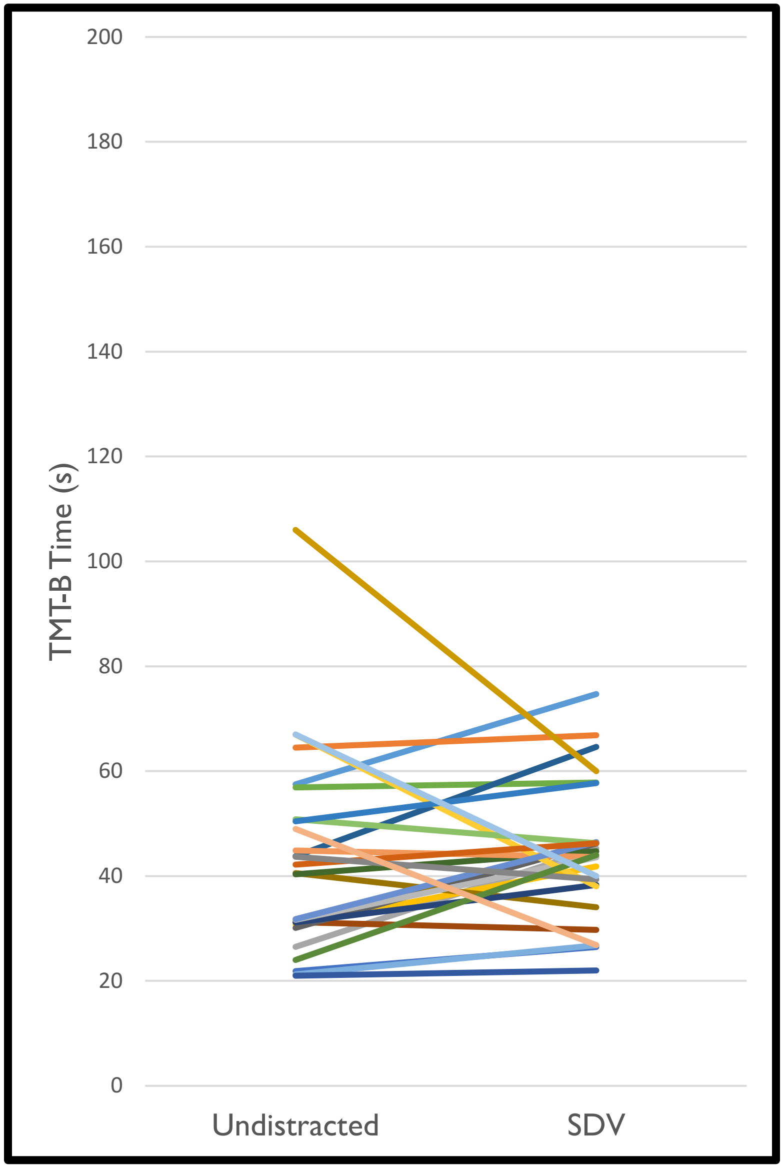

Figure 3.4: TMT-B Undistracted to SDV

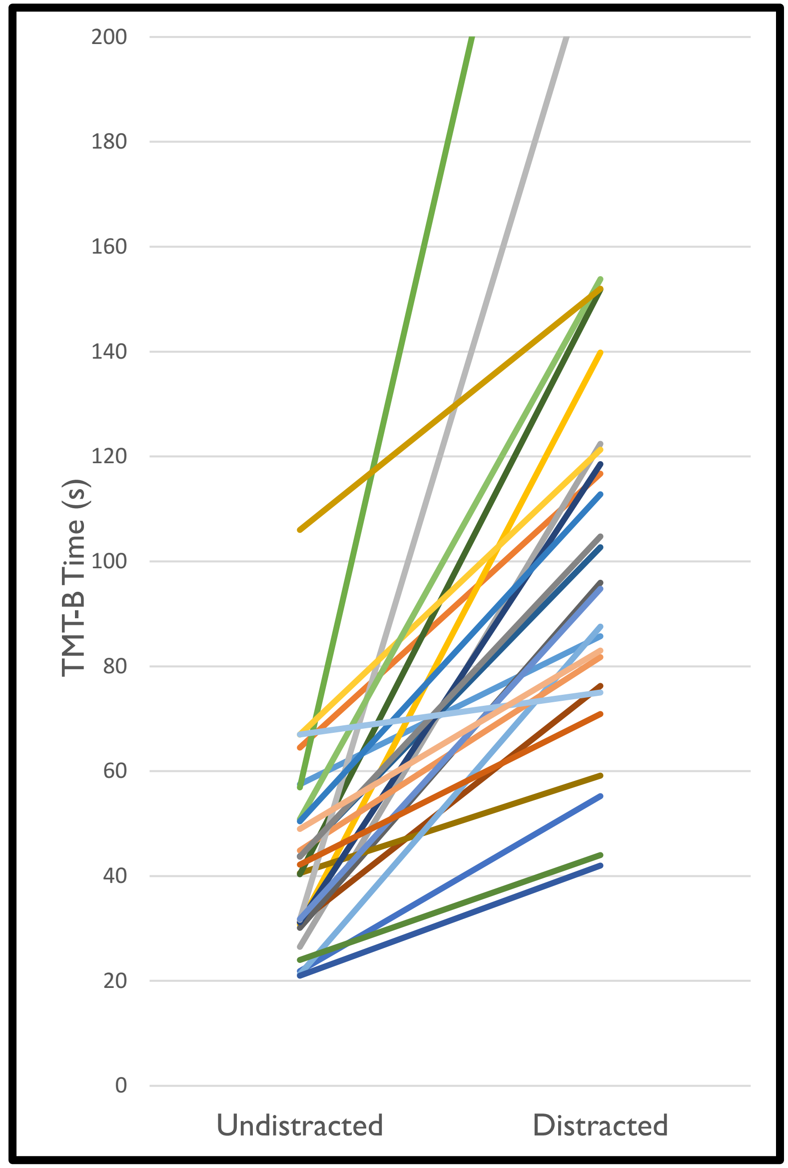

Figure 3.5: TMT-B Undistracted to Distracted

Chapter Four

Does the strong desire to void act as a source of diverted attention in older adults without lower urinary tract symptoms?

Abstract

Background There is a strong but unexplained association between falls and lower urinary tract symptoms (LUTS) in older people. It is known that diverted attention induces gait changes in older people that may increase the risk of falls. It has been suggested that urinary urgency acts as a source of diverted attention, and that it is this that explains the observed association between falls and LUTS. Furthermore, there is evidence that in young, healthy people the strong desire to void (SDV) can induces changes in cognitive function and gait. In this study we explored if SDV acts as a source of diverted attention in older volunteers without LUTS. **Methods** This was a repeated measures-within subjects design. Volunteers aged 65 years or older without LUTS (defined as a Bladder control Self-Assessment Questionnaire (B-SAQ) score of 4 or less) completed two tests of cognitive function, the Trail Making Test B (TMT-B) and Simple Reaction Time (SRT), under three experimental conditions; undistracted and with an empty bladder, distracted by the n back test, a known source of diverted attention, and when experiencing SDV. SDV was induced by asking participants to drink non-caffeinated fluids *ad libitum* until they experienced an urge to void that they could not defer further. **Results** 21 cognitively intact participants were recruited, 8 male and 13 female. The mean age was 74.4 years. SRT increased from a baseline of 451ms to 515ms when experiencing SDV and 885ms when distracted ($p<0.001$ for both comparisons). TMT-B time increased with distraction from 76.9s to 140.1s ($p<0.001$) but was not affected by SDV (increase to 81.1s, NS). **Conclusions** In this sample of cognitively intact, community-dwelling older adults without LUTS, the sensation of SDV induced an increase in SRT of 64ms, a greater increase than that induced by alcohol intoxication at the drink-drive limit or 40 hours of sleep deprivation. A similar but greater effect was induced by a distracting

task, suggesting that SDV may act as a source of diverted attention in cognitively intact, continent older people.

Background

Diverted attention, also referred to as dual tasking, is the concept whereby the performance of two simultaneous cognitive tasks leads to a deterioration in the performance of one or both tasks [1]. Understanding of the association between diverted attention and gait and falls risk has been building for the last two decades. In 1997, Lundin-Olsson and colleagues observed that a number of their patients in sheltered accommodation would "stop walking when talking", and they found that this behaviour was a predictor for the risk of falls with a positive predictive value of 83% [2]. A systematic review of dual tasking and gait in 2009 [3] reported a pooled odds ratio of 5.3 (95%CI 3.1 – 9.1) for falling when people had observable gait changes when walking under conditions of diverted attention. More recently, it was demonstrated that diverted attention induced changes in gait in older people including reduced gait speed [4] and increased gait variability [5].

There is a strong association between falls and lower urinary tract symptoms (LUTS) in older people, with those over the age of 65 experiencing LUTS being up to twice as likely to fall as those who do not [6-8]. The incidence and prevalence LUTS including urgency, frequency, nocturia, and urgency incontinence increase with increasing age [9, 10], which may result from changes to the central nervous system (CNS) as much as from changes to the bladder and lower urinary tract [11]. In positing potential explanations for the association between LUTS and falls, it has been suggested that the sensation of urinary urgency acts as a source of diverted attention leading to changes in gait and increasing the risk of falls [12]. There is increasing evidence that a bidirectional relationship exists between the lower urinary tract and the brain. In addition to the brain influencing the lower urinary tract, sensations from the lower urinary tract can exert effects on cognitive function. Functional brain imaging studies have demonstrated that the both the periaqueductal grey matter and pons, both areas central to the control of micturition, are activated during bladder distention, suggesting that the suppression of the sensation of urinary urge is an active, although unconscious, cognitive process [13].

While the lower urinary tract symptom of true urinary urgency, defined as a "sudden, compelling desire to pass urine that is difficult to defer" [14] may be difficult to induce in a laboratory setting, some limited work has examined the effect of a strong desire to void (SDV) on cognitive function. Lewis *et al.* demonstrated that SDV induced significant decline in the performance of computerised tests of psychomotor function in young, healthy volunteers [15]. In addition, SDV increases the reaction time in healthy young adults [16]. The impact of SDV on cognitive function and whether SDV might act a source of diverted attention in older adults without LUTS has not been studied.

The aim of this study was to explore if the sensation of SDV affects cognitive function in older adults without LUTS and to compare this impact with that of the n back test, a known source of diverted attention [17].

Methods

We used a repeated-measure within subjects design. Participants completed two cognitive tasks, the TMT-B and SRT, under three conditions: undistracted with an empty bladder, distracted by a known source of diverted attention (the n back test), and when experiencing SDV.

Participants

Participants were recruited through advertising in the local press and at local seniors' centres. Study participants were aged 65 or over, and did not have any significant LUTS, defined as a Bladder control Self-Assessment Questionnaire (B-SAQ) score [18] of less than 4. Exclusion criteria were being unable to understand written or spoken English, a diagnosis or evidence of cognitive impairment, defined as a Montreal Cognitive Assessment Score (MoCA) [19] of less than 26, performed at the time of recruitment, sensory or physical impairment that would prevent cognitive testing, the use of an intermittent or indwelling urinary catheter, and dialysis with anuria. Ethics approval was obtained from the local Research Ethics Office and participants received a small (C$10) honorarium in return from their time and travel expenses were reimbursed.

Measures

Following informed consent, participants completed two tests of cognitive function, TMT-B and SRT. The TMT-B, in which letters and numbers are alternately connected in ascending order (example given in Figure 4.1), is a validated test of executive function and is influenced by distraction [20, 21]. SRT is a measure of processing speed and fluid intelligence [22] and has also been shown to be affected by distraction [23]. SRT was measured using an online test [24], where participants pressed the spacebar on a standard computer keyboard as quickly as they could when an on-screen indicator changed colour. The same computer and internet connection were used for all participants.

Study Procedure

Participants complete the two cognitive tests as described above under the three conditions; *undistracted* and with an empty bladder, *distracted* by the simultaneous performance of the n back test, and when experiencing SDV. Under the *distraction* condition using the auditory n back test, the examiner reads a list of letters aloud at a comfortable volume. When a letter which is the same as the letter 2 prior in the sequence is read out, the participant indicates verbally that this has occurred. So, in the sequence "F, B, D, E, D, A, C…" the second D would elicit a positive response. The n back test relies on working memory and attention, and is a validated source of distraction; it is unimportant whether or not the responses are correct, as the attempt itself induces distraction [25]. The condition of *SDV* was induced by asking the participants to drink non-caffeinated fluids at a comfortable pace until they felt as desire to void so strong that they could no longer delay voiding. Specifically, we asked the participants to wait until they experienced a desire to void so strong that they would leave a movie theatre to void during an enjoyable film, a description chosen *a priori* as a familiar situation in which one would delay voiding for as long as possible. We did not ask participants to quantify their desire to void with a visual analog scale or other objective rating, but to wait until they had the strongest desire they could without actually being incontinent. Upon achieving this state, they alerted the research staff, who would then check that the participant was unable to delay voiding any further, and if not, the cognitive tasks were completed. If the participant indicated they could defer voiding, they were asked to continue drinking until they felt a stronger urge that they could not defer further. Following the completion of the cognitive tests the participants were allowed to go to the toilet and void.

Participants were told that if, during data collection, they felt unable to continue due to their SDV being so uncomfortable they feared imminent incontinence, they could abandon the testing at any time to go to the toilet. To increase data accuracy, participants completed the TMT-B twice and the SRT five times, with the mean time to complete the TMT-B and the mean SRT being recorded. All data collection was completed in a quiet room without extraneous distraction and within a few seconds walk of toilet facilities.

To ensure that learning effects were consistent and to ensure understanding and ability to complete the tests, all participants were given one practice run of a TMT-B and SRT prior to data collection. To reduce ordering effects, the three conditions (bladder empty, distracted by task, SDV) in which data were collected were randomised by the blind drawing of lots prepared in advance by an uninvolved staff member. Those participants randomised to perform the bladder empty or distracted conditions first were asked to go to the toilet to void prior to data collection, to ensure they had minimal or no sensation of the need to void.

Sample Size

Previous work by our group has demonstrated an increase in SRT with SDV in young, healthy volunteers of 15% [16], a Cohen's d effect size of 0.59. Based on this moderate effect, and using a within-subjects design, we aimed to recruit a minimum of 17 participants, calculated with G-Power 3 [26].

Statistical Analysis

Descriptive statistics were used to summarise demographic data. The data violated the assumption for sphericity required for repeated-measures ANOVA and therefore non-parametric analysis was performed using two-tailed Friedman's test followed by Wilcoxon signed rank tests for pairwise comparisons with Bonferroni correction for multiple comparisons in SPSS v25 (IBM Corp, Armonk, NY). Statistical significance was defined at $p<0.05$.

Results

21 people were recruited, 8 male and 13 female. The mean age was 74.4 years (SD 5.8). The mean MoCA was 27 (SD 1.3, range 26 – 30). The mean B-SAQ score was 1.76 (SD 1.22, range 0 – 3). All participants successfully completed data collection and there were no adverse incidents

or episodes of incontinence. All participants successfully achieved a desire to void which they could no longer defer. Demographic data are summarised in Table 4.1.

The mean SRT increased from 451ms in the undistracted condition to 515ms with SDV and 885ms with distraction, an increase of 15% and 96% respectively ($p<0.001$ for both). Mean TMT-B time was not statistically significantly different in SDV condition compared to the undistracted state, but was significantly increased by distraction. The results are summarised in Table 4.2. Data for individuals are displayed graphically in Figures 4.2 – 4.5. The results for SDV and TMT-B were not affected by the order in which testing occurred ($p=0.66$ and $P=0.62$ respectively).

Discussion

In this study we found that, in cognitively intact older people without LUTS, SDV induced a statistically significant increase in reaction time, that was smaller but in the same direction as a simultaneous distracting task. The increase in SRT of 65ms is greater than that induced by a blood alcohol level of 60mg/dl [27] (the legal limit for driving is generally between 0mg/dl and 80mg/dl), and from 40 hours of sleep deprivation [28].

Slower reaction times have also been associated with increased falls risk in older people. Richardson and colleagues demonstrated that, in people with diabetes, greater reaction time was associated with reduced unipedal stance time, increased frontal plane gait variability in response to perturbations when walking, and fall related injury [29]. The ability to prevent a fall depends on being able to react to a perturbation in gait, such as a stumble, before it reaches the state of being unrecoverable [30], a function of reaction time.

As in previous work in young adults, the time taken to complete the TMT-B was not affected by SDV. There are several potential explanations for this observation. As a more complex task involving numerous cognitive domains, other than executive function, (visual search and scanning, and psychomotor speed [31]), there may be more cognitive reserve available to overcome the distracting effects of SDV when completing the TMT-B. It could also be that the concentration required to complete the TMT-B is greater, and that this increased concentration is sufficient to suppress SDV even though the participant reported being unable to consciously defer voiding. Finally, there is evidence that older adults with OAB demonstrate impairment in TMT-B performance when compared to their continent peers, suggesting that a group without LUTS such as our participants may have had levels of TMT-B performance insensitive to the effect of SDV.

Holding the bladder in the storage phase requires the brain to actively ignore the sensation of the need to void. Functional MRI studies have demonstrated that during the suppression of both urge (the physiological sensation of a full bladder) and urgency (the sudden compelling desire to void that is difficult to defer), multiple areas of the brain are activated, including the frontal and pre-frontal cortices, the periaqueductal grey matter (PAG), and anterior cingulate gyrus (ACG) [32-34]. These areas are similar to those involved in suppression of unpleasant sensations [35], and SDV could clearly be considered an unpleasant sensation. Several of these areas, including the ACG and inferior frontal cortex, are also involved in the inhibition of motor tasks [36, 37].

LUTS are highly prevalent in later life [9] and are associated with falls [8]. These data demonstrate that SDV in older adults without LUTS induces an increase in reaction time, which could increase falls risk, and may be a source of diverted attention. In people with OAB there is continued, subconscious, cognitive activity to suppress the sensation of urgency [38]. Given this, it is possible that reaction time may also be increased by urinary urgency, acting as a source of diverted attention, and explain the association of urgency and increased risk of falls in people with LUTS.

Strengths and Limitations

This study is limited by its small sample size, although we exceeded our required sample size calculated from similar data, and the results were statistically significant and concordant with previous work in a younger cohort [16]. Both of the cognitive tests used are relatively quick and simple. This is advantageous, as it meant that our participants knew that there would only be a short period of cognitive testing between alerting the research staff of their SDV and being able to void, and therefore had the confidence to delay voiding as much as possible, but also may have failed to detect subtle cognitive changes in any of the three experimental conditions. Finally, we relied on a qualitative description of SDV without any attempt to quantify using visual analog scales or other quantified measure of SDV. However, we did give clear instructions to our participants that they should delay voiding as long as possible and gave a practical example of this. After voiding, the participants reported that they could not have delayed further.

Conclusions

In this sample of older adults without LUTS, the sensation of SDV induced a significant increase in SRT, which was smaller than but in the same direction as a simultaneous distracting task. This suggests that SDV may therefore be acting as a source of diverted attention. Given the known association between urinary urgency and other LUTS and falls in older adults, the action of bladder sensation as a distractor may partially explain this association. It is known that dual task training can improve gait and reduce falls risk under dual task conditions [39, 40]. Further research should establish if the influence of SDV on cognitive function can be reduced with dual-task training.

Table 4.1: Demographics

n=	21
Age	72.4 years
SD	5.8
Range	66 – 86
B-SAQ	
Mean	1.76
SD	1.22
Range	0 – 3

Table 4.2: Results

	Undistracted (Mean (SD)) 95%CI	SDV (Mean (SD)) 95%CI	Distracted (Mean (SD)) 95%CI	Undistracted to SDV	Undistracted to Distracted	Distracted to SDV
Reaction Time (ms)	451 (110) 404 - 498	515 (115) 466 - 564	885 (464) 687 - 1080	p<0.001	p<0.001	p<0.001
Trail Making B (sec)	76.9 (25.9) 65.8 - 88	81.1 (32.2) 67.3 – 94.9	140.1 (56.5) 116 - 164	p=0.566	p<0.001	p<0.001
Friedman's test with Wilcoxon's Signed Rank test for pairwise comparisons with Bonferroni correction						

