An Examination of the Relationship between Gait, Cognition and Risk of Falling in an Older Population Based Sample

by

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Declaration of originality

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Statement of authorship

This thesis includes papers for which Kara Martin (KM) was not the sole author. KM was the lead in this research as she participated in data collection, analysed the data and wrote the manuscripts. However, she was assisted by the co-authors whose contributions are detailed below.

1. The paper reported in Chapter 4:

Martin K, Wood A, Blizzard L, Callisaya M, Thomson R , Sanders L, Srikanth V, Cognitive Function, Gait and Gait Variability in Older People: a Population-Based Study. Submitted to the Journal of Gerontology, July 2011.

> The contribution of each author:
> KM participated in data collection, data management and cleaning, and comprised the initial draft of the manuscript. With LB, she undertook all the analyses and interpretation of the data, and completed revisions.
> AW helped with analyses and interpretation of the results and revised the manuscript.
> LB with KM undertook all the analyses and interpretation of the data and revised the manuscript.
> RT helped with analyses and interpretation of the results and revised the manuscript.
> MC helped with analyses and interpretation of the results and revised the manuscript.
> LS helped with analyses and interpretation of the results and revised the manuscript.
> VS was responsible for obtaining approvals, design and conduct of the study and helped with interpretation of the results and revised the manuscript

2. The paper reported in Chapter 5:

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Abstract

Falls are a significant public health problem for older people. Their prevention is important to reduce hospital admissions, and related loss of independence, morbidity and mortality. They have multiple risk factors, including impaired cognitive function and gait deterioration. Inter-relationships between cognitive function and gait in contributing to falls are poorly understood, with few data from population-based studies.

This thesis aimed to examine the associations between cognitive function, gait and the risk of falling in a series of studies conducted in a population-based sample of older people aged 60-86 years.

Cognitive functions were assessed from a battery of tests. Gait was assessed using the *GaitRite* walkway and a force platform. Falls-risk was assessed using the Physiological Profile Assessment, and falls were recorded prospectively using a 12-month diary.

In the first study, measurements of GI using the *GaitRite* walkway were compared with those on the same 28 subjects measured using a 200Hz force platform, considered to be the gold standard. The *GaitRite* walkway measurements had higher systematic error and inferior predictive validity for falls-risk.

In the second study, poorer processing speed and executive function/attention, but not deficits in memory or visuospatial ability, were independently associated with poorer gait. Deficits of processing speed, executive function and visuospatial ability were associated with increased intra-individual gait variability in double support phase, a measure of balance during gait.

In the third study, time to first lateral movement could be the best measure of gait initiation, given its consistent associations with surrogates of falls-risk and cognition, while also being most responsive to cognitive interference from dual-tasking.

In the fourth study, executive function, processing speed and visuospatial ability, but not memory, were independently associated with a surrogate measure of falls-risk.

In the final study, poorer executive and visuospatial functions predicted the risk of multiple falls. The associations between all cognitive functions and the risk of multiple falls were magnified in those with poorer sensorimotor function, gait speed or ambulatory activity.

These studies add significantly to knowledge about the relationships between cognitive functions, gait and the risk of falling, in community-dwelling older people. Consistent with prior studies, executive function and processing speed may either be involved in gait control or share the same neural substrate. Visuospatial ability, a higher cortical function reflecting sense of space and position, was associated with gait. Memory appeared to have the least influence. Cognitive function and physical sensorimotor impairments were found to interact in predicting multiple falls, suggesting that brain reserve capacity plays a role in compensating for physical frailty in older people. Lastly, these data substantially add to the issue of the choice of measure of gait initiation, and will guide future studies in this field.