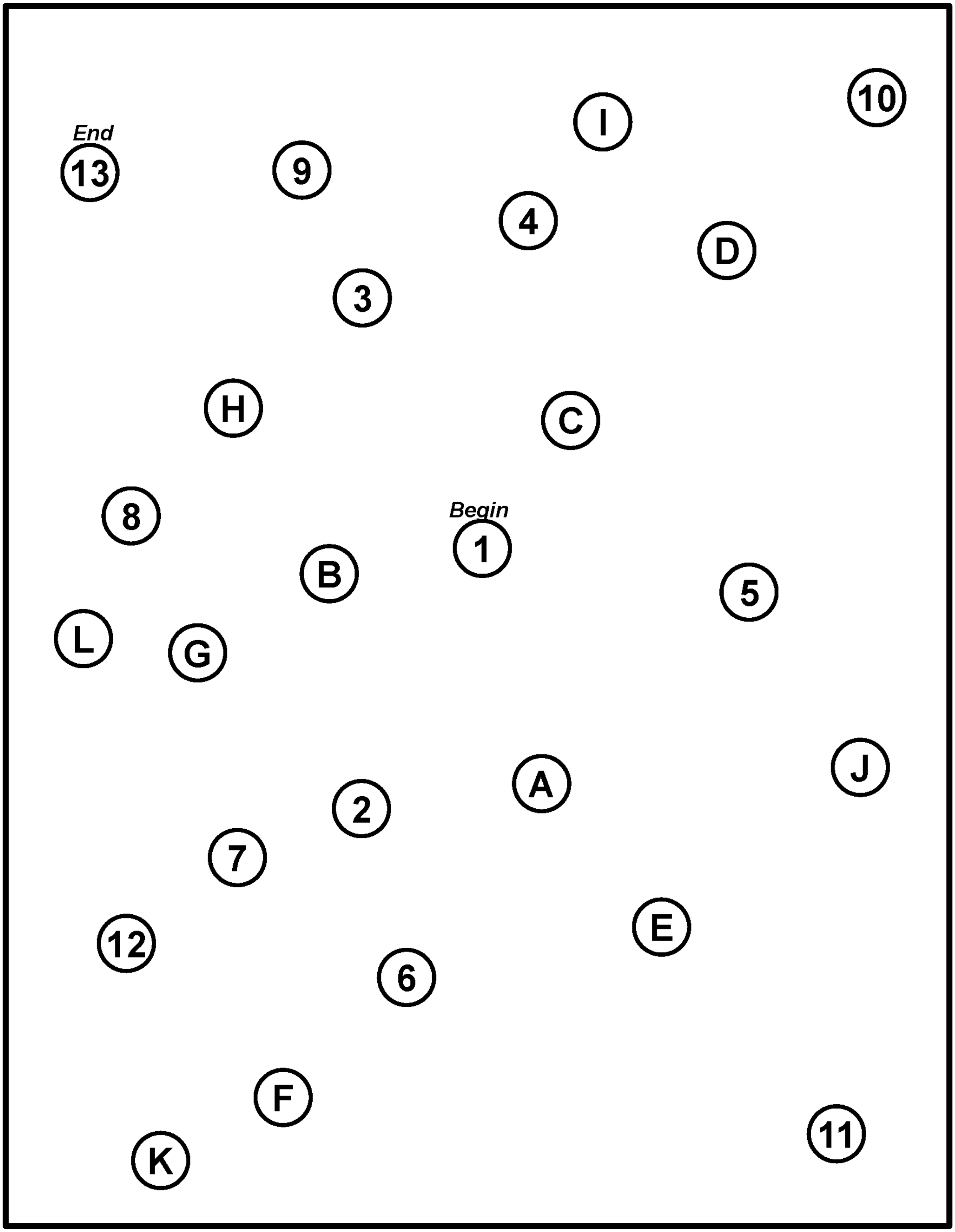

Figure 4.1: Trail Making B Test Example

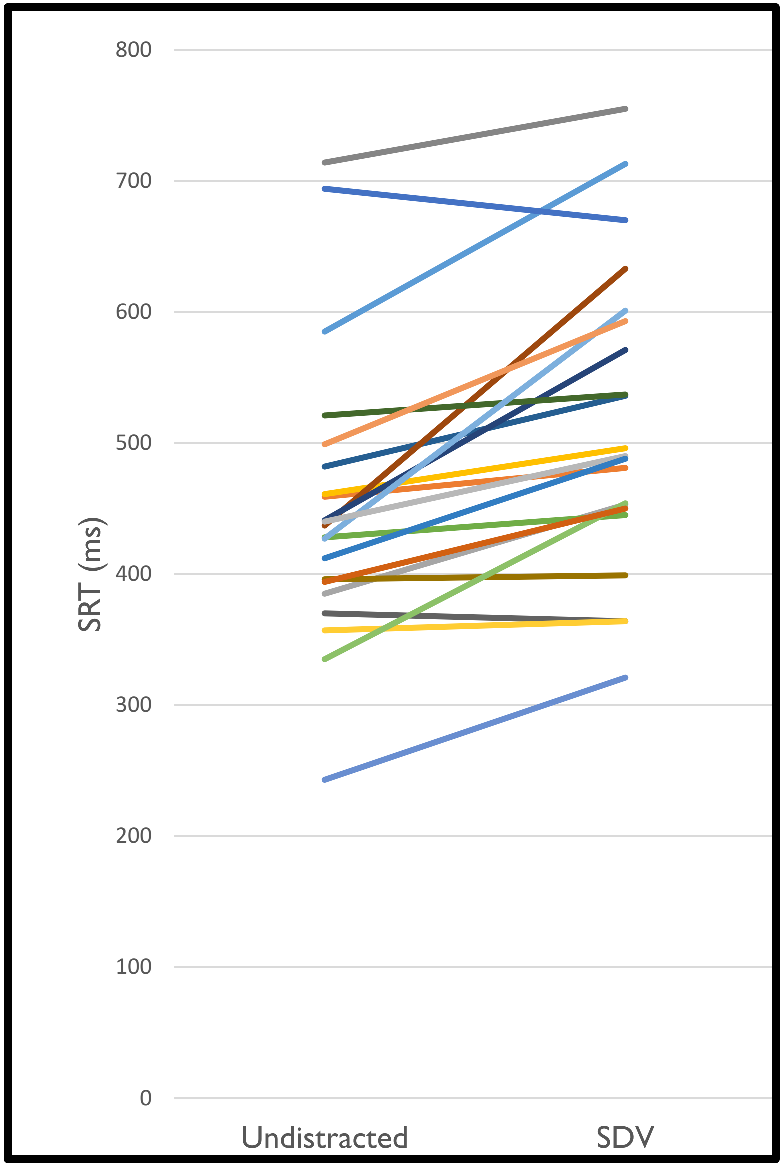

Figure 4.2: SRT Undistracted to SDV

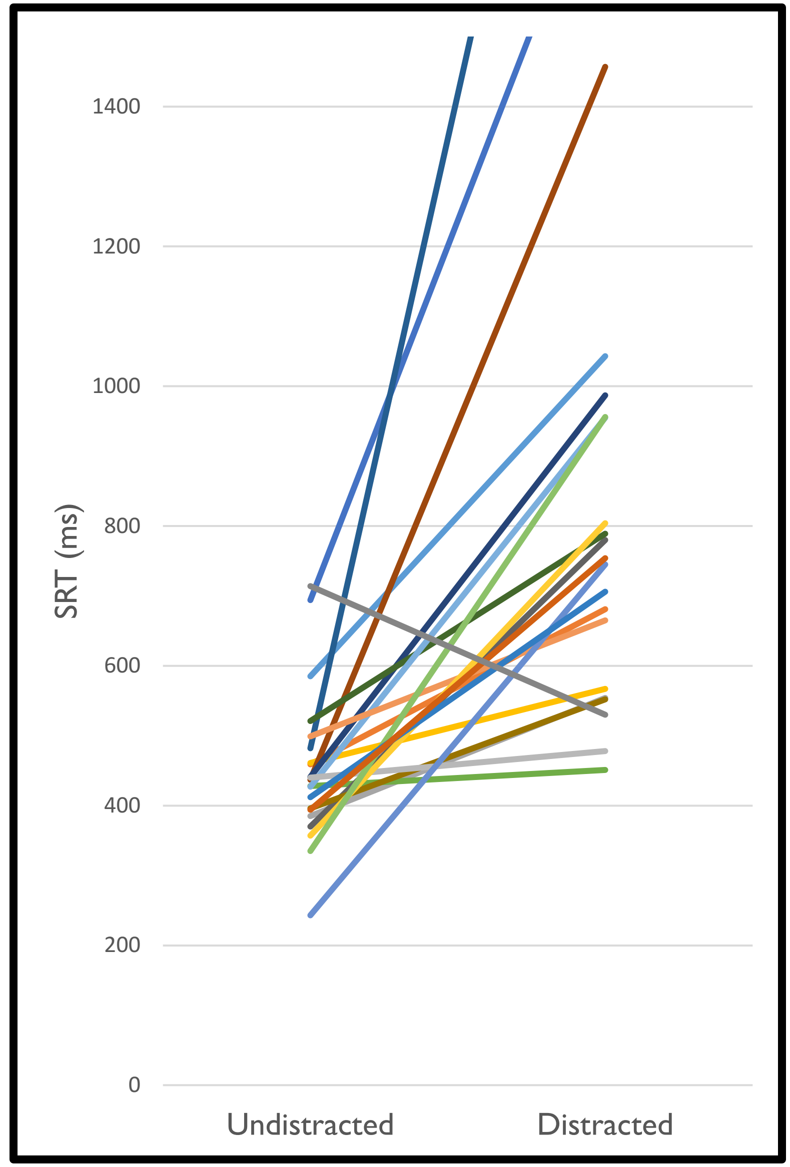

Figure 4.3: SRT Undistracted to Distracted

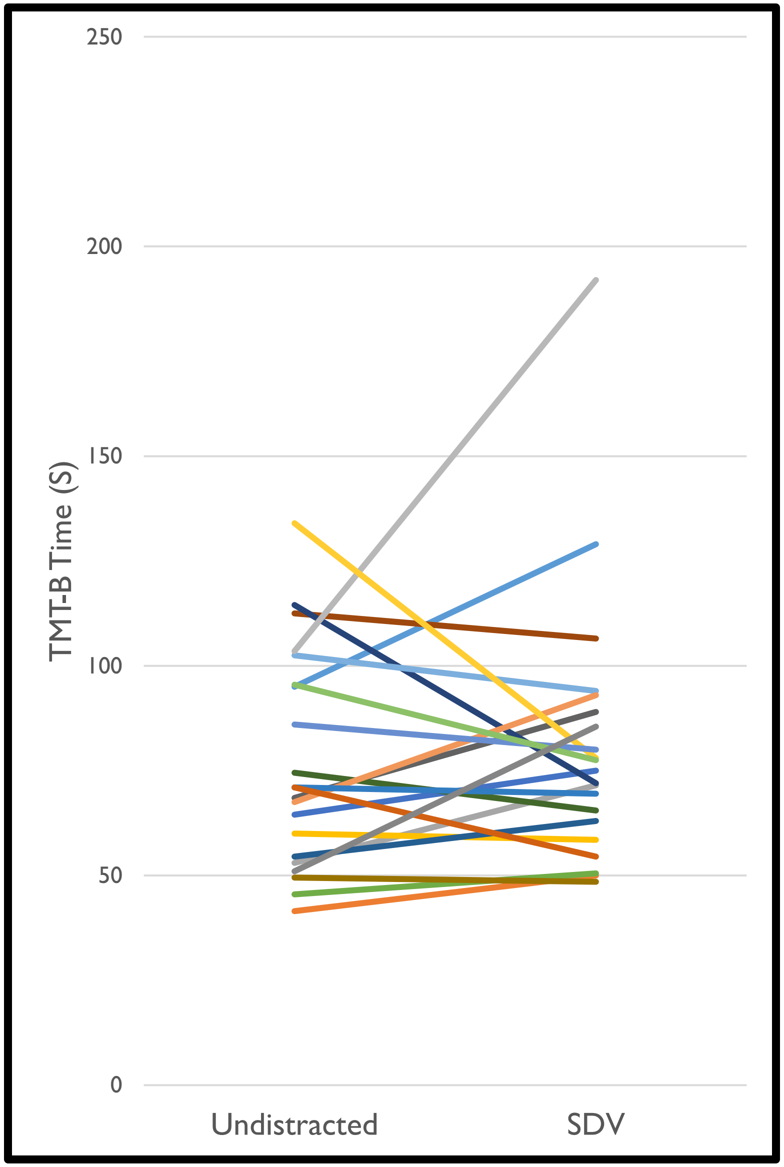

Figure 4.4: TMT-B Undistracted to SDV

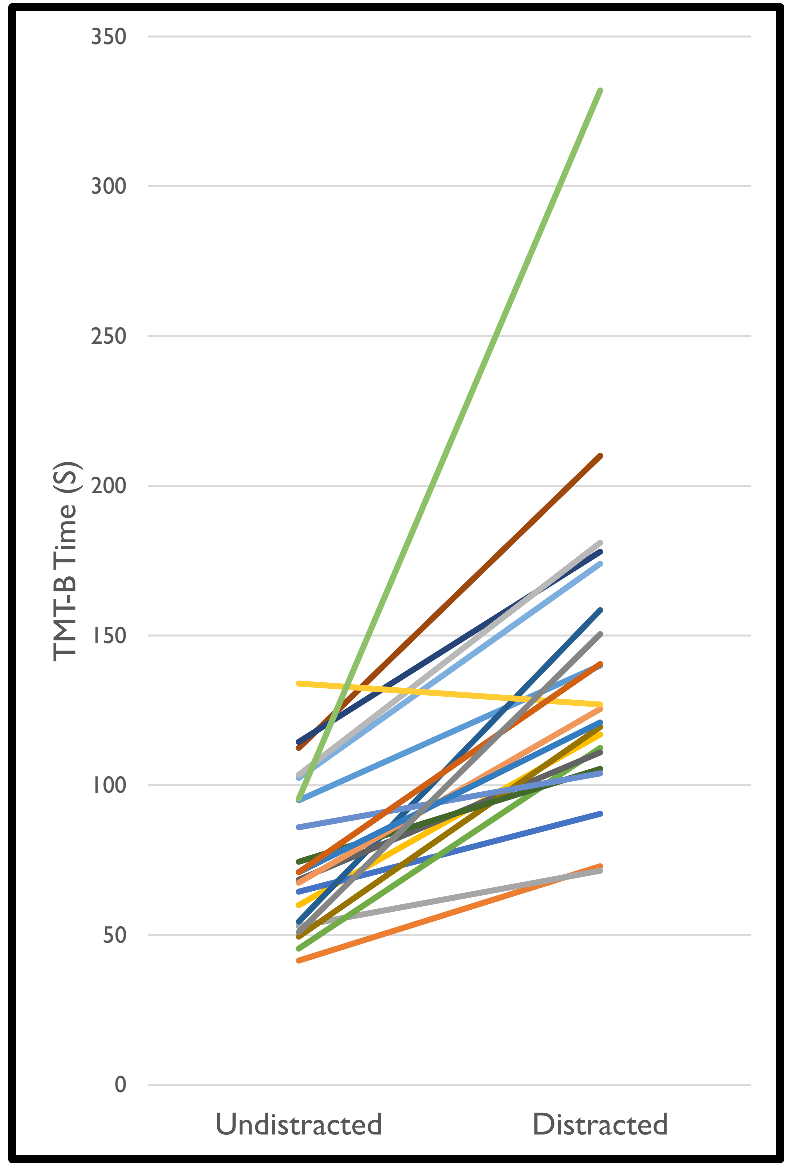

Figure 4.5: TMT-B Undistracted to Distracted

Chapter Five

Do older adults with OAB demonstrate impaired executive function compared to their peers without OAB?

Abstract

Background Maintaining urinary continence is not an automatic process, but relies on continuous processing of sensory signals from the bladder and suppression of the desire to void. Urinary incontinence (UI) and lower urinary tract symptoms (LUTS), including urinary urgency, frequency, and nocturia are highly prevalent among the general population; this prevalence rises in association with increasing age, and this may be in part due to changes in the central nervous system rather than the urinary tract. The aim of this study was to assess if older adults with overactive bladder (OAB) had demonstrable impairment in executive function. **Methods** This was a cross-sectional study comparing the performance of adults aged 65 and over with and without OAB on two cognitive tests, the Trail Making Test B (TMT-B) and simple reaction time (SRT). OAB was defined as urgency, with at least weekly urgency incontinence and a daytime urinary frequency of 8 or more. The control group were defined as a Bladder control Self-Assessment Questionnaire (B-SAQ) score of ≤4. **Results** 56 participants were recruited, of whom 35 met criteria for OAB. The OAB group took significantly longer to complete the TMT-B than the control group (103s vs 77s, p=0.003). There was no difference in the SRT. **Conclusion** In this sample of older adults, OAB was associated with measurable slower performance on the TMT-B, suggesting that impaired executive function is associated with OAB.

Background

Urinary incontinence (UI) and lower urinary tract symptoms (LUTS), including urinary urgency, frequency, and nocturia are highly prevalent amongst the general population; this prevalence rises in association with increasing age [1]. UI and LUTS are stigmatising conditions [2], which are often under-reported and under-treated, particularly in older individuals [3, 4]. The most commonly experienced LUTS are frequency, urgency and nocturia, which are components of overactive bladder syndrome (OAB) [5]. The most common form of UI in older people is urgency urinary incontinence (UUI), urine loss associated with urinary urgency, a sudden, compelling desire to void that is difficult to defer [5].

The maintenance of continence is not a wholly automatic process, but rather one which relies on the coordination of multiple areas of the brain, collating and processing sensory input from the bladder [6]. Sensory input from the lower urinary tract is conveyed by the pudendal and hypogastric nerves to multiple areas of the brain including the pontine micturition centre, the hypothalamus, the periaqueductal grey matter, and the frontal and pre-frontal cortices [6, 7]. These latter areas, which also play a role in executive function, also activate to suppress the sensation of urinary urge, allowing an individual to be consciously unaware of their bladder except at times of experiencing a desire to void. In the healthy individual, this sensation is suppressible, allowing voiding to occur only in at a time and place of one's own choosing.

Given the complexity of neurological control of continence, and evidence that urge is less well suppressed in older people [8], it is not surprising that OAB in older people may be as much a brain disease as a disorder of the bladder [9].

There is a strong association between LUTS and falls in older men [10] and women [11-14], with estimates of the odds ratios for falls in the presence of LUTS ranging from 1.5 to 2.3 [15]. This association has not been explained in the literature, but it has been suggested that the sensation of urinary urgency may exert deleterious cognitive effects by acting as a source of diverted attention [15], the concept where performing two simultaneous cognitive tasks leads to a decline in the performance of one or both of those tasks [16]. Diverted attention has been shown to lead to gait changes in older people [17, 18].

Although largely automatic [19], successful ambulation is reliant in part on executive function, with impairment of executive function being associated with slower gait speed and increased falls risk in older adults [20], and poor performance on executive function testing predicting increased falls risk five years before falls occurred [21]. Lower performance on tests of executive function, memory, and verbal IQ are associated with slower gait speed [22] and cognitively-intact older people with "poor" and "intermediate" performance on the Trail Making Test (TMT), a measure of executive function, were slower when completing an obstacle course than those with normal TMT performance [23].

Given that impairment in executive function is associated with both LUTS and falls, it may be that this impairment forms part of the known association between LUTS and falls by acting as a confounding factor. As part of a wider research program, this study aimed to examine the hypothesis that older adults with OAB may demonstrate impairment in executive function compared to their peers who do not have OAB.

Methods

This was a cross-sectional study comparing the performance of adults aged 65 years and over with and without OAB on two cognitive tests, one for executive function and the other for reaction time. The study was approved by the local research ethics committee, PRO00079683.

Recruitment and Participants

Potential participants were recruited by advertising in community newsletters for seniors. Participants were included if they were aged 65 or older, community-dwelling, and without a diagnosis of cognitive impairment or dementia, urinary catheter use (indwelling or intermittent self-catheterisation), on dialysis, diagnosed with neurodegenerative disease potentially causing cognitive impairment, or any subjective complaint of cognitive impairment. People were excluded if they were unable to understand English, to complete cognitive testing, for example due to sensory impairment such as blindness or colour blindness, inability to hold a pen, or being treated for OAB with either bladder antimuscarinics or β3 adrenoceptor agonists.

Procedures

Respondents to the adverts were screened by telephone and those who met the inclusion criteria were invited to participate. Following written informed consent, participants completed the Bladder control Self-Assessment Questionnaire (B-SAQ) [24], a self reported measure of LUTS and bother. Those without LUTS, defined as a B-SAQ of ≤4, comprised the control group, and those scoring 5 or higher comprised the OAB group. The OAB group also required a daytime frequency of 8 or more, urinary urgency, and urgency incontinence at least weekly for inclusion. The study was in a quiet office, free from distractions. Patient-reported demographic information, reported comorbidities, and prescribed medication were recorded, and a Charlson Comorbidity Index (CCI) [25] and anticholinergic burden (ACB) score [26] calculated for each participant as described in Appendix I. Participants were asked to void their bladder, then complete two tests of cognition, the Trail Making B Test (TMT-B) and a computer-based test of simple reaction time (SRT) [27]

The TMT-B is a validated test of cognition, testing visual search, scanning, mental flexibility, and executive function [28]. Participants were asked to link in sequence a series of 25 circles, each containing one of the letters A to L or the numbers 1 to 12. Normative data by age are available, suggesting, for those aged 65 – 69 years, a median time for completion of 68 seconds and 142.5 seconds in those aged 85 – 89 [28]. The time taken to complete the test and the number of errors made were recorded by a research assistant. The examiner did not interrupt or correct errors during the conduction of the test. To improve data accuracy and reduce the effects of a small number of delays, participants performed two different layouts of the TMT-B, with the mean time taken recorded.

To measure SRT, an online test [27] was used. Participants were asked press the spacebar on a standard computer keyboard as quickly as possible following a visual stimulus (an on-screen image changing from red to green) five times, with the mean reaction time reported by the software. SRT is among the most basic measures of processing speed [29] and correlates well with measures of fluid intelligence [30].

Statistical Analysis

Descriptive statistics were used to summarise participant characteristics. The differences between the groups were examined using two-way Fisher's Exact Test (for categorical variables with small sample size) and two-way independent samples t-test for continuous and ordinal variables which were normally distributed or the two-way Mann-Whitney U test for those which were not normally distributed and could not be transformed. For the purposes of analysis, the ACB score was treated as an ordinal variable.

For each cognitive test the time was recorded and compared between groups using a two-way independent samples t-test (for normally-distributed data) or two-way Mann-Whitney U-test (for non-normally distributed data). Statistical significance was pre-defined at $p<0.05$. Data were analysed using SPSS v25 (IBM Corp, USA).

Sample size

No previous work or pilot data were available from which to undertake a sample size analysis. We aimed to recruit at least 20 people per group to allow robust estimates of effect size in order to quantify the size of difference between the two groups.

Results

56 people were recruited, of whom 35 (62%) met the criteria for inclusion in the OAB group. The OAB group had more women than the control group (85% vs 62%, p=0.054, Fisher's exact test). No significant differences between the groups were seen with age, CCI, number of medications take, or ACB score. These data are summarised in Table 5.1 and graphically in Figures 5.1 – 5.3.

Time to complete the TMT-B was statistically significantly longer in the OAB group (OAB 103 seconds, control 77 seconds, relative difference 26%, p=0.003). There was no statistically significant difference in the number of errors made between the groups (2.28 vs 2.04, p=0.81). There was no difference in SRT between the groups (Table 5.2).

Discussion

Participants with symptoms of OAB took longer to complete the TMT-B than those without OAB, and no differences were seen between the OAB and non OAB groups in SRT. The two groups were similar in age, comorbidities, and medication use, and, none of the participants had subjective experience of any cognitive impairment.

The time taken to complete the TMT-B test is known to be a marker of frontal lobe and executive function [31], predominantly cognitive flexibility, but is not specific for sub-domains of executive function impairment {Kortte, 2002 #3593}. Normally, the bladder is held in a state of "tonic suppression of voiding, that is relaxed only when voiding is both desired and socially appropriate", through inhibition by the frontal lobes via the pre-frontal cortices inactivating the periaqueductal grey matter and in turn the pontine micturition centre [7]. Urinary urgency, and in turn OAB, could result from changes in the function of the frontal lobes [9]. Studies using functional MRI have identified changes in frontal lobe activation in patients with OAB [32, 33]. SRT is governed by visual and motor cortices as well as the somatosensory cortex [34]; it is unsurprising that, when the participants felt no desire to void, no difference in reaction time was observed, as neither the visual nor motor cortices are involved in bladder control. SRT is however influenced by SDV [35], and it may be that stimulation of the somatosensory cortex by the sensation of a full bladder acts as a source of diverted attention, thus impairing reaction time.

Walking without falling is also, at least in part, dependent on executive function [36] and community-dwelling older people with impairment in executive function have been shown to be at higher risk of falls [21, 37]. The impaired executive function, especially impaired cognitive flexibility, demonstrated by worse TMT-B performance time, in those with OAB may partially explain the association between urinary urgency, nocturia, urgency incontinence and falls in older adults. It has been suggested that the sensation of urgency acts as a source of diverted attention, inducing gait changes which may predispose a person to falling [15]. Those with impaired executive function may be less able to compensate for the additional cognitive demand of urinary urgency, and have greater susceptibility to the influence of urgency on their gait.

This study is limited by its small size and cross-sectional design, meaning that it is not possible to assign a direction of causality to the observed association. There is evidence from young, healthy volunteers without LUTS that the experience of SDV induces changes in reaction time [35] and impairment on the Stroop verbal reasoning task [38] suggesting a bidirectional relationship between processing speed and bladder function.

By ensuring our participants emptied their bladder immediately prior cognitive testing, we sought to minimise the afferent sensation from the bladder. Given that OAB may result from abnormal signalling from the bladder even at low volumes, it is possible that the OAB group were actively attempting to supress urgency and it is this that impaired their cognitive function by acting as a source of distraction. The use of functional imaging techniques such as functional MRI or functional Positron Emission Tomography may help delineate such effects in future studies. As our study was limited in scope, we did not conduct any brain imaging with participants. Given that the presence of white matter hyperintensities on MRI is associated with LUTS, falls, and other geriatric syndromes [39], it may be that our OAB group's impaired executive function was as a result of structural brain changes. Including imaging in future studies comparing cognitive function and process between people with and without OAB could increase the understanding of the underlying pathophysiological mechanisms.

We did not measure or examine falls risk or frequency of falls, and further work is needed to examine the links between LUTS, executive function, and falls risk in this context.

Conclusions

This small sample of cognitively intact older adults with OAB demonstrated impaired performance on a test of executive function, the time to complete the TMT-B, compared to a group of continent peers. This finding potentially informs part of the known association between falls and LUTS in older adults. Clinically, the identification of executive dysfunction by impaired TMT-B performance could also serve as a marker of risk of having or developing LUTS, leading to active case finding and/or pre-emptive bladder health training in older adults.

Table 5.1: Participant Characteristics

	OAB (Mean (SD))	Non-OAB (Mean (SD))	p=
n=	35	21	
Age Range	74.40 (5.6) 65 – 87	75.44 (5.9) 66 – 86	0.55
Sex (F:M)	30:5 (85%:15%)	13:8 (62%:32%)	0.05
Charlson Comorbidity Index	0.77 (1.21) Range 0 – 5	0.29 (0.64) Range 0 – 6	0.15
Number of Medications	2.17 (2.23) Range 0 – 7	2.21 (2.32) Range 0 – 8	0.80
Anticholinergic Burden Score	0.26(0.66) Range 0 – 2	0.19 (0.51) Range 0 – 3	0.77

Table 5.2: Cognitive Testing Results

	OAB n=35 (Mean (SD))	Non-OAB n=21 (Mean (SD))	Mean difference (95% CI)	p=
TMT-B time (s) Range	103.4 (33.13) 58 – 180	76.9 (25.95) 41 – 134	26.4 (9.5 – 43.4)	0.003
TMT-B Errors Range	2.29 (3.52) 0 – 10	2.05 (3.41) 0 – 8	0.24 (-1.17 – 2.16)	0.828
Reaction Time (ms) Range	480.3 (142.5) 313 – 913	463.9 (114.3) 321 – 714	36.64 (-57.0 – 89.9)	0.722

TMT-B: Trail Making Test B

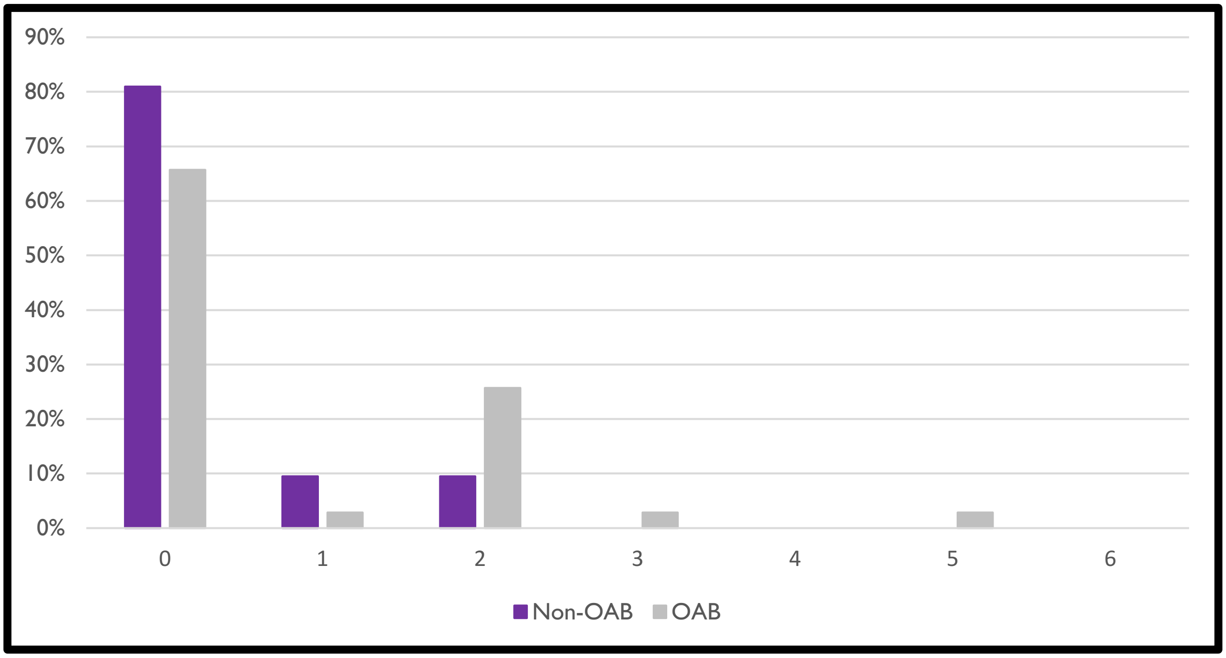

Figure 5.1: Charlson Comorbidity Index

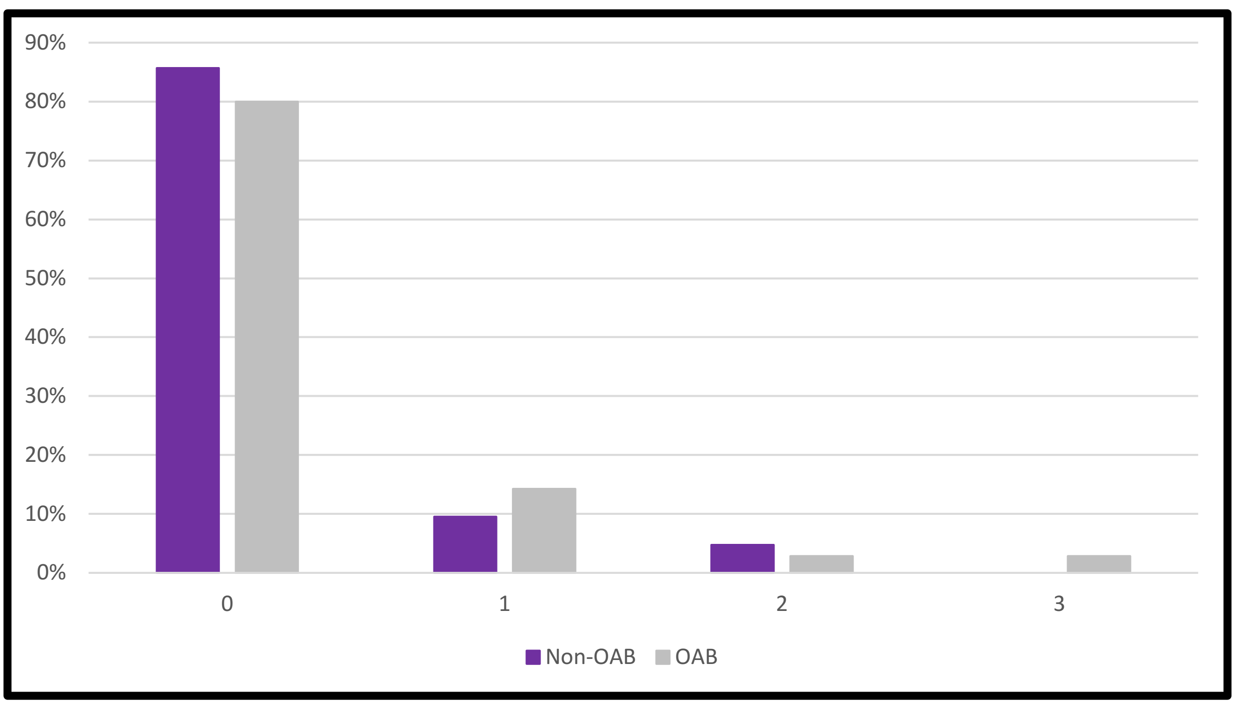

Figure 5.2: Prescribed Medications

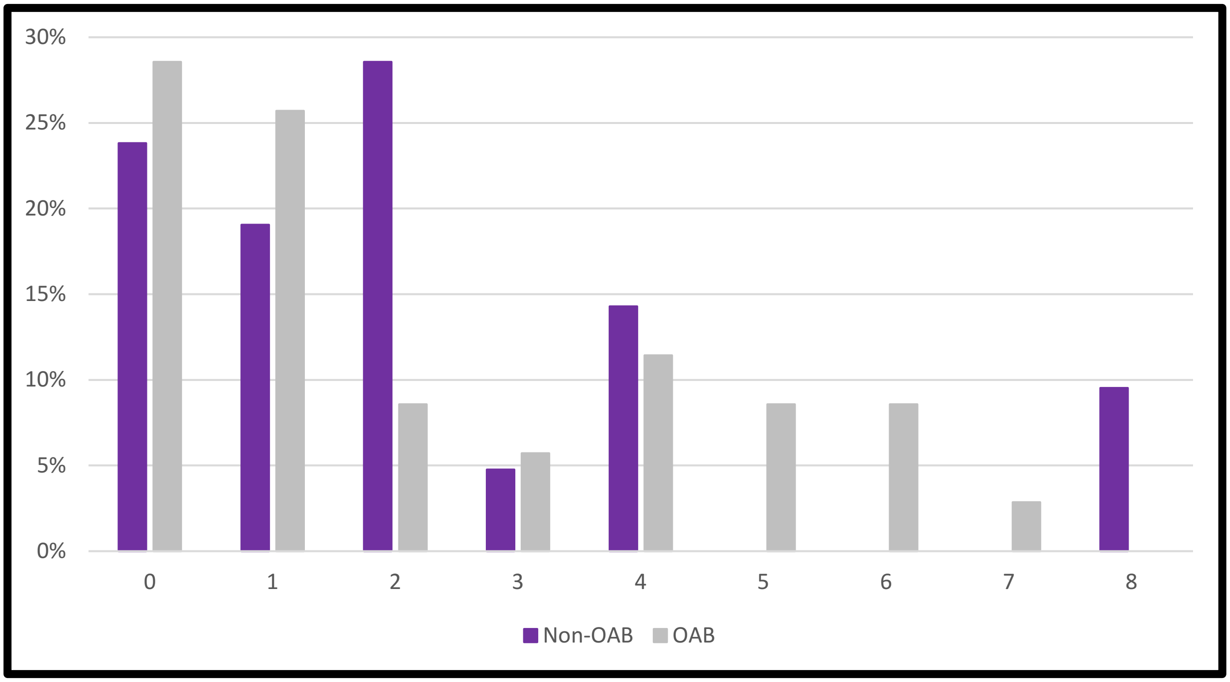

Figure 5.3: Anticholinergic Burden Score

Chapter Six

Measuring gait variables using motion capture in older women with urinary urgency: A pilot study

Abstract

Aim: There is a strong but as yet unexplained association between lower urinary tract symptoms (LUTS) and falls in older adults. A strong desire to void (SDV) can induce gait changes in middle-aged, continent women. This pilot study assessed the feasibility of using three-dimensional instrumented gait analysis (3D IGA) to analyze temporal-spatial and 3D gait parameters in older women with overactive bladder (OAB) while they experienced urinary urgency. **Methods** 11 women aged 65 years and over with OAB attended a gait laboratory for 3D dynamic motion capture during walking with and without experiencing SDV. Temporal-spatial and kinematic data were recorded walking on a flat, level floor **Results:** Of the 11 women recruited, 10 successfully completed data collection. There were no investigation-related adverse events. When experiencing urinary urgency, the participants' gait variability, measured by coefficient of variance of velocity, showed a moderate increase with an effect size (Cohen's d) of 0.36. Cadence reduced with a larger effect size (Cohen's d=0.64), and velocity reduced with a moderate (Cohen's d=0.36) effect size. There were no consistent changes in the 3D kinematic gait data in either the limbs or trunk. **Conclusions**: 3D IGA is a feasible and safe method to evaluate gait parameters in older women with OAB during the sensation of urinary urgency.

Introduction

Falls among older adults are frequent, multifocal in aetiology and have considerable impact in terms of mortality, quality of life, injury, pain and fear of falling [1]. Falls have high cost implications for health systems, with an annual cost of falls in the USA being approximately US$50 billion in 2015 [2], and C$2 billion in Canada in 2004, predicted to rise to C$4.4 billion by 2031 [3]. Lower urinary tract symptoms (LUTS) urinary incontinence (UI), nocturia, overactive bladder (OAB) and urinary urgency have been identified repeatedly as risk factors for falls [4-11]. In a study of 6,049 community based women, urgency incontinence which occurred at least weekly was independently associated with an increased risk of falling (OR = 1.26, 95%CI 1.14 – 1.40) and sustaining a fracture as a result of that fall (OR = 1.34, 95%CI 1.06 – 1.69) [9]. More recently, Nakagawa [4] described the relationship between nocturia, falls and increased risk of hip fracture in Japanese seniors. Similarly, Takazawa and Arisawa [12] reported that although either stress or urgency incontinence alone were not significantly associated with falls among frail older women, those with mixed incontinence (stress and urgency) were 3.05 times more likely (95%CI 1.01 – 10.2) to fall than those without. Both urinary urgency and incontinence were shown to be risk factors for falls in a Finnish study of 1016 adults 70 years and older [13]. A report of an economic analysis of data from the NOBLE survey [14] in those with OAB found increased risk of injury related to a fall (OR 2.26, 95%CI 1.46 – 3.51) and significant health care costs. Frequency of micturition and nocturia are also risk factors for falls in community dwelling older people. In a prospective study of 405 older Taiwanese living either at home or in seniors' housing, urinary frequency or incontinence were among six factors that predicted falls [15]. Data from a longitudinal health screening programme of ambulatory older people revealed that nocturia of at least twice nightly significantly increased risk of falls (OR 1.84, 95%CI 1.05 – 3.22), and the risk increased in those reporting more than three episodes of nocturia (OR 2.15, 95%CI 1.04 – 4.44) [6]. In hospital, the need to use the toilet has been reported to increase falls, especially among older people [16]. Urinary incontinence is also associated with increased falls in institutionalised older people [17].

Despite this, there has been little attention paid to the potential causes of this relationship, and the underlying causes of the association are unknown [18, 19]. A systematic review of interventions to prevent falls in older people included only one randomised controlled study of incontinence management, which was combined with exercise [20]. Preliminary work in elucidating the relationship of LUTS and falls was undertaken in a single study of middle-aged, continent women, where SDV induced changes in temporal-spatial gait parameters [21]. Gait variability, and in particular increased variability in stride length and gait speed, has been previously shown to be associated with increased falls risk [22, 23].

Objective

The objective of this pilot study was to investigate the feasibility, safety, and acceptability of recording temporal-spatial and 3D gait data in older women with OAB while they were experiencing urinary urgency, one of the LUTS associated with falls risk.

Methods

Design

A clinical gait study which measured participants walking under two conditions, bladder empty and when experiencing urinary urgency using a within-subject, repeated measure design.

Recruitment and Ethics

A convenience sample was recruited from a tertiary continence clinic. Included participants were female, aged 70 years or over, had a clinical diagnosis of OAB and able to ambulate without the use of aids. Participants were excluded if they had a Montreal Cognitive Score (MoCA) [24] of less than 22/30, used walking aids, or had chronic or progressive neurological, vestibular or musculoskeletal conditions that interfered with gait and balance such as Parkinson's disease, post stroke hemiplegia, Meniere's disease, multiple sclerosis, or end stage renal failure. Participants were also excluded if they were taking antimuscarinic medication for OAB, had an acute symptomatic urinary tract infection, or impaired bladder emptying, defined as a post void residual volume of 200ml. All participants gave informed, written consent. The study was approved by the local Research Ethics Committee, PRO00022975.

Instrumentation

Gait was assessed by three dimensional instrumented gait analysis (3D IGA), which uses an eight-camera optoelectronic motion capture system (Eagle Digital Camera, Motion Analysis Corporation, Santa Rosa, CA, USA) recorded at a collection rate of 120 Hertz (Hz) and normalised to 0 – 100% of the gait cycle [25].

Computer software allows for processing of data and produces a three dimensional image of the person moving. Graphed kinematic data are produced showing movements of the body segments.

Retro-reflective markers were placed on the skin over bony landmarks and then these positions are recorded by an optical tracking system. These markers were then used to create a biomechanical model of the participant walking across the lab. From this model, kinematics were generated for trunk, pelvis, hip, knee and ankle/foot motion. The marker set used is the modified Helen Hayes marker set for the lower body [25] with additional trunk markers on C7 and the sternum (Figure 6.1). Temporal spatial parameters were also recorded and included velocity, cadence, stride length, step length, step width and toe-off times. The variability in velocity and cadence were calculated as the coefficient of variance (COV), the standard deviation divided by the mean. The markers were placed, the system calibrated and gait analysis was performed by an experienced gait analyst in accordance with the lab's standard operating procedure. The number of participants able to successfully complete data collection, the rate of adverse events during data collection, and the time taken to perform the protocol formed the primary outcomes of interest. Secondary outcomes were gait and sway analysis and subjective field notes regarding the feasibility and acceptability of the experimental method. The gait analysis data were used to inform sample size calculation for planning a fully-powered study.

After data collection, participants were asked to give their views on the procedure, its acceptability, and for general comments on the experience of taking part in the project.

Study Procedure

On arrival at the gait lab, participants were asked to visit the toilet to empty their bladder and apply protective undergarments if desired. Reflective markers were applied. Gait analysis was performed in two states: "bladder empty", immediately after voiding, and "urgency", which was achieved by drinking non-caffeinated beverages *ad libitum* until the participant felt urinary urgency, a compelling desire to void which was difficult to defer [26]. The order of states was selected at random by the drawing of lots.

Dynamic motion capture:

Participants walked three lengths of the gait lab, a total distance of 27.5 meters, during dynamic motion capture, with the final walk being towards a nearby toilet. Participants walked in their usual footwear and at a self-selected pace. The temporal-spatial parameters and 3D motion capture curves for pelvic tilt, pelvic obliquity, hip extension and flexion, and knee flexion and extension were recorded. These were chosen *a priori* as the 3D gait parameters most likely to change as velocity and cadence changed, and with voluntary contraction of the pelvic floor to delay voiding.

Analysis

The primary outcome measure was the number of participants from whom all planned data were successfully collected. Temporal-spatial data were compared between the two states using a two-tailed dependent-samples T-test using SPSS v25 (IBM Corp, Armonk, NY). Statistical significance was set at <0.05. Cohen's d was calculated from the means and pooled standard deviations and used to calculate a sample size for a fully-powered study using G*Power 3 [27].

Kinematic data were interpreted and reported by an expert gait analyst to identify any consistent or repeated changes in gait between the two states, and compared to the lab's standardised data for "normal" adults, which are based on a group of healthy volunteers aged <60 in 2006. This analysis was blinded to the state (bladder empty/urgency) under which the walk was performed.

Field notes that included the participants' subjective observations of their experiences of participating to gain feedback on the experience of participating, and their bladder sensation and symptoms were also recorded as part of the protocol to ascertain a compelling desire to void and to informally assess the acceptability of the process to participants. A formal thematic analysis was not planned.

Results

Feasibility

11 women were recruited, with a mean age of 78 years (SD 6.26 years), and a mean MoCA of 26.3 (SD 2.58). 10 (91%) successfully completed the protocol. Only one participant was unable to complete any of the gait analysis because she was feeling unwell. The mean time for each data collection cycle was 330 seconds (range 120 – 660) for the bladder empty condition, and 353 seconds (range 180 – 720) in the urgency state. These data are summarised in Table 6.1.

Adverse Events

There were no falls, trips, or episodes of incontinence during data collection. The participant who did not complete the study (aged 85) arrived at the gait laboratory feeling nauseated, which she attributed to anxiety. During fluid loading her nausea increased and she vomited. Data collection was abandoned at this point. Her nausea was not felt to relate to the study and rapidly resolved after she vomited.

Gait Analysis

Temporal-spatial parameters

For those who were able to commence data collection, all gait data were successfully collected. No statistically significant changes in temporal-spatial gait parameters were observed. The variability of velocity, expressed as the coefficient of velocity (COV), did not show a significant increase; however, there was a difference between the means with a moderate effect size seen (Cohen's d 0.36), although this difference was not statistically significant. The cadence was reduced, with a moderate effect size (Cohen's d 0.64) without reaching statistical significance. These data are summarised in Table 6.2.

Using COV of velocity and cadence as primary outcome measures to power a full-size study, based on the Cohen's d of 0.4, would require 40 participants, assuming a one-tailed t-test for matched pairs and α=0.05 and β=0.8.

3D Gait analysis

The 3D kinematic data were reported by an expert gait analyst (JL), who was blinded to the state under which each walk was performed and the report of these data is summarised in Table 6.3. An example of the recorded gait data given as Figure 6.2. No consistent changes between the two states were observed. When compared to standardised normative data for young adults by an expert gait analyst, significant and highly variable differences were observed for all but one participant, with baseline gait abnormalities including differences in knee flexion, hip flexion and extension, and pelvic tilt. These are summarised in Table 6.3.

Participant Experience

Of the 10 participants who successfully completed data collection, all were satisfied with the experience and none expressed discomfort or embarrassment. Several participants expressed surprise at the length of time they were able to delay voiding in the gait lab and a commonly-expressed sentiment was "if I'd been at home, I'd have been to the toilet several times by now!" The time taken for all data collection to be completed was felt to be reasonable by the participants.

Discussion

This study has shown that 3D IGA is a feasible research tool in older women with OAB who ambulate independently, and that evaluation of gait using 3D IGA can be performed effectively and safely while participants experience urinary urgency. There were no consistent differences between the two states for the 3D motion capture data, and the kinematic gait data demonstrated that the participant's baseline gait was abnormal when compared to the lab's standardised gait patterns for young, healthy volunteers. This was a feasibility study which addressed the data collection method and was not powered to identify change in temporal-spatial or kinematic gait between the two bladder states. Moderate to large effect sizes for velocity, variability of velocity, and cadence were seen. Changes in gait parameters are associated with an increase in both falls risk and fear of falling [23, 28, 29]. Normal ageing has been associated with changes to gait including reduced gait speed [31], step length reduction [32], increased double stance time [33], and lower ankle plantar flexor power in late stance [34]. In addition, ageing is associated with an increased prevalence of conditions which may affect gait, such as osteoarthritis [35], and older people have greater gait variability than their younger counterparts [36].

This is the first trial to assess gait in older people with established OAB while experiencing urinary urgency, and the first to use 3D gait analysis. We successfully used this technique to assess temporal-spatial and kinematic gait parameters in participating older women with OAB.

The most significant limitation of this study was the challenge of distinguishing between SDV, a normal sensation, and urinary urgency, the sudden compelling desire to void which is difficult to defer [26]. The identification of true urgency remains a challenge in both clinical and research settings [37]. We asked our participants to alert the research staff when they were experiencing urgency, but clearly if they had experienced a *gradual* increase in the desire to void, the sensation they reported may have been physiological urge rather than pathological urgency. It is interesting that the participants often felt that their LUTS were better in the controlled setting of the gait lab. It is possible that by asking them to pay attention to their bladder sensation we influenced their experience of urgency. Mindfulness, the state of being aware of a feeling or sensation, has been suggested as a potential treatment for OAB [38]. It is known that people with OAB who report anxiety have more severe symptoms than those without [39], and it is also possible that we modulated this effect in the calm, controlled environment of the gait lab.

The recording of gait and sway using 3D IGA is a feasible research tool in older women with OAB, even while they are experiencing urinary urgency. However, 3D gait analysis did not show any consistent change and produced data with high intra-participant variability. This was felt by the reporting gait analyst to be far more variable than the gait of younger people. In the absence of consistent changes associated with urgency, we can conclude that the kinematic aspect of 3D gait analysis is not a useful tool to study the changes in gait associated with urinary urgency, but is a valid tool for collecting temporal-spatial data, which also has the advantage of being amenable to robust statistical analysis and, in this study demonstrated moderate effect sizes, allowing power calculations for a fully-powered study to be performed.

Conclusion

The recoding of temporal-spatial and 3D gait parameters in older women experiencing urinary urgency was feasible and there were no adverse events observed. Urinary urgency induced non-significant but moderate effects on gait parameters associated with an increased falls risk in older people, specifically reduced velocity, reduced cadence, and increased gait speed variability.

Table 6.1: Demographics and cycle descriptors

n=10	Mean	SD	
Age	78.1	6.26	
MoCA	26.3	2.58	Range 23 – 30
Total time in gait lab (minutes)	97	41	Range 46 – 174
Time for bladder empty cycle (secs)	330	137	NS (p=0.73)
Time for urgency cycle (secs)	353	160	
Time for fluid loading (minutes)	74	25	
Volume of fluid consumed (ml)	709	230	Range 250 – 1050

Table 6.2: Temporal-Spatial Gait Parameters

Measure	Bladder Empty (mean(SD))	Urgency (mean(SD))	p=	Cohen's D
Velocity	0.887 (0.2)	0.841 (0.19)	0.277	0.36
Velocity COV	0.218 (0.01)	0.263 (0.13)	0.279	0.36
Cadence	103.19 (9.4)	98.95 (11.3)	0.071	0.64
Cadence COV	0.036 (0.015)	0.035 (0.018)	0.88	0.05
Stride length	1.02 (0.15)	1.01 (0.14)	0.93	0.02
Stride Length COV	0.297(0.72)	0.3 (0.075)	0.78	0.08

Table 6.3: Kinematic data

Participant	Bladder empty	Urgency
1	Rapid hip extension in early stance. Small knee flexion Small posterior pelvic tilt	No change
3	Large pelvic tilt Increased hip extension Decreased knee flexion "Crouched" stance	Increase in pelvic obliquity Less crouched stance
4	Gait within normal limits	No change
5	Rapid hip extension in early stance Flexion absorption wave left knee	No change Loss of flexion absorption wave
6	Flexed knees bilaterally	No change
7	Rapid hip extension in early stance Increased knee extension	No change
8	Flexed knees Anterior pelvic tilt	No change
9	Increased knee flexion Decreased hip flexion	Smaller increase in knee flexion Smaller decrease in hip flexion
10	Anterior pelvic tilt	Reduced anterior pelvic tilt
11	Rapid hip extension in early stance Slight posterior pelvic tilt	No change

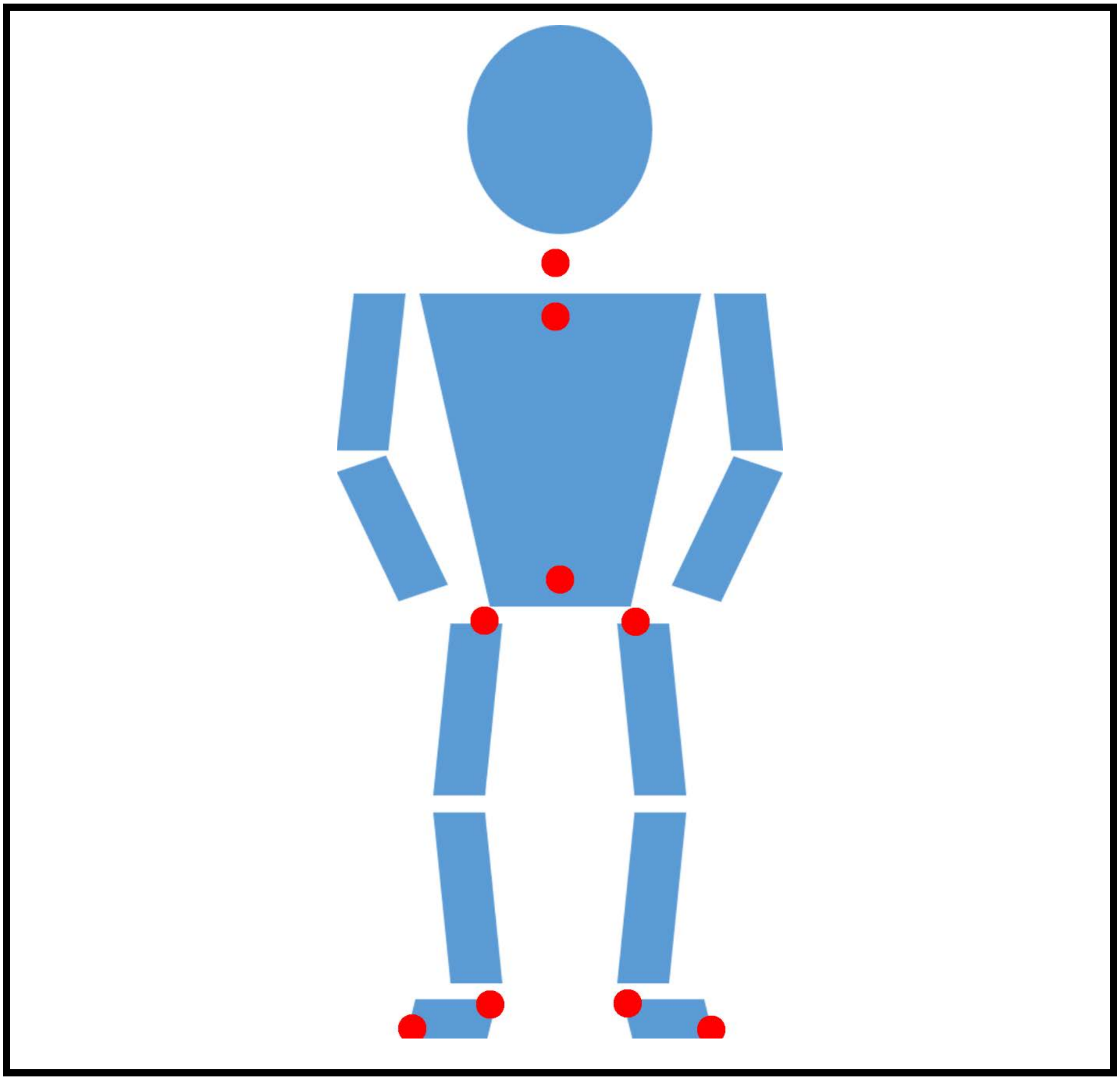

Figure 6.1: Placement of reflective markers

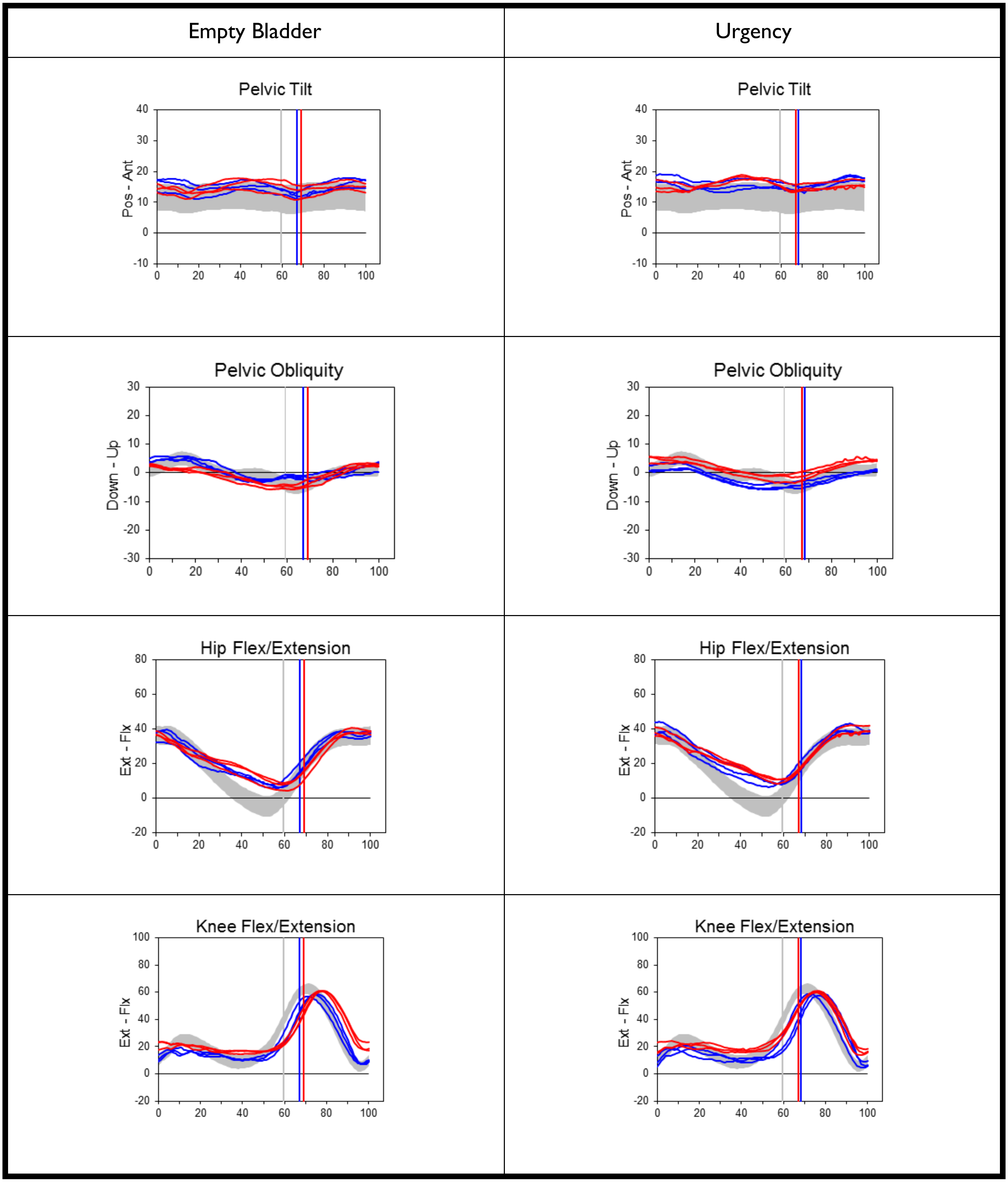

Figure 6.2: Kinematic Data Example

Y-axis - % of gait cycle. Red – right leg, Blue, left. Vertical line indicates foot off point for that limb.

Grey area indicates the lab normative data

Chapter Seven

Urinary urgency acts as a source of diverted attention leading to changes in gait in older adults with overactive bladder.

Abstract

Aims There is a well-recognised but unexplained association between lower urinary tract symptoms (LUTS) including urgency and urgency incontinence and falls in older people. It has been hypothesised that urinary urgency acts as a source of diverted attention, leading to gait changes which increase falls risk. This study aimed to assess if urinary urgency acts as a source of diverted attention in older adults with overactive bladder (OAB). **Methods** 27 community-dwelling adults aged 65 years and over with a clinical diagnosis of OAB underwent 3 Dimensional Instrumented Gait Analysis under three conditions; bladder empty, when experiencing urgency, and when being distracted by the n back test. Temporal-spatial gait and kinematic gait data were compared between each condition using repeated measures ANOVA.

Results Gait velocity reduced from 1.1ms^{-1} in the bladder empty condition to 1.0ms^{-1} with urgency and 0.9ms^{-1} with distraction ($p=0.008$ and $p<0.001$ respectively). Stride length also reduced, from 1.2m to 1.1m with urgency and 1.0m with distraction ($p<0.001$ for both). The presence of detrusor overactivity did not influence these results ($p=0.77$).

Conclusions In older adults with OAB, urinary urgency induces similar changes in gait to those caused by a distracting task, the n back test. This may be part of the explanation for the known association between falls and LUTS in older people. Future research should examine the effect of pharmacological treatment of OAB on gait and on the effect of dual-task training on gait when experiencing urgency.

Introduction

Falls, are the sixth leading cause of death in older adults, with the deaths of 2,691 Canadian seniors attributed to falls in 2008. Up to one third of people aged over 65, and half of those over 80, will fall in any given year [1]. Falls are often recurrent, with around half of people who fall experiencing another within 12 months [2]. Falls impair quality of life, cause individual pain and suffering, lead to functional decline [3], cause a fear of further falls [4] and are a significant cause of health resource use [5-7].

Urinary incontinence (UI) and lower urinary tract symptoms (LUTS) are common [8, 9] and the prevalence, particularly that of urgency and urgency incontinence, rises in association with increasing age [10] due to multiple factors including age-related changes to the lower urinary tract and central nervous system and increasing prevalence of concurrent medical conditions and polypharmacy [11].

There is a strong but unexplained association between LUTS and falls in older adults. In community-dwelling older women, those with at least weekly urgency incontinence had a higher rate of falls than those without, with an age-adjusted odds ratio (OR) of 1.46 (95%CI 1.32 – 1.61) [12]. In community dwelling men age over the age of 70, those with both storage and voiding symptoms had a higher rate of falls than those without [13]. A systematic review of the association between LUTS and falls, injuries, and fractures in men concluded that both UI and LUTS are associated with falls in older men, with evidence that urgency, nocturia and frequency were consistently associated with falls, but only frequency was associated with fractures [14].

Despite this well-described association, potential underlying causes remain unexplained and poorly explored [15]. It has been proposed that people with LUTS may rush to the toilet and trip [16, 17], or from being incontinent and then slipping in the resultant pool of urine [18]. The majority of falls in older adults with LUTS do not occur when getting to a toilet [19]. In people with Parkinson's Disease and LUTS only 14% of falls occurred when getting to a toilet [20].

When experiencing a strong desire to void (SDV), continent middle-aged women will slow their gait, not accelerate, and their step length decreases with an increase in gait variability [21]. A study of continent and incontinent women aged 65 years and over found that SDV influenced gait parameters in both groups, with shorter stride length and increased stance time when experiencing SDV, and that the incontinent group had a slower self-selected gait speed at baseline [22].

When two cognitive tasks are performed simultaneously the speed or quality of performance of one or both tasks is reduced; a concept known as dual-tasking or diverted attention [23]. Dual tasking is associated with changes in gait and increased falls risk in older people.

These changes in gait, such as reduced speed and stride length, and changes associated with an increased falls risk such as increased forward lean, have been demonstrated when secondary cognitive tasks are combined with walking [24-27]. The impact of diverted attention on gait is greater in older than in younger adults [28].

We hypothesised that the sensation of urinary urgency acts as a source of diverted attention in older adults with overactive bladder (OAB), and that this, at least in part, explains the observed association between falls and LUTS in older people.

Methods

Design

This was a within-subject repeated measure design. Using 3D Instrumented Gait Analysis (3D IGA), temporal-spatial and kinematic gait parameters were recorded during walking under three conditions, *undistracted*, *distracted*, and when experiencing *urgency*.

Recruitment and Ethics

Participants were recruited from a specialist continence clinic, by advertising in the local press, and by approaching local seniors' associations. Men and women were included if they were aged 65 or over, and had OAB-wet, defined as per the ICS definition of symptomatic urinary urgency [29, 30], with a daytime frequency of 8 or more, and urgency incontinence at least weekly. Exclusion criteria were cognitive impairment, defined as a Montreal Cognitive Assessment Score (MoCA) [31] of less than 26, executive dysfunction, defined as more than one error in the executive function parts of the MoCA (backward digit span, trail-marking test, word similarities, and word list generation) [32], pharmacological treatment of OAB with either anticholinergic or beta-adrenergic medication, the inability to walk 30 metres independently and without aids, the use of a urinary catheter, or dialysis with anuria, a diagnosis of neurological disease that may affect gait, such as Parkinson's, previous stroke or multiple sclerosis, or sensory impairment such as visual or hearing loss sufficient to interfere with the conduct of the study.

The study was approved by the local Heath Research Ethics Committee, PRO00054370.

Instrumentation

Gait was assessed with 3D IGA. This technique uses multiple cameras to record the positions of small reflective markers attached to the skin or clothing over bony prominences on the body [33]. Based on the findings of a pilot of this experimental method in older women experiencing urgency [34], markers were placed on the feet between the 2nd and 3rd metatarsal heads and posterior aspect of the calcaneus bilaterally, and on C7 posteriorly and the sternal notch anteriorly to measure movement of the trunk. Computer software (Visual 3D Professional, C-Motion, Inc., Germantown, MD, USA) allows for processing of these data and produces a three-dimensional image of the person moving. From this, highly accurate measurements of the position of the body in time and space can be taken and converted to temporal-spatial and kinematic measures. The optical systems were calibrated at the beginning of each session of data collection and the markers were placed by an experienced and expert gait analyst (JL) in accordance with the gait laboratory's standard procedures.

Participants walked the length gait lab thrice wearing their normal footwear and the final three gait cycles (six steps) were analysed. This was to allow the participants to get to a steady, self-selected speed, and to ensure sufficient gait cycles were available in case of camera or other data capture failure. The participants were not told which cycle was used for analysis to maintain data integrity.

Temporal-spatial gait data

For each step, the point of heel strike was identified and the position of the midfoot at this time marked. From this, velocity, cadence, stride length, and step width were calculated for each step and the mean value of the three gait cycles recorded.

Kinematic data

Trunk lean was quantified by measuring the angle subtended the C7 and sternal notch markers, with the mean and range recorded. Foot-floor angle, defined as the angle subtended by the calcaneal and metatarsal marker at the point of heel strike, was also recorded. These were selected *a priori* to assess front-to-back lean, a measure associated with increased falls risk [35], and as a measure of a "flat-footed" or shuffling gait. A pilot study by our group found that more detailed kinematic data of leg motion was highly variable between individuals and did not provide useful data for analysis [34].

Study Procedure

Following informed consent, participants underwent multichannel subtracted cystometry according to standard ICS-approved protocol [36]. This was interpreted by an independent clinician and categorised as to the presence or absence of detrusor overactivity (DO) to allow a subgroup analysis and investigate the influence of urgency due to DO on any gait effects. Those who declined to have this test were not excluded from gait analysis.

Participants then attended the gait laboratory, where a research assistant completed the Berg Balance Score (BBS) [37], the Activities-specific Balance Confidence (ABC) score [38], and a LUTS severity score, the sex-specific International Consultation on Incontinence Questionnaire (ICIQ) [39, 40], and were asked about any falls, trips, or stumbles in the previous three months. The storage and incontinence subscales and associated bother scores were extracted from the sex-specific ICIQ questionnaires.

Reflective markers were applied and the participant then underwent gait analysis under three conditions; undistracted and with an empty bladder, when being distracted by the auditory n back test, and when experiencing urinary urgency. To reduce ordering effects, the order of state was determined by the blind drawing of lots at random. The study procedure was explained again and the location of the nearby toilet facilities shown.

The auditory n back test is a validated source of diverted attention [41]. To perform the auditory n back test the examiner reads a list of letters aloud at a comfortable volume. When a letter which is the same as the letter 2 prior in the sequence is read out, the participant indicates verbally that this has occurred. So, in the sequence "F, B, D, E, D, A, C…" the second D would elicit a positive response. The n back test relies on working memory and attention, and is a validated source of distraction; it is unimportant whether or not the responses are correct, as the attempt itself induces distraction [42]. Participants were asked to commence walking after the research assistant began reading the list of letters for the n back test and the n back continued until the participant had completed walking the gait lab.

To induce urgency, participants drank non-caffeinated fluids *ad libitum* at a comfortable pace until they experienced a compelling desire to void that was difficult to defer. When participants indicated that they needed to void, the examiner checked that they were unable to delay voiding any longer. If the participant did not absolutely have to go to void, they were encouraged to wait until they had an unsuppressible desire to void. At this point they undertook gait analysis, with the final walk being towards the toilet. All three walks were completed on the same visit to the gait laboratory.

Statistical Analysis

For each gait parameter, the mean velocity, cadence, stride length, and step width were compared from the bladder empty condition to urgency and to distraction using two-tailed paired samples t-tests, having demonstrated normality with the Shapiro-Wilk test. Statistical significance was pre-defined at $p<0.05$. The primary outcome measure was the change in gait velocity under each of the three conditions, as this has been shown to be influenced by urinary urge [21, 22]. Trunk lean data were not normally distributed and were compared using two-tailed Wilcoxon's signed rank tests. Subgroup analysis by the presence or absence of DO was performed using a mixed ANOVA for velocity, the primary outcome measure, using the classification of DO/Non-DO as a between-subject factor, to allow the impact of DO as a proxy for true urgency rather than urge to be assessed. Analysis was performed with using SPSS v25 (IBM Corp, Armonk, NY).

Sample Size Calculation

Verghese *et al.* [43] studied gait velocity under dual-task conditions in older adults, and found a reduction from a mean of $104.7cms^{-1}$ (SD 17.42) while walking with no distraction, to $72.2cms^{-1}$ (SD 28.17) while walking under dual-task conditions. The Cohen's d for effect size of these data is 1.388. Assuming a similar change in our study population, with α=0.5 and β=0.8, and using participants as their own controls, our minimum required sample size was **10**, calculated using G*Power [44].

Given that the effect size associated with urinary urgency in the older adult population is unknown, in order to minimise our risk of type 2 error we aimed to over-recruit by at least 100%.

Results

27 participants, 22 female and 5 male, were recruited and successfully completed data collection. The mean age was 75 years (SD 5.9). 7 participants had evidence of DO, and in 14 it was absent. 6 participants (3 men, 3 women) declined to undergo multichannel cystometry. In the female participants, the mean ICIQ F-LUTS storage symptom score was 7.8 (SD 2.2) and mean bother score 20 (SD 7.3), and the incontinence score 9.2 (SD 4.3) and bother 27.9 (SD 13.2). In the male participants, the equivalent mean scores were 7.2 (SD 1.2), 25.6 (SD 6.0), 7.0 (SD 2.1) and 24.2 (SD 4.9) respectively. The mean Berg Balance Score was 52.5 (SD 3.0) and Activities-specific Balance Confidence Score 83.2% (SD 16.4). No participants reported any slips, trips, or falls in the three months prior to recruitment. These results are summarised in Table 7.1.