Acknowledgements

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List of abbreviations

AA	Ambulatory activity (steps/day)
ABS	Australian Bureau of Statistics
AD	Alzheimer's disease
AMTI	Advanced Mechanical Technology Inc
CI	Confidence interval
COWAT	Controlled Oral Word Association Test
D	Absolute difference
DSP	Double support phase
F	Force platform
FLM	First lateral movement
G	*GaitRite* walkway
GDS	Geriatric Depression Scale
GI	Gait initiation
HVLTR	Hopkins Verbal Learning Test Revised.
ICC	Intraclass correlation coefficient
IQR	Inter-quartile range
MMSE	Mini Mental State Examination
MRI	Magnetic Resonance Imaging
PPA	Physiological Profile Assessment
ProFaNE	Prevention of Falls Network Europe
r	Pearson's product-moment correlation coefficient
RR	Risk ratio
SD	Standard deviation
SE	Standard error
TASCOG	The Tasmanian Study of Cognition and Gait
WAIS-III	Wechsler Adult Intelligence Scale – 3rd Edition

Publications

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Other publications

Srikanth V, Beare R, Blizzard L, Phan T, Stapleton J, Chen J, Callisaya M, Martin K, Reutens D. Cerebral white matter lesions, gait, and the risk of incident falls: a prospective population-based study. *Stroke* 2009; 40:1:175-180.

Srikanth V, Sanders L, Callisaya M, Martin K, Phan T. Brain aging and gait. *Aging Health* 2010; 6:1:123-131.

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Martin K, Blizzard L, Garry M, Thomson R, McGinley J, Srikanth V. Effects of age, sex and dual tasking on gait initiation – the Tasmanian study of cognition and gait (TASCOG). Australian New Zealand Society for Geriatric Medicine, September 2008, Melbourne, Victoria. Poster presentation.

Martin K, Wood A, Blizzard L, Callisaya M, Thomson R, Sanders L, Srikanth V. The relationships between cognitive function, gait and gait variability in older people: a population-based study. Gait and Mental Function, February 2010, Washington, DC, USA. Poster presentation.

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Chapter 1:   Introduction

1.1   Background

Falls by older people are a significant public health problem. Their prevention is important to reduce hospital admissions, and related loss of independence, morbidity and mortality [1, 2]. There are multiple risk factors for falls, including impaired cognitive function [3-6] and gait deterioration [7-9], both of which are common in older people [10-14]. The inter-relationships between cognitive function and gait in contributing to falls are poorly understood, with few data from population-based studies.

1.2   Falls in older people

The first attempt to define falls was made in 1987 by the Kellogg International Working Group on the Prevention of Falls in the Elderly [15]. They defined a fall as "unintentionally coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or epileptic seizure". This definition of a fall is only useful when addressing balance or sensorimotor impairments and not useful when addressing cardiovascular and neurological causes of falls (such as syncope and transient ischemic attacks). Many researchers have adapted the Kellogg definition of falls to enable the investigation of falls due to these other causes.

This has led to a proliferation of definitions. In a recent systematic review on interventions to prevent falls, it was noted that there was neither a standard definition of falls, nor a method of identifying when a fall had occurred [16]. The authors reported that some studies counted a fall only if the body had made contact with the ground, whereas other studies classified a fall as having occurred if the body had made contact with furniture and even walls. Some studies excluded falls due to environmental hazards or syncope and other acute medical events, whereas others included some or all of the above [16]. These inconsistencies in definition led the Prevention of Falls Network Europe (ProFaNE) to organise a team of international experts to meet to develop a standard definition of falls. The consensus statement

from that meeting was that a fall be defined as "an unexpected event in which the person comes to rest on the ground, floor, or lower level" [17].

Measurement of falls

It was also noted in the recent systematic review that there is a wide range of methods for collecting falls data [16]. Falls can be, and have been, measured in three ways: observationally, retrospectively and prospectively. Observational methods include routine surveillance or inspection of health care records, which are limited by the quality of reporting. In community-based studies, health care records may miss over 80% of fall events compared to self-report methods [16, 18].