Adverse events

There were no trips or falls during gait analysis and no episodes of incontinence. No participant developed a symptomatic urinary tract infection following cystometry. All participants tolerated fluid loading well without episodes of nausea or vomiting.

Gait Analysis

Temporal-spatial Data

Self selected gait velocity was reduced from 1.1ms^{-1} at baseline to 1.0ms^{-1} when experiencing urgency, and 0.8 ms^{-1} when distracted. The change from baseline to both states was statistically significant (p=0.008 and p<0.001). Likewise, stride length was reduced, from 1.19m to 1.12m with urgency and 1.0m with distraction (p<0.001 for both comparisons). Cadence was significantly reduced by distraction (110steps/min to 94 steps/min, p<0.001) but not by urgency. Step width was unaffected by urgency (10.8cm to 10.9cm, NS) but was increased by distraction, to 12.0cm (p=0.25). These results are summarised in Table 7.2.

Kinematic Data

One participant was too tall for kinematic data collection of trunk lean, as the C7 marker left the field of view of the camera during walking. Neither urgency nor distraction increased the range of lean, indicating no increase in front-to-back sway while walking. These data are summarised in Table 7.3.

Discussion

These demonstrate that gait, velocity and stride length, are similarly affected by both urgency and diverted attention. It is therefore likely that the sensation of urgency acts as a source of diverted attention in older adults with OAB.

Participants had moderate LUTS, based on the mean filling subscale score of 7.8/15, with moderate degree of bother. Participants' BBS and ACB scores indicated that that they were at low risk of falls [37] and were highly confident in their balance [38].

We demonstrated a *decrease* in velocity and step length with both urgency and diverted attention, which is similar to the effect observed with SDV in continent, middle-aged women [21]. These findings add further evidence to dispute the notion that urinary urgency and urgency incontinence may lead to falls by inducing people to run to the toilet [17]. The observed small decrease in foot-floor angle (FFA) with both urgency and distraction is unlikely to be clinically significant; although no normative data for FFA exist in adults, the reported standard deviation of FFA in children is 2.8° [45]. The observed C7-Sternal angle changes indicated that people leant forwards when walking with urgency. Contracting the pelvic floor induces a posterior pelvic tilt [46], and it is possible that our participants compensated for that by leaning their trunk forward, although we were unable to assess pelvic floor contraction directly.

Neither continence nor walking are completely automatic processes. Maintaining continence relies on the processing of sensory input from the urothelium and detrusor, processed in multiple areas of the brain including the periaqueductal grey matter, the frontal and prefrontal cortices, and the pons [47]. Despite being largely automatic [48], gait and balance also require highly complex integration of sensory information from the vestibular, ocular, and proprioceptive systems, being integrated in the frontal and parietal regions of the brain [49]. As such, both maintaining continence and walking without falling are tasks which require active sensory input and cognitive processing. Both have been shown to be more common in the frail [50, 51], the cognitively impaired [52, 53], and in those with cerebral white matter disease [54, 55].

Diverted attention induces deleterious gait changes in older people [56]. How diverted attention causes decline in simultaneous tasks is debated in the literature. Briefly, there are three main models; *capacity sharing*, which suggests the brain has a finite capacity for global function, and if simultaneous tasks exceed this threshold, performance declines, *bottleneck (or task-switching)*, which suggests that individual brain areas can only perform one function at a time, so if the competing tasks require the same pathway, a bottleneck occurs, slowing processing and *cross-talk model*, which suggests that simultaneous tasks are more difficult if they both require similar sensory input [23]. In all these models, prioritisation occurs, in that a subconscious decision is made to devote greater cognitive resource to one task over another. In this study, none of the participants experienced incontinence, suggesting that our participants prioritised their bladder control over gait, hence the deterioration in gait parameters.

It is always challenging to differentiate between *urgency*, the sudden compelling desire to void that is difficult to defer, and *urge*, the physiological sensation of a full bladder. All our participants had a diagnosis of OAB with urgency and urgency incontinence, but we made no attempt to quantify the desire to void with a visual analogue scale (VAS) or similar tool such as the Urgency Sensation Scale [57], as we explained clearly that the participant should delay voiding until they could absolutely not delay further, which would by definition correspond to a 4 on the USS or a 10 on a VAS, and that adding a further test between urgency and walking may have increased the risk of UUI during the study.

We used multi-channel pressure subtracted cystometry to classify our participants into DO/non-DO, as the finding of DO would increase our confidence that pathological urgency was being reported. However, the presence or absence of DO on cystometry had no effect on the results, suggesting that either our participants were experiencing true urgency, or that any SDV in older people with OAB acts as a source of diverted attention, whether it be a strong sensation of urinary urge or pathological urgency.

Despite calls [58], no intervention trial has been performed to investigate whether treating OAB reduces the risk of falls. Possible interventions include pharmacological management of OAB or a potential for dual task training, which has been shown to improve gait under conditions of diverted attention [59]. This may not only reduce the risk of falls but also allow control of OAB symptoms.

Strengths and Limitations

This is the first study to use 3D-IGA to record temporal-spatial and kinematic gait data from older people with OAB and compare gait under the conditions of urgency and distraction. 3D capture technology allows highly accurate measurements of gait and joint position, and therefore gait velocity. We averaged the final 3 gait cycles of the walk for analysis, We were therefore unable to assess gait variability, which has been previously shown to increase with urinary urge [21] and diverted attention [28]. The study is limited by its small sample size, although we over-recruited based on the sample size calculation, and the small number of participants with demonstrable DO on cystometry, limiting the confidence in the conclusions from the subgroup analysis by presence or absence of DO.

Conclusion

These findings support the hypothesis that urgency acts as a source of diverted attention in older people with OAB, leading to changes in gait. This may explain the known association between falls and LUTS in older adults.

Table 7.1: Demographic Data

n=27, 22 female, 5 male

7 DO on Urodynamics (all female), 14 no DO, 6 declined urodynamics (3 male, 3 female)

	Mean	SD	Range
Age	75	5.9	65 – 87
Montreal Cognitive Assessment Score	27.6	1.4	26 – 30
Berg Balance Score	52.5	3.0	46 – 56
Activities-specific Balance Confidence Score	83.2	16.4	46 – 99
ICIQ F-LUTS Storage Score	6.76	2.21	2 – 11
ICIQ F-LUTS Storage Score Bother	20.1	7.27	3 – 28
ICIQ F-LUTS Incontinence Score	9.2	4.32	3 – 18
ICIQ F-LUTS Incontinence Score Bother	27.9	13.2	4 – 50
ICIQ M-LUTS Storage Score	7.2	1.3	6 – 9
ICIQ M-LUTS Storage Score Bother	25.6	6.07	17 – 33
ICIQ M-LUTS Incontinence Score	7	2.12	4 – 9
ICIQ M-LUTS Incontinence Score Bother	24.2	4.87	19 – 31

ICIQ F-LUTS/M-LUTS: International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Female/Male

Table 7.2: Temporal Spatial Gait Analysis

Gait Parameters (n=27)						
	Baseline (mean(SD)) 95% CI	Urgency (mean(SD)) 95% CI	Distraction (mean(SD)) 95% CI	Baseline to Urgency Significance Mean Difference (95% CI)	Baseline to Distraction Significance Mean Difference (95% CI)	SDV to Distraction Significance Mean Difference (95% CI)
Velocity (m/s)	1.1 (0.16) 1.02 – 1.15	1.0 (0.15) 0.96 – 1.07	0.8 (0.19) 0.72 – 0.87	p=0.008 0.9 (0.02 – 0.13)	p<0.001 0.29 (0.19 – 0.4)	p<0.001 0.2 (0.15 – 0.174)
Cadence (steps/min)	110 (9.08) 106 - 113	108 (11.2) 104 - 113	94 (18.14) 87 - 101	p=0.805 1.3 (-1.7 – 4.3)	p<0.001 16 (8.0 – 23.9)	p<0.001 1.3 (-4.3 – 1.6)
Stride Length (m)	1.19 (0.16) 1.12 – 1.24	1.12 (0.13) 1.07 – 1.17	1.0 (0.13) 0.96 – 1.05	p<0.001 0.65 (0.03 – 0.99)	p<0.001 0.17 (0.13 – 0.23)	p<0.001 0.12 (0.73 – 0.16)
Step Width (cm)	10.8 (0.7) 9 – 12	10.9 (0.7) 9 – 12	12.0 (0.6) 11 – 13	p>0.99 0 (-0.9 – 1.2)	p=0.25 1.2 (0.1 – 2.3)	p=0.154 1.1 (-3 – 2.4)
Repeated-measures ANOVA with Bonferroni correction						

Table 7.3: Kinematic Gait Analysis

Kinematic Measure (n=26)				Significance		
	Baseline (mean(SD))	Urgency (mean(SD))	Distraction (mean(SD))	Baseline to Urgency	Baseline to Distraction	Urgency to Distraction
Foot Floor Angle (°)	22 (4.5)	21.5 (3.68)	19.0 (4.22)	p=0.044	p<0.001	p<0.001
C7-Sternal Angle mean (°)	34.7 (7.0)	35.8 (7.3)	35.3 (7.7)	p=0.012	p=0.23	p=0.23
C7-Sternal Angle range (°)	6.0 (2.4)	6.1 (1.6)	6.5(2.6)	p=0.82	p=0.44	p=0.92
Wilcoxon Signed-Rank Tests for pairwise comparison with Bonferroni correction						

Chapter Eight

Discussion, Synthesis, and Future Research

Summary and synthesis of the thesis

Previous epidemiological research has identified a strong association between lower urinary tract symptoms (LUTS) including urgency, incontinence, and nocturia, and falls in older adults [1-5]. Little attention has been paid to the potential causes of this association [6], and despite calls in the literature, no intervention trial has been performed to assess the effect of treating LUTS on falls risk [7]. Given the high prevalence of LUTS in the general population, in particular in older people [8, 9], and the significant and potentially fatal consequences of falls in this group [10], understanding the potential causes of this association provides valuable insights into developing potential therapeutic interventions.

The overarching theme of the research for this dissertation was to assess whether the sensation of a strong desire to void (SDV) in those without overactive bladder (OAB) and urgency in those with OAB acts as a source of diverted attention, and whether that may partly explain the association between falls and LUTS in older adults. The series of studies establishes a foundation and direction for development of a program of research in this area.

In Chapter Three the impact of SDV and a distracting task on two simple tests of cognition, the Trail Making B (TMT-B) test and Simple Reaction Time (SRT), in young, healthy volunteers without LUTS was examined. Under controlled conditions, we demonstrated that SDV caused an increase in reaction time that was both statistically significant and was large enough to have real-world impact, being greater than that induced by being over the drink-drive limit. This change was smaller but similar to the change induced by a distracting cognitive task, suggesting that the sensation of SDV was acting as a source of diverted attention.

Chapter Four describes an essentially identical experiment in older adults without LUTS. Akin to the younger cohort, the sensation of SDV generated an increase in SRT, again similar to but smaller than that induced by distraction, and was slightly larger than the effect seen in the younger group.

The findings from Chapters Three and Four demonstrate that, even in those without OAB, the sensation of SDV induces measurable deterioration in cognitive performance, specifically SRT. These results are concordant with previous research assessing the impact of SDV on cognitive function in healthy volunteers Lewis *et al.* found that, in a small sample of young adults without LUTS, SDV led to a decline in performance of tests of attention and working memory [11]. Similarly, Tuk *et al.* demonstrated similar results in a cohort of young adults using SDV as a model of inhibition, finding that SDV resulted in increased impulsive behaviour and decreased performance on the Stroop colour naming task [12].

SRT has been used as a diagnostic test for "senility" [13], shown to correlate with the Addenbrooke Cognitive Examination in healthy older people [14], and with a test of general mental ability, the Alice Heim 4, in middle–aged people [15], as well as with increased mortality in a population-based cohort study [16]. In older adults, the presence of white matter hyperintensities (WMH) on brain imaging is associated with impaired reaction time in the absence of dementia [17], and impairment more complex measures of reaction time, such as choice stepping reaction time (CSRT), in which people step onto one of four lights as quickly as possible after it illuminates, is associated with increased falls risk, with those classified as "fallers" having a higher CRST (1322ms) than "non-fallers" (1168ms) [18].

This thesis is the first work which directly compares the cognitive impact of SDV to a validated source of diverted attention, to assess the impact of SDV on reaction time, and the first to provide evidence that SDV acts as a source of diverted attention in young and old adults.

Why, then, does this effect not increase the risk of falls in those without LUTS? Firstly, it may, but given that those without LUTS are used as the comparator group when calculating the effect of LUTS on falls risk this will not be apparent. It may be that there is an increased risk of falls in people without LUTS when they have SDV, however the vast majority of the time people do not get to the point of SDV that we induced, as they will void well before reaching the state induced in our participants. Secondly, as discussed in Chapter Two, there is evidence that the suppression of urge requires greater cerebral activity and therefore cognitive input in older people and those with OAB [19, 20]. It is therefore conceivable that in those without OAB, the cognitive demands of maintaining continence occur only when experiencing the relatively unusual state of a very strong desire to void. Finally, older adults with OAB are more likely to have cerebral white matter hyperintensities on MRI [21], take more medication [22, 23], have more comorbidities [24], and are more likely to be frail [25]. They could therefore be less able to compensate for the cognitive effects of urgency or SDV, and therefore have a demonstrable increase in falls risk.

Chapter Five compared the cognitive performance of two groups of older adults with and without OAB. In this study we used the same cognitive tests and in Chapters Three and Four, but this time measured performance at baseline; undistracted and with an empty bladder. We demonstrated that, despite being similar in terms of age, Charlson Comorbidity Index, number of coexistent medications and anticholinergic cognitive burden score, those with OAB had significantly worse performance on the TMT-B, a measure of executive function, predominantly cognitive flexibility [26]. This is concordant with previous work which demonstrates age-related changes to the structure of the brain are associated with LUTS [19, 27, 28], and evidence that impaired executive function is associated with mixed incontinence [29]. The demonstration of impaired executive function on a simple desktop test may be clinically relevant as successful ambulation – walking without falling – and gait speed are dependent on executive function [30]. We can therefore hypothesise that part of the explanation for the association between falls and LUTS is from the common cause of impairment in executive function, which may in turn be due to the accumulation of WMH in the brain, other pathological changes to the brain, or the changes associated with ageing; those with a greater WMH burden being more likely to develop gait impairment, falls, LUTS and cognitive impairment [21].

The results presented in Chapter Five are in agreement with those of by Lussier *et al.* who demonstrated that, in a group of women aged 60 years and older, those with mixed incontinence had worse performance on a battery of tests of executive function compared to those with stress incontinence or who were continent [29]. However, Morris *et al.*, when comparing women aged 60 years and older with and without OAB, found no difference in the performance on the Stroop colour dot test, maze tracing spend, and the Wisconsin card-sorting test, but did demonstrate higher attentional demand, which may fit with the concept of urgency as a source of diverted attention [31].

From a clinical perspective, these results suggest that the finding of impaired executive function should prompt active case finding for LUTS and the offer of investigation and treatment. From a research standpoint, prophylactic intervention, such as bladder health education [32], may be beneficial in preventing the development of LUTS in those with executive dysfunction. This is discussed further below.

Chapter Seven describes a study to analyse the impact of urinary urgency on temporal-spatial gait parameters, specifically, gait velocity, stride length, and cadence, and to compare those changes to the changes caused by distraction in older people with OAB. Both urgency and distraction induced reductions in gait speed and stride length by approximately 10% and 6% respectively. These results are informative as reduced gait speed is associated with an increased risk of falls [33-37], although some authors have suggested that reduced gait speed is an adaptive response to perceived falls risk and a compensation for that risk [38]. The magnitude of reduction observed in this study, of approximately $10cms^{-1}$, confers a relative risk increase for falling of around 7% [37]. Reduced stride length has been also been suggested to be a protective adaptation to falls risk, with older women who are highly concerned about falling having shorter strides [39]. Walking under dual-task conditions has been repeatedly shown to affect gait [40-45]. These findings support the hypothesis that, in older adults with OAB, urgency acts as a source of diverted attention, leading to changes in gait. This is the first study to demonstrate gait changes with both urgency and a validated source of diverted attention. Here we demonstrated that both urgency and distraction induced changes in gait, with both states causing participants to slow down and take shorter strides, a finding similar to that observed in continent, middle-aged women [46].

This was the first trial to use 3D instrumented gait analysis (3D-IGA) during urinary urgency, allowing analysis of kinematic changes to gait. Analysis of the kinematic data suggested that the sensation of urgency caused a small but detectable increase in forward lean, a change not induced by distraction, suggesting that this is likely not a not a result of cognitive influence, but may be a physical adaptation. Although prior research has identified that ankle dorsiflexion increases the strength of a voluntary pelvic floor contraction [47], and contraction of the pelvic floor induces a posterior pelvic tilt [48], there are no data analysing the dynamic motion of the trunk when walking with a contracted pelvic floor. Intuitively, it would seem that contracting one's pelvic floor may affect posture, and clinical experience suggests that when attempting to contract their pelvic floor people, women, will contract several other muscles including the gluteal and abdominal muscles. This has potential for an investigative avenue (discussed below). We also demonstrated a small but statistically significant decrease in foot-floor angle (FFA), and although this finding is likely too small to be clinically relevant – the standard deviation of FFA in children with normal gait has been reported as ±2.8° [49]; no normative data in older adults are available.

Distinguishing between urgency and urge or SDV in an experimental model is always challenging. Participants in this study underwent urodynamics to allow an assessment of the influence of detrusor overactivity (DO) on the effect of urgency on gait – although small numbers of our participants had DO, there was no appreciable impact on the results.

Synthesis and updating the conceptual framework

How, then, do these results alter the conceptual framework of links between LUTS and falls outlined in our original diagram (Figure 8.1)? Firstly, these results provide further evidence that people experiencing urgency in an experimental setting do not rush to get to the toilet; indeed they slow down, taking shorter steps with a reduced gait speed. It is conceivable that in a "real world" setting people experiencing SDV or urgency do increase their gait, but this has not been examined, and these results provide greater weight to argument that that people with OAB are running to the toilet as an explanation for the association between LUTS and falls should be removed from the collective consciousness and from the literature. Secondly, they suggest that older adults with OAB exhibit impaired executive function, which may well have a bidirectional relationship with both falls and OAB. Thirdly, we have demonstrated an increase in reaction time when experiencing SDV, which may reduce an individual's ability to compensate for instability and prevent a stumble turning into a fall [50], and finally, they provide support for the hypothesis that both urinary urge and urgency act as a source of diverted attention, and in particular that in older adults with OAB this effect is sufficiently large to induce gait changes which are associated with an increased risk of falls.

The theoretical framework proposed in Chapter Two can be modified in the light of these results. We have generated further evidence that people experiencing urgency or SDV do not rush, and this potential link can now be removed from the proposed framework. Impaired executive function emerges as a potential risk factor of both falls and LUTS, allowing a new connection to be added. There is good evidence that urgency is acting as a source of diverted attention, inducing both gait changes and an increase in reaction time, both of which contribute to falls risk. This adds a new link between LUTS and falls. These changes allow an updated conceptual framework to be produced (Figure 8.2).

Future Direction and Further Research

Knowledge Translation

Although the association between falls and LUTS is well established [4, 5, 51], there is a significant knowledge to practice gap. Although urinary incontinence is included in some falls assessment tools, including the Johns Hopkins Fall Risk Assessment Tool [52], and the National Institute of Clinical Excellence in the UK recommends assessment of LUTS in the prevention of falls [53], many commonly used falls assessment tools do not involve an assessment of continence status, including STRATIFY [54] and the Morse Fall Scale [55]. Furthermore, despite guideline recommendations, rates of assessment of continence following a fall are low [56]. Advancing the understanding of the potential links between falls and LUTS in older adults can feed into knowledge translation.

Investigative Avenues

There are a number of potential future avenues of investigation arising from this work. They include further investigative research to assess the impact of urgency or SDV in a real world setting on gait, influence of SDV and/or voluntary pelvic floor contraction on gait in younger people, assessing the impact of urgency on cognitive function in older and younger adults with OAB, studies using functional brain imaging, and intervention trials to reduce falls risk in older people with LUTS.

The results presented here are further lab-based evidence that SDV and urgency lead to a decrease in gait speed, but the artificial environment of the gait lab may be a factor affecting this. Real world data using body-worn accelerometers to record gait speed coupled with bladder diaries to record bladder sensations, be they SDV in healthy volunteers or urgency in those with

OAB, or recording the gait speed of people entering and leaving public washrooms would be interesting.

To date, no intervention trial has demonstrated that treating OAB in older adults reduces the risk of falls. Intervention trials to reduce falls risk are challenging – a "recurrent faller" will experience two or three falls a year, and therefore a trial using falls as a primary outcome measure will require either large numbers or several years of follow up. The trials included in the Cochrane review of falls prevention programmes included a total of 20,000 participants followed for up to three years (median 247 participants per trial) [57], and this was for multicomponent interventions. A single intervention, dual task training for those with OAB, would likely need even larger numbers to demonstrate a reduction in falls risk. However, as we have demonstrated, there are measurable gait changes induced by urgency, and these could be used as a surrogate outcome measure.

We used 3D IGA to assess gait, which has the advantage of demonstrating changes in posture, such as forward lean, and of being extremely accurate as it samples position 120 times per second. However, extracting temporal-spatial measures from the 3D IGA is a specialist and time-consuming process. A pressure sensitive mat, such as the GAITrite™ system, allows automatic processing of temporal-spatial data and requires no specific staff to utilise, but cannot assess kinematic data. Given that we have demonstrated both temporal-spatial and kinematic changes, it would be reasonable to use a pressure mat rather than a full 3D IGA in future work.

Therapeutic Avenues

Two potential therapeutic interventions could be investigated. Firstly, there are several pharmaceutical interventions that have demonstrated efficacy in OAB. Some, such as oxybutynin, have demonstrable and deleterious cognitive effects [58], and would therefore not be suitable for investigating if treating OAB ameliorates the cognitive impact of urgency. However, there is evidence that several available agents, including trospium [59], darifenacin [60], solifenacin [61] and fesoterodine [62] do not cause cognitive impairment in short-term studies. A crossover trial of gait and balance at baseline and experiencing urgency and again following drug treatment with one of the latter agents would be an appropriate investigative avenue. This has the advantage of being blinded, as a placebo could be used for the comparator arm.

Dual task physiotherapy, involving strength and balance work combined with a simultaneous distracting task, has been shown to be effective in improving gait under dual task conditions and reducing the impact of distraction on gait. Given that the evidence here presented suggests that gait when experiencing urgency is a dual-task condition, it would be reasonable to suggest that dual task physiotherapy can improve gait when experiencing urinary urgency and may also allow control of OAB symptoms. This trial could be a pre- post design, with a cohort of older adults having gait analysis with and without urgency before and after undertaking a program of dual-task physiotherapy, or as a randomised design with standard balance physiotherapy as the comparator arm.

Other areas of research include follow on some of the other findings. Firstly, although we have demonstrated an increase in reaction time in asymptomatic individuals when experiencing SDV, we have not examined this effect in older adults with OAB experiencing urgency. It seems reasonable to hypothesise that the effect would be greater in this population. Replication of the study in reaction time with older participants with established OAB would be informative.

Replication of postural changes associated with urgency/SDV and understanding of postural changes with pelvic floor contraction would also be worthy of investigation. An exploratory trial of 3D IGA with healthy volunteers who are able to voluntarily contract their pelvic floor would help to delineate this, with participants walking in the gait lab normally and while performing a continued pelvic floor contraction. Intra-vaginal devices to assess pelvic floor contraction are available and would confirm a successful pelvic floor contraction, although consent and ethical issues need addressing.

The limitations of this work also require further investigation. We did not formally assess frailty in our participants. They did not report recent falls, but this may be subject to recall bias. Prospectively and robustly collecting falls data in future studies would avoid this, but increase the time required. We recruited community-dwelling older people, and our mean gait speed in the undistracted state was $1.1ms^{-1}$, suggesting that these were not frail individuals. It may well be that the frail are more vulnerable to the distracting effects of urgency and/or SDV. It would be valuable to assess the impact of LUTS on the cognitive processing in both cognitively intact frail older adults and in those with cognitive impairment. Gait analysis in those who use walking aids may be challenging, but by using a repeated-measures design with individuals as their own controls this is possible. We did not undertake any measurement of changes in brain activity or blood flow that could further inform our understanding of changes occurring with SDV/urgency and diverted attention. Previous studies using functional brain imaging to assess brain activation during urgency, using both functional MRI and functional PET scanning [63, 64], as well as infrared assessment of cerebral blood flow [65] have been informative. It would be a worthwhile endeavour to use these imaging techniques to assess brain activation during both urgency and distraction to assess the similarities and differences in activation. These imaging techniques are technically challenging and expensive, and may not be feasible in the current funding environment.

Conclusions

This thesis has examined the effect of lower urinary tract symptoms and sensations on cognitive function in asymptomatic older and younger adults and in older adults with OAB. The consistent finding has been that a sensation of a SDV, be that physiological urge or pathological urgency, acts as a source of diverted attention leading to demonstrable and significant changes in cognitive function and gait. These results suggest a novel avenue for future intervention studies for older adults with OAB.

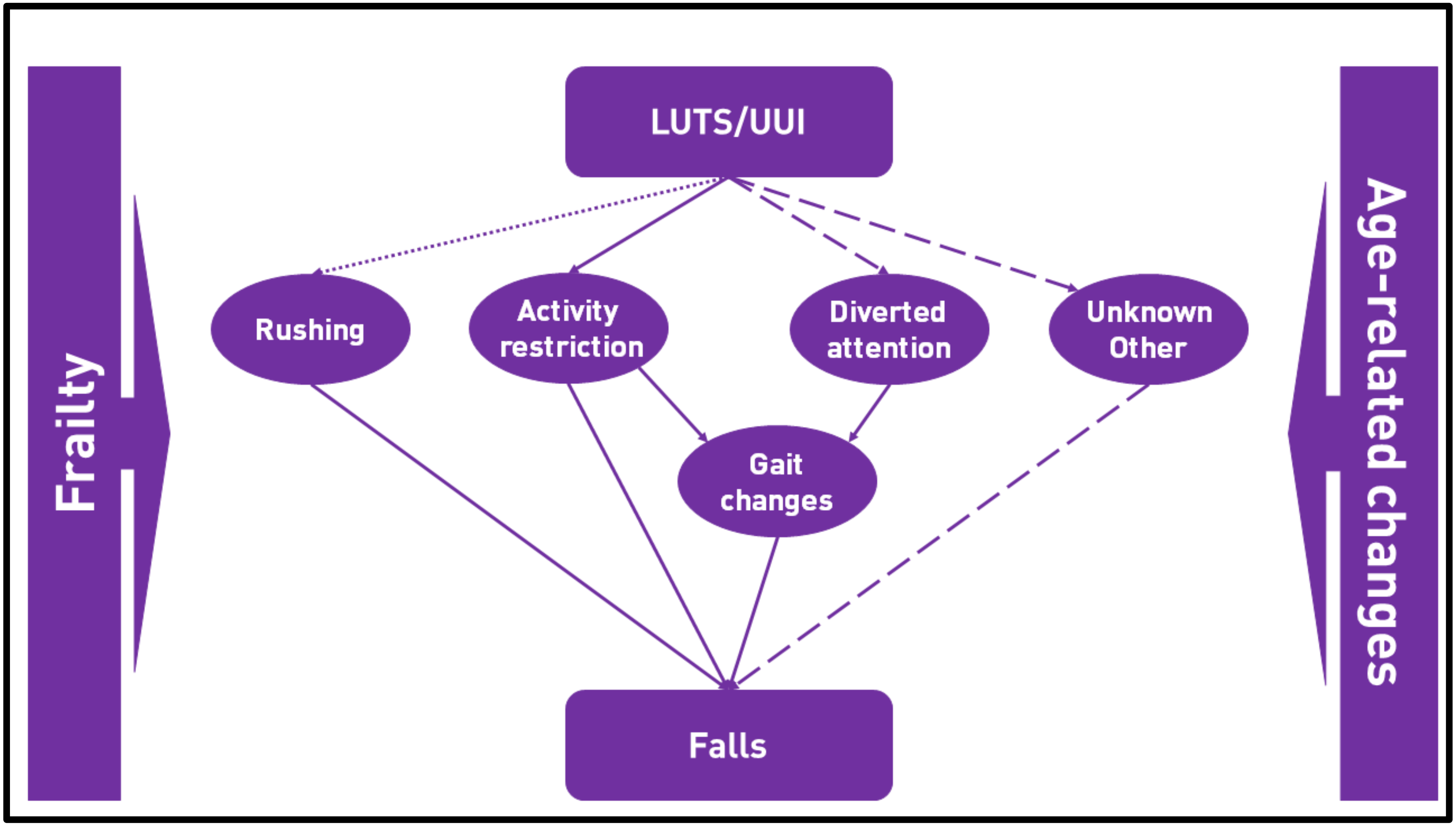

Figure 8.1: Initial conceptual framework of the links between LUTS and falls

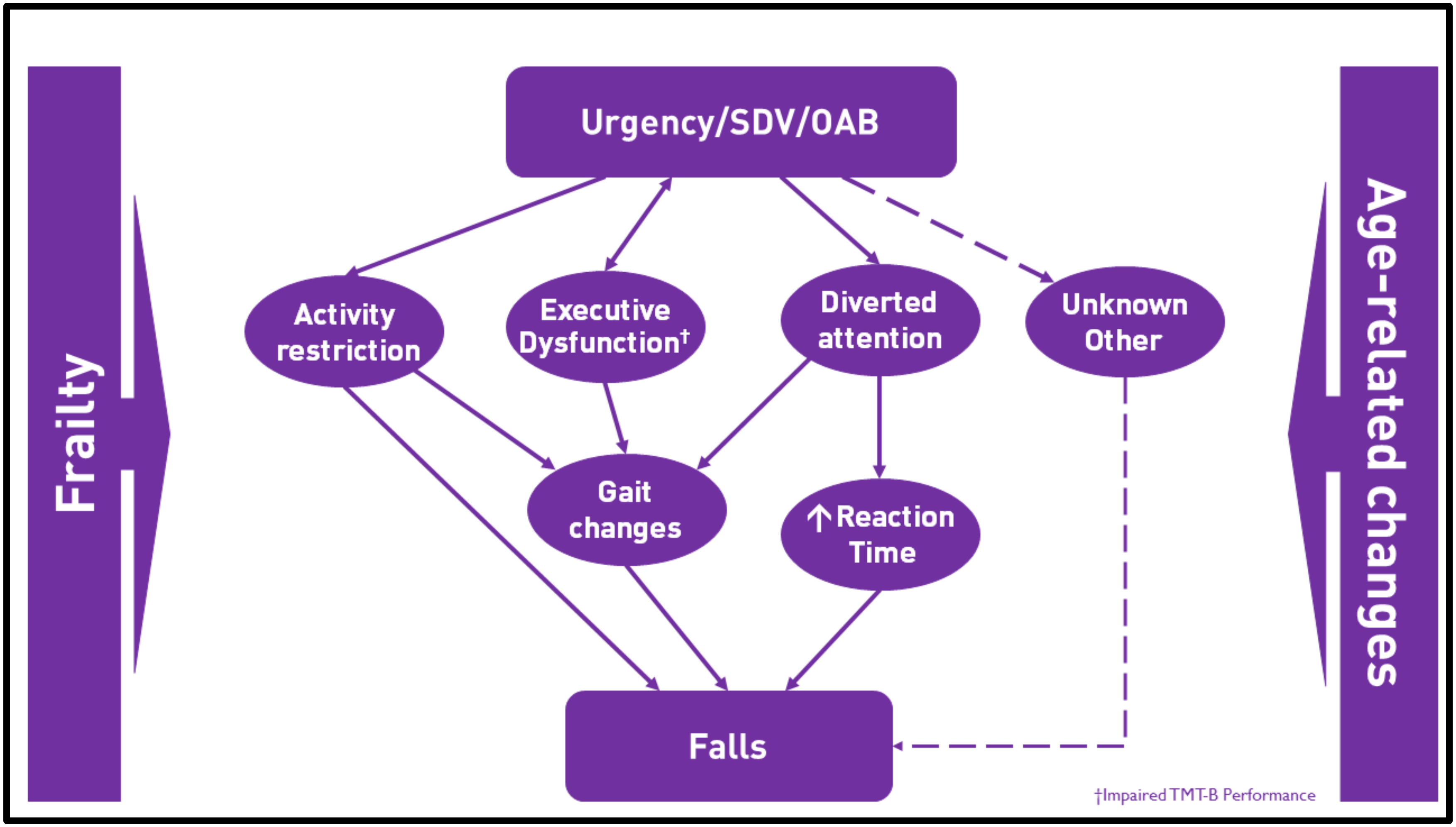

Figure 8.2: Updated conceptual framework of the links between LUTS and falls.

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Appendix I

Measures Used

The following measures are used throughout this work.

Activities-Specific Balance Confidence Scale	Self-reported measure of balance confidence when performing 16 variety of activities, each leading with the stem "how confident are you that you will not lose your balance or become unsteady when you…". Each item is rates as a percentage and the average percentage reported. A score of >80% indicates a high level of physical functioning [1]. The score has been widely validated in a range of patient groups [2]
Anticholinergic Burden Scale	A method of quantifying the total anticholinergic load of medication. Each drug is assigned a score; 0 for no anticholinergic effect, 1 for in vitro but unproven in vivo anticholinergic effect, 2 for moderate in vivo anticholinergic effect, and 3 for severe in vivo anticholinergic effect. Higher total scores have been associated with the development of cognitive impairment [3, 4].
Berg Balance Scale	Test of static and dynamic balance abilities. 14 simple balance tasks including standing from sitting, pivot transfer, standing with eyes closed, and stepping on and off a step, rated from 0 (unable) to 4 (independent). Scores range from 0 to 56, with a score of <40 being associated with increased falls risk [5]. It has excellent inter- and intra-rater reliability [6].

Bladder Self-control Assessment Questionnaire	A short (4 item) self-reported questionnaire incorporating lower urinary tract symptoms and bother score, validated for the screening for LUTS in men and women. A score of 4 or more indicates that an individual may wish to seek help for their LUTS [7]
Charlson Comorbidity Index	Categorises comorbidities of patients based on the International Classification of Diseases (ICD) diagnosis codes. Each comorbidity category has an associated weight (from 1 to 6), based on the adjusted risk of mortality or resource use, and the sum of all the weights results in a single comorbidity score for a patient. A score of zero indicates that no comorbidities were found. A higher score indicates increased mortality but has little relationship to function [8].
ICIQ-FLUTS	Self-reported questionnaire for evaluating female lower urinary tract symptoms and impact on quality of life (QoL). It covers 12 items relating to lower urinary tract symptoms with an assessment of impact of bother and has been validated in community-dwelling women [9].
ICIQ-MLUTS	Self-reported questionnaire for evaluating male lower urinary tract symptoms and impact on quality of life (QoL) in men. It covers 13 lower urinary tract symptoms and has an assessment of associated bother [10]
Montréal Cognitive Assessment	Screening test for cognitive impairment, assessing numerous cognitive domains including recall, visuospatial, execute function including an adapted TMT-B, phonemic fluency task, sustained attention, concentration, language, repetition, and

	orientation. It is validated for the detection of mild cognitive impairment in community-dwelling older adults [11].
Trail Making B Test	A paper-based test of executive function, involving visual search speed, scanning, speed of processing, and mental flexibility. Participants connect a series of circles alternating between numbers and letters with the time taken recorded [12].

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Appendix II

Chapter 3 Documentation

- Recruitment Poster
- Patient Information Letter
- Consent Form
- Ethics Approval
- Bladder control Self Assessment Questionnaire
- Trail Making B Test
- N back Test

Recruitment Poster

Volunteers needed for research project

“Is the strong desire to void a source of diverted attention in healthy volunteers?”

We are looking for healthy volunteers to participate in a study looking at how having a full bladder affects reaction time and problem solving ability.

Participants will need to attend the University of Alberta for around 3 hours and will receive a small gift to say thanks.

For more information contact:

Dr. William Gibson on 780-492-0133 or wgibson@ualberta.ca

This study has been reviewed by the University of Alberta Research Ethics Office: Reference PRO00072171

Patient Information Letter

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

Study Title: Is the strong desire to void a source of diverted attention in healthy volunteers?

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Background

- Thank you for expressing an interest in taking part in our research study.
- This study will provide valuable information about how the feeling of needing to pee affects how people are able to think and solve problems.

Purpose

- It is well known that older people who have bladder problems are more likely to fall than people who do not. We do not know why this is. We think it may be because the feeling of needing to pee is distracting and causes people to walk differently. This might increase their chance of falling over. As part of a larger program of research, this study will investigate how young, healthy people's ability to perform simple tasks is affected by having a full bladder and compare this to how they perform the same tasks when they are being distracted.

Study Procedures

- The study will involve one visit to the Division of Geriatric Medicine at the University of Alberta. We will pay for your travel and parking costs.
- During the visit we will explain the study in detail and ask you to sign a consent form.
- We will then ask you to complete a questionnaire called the Bladder Control Self-Assessment Questionnaire. This is a quick screening tool for problems with bladder control.
- We will then ask you to compete a test called the Trail Making B. This is a paper-based test of thinking speed. We will also test your reaction time by asking you to press the spacebar on a keyboard as quickly as possible after seeing an icon change colour on the screen.

- You will do these tests under three conditions;
    - When you are relaxed and undistracted
    - When you are being distracted by performing a second task at the same time
    - When you have a full bladder and feel that you need to pee
- In order to reach the point of having a full bladder we will ask you to drink water of juice at a comfortable rate, until you experience a strong desire to empty your bladder. We will want you to get your bladder as full as you can, until you feel that you need to get to a toilet soon, sufficient that if you were watching a movie you would step out of the theatre to pee.
- We expect that you will be in the department for a maximum of three hours.

Benefits

- You will not benefit directly from the study.
- We hope that the study will provide valuable information to explain the reason people with bladder trouble may fall over, and help us design a treatment to reduce this risk.
- There are no costs to you for participating in this study.
- We will pay for your travel and parking for the visit in the study. We will give you a Tim Horton's gift card for $10 to thank you for taking part. You will be eligible for the reimbursements and gift card should you choose to withdraw from the study before data collection is complete.

Risk

- There are no major risks to people taking part in the study. The feeling of having a very full bladder is uncomfortable but short-lived. Should the desire to void become too strong data collection may be stopped and you can go empty your bladder.

Voluntary Participation

- You do not have to take part in this study, it is entirely up to you to decide
- If you decide not to be involved this will not affect any health are you receive now or in the future.
- You may withdraw from the study at any time. If you withdraw before data collection is finished then none of the information collected about you will be used in the final analysis.

Confidentiality & Anonymity

- Your data and information will be kept confidential.
- Only the research team will have access to the data.

- All the information about you will be identified with a code number assigned to you, and the list of people's personal information corresponding to their code will be kept in a locked cabinet. This will be stored for 5 years and then destroyed.
- During the study we will be collecting data about you. We will do everything we can to make sure that this data is kept private. No data relating to this study that includes your name will be released outside of the researcher's office or published by the researchers. Sometimes, by law, we may have to release your information with your name so we cannot guarantee absolute privacy. However, we will make every legal effort to make sure that your information is kept private.

Further Information

The study will be used to produce academic papers and Dr Gibson's PhD thesis. If you would like to receive copies of these please ask and we would be happy to send you an electronic copy.

If you have any further questions regarding this study, please do not hesitate to contact Dr Gibson at wgibson@ualberta.ca or 780 492 0133.

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615 quoting reference PRO00072171.

Consent Form

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

CONSENT

Title of Study: Is the strong desire to void a source of diverted attention in healthy volunteers?

Principal Investigator(s): Dr William Gibson **Phone Number(s): 780 248 1969**
Study Coordinator: Rachel Morrison **Phone Number(s): 780 248 1969**

	YES	NO
Do you understand that you have been asked to be in a research study?	○	○
Have you read and received a copy of the attached Information Sheet?	○	○
Do you understand the benefits and risks involved in taking part in this research study?	○	○
Have you had an opportunity to ask questions and discuss this study?	○	○
Do you understand who will have access to the information you provide?	○	○
Do you understand that you are free to leave the study at any time, without having to give a reason and without affecting your future medical care?	○	○
Has the issue of confidentiality been explained to you?	○	○

Who explained this study to you?

I agree to take part in this study

Signature of research participant ________________________

Printed Name ________________________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Researcher ________________________

Printed Name ________________________

Ethics Approval

Approval Form

Date:	June 16, 2017
Study ID:	Pro00072171
Principal Investigator:	William Gibson
Study Title:	Is the strong desire to void a source of diverted attention in healthy volunteers?
Approval Expiry Date:	Friday, June 15, 2018

Approved Consent Form:	Approval Date 6/16/2017	Approved Document Consent form.docx

Sponsor/Funding Agency:	University of Alberta Faculty of Medicine and Dentistry	FOMD

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel . Your application, including the following, has been reviewed and approved on behalf of the committee;

- Advert (6/6/2017)
- Detailed Information Letter (6/6/2017)
- Protocol V1 (5/5/2017)
- Bladder Self Assessment Questionnaire (5/15/2017)
- Trailmaking B Test (5/15/2017)

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date, you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health Services approvals should be directed to (780) 407-6041. Enquiries regarding Covenant Health should be directed to (780) 735-2274.

Sincerely,

Anthony S. Joyce, PhD.
Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Bladder control Self Assessment Questionnaire

Is the strong desire to void a source of diverted attention in healthy volunteers?

Study ID:

Bladder Self-Control Assessment Questionnaire

Please put the number that applies to you in the boxes shown by the arrows based on the following

Not at all 0 A little 1 Moderately 2 A Great Deal 3

☐ Is it difficult to hold urine when you get the urge to go?

How much does it bother you? ☐

☐ Do you have a problem with going to the toilet too often during the day?

How much does it bother you? ☐

☐ Do you have to wake from sleep at night to pass urine?

How much does it bother you? ☐

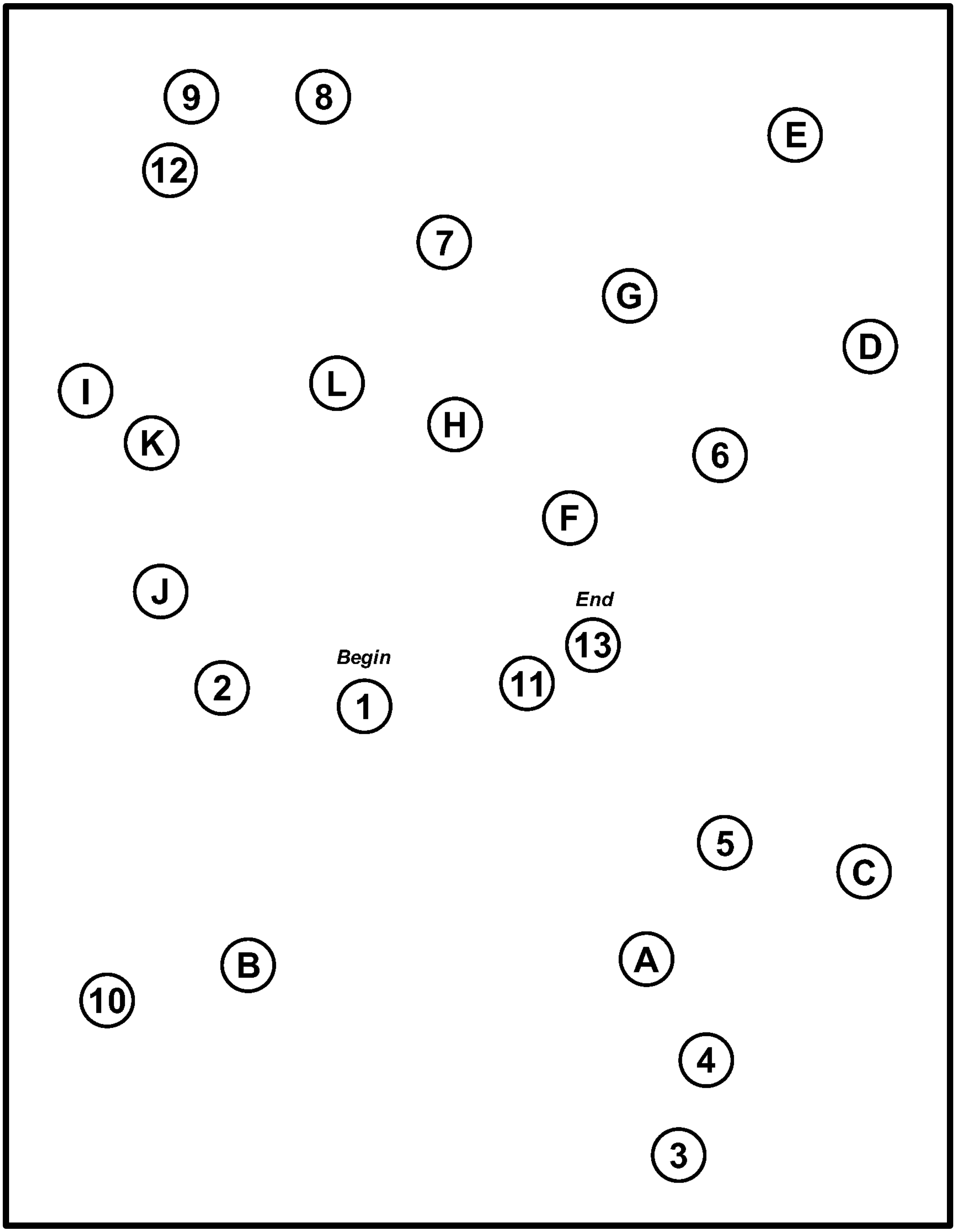
☐ Do you leak urine?

How much does it bother you? ☐

☐ Total Symptom Score

Total Bother Score ☐

Trail Making B Test Example



Auditory n back test

Read down each column in a clear voice, allowing 1 second per letter. The shaded cells indicate that this should elicit a response. Do not alter your tone for this letter.

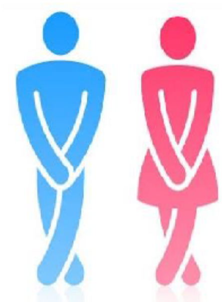
D	T	G
K	V	K
G	Q	Q
P	V	K
G	K	G
C	D	T
T	K	C
G	V	D
T	D	C
K	C	T
T	D	P
Q	C	T
V	T	P
V	T	D
P	V	V
K	T	C
T	K	K
K	C	C
G	K	P
Q	Q	D

Appendix III

Chapter 4 Documentation

- Newspaper Advert
- Patient Information Letter
- Consent Form
- Ethics Approval
- Montreal Cognitive Assessment
- Bladder Self-Control Assessment Questionnaire
- Trail Making B Test Example
- N back Test

Newspaper Advert



Are you 65+ years old?

Did you know: 1 in 4 women and 1 in 10 men suffer from bladder control problems?

We are looking for healthy participants, or those who struggle with bladder control

Study Information

Researchers at the University of Alberta are investigating how the feeling of needing to pee affects people's ability to think and solve problems, and how people with and without bladder problems perform on some simple tasks.

Study Will Require

- One visit to the University of Alberta
- Performing two tests of cognition
- The study will take about 1 hour to complete

Contact Us

Asad Makhani or Dr. Gibson
780-248-1969
makhani@ualberta.ca

This study has received Health Research Ethics Board approval (Pro00081048)
Tel: 780-492-2615

Patient Information Letter

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

Study Title: Is the strong desire to void a source of diverted attention in older adults without lower urinary tract symptoms?

Study Coordinator:

Asad Makhani
Clinical Sciences Building
University of Alberta
Edmonton, AB, T6G 2P4
makhani@ualberta.ca
780 248 1969

Supervisor:

Dr. William Gibson
Clinical Sciences Building
University of Alberta
Edmonton, AB, T6G 2P4
wgibson@ualberta.ca
780 248 1969

Background

- Thank you for expressing an interest in taking part in our research study.
- This study will provide valuable information about how the feeling of needing to pee affects how people are able to think and solve problems.

Purpose

- It is well known that older people who have bladder problems are more likely to fall than people who do not. We do not know why this is. We think it may be because the feeling of needing to pee is distracting and causes people to walk differently. This might increase their chance of falling over. As part of a larger program of research, this study will investigate how people's ability to perform simple tasks is affected by having a full bladder and compare this to how they perform the same tasks when they are being distracted.

Study Procedures

- The study will involve one visit to the Division of Geriatric Medicine at the University of Alberta. We will pay for your travel and parking costs.
- During the visit we will explain the study in detail and ask you to sign a consent form.
- We will then ask you to complete a questionnaire called the Bladder Control Self-Assessment Questionnaire. This is a quick screening tool for problems with bladder control and takes around a minute to complete.
- We will then ask you to complete a test of cognition called the Montreal Cognitive Assessment. This takes about 10 minutes and is a test of how your brain is working. If you score below a certain level on this test, we

will not be able to use you for our study. It may suggest that your memory or similar is not as good as it used to be. There are lots of causes of this and we will advise you to see your doctor to discuss these.

For the study itself we will;

- We will then ask you to compete a test called the Trail Making B. This is a paper-based test of thinking speed. We will also test your reaction time by asking you to press the spacebar on a keyboard as quickly as possible after seeing an icon change colour on the screen.
- You will do these tests under three conditions;
    - When you are relaxed and undistracted
    - When you are being distracted by performing a second task at the same time
    - When you have a full bladder and feel that you need to pee
- In order to reach the point of having a full bladder we will ask you to drink water of juice at a comfortable rate, until you experience a strong desire to empty your bladder. We will want you to get your bladder as full as you can, until you feel that you need to get to a toilet soon, sufficient that if you were watching a movie you would step out of the theatre to pee.
- We expect that you will be in the department for a maximum of three hours.

Benefits

- You will not benefit directly from the study.
- We hope that the study will provide valuable information to explain the reason people with bladder trouble may fall over, and help us design a treatment to reduce this risk.
- There are no costs to you for participating in this study.
- We will pay for your travel and parking for the visits in the study. We will give you a Tim Horton's gift card for $10 to thank you for taking part. You will receive this even if you decide to withdraw from the study after attending.

Risk

- There are no major risks to people taking part in the study. The feeling of having a very full bladder is uncomfortable but short-lived. There is a small risk that if you delay going to the bathroom too long you may have an accident. However it is completely up to you when you go to the toilet, and it is very close.

Voluntary Participation

- You do not have to take part in this study, it is entirely up to you to decide
- If you decide not to be involved this will not affect any health are you receive now or in the future.

- You may withdraw from the study at any time. If you withdraw before data collection is finished then none of the information collected about you will be used in the final analysis.

Confidentiality & Anonymity

- Your data and information will be kept confidential.
- Only the research team will have access to the data.
- All the information about you will be identified with a code number assigned to you, and the list of people's personal information corresponding to their code will be kept in a locked cabinet. This will be stored for 5 years and then destroyed.

If you have any further questions regarding this study, please do not hesitate to contact Dr Gibson at wgibson@ualberta.ca or 780 492 0133

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615 and quote project **PRO00081048**.

Consent Form

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

CONSENT

Title of Study: Is the strong desire to void a source of diverted attention in older adults without lower urinary tract symptoms?

Principal Investigator(s): Dr William Gibson **Phone Number(s): 780 248 1969**
Study Coordinator: Asad Makhani **Phone Number(s): 780 248 1969**

	YES	NO
Do you understand that you have been asked to be in a research study?	○	○
Have you read and received a copy of the attached Information Sheet?	○	○
Do you understand the benefits and risks involved in taking part in this research study?	○	○
Have you had an opportunity to ask questions and discuss this study?	○	○
Do you understand who will have access to the information you provide?	○	○
Do you understand that you are free to leave the study at any time, without having to give a reason and without affecting your future medical care?	○	○
Has the issue of confidentiality been explained to you?	○	○

Who explained this study to you?

I agree to take part in this study

Signature of research participant ____________________

Printed Name ____________________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.
Signature of Researcher ____________________

Printed Name ____________________

Ethics Approval

8/14/2019 https://remo.ualberta.ca/REMO/sd/Doc/0/KGNJL8FSOLC4J70AO1LADD9T2A/fromString.html

Approval Form

Date:	May 29, 2018
Study ID:	Pro00081048
Principal Investigator:	William Gibson
Study Title:	Is the strong desire to void a source of diverted attention in older adults without lower urinary tract symptoms?
Approval Expiry Date:	Tuesday, May 28, 2019

Approved Consent Form:

Approval Date	Approved Document
5/29/2018	Detailed information letter.pdf
5/29/2018	Consent form.pdf

Sponsor/Funding Agency: University of Alberta Faculty of Medicine and Dentistry FOMD

RSO-Managed Funding:

	Project ID	Project Title	Speed Code	Other Information
View	RES0041138	Is the strong desire to void a source of diverted attention in older adults without lower urinary tract symptoms?		

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel. Your application, including the following, has been reviewed and approved on behalf of the committee;

- Seniors Centre Advert V2 (5/18/2018)
- Telephone Script (5/11/2018)
- Protocol (4/13/2018)

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date, you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health Services approvals should be directed to (780) 407-6041. Enquiries regarding Covenant Health should be directed to (780) 735-2274.

Sincerely,

Anthony S. Joyce, PhD.
Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

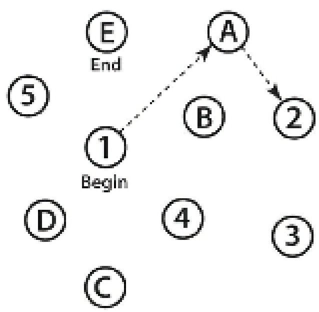
https://remo.ualberta.ca/REMO/sd/Doc/0/KGNJL8FSOLC4J70AO1LADD9T2A/fromString.html 1/2

Montreal Cognitive Assessment

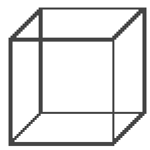
MONTREAL COGNITIVE ASSESSMENT (MOCA®)
Version 8.1 English

Name:
Education: Date of birth:
Sex: DATE:

VISUOSPATIAL / EXECUTIVE | POINTS



[ ]

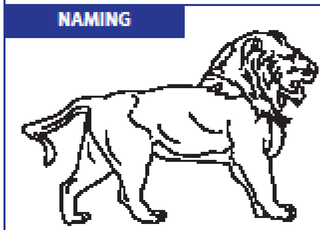


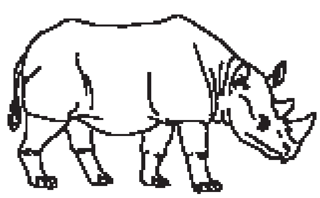
Copy cube [ ]

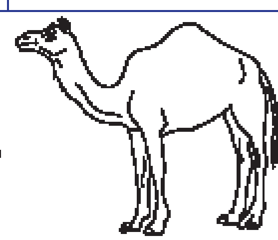
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands __/5

NAMING

 [ ]

 [ ]

 [ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1ST TRIAL					
2ND TRIAL					

NO POINTS

ATTENTION Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order. [ ] 2 1 8 5 4
Subject has to repeat them in the backward order. [ ] 7 4 2 __/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B __/1

Serial 7 subtraction starting at 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0** __/3

LANGUAGE Repeat: I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] __/2

Fluency: Name maximum number of words in one minute that begin with the letter F. [ ] _____ (N ≥ 11 words) __/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler __/2

DELAYED RECALL

(MIS)	Has to recall words	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
X3	WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]	
X2	Category cue						MIS = ____/15
X1	Multiple choice cue						

Memory Index Score (MIS) __/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City __/6

© Z. Nasreddine MD www.mocatest.org MIS: /15
(Normal ≥ 26/30) TOTAL __/30
Add 1 point if ≤ 12 yr edu
Administered by: ______________________
Training and Certification are required to ensure accuracy

Bladder Self control Assessment Questionnaire

Is the strong desire to void a source of diverted attention in older people without lower urinary tract symptoms?

Study ID:

Bladder Self-Control Assessment Questionnaire

Please put the number that applies to you in the boxes shown by the arrows based on the following

Not at all 0 A little 1 Moderately 2 A Great Deal 3

☐ Is it difficult to hold urine when you get the urge to go?

How much does it bother you? ☐

☐ Do you have a problem with going to the toilet too often during the day?

How much does it bother you? ☐

☐ Do you have to wake from sleep at night to pass urine?

How much does it bother you? ☐

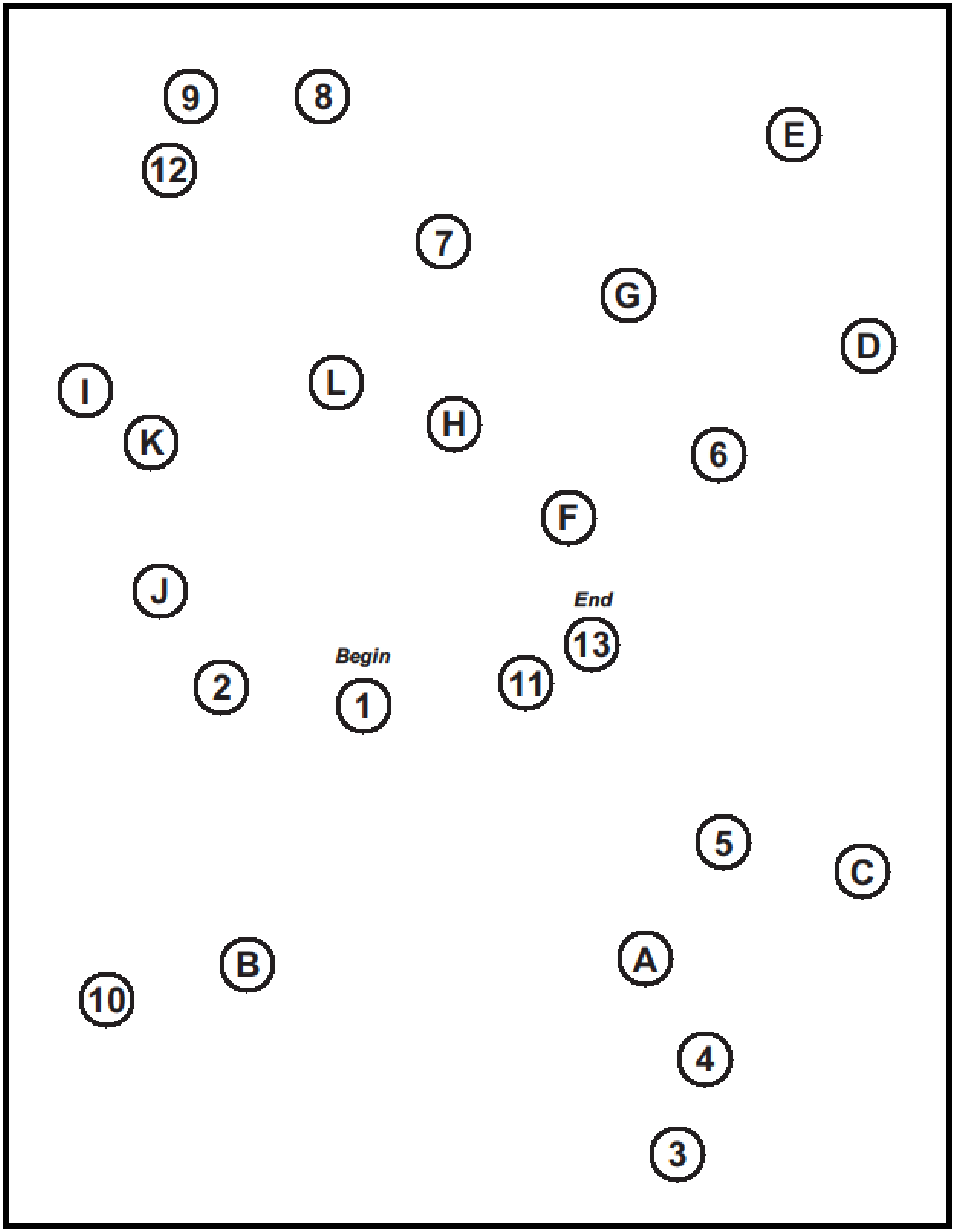
☐ Do you leak urine?

How much does it bother you? ☐

☐ Total Symptom Score

Total Bother Score ☐

Trail Making B Test Example



N back Test

Auditory n back test

Read down each column in a clear voice, allowing 1 second per letter. The shaded cells indicate that this should elicit a response. Do not alter your tone for this letter.