A retrospective account of falls involves asking a participant – by telephone call, face-to-face interview or postal questionnaire – if they have fallen during a previous time period (for example, the last 12 months). This method relies on accuracy of recall and can produce under- or over-estimates of falls. The limitations of retrospective falls ascertainment were highlighted in a study of 304 older adults, which showed that between 13 and 32% of people did not recall that they had had a fall over a 12 month period [19].

The prospective method, utilised in this thesis, involves recording of falls in a calendar, diary or postcard as they occur during a period of follow-up (for example, the next 12 months). The recordings are retrieved on a regular basis (weekly, monthly or every couple of months) during the follow-up period. Reminder telephone calls may be made to ensure ongoing maintenance of the falls diary [16, 17]. Whilst prospective methods are generally superior because there is less reliance on recall, the problems of over- or under-reporting are not eliminated [16]. In a study of 96 healthy, community-dwelling women, Hill et al. [20] reported that the use of falls diaries with follow up phone calls improved falls recall by 14.8%.

Incidence of falls in older people

Around a third of people aged over 65 years can expect to have a fall in a one year period [4, 21, 22], and around half of those can expect multiple falls [23, 24].There is considerable variation in reported occurrence of falls, however. Fall rates per annum in population-based samples have been reported to be as low as 13.2% and as high as

49% [3, 4, 25-29]. The percentage of people who fall more than once in a one year period is reported to range from 11% to 22% [26-29].

There have also been different fall rates reported for men and women. In a study of people over 70 years, Campbell et al. [3] found that 40% of women fell in a one year period, compared with only 28% in men. Fall rates are also reported to rise with increasing age [30], with up to 50% of people over 85 years reporting falls in a one year period [31].

Consequences of falls

The costs and consequences of falls are significant to the person, family and the community as a whole. Falls can lead to injury, hospitalization or institutionalization, loss of independence, morbidity and even mortality [1, 2]. Up to 60% of falls result in an injury [32] and whilst most of these injuries are minor – for example bruising [32] – around 25% will result in a more serious injury [4] including fracture [4, 32]. In addition, falls are the leading cause of injury-related hospitalisation [33] and increase the risk of admission to aged-care facilities [34] and mortality [35] in older people. Even a non-injurious fall can lead to fear of future falling, loss of independence and confidence, and reduced activity levels in older people [36].

The financial costs of falls to the community are large, with an estimated total cost of US $19 billion [35, 37] in the United States of America in the year 2000 and AUD $287 million in Australia per annum in 1999 [22]. These costs are expected to increase in the future. In 2006, 500 million people worldwide were over the age of 65 years and that figure is estimated to rise to one billion people by 2030 [23, 38], The costs of falls are estimated to double by 2020 [37] and, as a result, exceed AUD $1.3 billion in Australia by 2051 [39].

1.3   Established risk factors for falls

Falls are thought to be a result of a combination of intrinsic and extrinsic factors. Intrinsic factors include poor balance, cognitive impairment, visual impairment and muscle weakness [9]. Extrinsic factors include being on multiple medications or psychoactive medications, and environmental triggers such as obtrusive objects, poor lighting and undiscernible edges that may cause the person to trip over. Risk of falling is reduced for persons with better physical functioning, good balance and

higher level cognitive processing abilities [40-42]. The presence of multiple risk factors increases the risk of falling [4, 43], with around a 10% risk of falling for older people with at most one risk factor, and up to a 70% risk of falling for those with 4 or more risk factors [43].