D	I	G
K	V	K
G	Q	Q
P	V	K
G	K	G
C	D	T
T	K	C
G	V	D
I	D	C
K	C	I
T	D	P
Q	C	T
V	T	P
V	T	D
P	V	V
K	T	C
T	K	K
K	C	C
G	K	P
Q	Q	D
B	D	P
Q	Q	Q
G	A	P
C	T	T
Q	V	V
D	D	T
C	G	G
D	D	P

Appendix IV

Chapter 5 Documentation

- Recruitment Poster
- Newspaper Advert
- Patient Information Letter (Control group)
- Patient Information Letter (OAB Group)
- Consent Form
- Ethics Approval
- Bladder Self-Control Assessment Questionnaire
- Trail Making B Test Example
- N back Test

Recruitment Poster

Are you 65+ years old and in good health?

Researchers at the University of Alberta are looking for healthy seniors to take part in research to see how the feeling of needing to pee affects people's ability to think and solve problems, and how people with and without bladder perform on some simple tasks.

If you are interested in participating in either study and would like to hear more, please contact:

Asad Makhani or Dr. William Gibson at 780-248-1969 (24 hour voicemail) or makhani@ualberta.ca in complete confidence.

These studies have received Health Research Ethics Board approval PRO00081048 and PRO00079683

For information about research ethics call 780-492-2615

Healthy seniors study
780-248-1969 or makhani@ualberta.ca

Healthy seniors study
780-248-1969 or makhani@ualberta.ca
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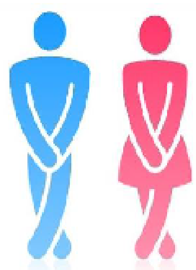
780-248-1969 or makhani@ualberta.ca

Newspaper Advert



Are you 65+ years old?

Did you know: 1 in 4 women and 1 in 10 men suffer from bladder control problems?

We are looking for <u>healthy participants</u>, or those who <u>struggle with bladder control</u>

Study Information

Researchers at the University of Alberta are investigating how the feeling of needing to pee affects people's ability to think and solve problems, and how people with and without bladder problems perform on some simple tasks.

Study Will Require

- One visit to the University of Alberta
- Performing two tests of cognition
- The study will take about 1 hour to complete

Contact Us

Asad Makhani or Dr. Gibson
780-248-1969
makhani@ualberta.ca

This study has received Health Research Ethics Board approval (Pro00081048)
Tel: 780-492-2615

Patient Information Letter (Control Group)

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

Study Title: Do older adults with Overactive Bladder demonstrate impairment in executive function compared to their peers without OAB?

Research Lead

Dr William Gibson
Clinical Sciences Building
University of Alberta
Edmonton, AB, T6G 2P4
wgibson@ualberta.ca
780 248 1969

Background

- Thank you for expressing an interest in taking part in our research study.
- This study has been funded by a grant from the Canadian Geriatrics Society, provided by Pfizer. These organisations had no part in the design of the study.

Purpose

- **Bladder problems, such as an overactive bladder (OAB) are common in the older people, with up to 50% of men and 60% of women over 70 years have symptoms of OAB. Research studies have shown that symptoms of OAB can increase the risk of falls, and that people with OAB may show changes in their brains compared to healthy people. We want to investigate the reason for this association.**
- We are interested in how people who have a bladder problem called **overactive bladder** perform on some simple cognitive tests compared to people who do not have bladder problems. We think that people with overactive bladder will do less well on these tests, which would suggest that overactive bladder may be caused by changes in the brain rather than the bladder. We hope to use this information to develop new treatments.
- **We are interested in your participation in our study because you are not diagnosed with an overactive bladder and are not taking medications for an overactive bladder.**

Study Procedures

- We will first complete a brief questionnaire called the Bladder Symptom Self-Assessment Questionnaire. This will identify if you have any bladder issues ***(this will help ensure you do not have a bladder problem)*. If the questionnaire does suggest a bladder problem, such as incontinence, then we will offer you an**

offer you an appointment at the Glenrose Hospital Continence Clinic for an assessment by a specialist, but cannot be part of the study at this time.

- Participants will then complete two tests of brain function. The first is the **trail making B test**, in which you will link a series of circles, each of which contains a number or a letter. The second is a **reaction time test**, in which you watch a screen and press the spacebar on the keyboard when an icon changes colour. We will record the time it takes you to complete these tests. We are doing these tests in two groups of people; those who have an overactive bladder, and those who do not. We will compare the test results between the two groups. Completing the two tests will take around ten to fifteen minutes.
- You may withdraw from the study at any time.

Benefits

- You will not benefit directly from the study.
- We hope that the study will provide valuable information to explain the causes of bladder problems in people of your age and help us develop new treatments.
- There are no costs to you for participating in this study.

Risk

- There are no risks to people taking part in the study. We appreciate that it can be embarrassing or awkward to discuss problems such as incontinence. We deal with bladder problems all the time and they are very common, and we will deal with you sensitively and respectfully. If you find the cognitive tests much more difficult than we would expect, which might suggest a problem with how your brain is functioning, we will suggest that you make an appointment with your doctor to discuss this. This is very unlikely unless you have noticed other problems with your memory.

Voluntary Participation

- You do not have to take part in this study, it is entirely up to you to decide.
- If you decide not to be involved this will not affect any health care you receive now or in the future.
- You may withdraw from the study at any time until we complete data collection.

Confidentiality & Anonymity

- Your data and information will be kept confidential.
- Only the research team will have access to the data.

- All the information about you will be identified with a code number assigned to you, and the list of people's personal information corresponding to their code will be kept in a locked cabinet. This will be stored for 5 years and then destroyed.
- During the study we will be collecting data about you. We will do everything we can to make sure that this data is kept private. No data relating to this study that includes your name will be released outside of the researcher's office or published by the researchers. Sometimes, by law, we may have to release your information with your name so we cannot guarantee absolute privacy. However, we will make every legal effort to make sure that your information is kept private.

If you have any further questions regarding this study, please do not hesitate to contact Dr Gibson at wgibson@ualberta.ca or 780 248 1969

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615 and reference project **Pro00079683**.

Patient Information Letter (OAB Group)

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

Study Title: Do older adults with Overactive Bladder demonstrate impairment in executive function compared to their peers without OAB?

Research Lead

Dr William Gibson
Clinical Sciences Building
University of Alberta
Edmonton, AB, T6G 2P4
wgibson@ualberta.ca
780 248 1969

Background

- Thank you for expressing an interest in taking part in our research study.
- This study has been funded by a grant from the Canadian Geriatrics Society, provided by Pfizer. These organisations had no part in the design of the study.

Purpose

- **An overactive bladder (OAB) is common in older people, with up to 50% of men and 60% of women over 70 years having symptoms of OAB. Previous research studies have shown that symptoms of OAB can increase the risk of falls, leading to injury, and that older people with OAB can show changes in how their brains work.**
- We are interested in how people like you who have a bladder problem called **overactive bladder (OAB)** perform on some simple cognitive tests compared to people who do not have bladder problems. We think that people with overactive bladder will do less well on these tests, which would suggest that overactive bladder may be caused by changes in the brain and not just the bladder. We hope to use this information to develop new treatments.
- We have asked you to participate in this study because you meet our inclusion criteria of an OAB diagnosis, have had symptoms of OAB for the last 3 months and are not currently taking medications for OAB. Taking part is completely voluntary.

Study Procedures

- **After your appointment, we will invite you to join us in a separate room, where you will complete two tests of brain function for approximately ten to fifteen minutes.** The first is the **trail making B test**, in which you will link a series of circles, each of which contains a number or a letter. The second is a **reaction time test**, in which you watch a screen and press the spacebar on the keyboard when an icon changes colour. We will record the time it takes you to complete these tests. We estimate that these tests will take around ten to fifteen minutes to complete.

- We are comparing two groups of people: one group with overactive bladder, and a group of volunteers without bladder problems. As you have been diagnosed with an overactive bladder you have been asked to participate.

Benefits

- You will not benefit directly from the study.
- There are no costs to you for participating in this study.
- We hope that the study will provide valuable information to explain the causes of bladder problems in people of your age and help us develop new treatments.

Risk

- There are no risks to people taking part in the study.

Voluntary Participation

- You do not have to take part in this study, it is entirely up to you to decide.
- If you decide not to be involved this will not affect any health care you receive now or in the future. We will continue to see you in clinic as a patient if you wish and your treatment will be unaffected. Your doctor will not be informed that you did or did not take part in the study.
- **You may withdraw from the study at any time until we complete data collection.**

Confidentiality & Anonymity

- Your data and information will be kept confidential.
- Only the research team will have access to the data.
- All the information about you will be identified with a code number assigned to you, and the list of people's personal information corresponding to their code will be kept in a locked cabinet. This will be stored for 5 years and then destroyed.
- During the study we will be collecting data about you. We will do everything we can to make sure that this data is kept private. No data relating to this study that includes your name will be released outside of the

researcher's office or published by the researchers. Sometimes, by law, we may have to release your information with your name so we cannot guarantee absolute privacy. However, we will make every legal effort to make sure that your information is kept private.

If you have any further questions regarding this study, please do not hesitate to contact Dr Gibson at wgibson@ualberta.ca or 780 492 0133

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615 and reference project **Pro00079683**.

Consent Form

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

CONSENT FORM

Title of Study: Do older adults with Overactive Bladder demonstrate impairment in executive function compared to their peers without OAB??

Principal Investigator(s): Dr William Gibson **Phone Number(s): 780 248 1969**

	YES	NO
Do you understand that you have been asked to be in a research study?	◯	◯
Have you read and received a copy of the attached Information Sheet?	◯	◯
Do you understand the benefits and risks involved in taking part in this research study?	◯	◯
Have you had an opportunity to ask questions and discuss this study?	◯	◯
Do you understand that you are free to leave the study at any time, without having to give a reason and without affecting your future medical care?	◯	◯
Has the issue of confidentiality been explained to you?	◯	◯
Do you understand who will have access to your records, including personally identifiable health information?	◯	◯

Who explained this study to you?

I agree to take part in this study

Signature of research participant ______________________

Printed Name ______________________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Researcher ______________________

Printed Name ______________________

Ethics Approval

Approval Form

Date:	May 17, 2018
Study ID:	Pro00079683
Principal Investigator:	William Gibson
Study Title:	Do older adults with Overactive Bladder demonstrate impairment in executive function compared to their peers without OAB?
Approval Expiry Date:	Thursday, May 16, 2019
Approved Consent Form:	Approval Date 5/17/2018 — Approved Document Consent form.pdf
Sponsor/Funding Agency:	University of Alberta Faculty of Medicine and Dentistry FOMD

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel. Your application, including the following, has been reviewed and approved on behalf of the committee;

- Seniors Centre Advert (5/11/2018)
- Detailed Information Sheet (5/11/2018)
- Detailed Information for Participants with OAB (5/11/2018)
- Protocol (5/11/2018)

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. Subject consent for access to identifiable health information is required for the research described in the ethics application, and appropriate procedures for such consent have been approved by the HREB Health Panel. In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (Thursday, May 16, 2019), you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health approval should be directed to (780) 407-6041. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,

Doug Hill, PEng, MBA
Associate Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Bladder Self Control Assessment Questionnaire

Is the strong desire to void a source of diverted attention in older people without lower urinary tract symptoms?

Study ID:

Bladder Self-Control Assessment Questionnaire

Please put the number that applies to you in the boxes shown by the arrows based on the following

Not at all 0 A little 1 Moderately 2 A Great Deal 3

☐ Is it difficult to hold urine when you get the urge to go?

How much does it bother you? ☐

☐ Do you have a problem with going to the toilet too often during the day?

How much does it bother you? ☐

☐ Do you have to wake from sleep at night to pass urine?

How much does it bother you? ☐

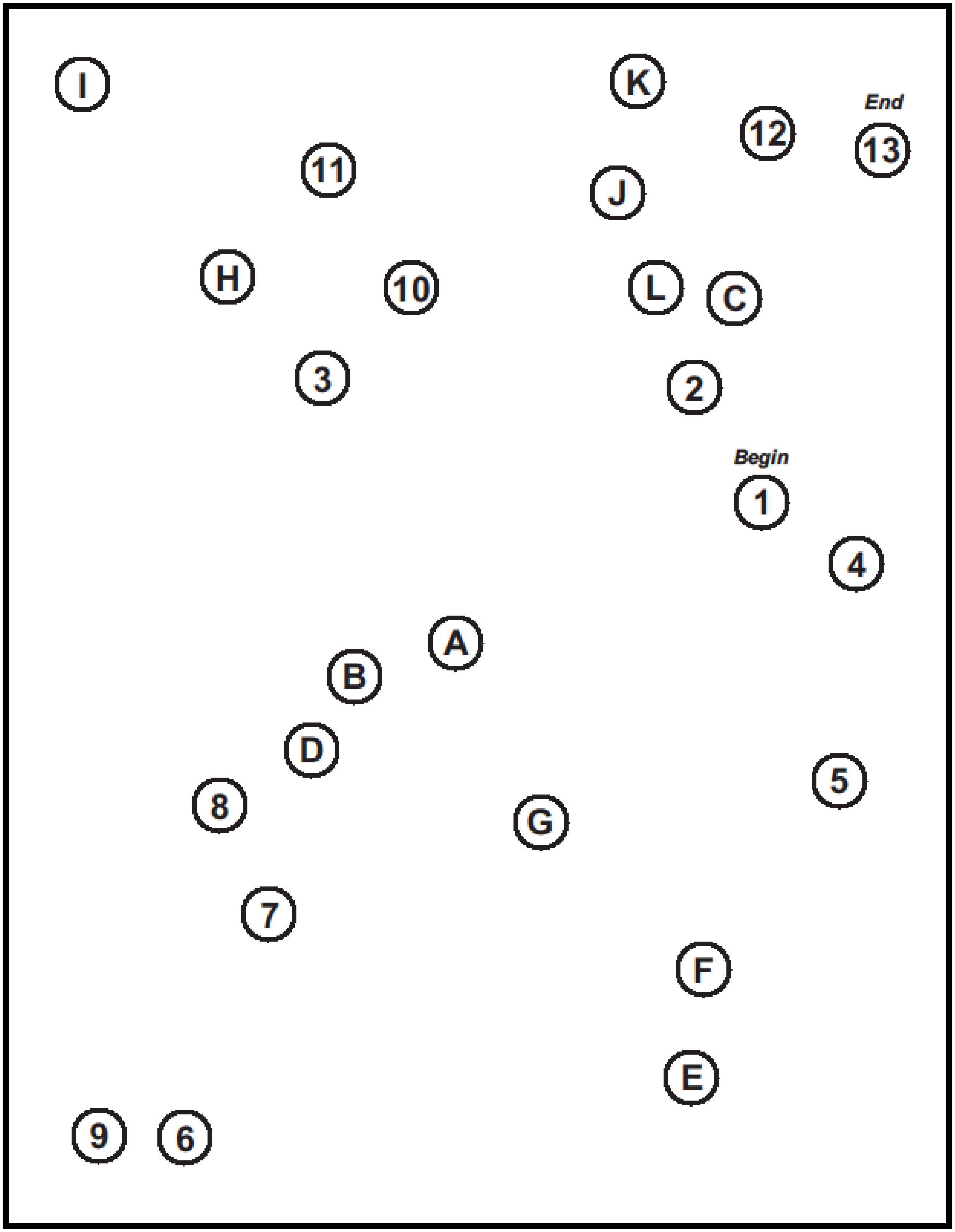
☐ Do you leak urine?

How much does it bother you? ☐

☐ Total Symptom Score

Total Bother Score ☐

Trail Making B Test Example



Auditory n back test

Read down each column in a clear voice, allowing 1 second per letter. The shaded cells indicate that this should elicit a response. Do not alter your tone for this letter.

D	I	G
K	V	K
G	Q	Q
P	V	K
G	K	G
C	D	T
T	K	C
G	V	D
I	D	C
K	C	I
T	D	P
Q	C	T
V	T	P
V	T	D
P	V	V
K	T	C
T	K	K
K	C	C
G	K	P
Q	Q	D
B	D	P
Q	Q	Q
G	A	P
C	T	T
Q	V	V
D	D	T
C	G	G
D	D	P

Appendix V

Chapter 6 Documentation

- Patient Information Letter
- Consent Form
- Ethics Approval
- Montreal Cognitive Assessment
- Kinematic Data
    - Y-axis - % of gait cycle. Red – right leg, Blue, left. Vertical line indicates foot off point for that limb.
    - Grey area indicates the lab normative data (mean ± 1SD)

Patient Information Letter

INFORMATION SHEET

A pilot study to examine the influence of urinary urgency on sway and gait in older women with overactive bladder.

Principal Investigators
Dr. Adrian Wagg, Faculty of Medicine and Dentistry, University of Alberta
Dr. Kathleen Hunter, Faculty of Nursing University of Alberta
Dr. Jo Booth, School of Health Glasgow Caledonian University, Glasgow UK

Co-Investigators
Justin Lewicke MBA B.Sc. Kin, Glenrose Rehabilitation Hospital
Vicki Buttar B.Sc. PT, Glenrose Rehabilitation Hospital

Background: Falls often have serious consequences for older people. Not only can they result in injury but the fear of falling can mean that people stop going out and may no longer be able to live their lives as they would wish. While there are many causes of falls, bladder problems or having to rush to the washroom, have been associated with an increased risk of falling. We are interested in the reasons that having to rush to empty your bladder (called urinary urgency) might lead to an increased risk of falling.

Purpose: You are being asked to take part in a research study which will examine why people who have urinary urgency are at an increased risk of falling. You are being asked because you have the bladder problem which includes urgency and, although you may not have fallen because of this, you would be able to help the researchers understand how bladder problems might affect walking patterns and perhaps make walking more unstable.

Procedures: Participation in this study involves filling in a questionnaire about your bladder problems, to allow the researchers to check that you do have urinary urgency as a symptom and then attending the Syncrude gait analysis lab for the investigation which will take approximately 2 hours; an appointment will be arranged for you. On arrival at the lab, and after introductions to the team, you will be asked to empty your bladder and, should you so wish, be given a protective pad to use in your underwear to protect against any incontinence. One of the investigators will then apply some markers to your body which allow the way you stand and walk to be recorded on camera (there will be no pictures of you recorded, only of the markers). You will then be asked to stand still for a while on the test pad whilst the position of your body (the markers) is recorded. You will be asked to do this with your eyes open and with your eyes closed on both a soft and hard surface. You will then be asked to sit on a chair. The researchers will then record you standing up from the chair, walking along a path in the lab and then sitting again.

You will then be asked to sit for a while and drink to fill your bladder. As soon as you feel an urgent need to visit the washroom, the researchers will ask you to do the standing and walking tests again. Should you be unable to complete the tests because of your need to empty your bladder then you can visit the washroom at any time.

The researchers are interested in the results of the test and the practicality of performing all of the parts of the test; they will ask you about your opinions and feelings about the testing at the end.

Possible Benefits: Although there is little direct benefit to you of taking part in this study; the researchers will be able to gain more of an insight in to the way in which bladder problems affect walking patterns and contribute to the risk of falling. This information may well, in future, help others who have fallen when rushing to the washroom and may also help prevent the problem from occurring.

Possible Risks: Although this study is fairly safe, there is the risk of accidental urine loss if there is a very urgent need to visit the washroom during the testing and you do not make it on time. The researchers will provide protective pads in case of this and to prevent accidental wetting of clothes. There will be someone in the gait analysis lab at all times to ensure that the risk of falling during the test is minimal.

Confidentiality: Personal health records relating to this study will be kept confidential. Any information collected about you during this study will not identify you by name, only by a coded number. Your name will not be disclosed outside the research clinic. Any report published as a result of this study will not identify you by name.

For this study, the study doctor may need to access your personal health records for health information such as past medical history and test results. The health information collected as part of this study will be kept confidential unless release is required by law, and will be used only for the purpose of the research study. By signing the consent form you give permission to the study staff to access any personally identifiable health information which is under the custody of other health care professionals as deemed necessary for the conduct of the research. The University of Alberta and the HREB may have access to research data to verify its accuracy

By signing the consent form you give permission for the collection, use and disclosure of your medical records. In Canada, study information is required to be kept for 5 years. Even if you withdraw from the study, the medical information which is obtained from you for study purposes will not be destroyed. You have a right to check your health records and request changes if your personal information is incorrect.

Voluntary Participation: You are free to withdraw from the research study at any time, and your continuing medical care will not be affected in any way. If the study is not undertaken or if it is discontinued at any time, the quality of your medical care will not be affected. If any knowledge gained from this or any other study becomes available which could influence your decision to continue in the study, you will be promptly informed.

Reimbursement of Expenses: Costs you incur (travel, parking) as part of the study will be reimbursed. Drinks and light refreshment will be provided as part of the study

Compensation for Injury: If you become ill or injured as a result of participating in this study, necessary medical treatment will be available at no additional cost to you. By signing this consent form you are not releasing the investigator(s), institution(s) and/or sponsor(s) from their legal and professional responsibilities.

Contact Names and Telephone Numbers:
If you have concerns about your rights as a study participant, you may contact the Research Ethics Office at (780)492-2615. This office has no affiliation with the study investigators.

Please contact any of the individuals identified below if you have any questions or concerns:

	daytime telephone:	other times:
Dr. Adrian Wagg	780-492-5338	Removed for Publication
Dr. Kathleen Hunter	780-492-8941	

Consent Form

CONSENT FORM

Part 1 (to be completed by the Principal Investigator):

Title of Project: A pilot study to examine the influence of urinary urgency on sway and gait in older women with overactive bladder

Principal Investigator(s):		Phone Number(s):
Dr. Adrian Wagg		780-
Dr. Kathleen Hunter		780-492-8941
Dr. Jo Booth		UK
Co-Investigator(s):	Contact Names:	Phone Number(s):
Justin Lewicke		
Vicki Buttar		

Part 2 (to be completed by the research subject):

	Yes	No
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to withdraw from the study at any time, without having to give a reason and without affecting your future medical care?	☐	☐
Has the issue of confidentiality been explained to you?	☐	☐
Do you understand who will have access to your records, including personally identifiable health information?	☐	☐
Do you want the investigator(s) to inform your family doctor that you are participating in this research study? If so, give his/her name ___________________	☐	☐

Who explained this study to you?

____

I agree to take part in this study: YES ☐ NO ☐

Signature of Research Subject

____

(Printed Name)

____

Date:______________________________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator or Designee ________________________________ Date __________

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE RESEARCH SUBJECT

Ethics Approval

8/19/2019 Ethics approval gait lab pilot.html

Approval Form - HIA Consent

Date:	July 11, 2011
Principal Investigator:	Adrian Wagg
Study ID:	Pro00022975
Study Title:	A pilot study to examine the influence of urinary urgency on sway and gait in older women with overactive bladder.
Approval Expiry Date:	July 9, 2012

Thank you for submitting the above study to the Health Research Ethics Board - Biomedical Panel. Your application has been reviewed and approved on behalf of the committee. The following documents are included in this approval: Study Protocol, Recruitment Letter, Consent to Release Contact Information as well as the Study Consent Form and Information Sheet.

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. Subject consent for access to identifiable health information is required for the research described in the ethics application, and appropriate procedures for such consent have been approved by the HREB - Biomedical Panel. In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (July 9, 2012), you will have to re-submit an ethics application.

The membership of the Health Research Ethics Board - Biomedical Panel complies with the membership requirements for research ethics boards as defined in Division 5 of the Food and Drug Regulations and the Tri-Council Policy Statement. The HREB - Biomedical Panel carries out its functions in a manner consistent with Good Clinical Practices.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health administrative approval, and operational approval for areas impacted by the research, should be directed to the Alberta Health Services Research Administration office, #1800 College Plaza, phone (780) 407-6041.

Sincerely,

S.K.M. Kimber, MD, FRCPC

Chair, HREB Biomedical

Note: This correspondence includes an electronic signature (validation and approval via an online system).

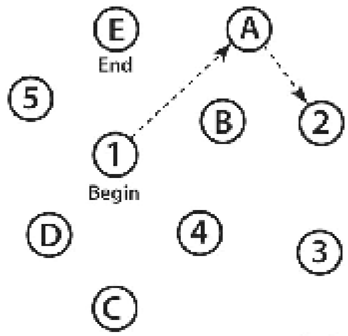
file://storeit.med.ualberta.ca/Profiles/UserProfiles/XenDesktop/billgibson/Documents/THESIS/Stuff for Appendices/Chapter 6/Ethics approval gait lab p... 1/1

Montreal Cognitive Assessment

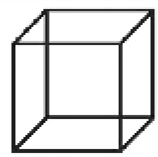
MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE



[ ]



Copy cube

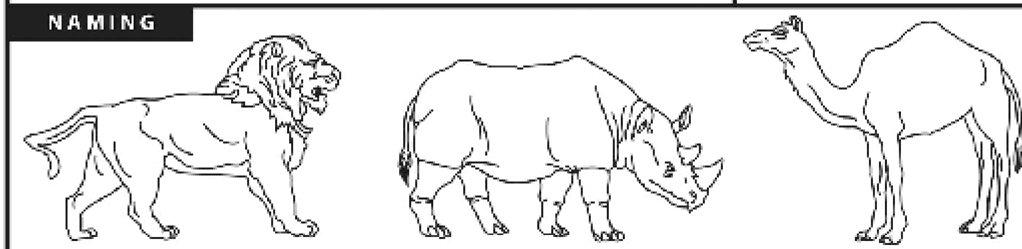
[ ]

Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING



[ ] [ ] [ ]

___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2

___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

___/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]

___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

___/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

___/2

DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

___/5

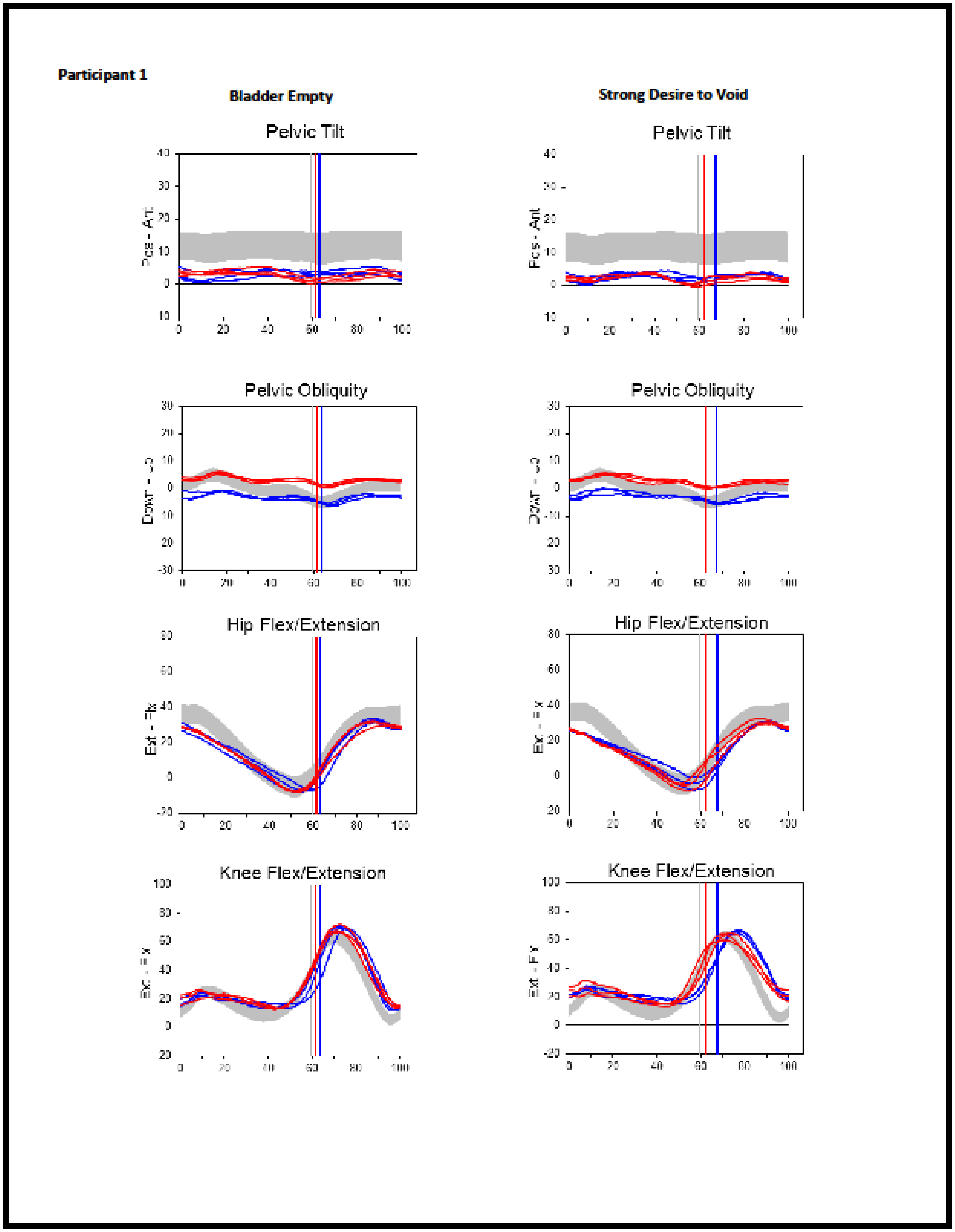
ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

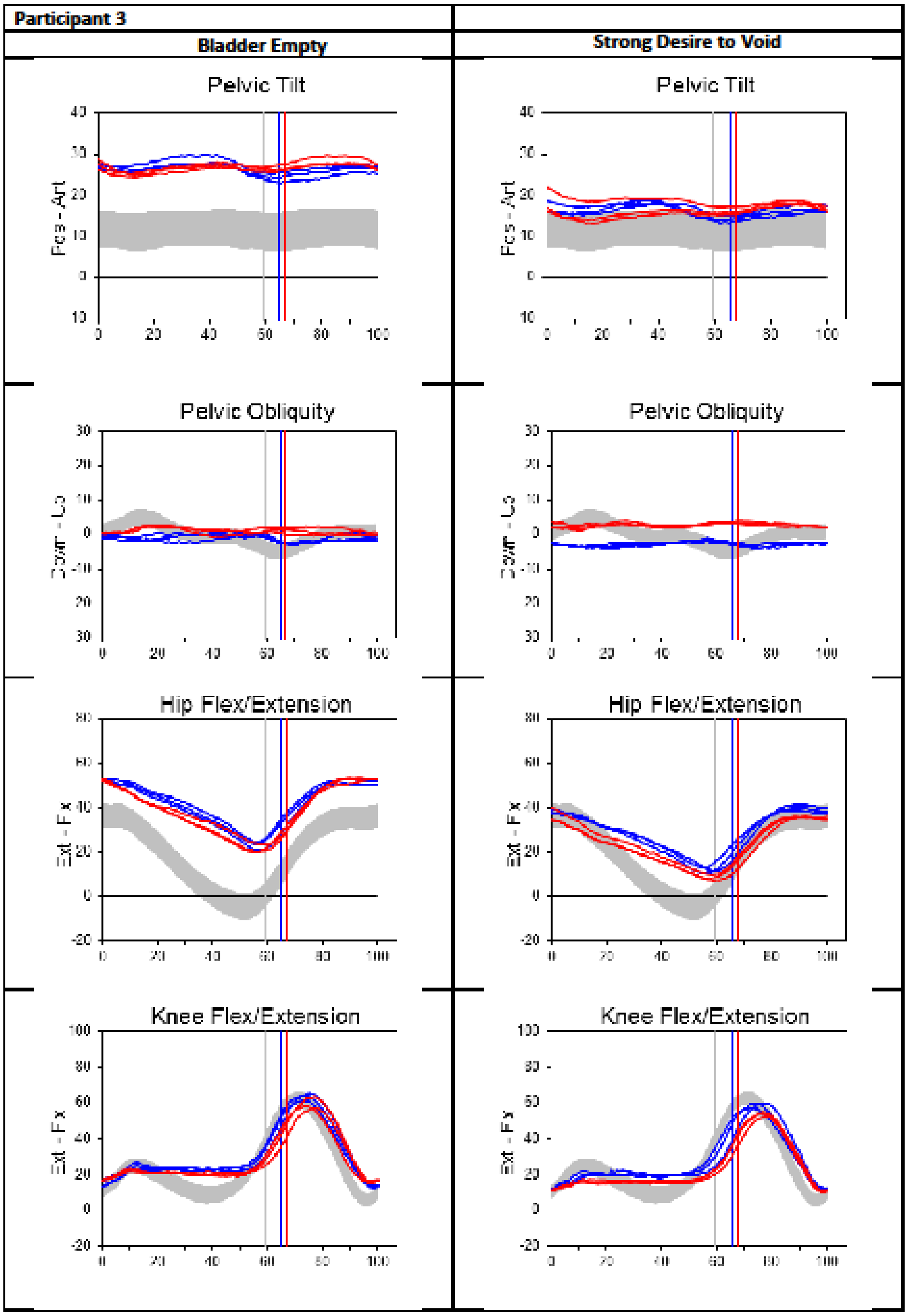
___/6

 www.mocatest.org Normal ≥ 26 / 30 TOTAL ___/30
Add 1 point if ≤ 12 yr edu

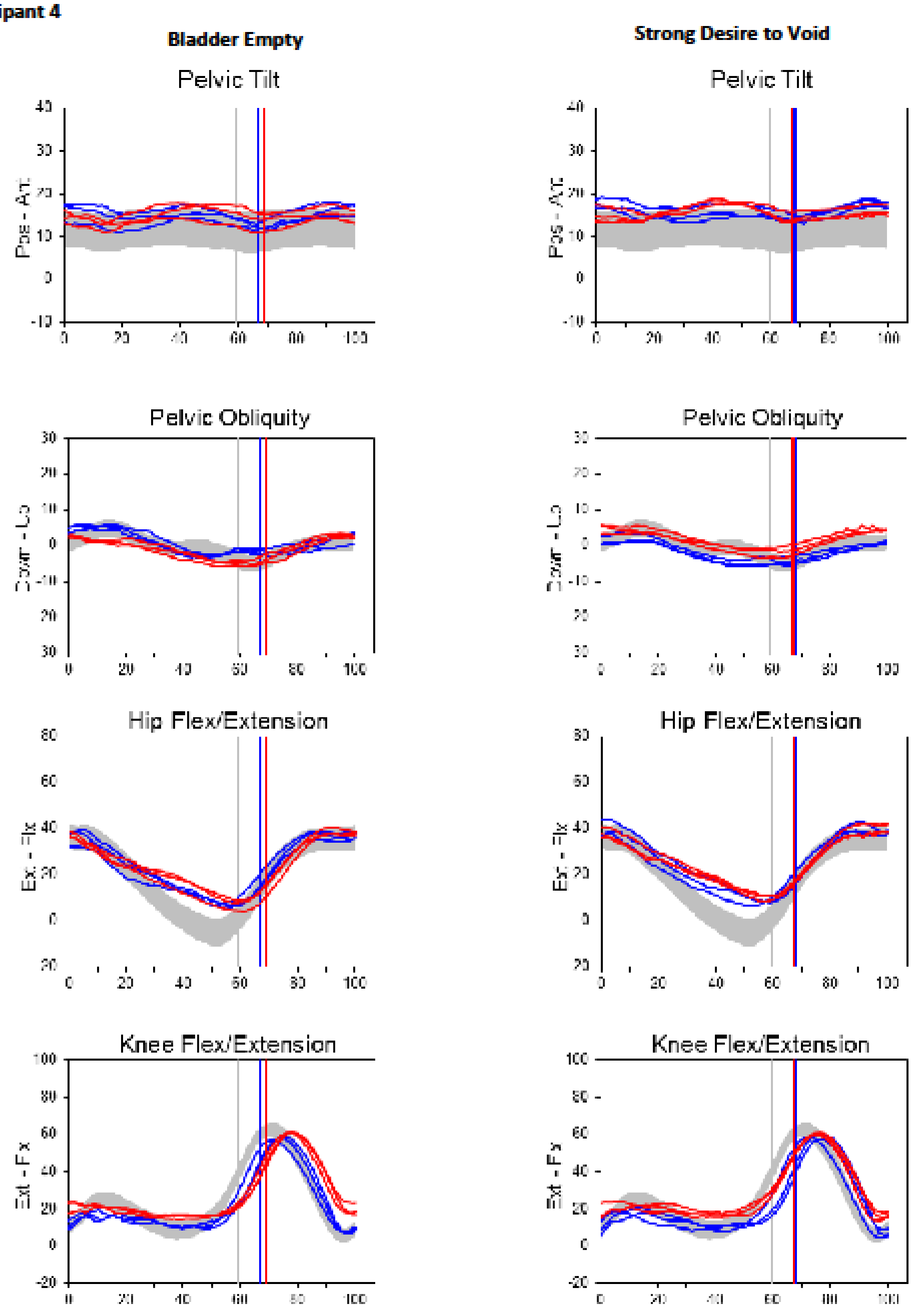
Administered by: ______________________

Kinematic Data



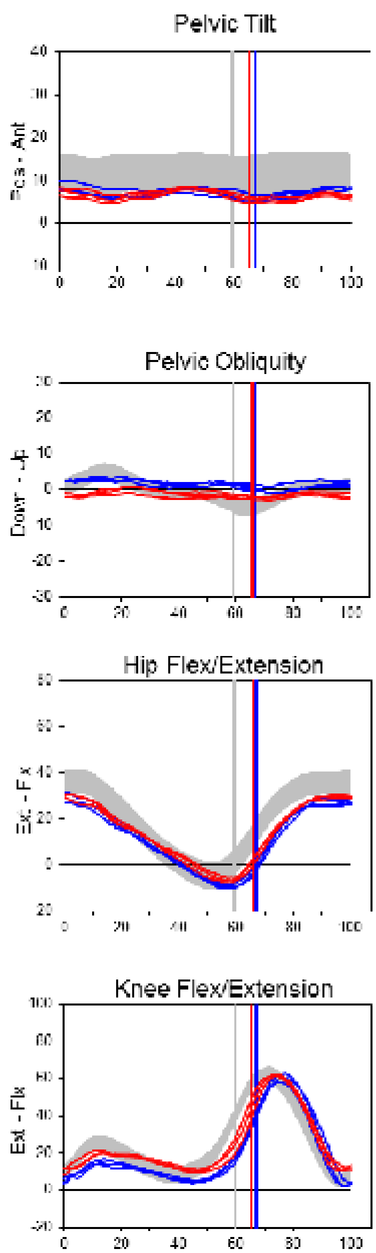

Participant 3
Bladder Empty
Strong Desire to Void
Pelvic Tilt
Pelvic Tilt
Pelvic Obliquity
Pelvic Obliquity
Hip Flex/Extension
Hip Flex/Extension
Knee Flex/Extension
Knee Flex/Extension

Participant 4

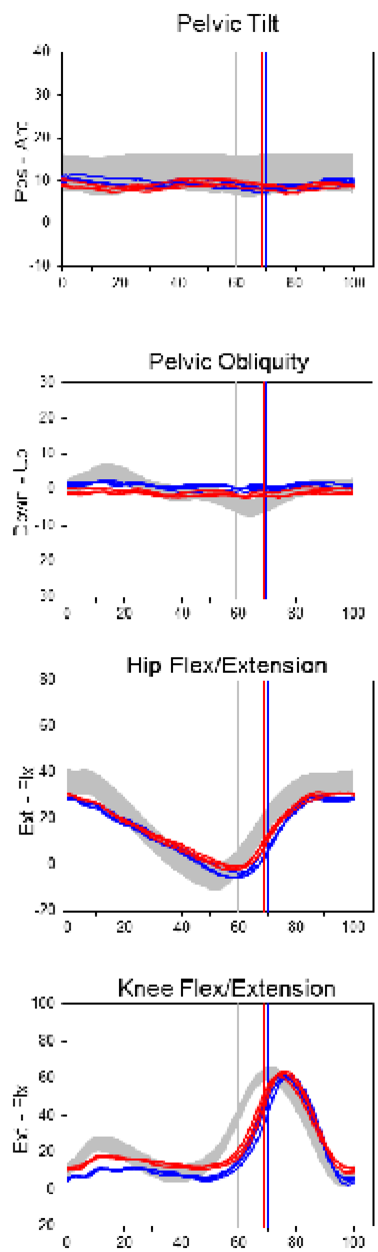


Participant 5

Bladder Empty

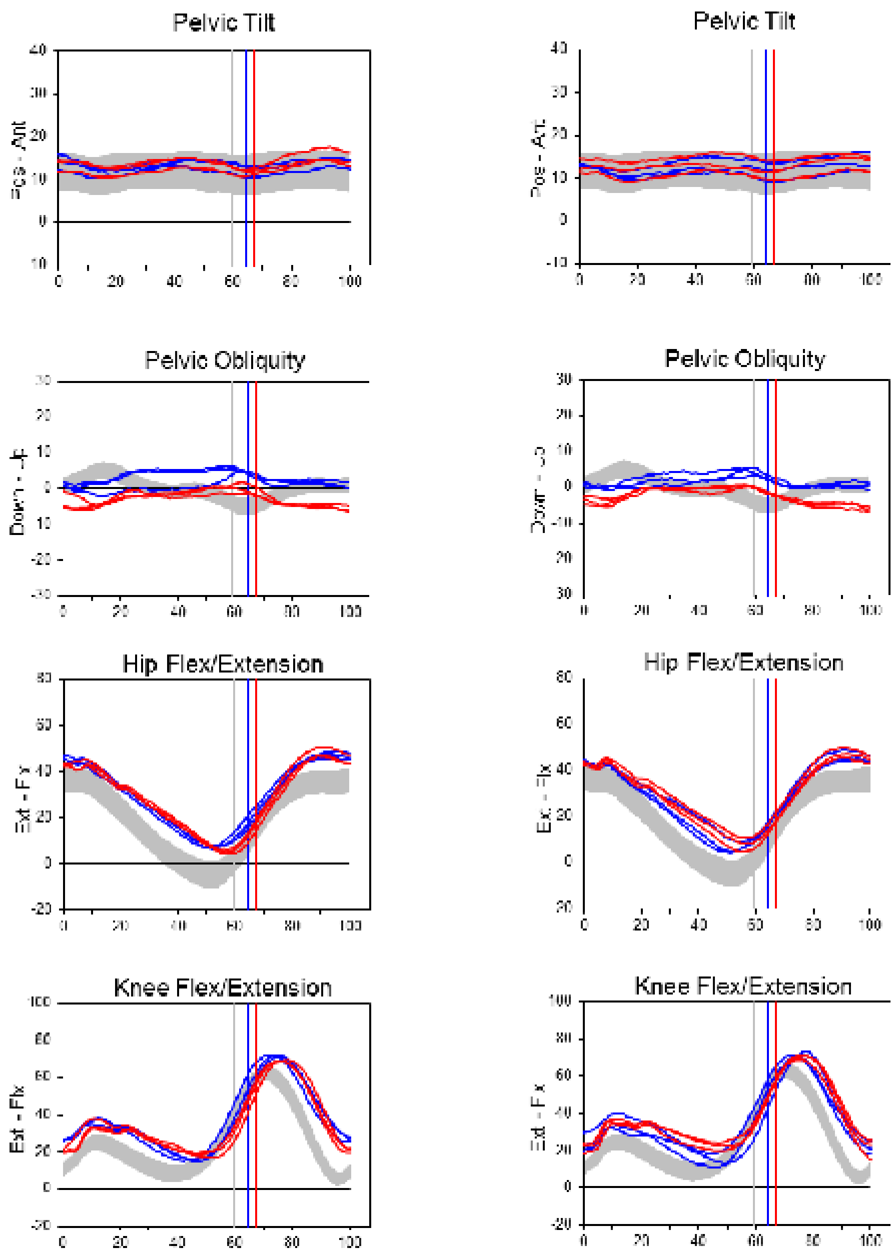


Strong Desire to Void



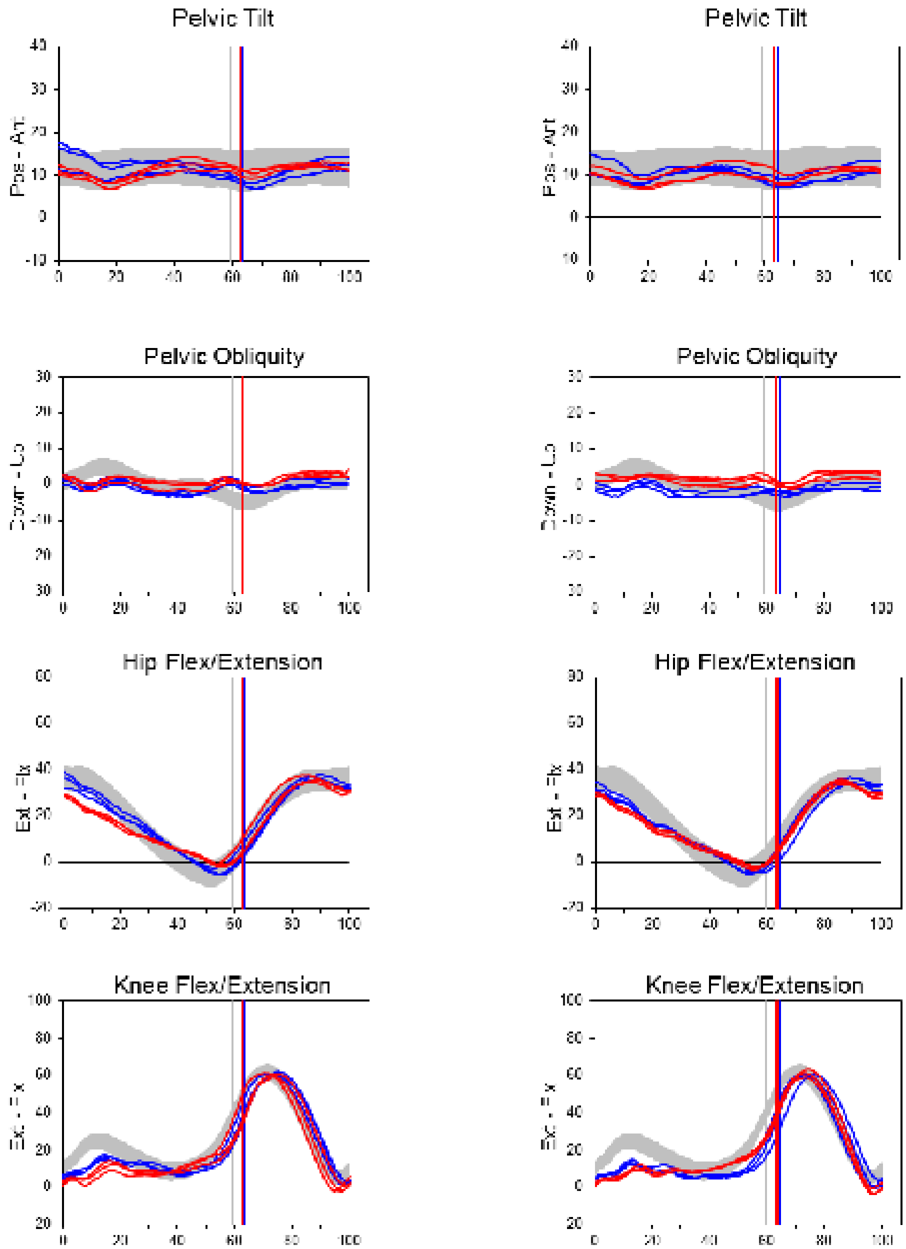
Participant 6

Bladder Empty **Strong Desire to Void**



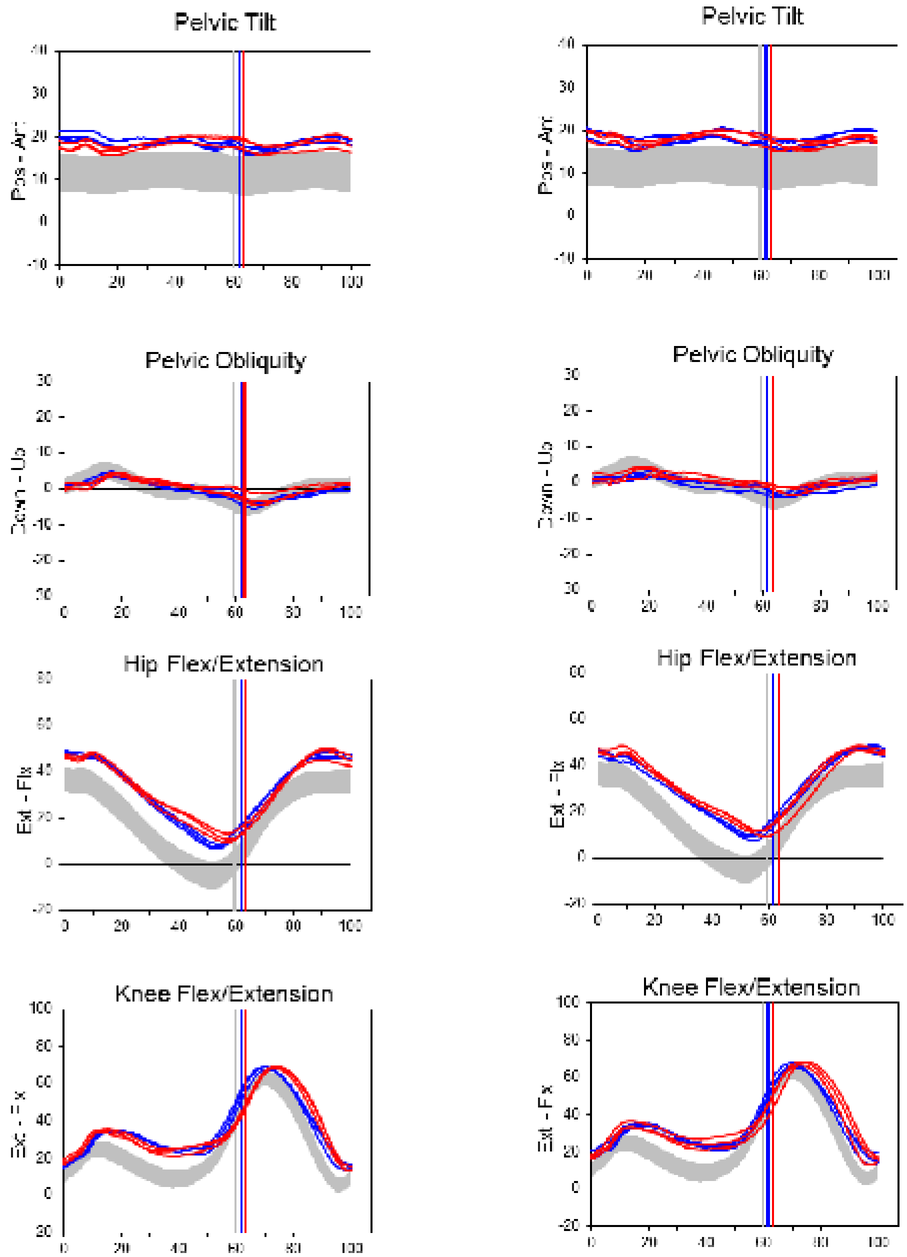
Participant 7

Bladder Empty | **Strong Desire to Void**



Participant 8

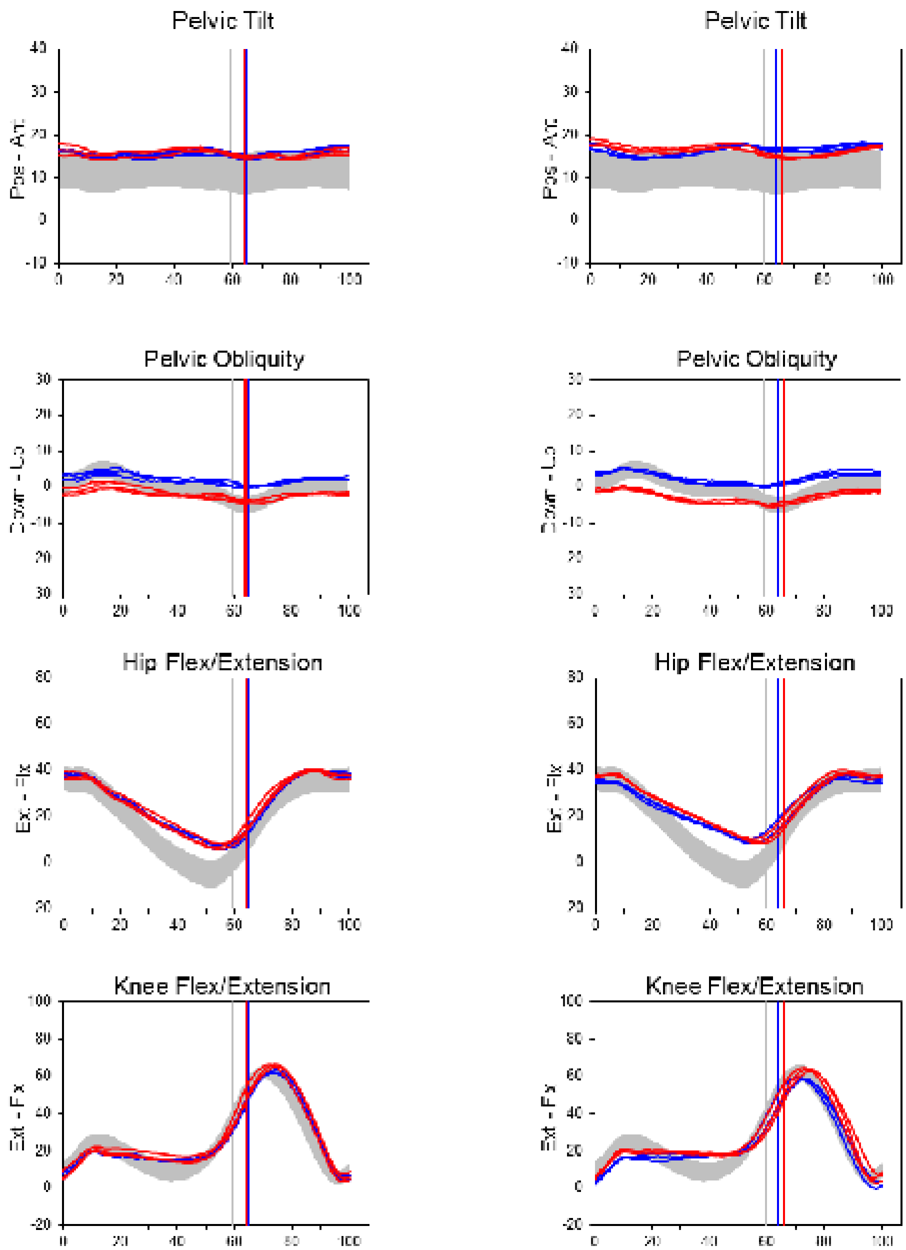
Bladder Empty **Strong Desire to Void**



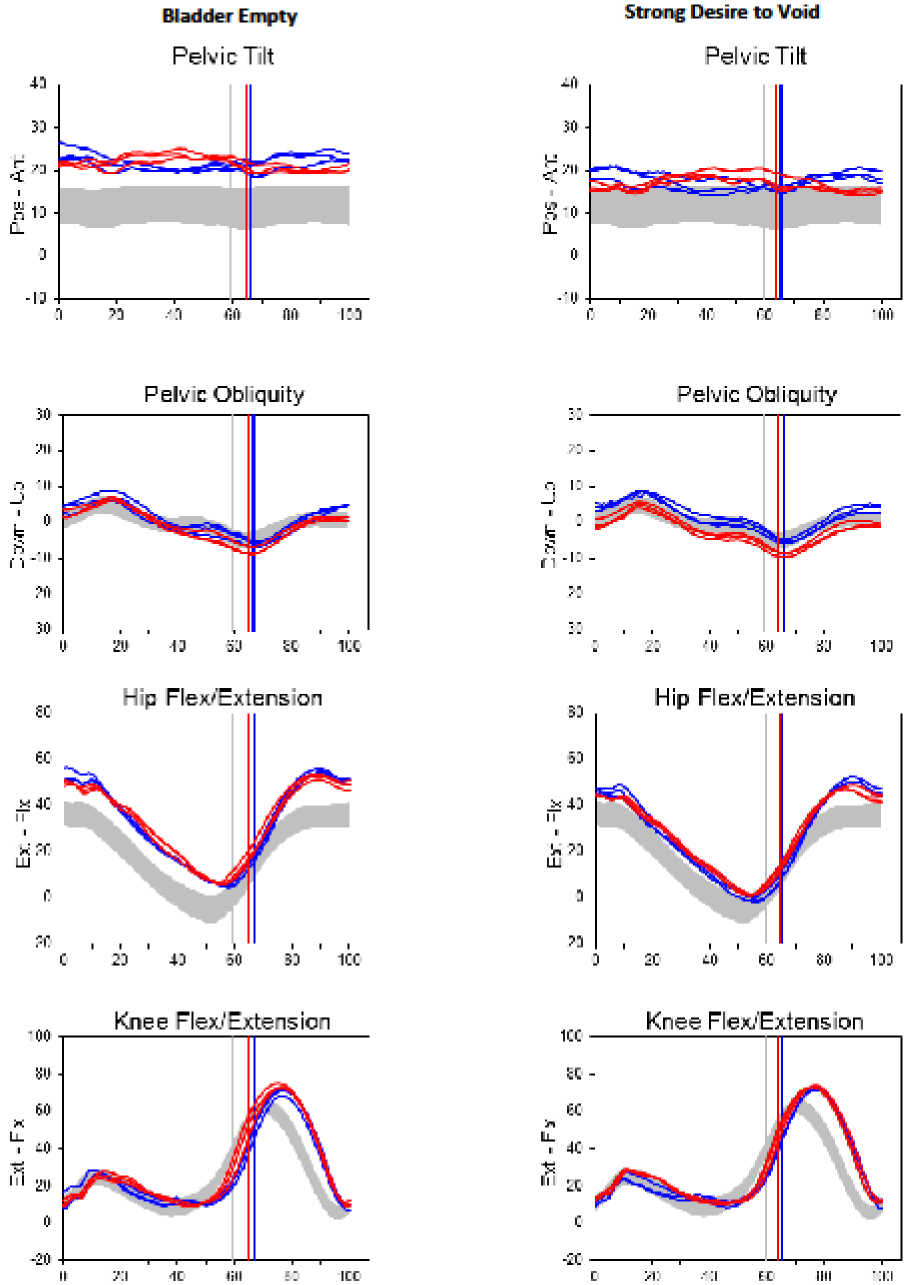
8

Participant 9

Bladder Empty **Strong Desire to Void**

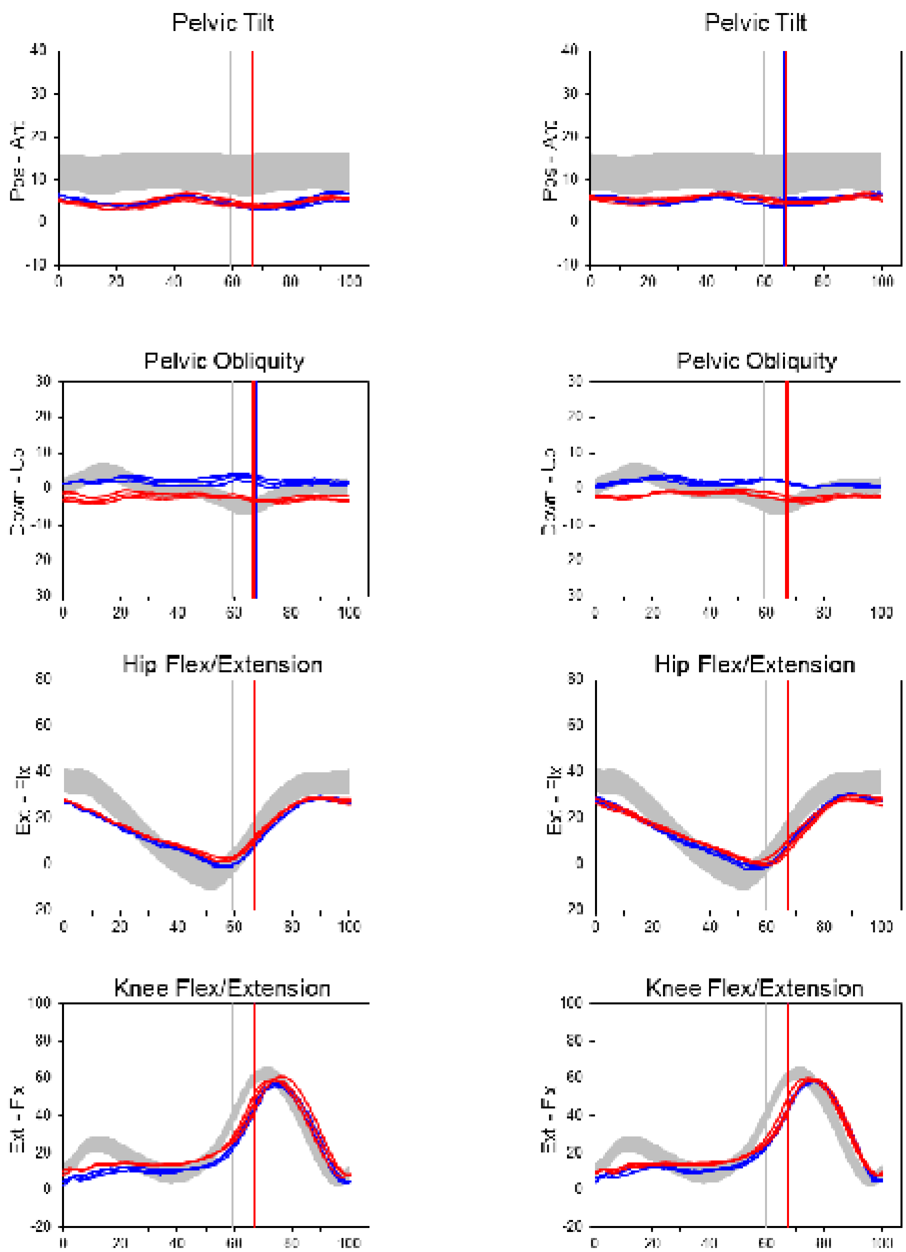


Participant 10



Participant 11

Bladder Empty **Strong Desire to Void**

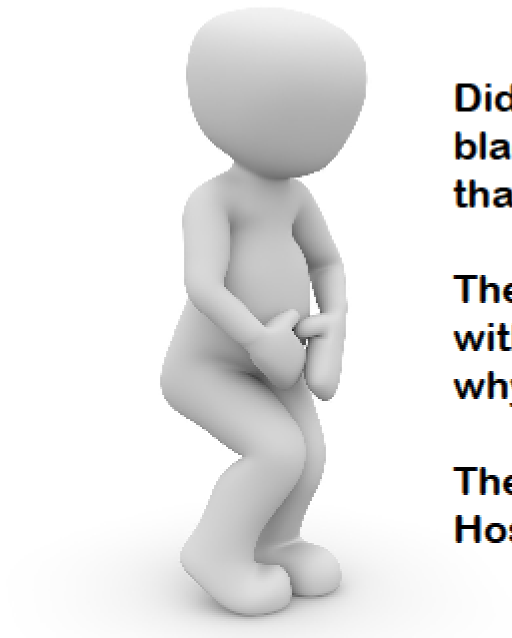


Appendix VI

Chapter 7 Documentation

- Recruitment Poster and Press Advert 1
- Recruitment Poster and Press Advert 2
- Initial Contact Letter
- Patient Information Letter
- Consent Form
- Ethics Approval
- Montreal Cognitive Assessment
- Berg Balance Score
- Activity Based Confidence Score
- ICIQ-FLUTS
- ICIQ-MLUTS

Recruitment Poster 1 and Press Advert 1



Did you know that people with overactive bladder (OAB) are more likely to have a fall than people without bladder problems?

The University of Alberta is recruiting people with OAB for a research study to investigate why this might be.

The study involves three visits to the Glenrose Hospital.

For more information contact:

Dr. William Gibson on 780-492-0133 or wgibson@ualberta.ca

Recruitment Poster 2 and Press Advert 2

Did you know that people with overactive bladder (OAB) are more likely to have a fall than people without bladder problems?

The University of Alberta is recruiting people with OAB for a research study to investigate why this might be.

The study involves three visits to the Glenrose Hospital.

For more information contact:

Dr. William Gibson on 780-492-0133 or wgibson@ualberta.ca

Initial Contact Letter

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

1-198 Clinical Sciences Building
11350 – 83 Avenue
Edmonton, Alberta
Canada T6G 2P4
Tel: 780.492.5338
Fax: 780.492.2874
www.ualberta.ca

Dear [partipant],

Many thanks for expressing an interest in our study. This letter is to give you some more information about it.

What are you trying to find out?
We know that people who suffer from bladder problems like yours, called overactive bladder, are almost twice as likely to fall over than people who do not. Why this is the case isn't understood. We think that it may relate to how the feeling of needing to pee distracts people, and we hope that this study will give us useful information to develop a treatment for overactive bladder which does not involve drugs.

What does the study involve?
We are asking people who have overactive bladder to come to the Glenrose Hospital for the day. While there, we will fit them with reflective markers and watch how they walk three times. Once normally, once while performing a mental task which is distracting, and once when needing to pee. You will need to attend the Glenrose hospital three times in total– once to go through your medical history and check you are suitable for the study, then once to perform a test of the bladder called urodynamics, and then once to collect the walking information.

What happens at each visit?
The first visit will involve seeing a doctor to review your medical history and talk about the problems you have with your bladder. There will be a basic examination and a scan of your bladder. This will ensure that you are suitable to enter the study.
The second visit is to have a test called urodynamics. This is a test which is performed by a specialist nurse, which involves having a thin tube called a catheter placed into the bladder and rectum. The test takes around half an hour.
The third visit is to collect the data. This will take place in the Gait Laboratory at the Glenrose. We will ask you to walk approximately 10 meters which we use a system of cameras to analyse how you walk. We will repeat this three times, once walking normally, once while you are doing a mental task, and once when you have a full bladder. We will fill your bladder by asking you to drink until you feel an urgent need to pee. There is a toilet very close to the test and we will provide you with an absorbent pad to wear just in case if you would like.

What happens next?
One of the research team will phone you in a few days to discuss things further, and you can ask any questions you may have. If you are still interested in taking part we will arrange for you to come to the Glenrose Hospital for the first visit. If you do not want to take part then we will offer to see you in clinic as an ordinary patient. **You are under absolutely no obligation to take part in the study and can say no or withdraw at any time without any problem.**

Thanks again for your interest

Dr William Gibson

Patient Information Letter

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

Study Title: The impact of urinary symptoms on gait: is urinary urgency a source of diverted attention leading to gain changes and falls in older people with overactive bladder?

Research Investigator:

Dr William Gibson
Clinical Sciences Building
University of Alberta
Edmonton, AB, T6G 2P4
wgibson@ualberta.ca
780 492 0133

Supervisor:

Professor Adrian Wagg
Clinical Sciences Building
University of Alberta
Edmonton, AB, T6G 2P4
adrian.wagg@ualberta.ca
780 492 5338

Background

- Thank you for expressing an interest in taking part in our research study.
- The results of this study will be used towards Dr Gibson's PhD thesis. It will also provide valuable information. This may help us understand why older people who suffer from urinary incontinence are more likely to fall over.
- This study has been partially funded by a grant from Astellas Pharma via the Canadian Urological Association and Astellas. These organisations had no part in the design of the study.

Purpose

- It is well known that people over the age of 65 who have bladder problems are more likely to fall than people who do not. We do not know why this is. We think it may be because the feeling of needing to pee is distracting and causes people to walk differently. This might increase their chance of falling over. We are recruiting people with the condition overactive bladder (OAB), which is the commonest cause of bladder problems in older people.

Study Procedures

- The study will involve 3 visits to the Glenrose Hospital in Edmonton. We will pay for your travel and parking costs.

- The first visit will be to see a doctor. During this visit we will explain the study in more detail and review your symptoms and medical history. If you are suitable to take part in the study we will ask you to sign a consent form and arrange for you to attend for the second and third visits.
- The second visit is to have a test called "multi-channel subtraction cystometry", also known as urodynamics. This is a test of how your bladder functions and whether or not you have a condition known as "detrusor overactivity". This is important as not everyone who has OAB has DO so we will look at our results for both groups separately to see if this makes a difference.
- The third visit is to perform the experiment itself. This will involve using a sophisticated system of cameras to map how you walk in different circumstances. You will walk normally, when you really need to pee, and when you are doing a task which we know is distracting. We will then compare the three walks to see if your walking is affected. We will place markers on your clothes to help us record your walking pattern. If you would like we will provide you with a pad to guard against any leaks for the walk while have an urgent need to pee. We will ask you to drink until you feel an urgent need to empty your bladder. There is a toilet at the end of the test walk for you to use.
- After the study, if you would like us to, we will see you in our clinic to treat your bladder problems
- We will collect the following information from you;
    - Your medical history, medications taken, and information about your bladder problems.
    - The results from the cystometry test
    - Information from the walking tests.
    - No information collected about you will be identifiable by anyone outside the study team. When you enter the study you will be given a code number which will only be connected to your personal information kept on a secure master list which away at the University of Alberta. We will make the results of the cystometry available on your Alberta Healthcare records unless you ask us not to, as this may be useful for your doctor in the future. Your AHS record is completely confidential.

Benefits

- You will not benefit directly from the study, other than by seeing a specialist in incontinence.
- We hope that the study will provide valuable information to explain the reason people with bladder trouble may fall over, and help us design a treatment to reduce this risk.
- There are no costs to you for participating in this study.
- We will pay for your travel and parking for the visits in the study, and you will receive a Tim Horton's gift card for $15 to thank you for taking part.

Risk

- There are no major risks to people taking part in the study. There is a chance that you may fall over while walking or lose control of your bladder. The risk of this happening is no higher than it would be in everyday life. We will provide you with an absorbent pad to wear if you would like.

Voluntary Participation

- You do not have to take part in this study, it is entirely up to you to decide
- If you decide not to be involved this will not affect any health are you receive now or in the future ,. We will offer to see you in clinic as a patient if you wish and your treatment will be unaffected.
- You may withdraw from the study at any time. If you withdraw before the end of the third visit then none of the information collected about you will be used in the final analysis.
- If you decide to withdraw from the study we will offer to see you in clinic to treat your bladder problems.

Confidentiality & Anonymity

- Your data and information will be kept confidential.
- Only the research team will have access to the data.
- All the information about you will be identified with a code number assigned to you, and the list of people's personal information corresponding to their code will be kept in a locked cabinet. This will be stored for 5 years and then destroyed.
- If we find an unrelated heath problem we will discuss this with you and inform your family doctor if you wish. For example, we will test your urine, which may find undiagnosed diabetes.

Further Information

The study will be used to produce academic papers and Dr Gibson's PhD thesis. If you would like to receive copies of these please ask and we would be happy to send you an electronic copy.

If you have any further questions regarding this study, please do not hesitate to contact Dr Gibson at wgibson@ualberta.ca or 780 492 0133

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615.

Consent Form

DIVISION OF GERIATRIC MEDICINE
DEPARTMENT OF MEDICINE

CONSENT

Title of Study: The impact of urinary symptoms on gait: is urinary urgency a source of diverted attention leading to gait changes and falls in older people with overactive bladder?

Principal Investigator(s): Dr Adrian Wagg — **Phone Number(s): 780 492 5338**
Study Coordinator: Dr William Gibson — **Phone Number(s): 780 492 0133**

	YES	NO
Do you understand that you have been asked to be in a research study?	○	○
Have you read and received a copy of the attached Information Sheet?	○	○
Do you understand the benefits and risks involved in taking part in this research study?	○	○
Have you had an opportunity to ask questions and discuss this study?	○	○
Do you understand that you are free to leave the study at any time, without having to give a reason and without affecting your future medical care?	○	○
Has the issue of confidentiality been explained to you?	○	○
Do you understand who will have access to your records, including personally identifiable health information?	○	○

Do you want the investigator(s) to inform your family doctor that you are participating in this research study and the results of the assessment and tests? If so, give his/her name.

Who explained this study to you?

I agree to take part in this study

Signature of research participant ______________________

Printed Name ______________________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Researcher ______________________

Printed Name ______________________

Ethics Approval

Approval Form

Date:	November 8, 2016
Study ID:	Pro00054370
Principal Investigator:	Adrian Wagg
Study Title:	**Is urinary urgency a source of diverted attention leading to gait changes and falls in older people with overactive bladder?**
Approval Expiry Date:	Tuesday, November 7, 2017

Approved Consent Form:

Approval Date	Approved Document
11/8/2016	Detailed information.docx
11/8/2016	Consent form.docx

Sponsor/Funding Agency:

Canadian Urological Association	CUA
Pfizer Canada Inc.	PFIZE

RSO-Managed Funding:

	Project ID	Project Title	Speed Code	Other Information
View	RES0028112	urinary urgency as a source of diverted attention		

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel . Your application, including the following, has been reviewed and approved on behalf of the committee;

- Clinic Poster 1 (10/28/2016)
- Clinic Poster 2 (7/27/2016)
- Press Advert 1 (7/27/2016)
- Press Advert 2 (7/27/2016)
- Initial Contact Letter v1 (11/7/2016)
- Phone FITT (11/7/2016)
- ICIQ-MLUTS (11/7/2016)
- ICIQ-FLUTS (11/7/2016)
- ABC-Scale (11/7/2016)
- Berg Balance Scale (11/7/2016)
- Protocol (11/7/2016)

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. Subject consent for access to identifiable health information is required for the research described in the ethics application, and appropriate procedures for such consent have been approved by the HREB Health Panel. In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

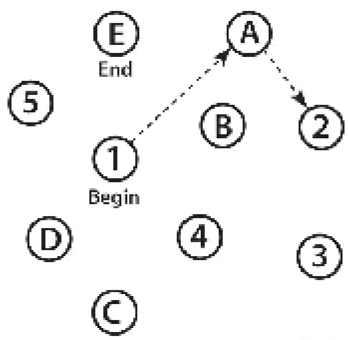
A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (Tuesday, November 7, 2017), you will have to re-submit an ethics application.

Montreal Cognitive Assessment

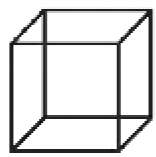
MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE



[ ]



Copy cube

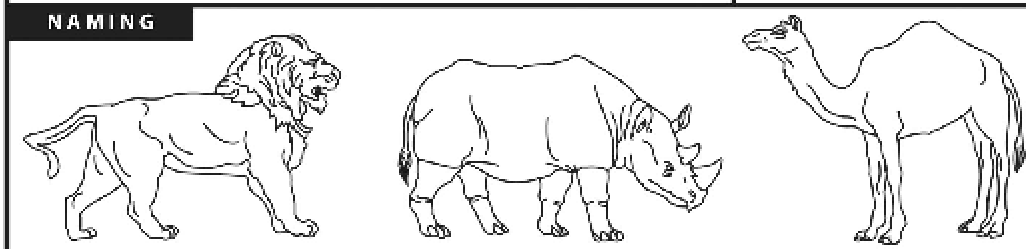
[ ]

Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING



[ ] [ ] [ ] ___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2 ___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B ___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** ___/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] ___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) ___/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler ___/2

DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	___/5
Optional	Category cue							
	Multiple choice cue							

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City ___/6

© Z.Nasreddine MD **www.mocatest.org** Normal ≥ 26 / 30 TOTAL ___/30

Administered by: ________________________ Add 1 point if ≤ 12 yr edu

Berg Balance Scale

The Berg Balance Scale (BBS) was developed to measure balance among older people with impairment in balance function by assessing the performance of functional tasks. It is a valid instrument used for evaluation of the effectiveness of interventions and for quantitative descriptions of function in clinical practice and research. The BBS has been evaluated in several reliability studies. *A recent study of the BBS, which was completed in Finland, indicates that a change of eight (8) BBS points is required to reveal a genuine change in function between two assessments among older people who are dependent in ADL and living in residential care facilities.*

Description:
14-item scale designed to measure balance of the older adult in a clinical setting.

Equipment needed: Ruler, two standard chairs (one with arm rests, one without), footstool or step, stopwatch or wristwatch, 15 ft walkway

Completion:

Time: 15-20 minutes

Scoring: A five-point scale, ranging from 0-4. "0" indicates the lowest level of function and "4" the highest level of function. Total Score = 56

Interpretation:
41-56 = low fall risk
21-40 = medium fall risk
0 –20 = high fall risk

A change of 8 points is required to reveal a genuine change in function between 2 assessments.

Berg Balance Scale

Name: ______________________________ Date: ________________

Location: ___________________________ Rater: ________________

ITEM DESCRIPTION	SCORE (0-4)
Sitting to standing	______
Standing unsupported	______
Sitting unsupported	______
Standing to sitting	______
Transfers	______
Standing with eyes closed	______
Standing with feet together	______
Reaching forward with outstretched arm	______
Retrieving object from floor	______
Turning to look behind	______
Turning 360 degrees	______
Placing alternate foot on stool	______
Standing with one foot in front	______
Standing on one foot	______

Total ______

GENERAL INSTRUCTIONS

Please document each task and/or give instructions as written. When scoring, please record the lowest response category that applies for each item.

In most items, the subject is asked to maintain a given position for a specific time. Progressively more points are deducted if:

- the time or distance requirements are not met
- the subject's performance warrants supervision
- the subject touches an external support or receives assistance from the examiner

Subject should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on or how far to reach are left to the subject. Poor judgment will adversely influence the performance and the scoring.

Equipment required for testing is a stopwatch or watch with a second hand, and a ruler or other indicator of 2, 5, and 10 inches. Chairs used during testing should be a reasonable height. Either a step or a stool of average step height may be used for item # 12.

Berg Balance Scale

SITTING TO STANDING
INSTRUCTIONS: Please stand up. Try not to use your hand for support.
( ) 4 able to stand without using hands and stabilize independently
( ) 3 able to stand independently using hands
( ) 2 able to stand using hands after several tries
( ) 1 needs minimal aid to stand or stabilize
( ) 0 needs moderate or maximal assist to stand

STANDING UNSUPPORTED
INSTRUCTIONS: Please stand for two minutes without holding on.
( ) 4 able to stand safely for 2 minutes
( ) 3 able to stand 2 minutes with supervision
( ) 2 able to stand 30 seconds unsupported
( ) 1 needs several tries to stand 30 seconds unsupported
( ) 0 unable to stand 30 seconds unsupported

If a subject is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item #4.

SITTING WITH BACK UNSUPPORTED BUT FEET SUPPORTED ON FLOOR OR ON A STOOL
INSTRUCTIONS: Please sit with arms folded for 2 minutes.
( ) 4 able to sit safely and securely for 2 minutes
( ) 3 able to sit 2 minutes under supervision
( ) 2 able to able to sit 30 seconds
( ) 1 able to sit 10 seconds
( ) 0 unable to sit without support 10 seconds

STANDING TO SITTING
INSTRUCTIONS: Please sit down.
( ) 4 sits safely with minimal use of hands
( ) 3 controls descent by using hands
( ) 2 uses back of legs against chair to control descent
( ) 1 sits independently but has uncontrolled descent
( ) 0 needs assist to sit

TRANSFERS
INSTRUCTIONS: Arrange chair(s) for pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair.
( ) 4 able to transfer safely with minor use of hands
( ) 3 able to transfer safely definite need of hands
( ) 2 able to transfer with verbal cuing and/or supervision
( ) 1 needs one person to assist
( ) 0 needs two people to assist or supervise to be safe

STANDING UNSUPPORTED WITH EYES CLOSED
INSTRUCTIONS: Please close your eyes and stand still for 10 seconds.
( ) 4 able to stand 10 seconds safely
( ) 3 able to stand 10 seconds with supervision
( ) 2 able to stand 3 seconds
( ) 1 unable to keep eyes closed 3 seconds but stays safely
( ) 0 needs help to keep from falling

STANDING UNSUPPORTED WITH FEET TOGETHER
INSTRUCTIONS: Place your feet together and stand without holding on.
( ) 4 able to place feet together independently and stand 1 minute safely
( ) 3 able to place feet together independently and stand 1 minute with supervision
( ) 2 able to place feet together independently but unable to hold for 30 seconds
( ) 1 needs help to attain position but able to stand 15 seconds feet together
( ) 0 needs help to attain position and unable to hold for 15 seconds

Berg Balance Scale continued…

REACHING FORWARD WITH OUTSTRETCHED ARM WHILE STANDING
INSTRUCTIONS: Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can. (Examiner places a ruler at the end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the distance forward that the fingers reach while the subject is in the most forward lean position. When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.)
( ) 4 can reach forward confidently 25 cm (10 inches)
( ) 3 can reach forward 12 cm (5 inches)
( ) 2 can reach forward 5 cm (2 inches)
( ) 1 reaches forward but needs supervision
( ) 0 loses balance while trying/requires external support

PICK UP OBJECT FROM THE FLOOR FROM A STANDING POSITION
INSTRUCTIONS: Pick up the shoe/slipper, which is in front of your feet.
( ) 4 able to pick up slipper safely and easily
( ) 3 able to pick up slipper but needs supervision
( ) 2 unable to pick up but reaches 2-5 cm(1-2 inches) from slipper and keeps balance independently
( ) 1 unable to pick up and needs supervision while trying
( ) 0 unable to try/needs assist to keep from losing balance or falling

TURNING TO LOOK BEHIND OVER LEFT AND RIGHT SHOULDERS WHILE STANDING
INSTRUCTIONS: Turn to look directly behind you over toward the left shoulder. Repeat to the right. (Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.)
( ) 4 looks behind from both sides and weight shifts well
( ) 3 looks behind one side only other side shows less weight shift
( ) 2 turns sideways only but maintains balance
( ) 1 needs supervision when turning
( ) 0 needs assist to keep from losing balance or falling

TURN 360 DEGREES
INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.
( ) 4 able to turn 360 degrees safely in 4 seconds or less
( ) 3 able to turn 360 degrees safely one side only 4 seconds or less
( ) 2 able to turn 360 degrees safely but slowly
( ) 1 needs close supervision or verbal cuing
( ) 0 needs assistance while turning

PLACE ALTERNATE FOOT ON STEP OR STOOL WHILE STANDING UNSUPPORTED
INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touched the step/stool four times.
( ) 4 able to stand independently and safely and complete 8 steps in 20 seconds
( ) 3 able to stand independently and complete 8 steps in > 20 seconds
( ) 2 able to complete 4 steps without aid with supervision
( ) 1 able to complete > 2 steps needs minimal assist
( ) 0 needs assistance to keep from falling/unable to try

STANDING UNSUPPORTED ONE FOOT IN FRONT
INSTRUCTIONS: (DEMONSTRATE TO SUBJECT) Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot. (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject's normal stride width.)
( ) 4 able to place foot tandem independently and hold 30 seconds
( ) 3 able to place foot ahead independently and hold 30 seconds
( ) 2 able to take small step independently and hold 30 seconds
( ) 1 needs help to step but can hold 15 seconds
( ) 0 loses balance while stepping or standing

STANDING ON ONE LEG
INSTRUCTIONS: Stand on one leg as long as you can without holding on.
( ) 4 able to lift leg independently and hold > 10 seconds
( ) 3 able to lift leg independently and hold 5-10 seconds
( ) 2 able to lift leg independently and hold ≥ 3 seconds
( ) 1 tries to lift leg unable to hold 3 seconds but remains standing independently.
( ) 0 unable to try of needs assist to prevent fall

( ) TOTAL SCORE (Maximum = 56)

Activity Based Confidence Score

Patient Name: ____ Date: ______________________

The Activities-specific Balance Confidence (ABC) Scale*

Instructions to Participants: For each of the following activities, please indicate your level of confidence in doing the activity without losing your balance or becoming unsteady from choosing one of the percentage points on the scale from 0% to 100% If you do not currently do the activity in question, try and imagine how confident you would be if you had to do the activity. If you normally use a walking aid to do the activity or hold onto someone, rate your confidence as if you were using these supports.

0%	10	20	30	40	50	60	70	80	90	100%
No Confidence										Completely Confident

How confident are you that you will not lose your balance or become unsteady when you...

1. ...walk around the house? _____%
2. ...walk up or down stairs? _____%
3. ...bend over and pick up a slipper from the front of a closet floor? _____%
4. ...reach for a small can off a shelf at eye level? _____%
5. ...stand on your tip toes and reach for something above your head? _____%
6. ...stand on a chair and reach for something? _____%
7. ...sweep the floor? _____%
8. ...walk outside the house to a car parked in the driveway? _____%
9. ...get into or out of a car? _____%
10. ...walk across a parking lot to the mall? _____%
11. ...walk up or down a ramp? _____%
12. ...walk in a crowded mall where people rapidly walk past you? _____%
13. ...are bumped into by people as you walk through the mall? _____%
14. ...step onto or off of an escalator while you are holding onto a railing? _____%
15. ...step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing? _____%
16. ...walk outside on icy sidewalks? _____%

*Powell LE & Myers AM. The Activities-specific Balance Confidence (ABC) Scale. Journal of Gerontology Med Sci 1995; 50(1):M28-34.

Total ABC Score: __________

Scoring: ____________ **/ 16 =** | __________% of self confidence |

Total ABC Score

MEDICARE PATIENTS ONLY
100% - _____% Function = _____% Impairment

Patient Signature: ____ Date: ______________________

Therapist Signature: ____ Date: ______________________

ICIQ F-LUTS

ICIQ-FLUTS Long Form 08/04

Initial number

CONFIDENTIAL

DAY MONTH YEAR
Today's date

Urinary symptoms

Many people experience urinary symptoms some of the time. We are trying to find out how many people experience urinary 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.

1. Please write in your date of birth:

DAY MONTH YEAR

2a. How often do you pass urine during the day?

one to six times ☐	0
seven to eight times ☐	1
nine to ten times ☐	2
eleven to twelve times ☐	3
thirteen or more times ☐	4

2b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

3a. During the night, how many times do you have to get up to urinate, on average?

none ☐	0
one ☐	1
two ☐	2
three ☐	3
four or more ☐	4

3b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

4a. Do you have a sudden need to rush to the toilet to urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

4b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

5a. Does urine leak before you can get to the toilet?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

5b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

6a. Do you have pain in your bladder?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

6b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

7a. How often do you leak urine?

never	☐	0
once or less per week	☐	1
two to three times per week	☐	2
once per day	☐	3
several times per day	☐	4

7b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 **1** **2** **3** **4** **5** **6** **7** **8** **9** **10**
not at all ... a great deal

8a. Does urine leak when you are physically active, exert yourself, cough or sneeze?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

8b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 **1** **2** **3** **4** **5** **6** **7** **8** **9** **10**
not at all ... a great deal

9a. Do you ever leak urine for no obvious reason and without feeling that you want to go?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

9b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 **1** **2** **3** **4** **5** **6** **7** **8** **9** **10**
not at all ... a great deal

10. How much urinary leakage occurs?

no leakage	☐	0
drops/pants damp	☐	1
dribble/pants wet	☐	2
floods, soaking through to outer clothing	☐	3
floods, running down legs or onto floor	☐	4

11a. Is there a delay before you can start to urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

11b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

12a. Do you have to strain to start urinating?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

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

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

13a. Do you stop and start more than once while you urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

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

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

14a. Do you leak urine when you are asleep?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

14b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

15a. Would you say that the strength of your urinary stream is...

not reduced	☐	0
reduced a little	☐	1
quite reduced	☐	2
reduced a great deal	☐	3
no stream	☐	4

15b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

16. Have you ever blocked up completely so that you could not urinate at all and had to have a catheter to drain the bladder?

no	☐	0
yes, once	☐	1
yes, twice	☐	2
yes, more than twice	☐	3

17a. Do you have a burning feeling when you urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

17b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

18a. How often do you feel that your bladder has not emptied properly after you have urinated?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

18b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

19. Can you stop the flow of urine if you try while you are urinating?

yes, easily	☐	0
yes, with difficulty	☐	1
no, cannot stop it flowing	☐	2

Thank you very much for answering these questions.

ICIQ M-LUTS

Initial number

ICIQ-MLUTS Long Form 08/04

CONFIDENTIAL

DAY MONTH YEAR
Today's date

Urinary symptoms

Many people experience urinary symptoms some of the time. We are trying to find out how many people experience urinary 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.

1. Please write in your date of birth: DAY MONTH YEAR

2a. During the day, how many times do you urinate, on average?

one to six times ☐	0
seven to eight times ☐	1
nine to ten times ☐	2
eleven to twelve times ☐	3
thirteen times or more ☐	4

2b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

3a. During the night, how many times do you have to get up to urinate, on average?

none ☐	0
one ☐	1
two ☐	2
three ☐	3
four or more ☐	4

3b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

4a. Do you have a sudden need to rush to the toilet to urinate?

never ☐	0
occasionally ☐	1
sometimes ☐	2
most of the time ☐	3
all of the time ☐	4

4b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

5a. Does urine leak before you can get to the toilet?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

5b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

6a. Do you have pain in your bladder?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

6b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

7a. Does urine leak when you cough or sneeze?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

7b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

8a. Do you ever leak for no obvious reason and without feeling that you want to go?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

8b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

9a. Is there a delay before you can start to urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

9b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

10a. Do you have to strain to <u>start</u> urinating?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

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

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

11a. Do you have to strain to continue urinating?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

11b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

12a. Do you usually urinate standing up or sitting down?

standing up	☐	0
sitting down	☐	1

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

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

13a. Would you say that the strength of your urinary stream is...

normal	☐	0
occasionally reduced	☐	1
sometimes reduced	☐	2
reduced most of the time	☐	3
reduced all of the time	☐	4

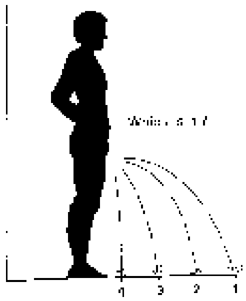
13b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

14. Do you think you have *always* had a weak stream?

no	☐	0
yes	☐	1

15. Would you say that the strength of your urinary stream is...
(please ring one number)



(from Peeling, 1989)

16a. Do you stop and start more than once while you urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

16b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all … a great deal

17a. Do you have a burning feeling when you urinate?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

17b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all … a great deal

18a. How often do you feel that your bladder has not emptied properly after you have urinated?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

18b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

19a. Does your urine stream end with a dribble?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

19b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

20a. How often have you had a slight wetting of your pants a few minutes after you had finished urinating and had dressed yourself?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

20b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

21a. Do you leak urine when you are asleep?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

21b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

22a. If you leak urine during the day, do you have to change your clothes or wear pads?

no, urine does not leak	☐	0
yes, change underpants	☐	1
yes, change clothes	☐	2
I wear pads	☐	3

22b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

23a. Do you have to urinate again (within 15 minutes) after you thought you had finished urinating?

never	☐	0
occasionally	☐	1
sometimes	☐	2
most of the time	☐	3
all of the time	☐	4

23b. How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

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

24. Have you ever blocked up completely so that you could not urinate at all and had to have a catheter passed to drain the bladder ?

no	☐	0
yes, once	☐	1
yes, twice	☐	2
yes, more than twice	☐	3

Thank you very much for answering these questions.