Impairments in sensory and motor systems, which increase with age, are implicated as causes of falls [44]. The abilities in question include vision, lower limb proprioception and muscle strength, reaction time and balance [44, 45]. Vision encompasses contrast sensitivity, glare sensitivity, dark adaptation and depth perception [44]. Impairments in vision may lead to poorer balance, tripping over obstacles, difficulty with uneven surfaces and problems navigating through the environment [46]. Proprioception refers to the ability to sense the position of a limb (in this case lower limb) or joint in relation to the rest of the body. Impaired proprioception may lead to inadequate foot clearing over obstacles and difficulty walking on uneven surfaces. Lower-limb muscle strength is generally weaker in fallers than non-fallers [46]. Knee extension weaknesses, in particular, are known to be associated with an increased risk of falls and fractures [44, 47]. Muscle weakness may also lead to inadequate foot clearance over obstacles, but also shorter endurance and poor balance and body control. Reaction time is the time elapsed from a stimulus to completion of a desired task and declines significantly with age, with a median slowing of around 26% in reaction time from the third decade of life to the seventh [44]. Slow reactions may decrease the ability to correct postural imbalances, and thus result in falls. All of these functions can impact on a person's balance – the ability to maintain an upright stance or steadiness in spite of instability or external perturbations – and balance itself is an important risk factor for falls [44].

It is widely known that older people have a higher risk of falls and that females have a greater risk than males [31, 44, 48-51]. Independently of age and sex, several other factors have been shown to increase the risk of falls. Medication use, and in particular taking multiple medications, is a potentially reversible risk factor for falls [3, 7, 24, 44, 49, 52-57]. Similarly, the surrounding environment can contribute to falls. Tripping over objects and slipping on surfaces are causes of falls, and O'Keefe et al. [58] showed that bedrails can also increase the risk of falls.

In a population-based study of 761 subjects aged 70 years and older, a higher risk of falls in men was associated with decreased levels of physical activity, history of stroke and arthritis of the knees. For women, increased risk was associated with medications, standing systolic blood pressure lower than 110mmHg, and muscle weakness [59]. In a population-based study of community-living older people in Germany, factors such as living alone, poor health status, use of varifocals and depression, in addition to older age and female sex, were shown to predict falls in univariable analysis [48].

In another prospective study of community-dwelling older adults with a three year follow-up [60], a history of falls, dizziness, functional limitations, weak grip strength, low body weight, a fear of falling, the presence of animals (particularly dogs or cats), a higher education level and alcohol consumption were identified as predictors of recurrent falls.

An increased risk of falls due to these individual factors has been reproduced in several other studies. Factors that increase falls that have been reproduced in more than one study are: depression [44, 48, 49, 54, 59], medical conditions (such as Parkinson's disease [44, 48, 61, 62], arthritis [3, 24, 44, 49, 53], stroke [3, 44], dementia [44, 54, 55] and orthostatic hypotension [7, 9, 57]), incontinence [44, 48], low body mass index [49, 53], poor self-perceived health status [48, 50], poor performance on the instrumental activities of daily living [7, 44, 50] and living alone [44, 48].

In addition to these physiological measures, cognitive function and gait are key intrinsic abilities that may be associated with a risk of falling [3, 4, 8, 9].

1.4   Cognitive function as a risk factor for falls

Reduced cognitive function has been identified as an important risk factor for falling in specific patient groups [25, 63-72] and more generally in population-based studies [3-6]. Most research into cognitive function and falls has focused on general cognitive function as assessed by instruments such as the Folstein Mini Mental Status Examination (MMSE) [73]. An emerging focus has been placed on studying the effects of more specific cognitive functions, mainly executive function, attention

and memory [5, 6, 72, 74], because it is thought that decline in cognitive function occurs non-uniformly across domains [75] and studying levels of and changes in specific cognitive abilities may better elucidate the pathways leading to falls.

The most widely-researched cognitive functions with respect to falls are executive function, attention and processing speed [72, 74, 76]. There is little information on the effects of other cognitive functions including memory and visuospatial ability. It is thought that these instrumental functions (memory and visuospatial ability) rely on the more fundamental functions (executive function, attention and processing speed) to be intact in order to achieve full functionality [77]. The associations between specific cognitive functions and falls are investigated in **Chapter 6** (falls-risk) and **Chapter 7** (incident falls).

Fundamental cognitive functions

Certain cognitive functions provide the fundamental framework necessary for other more specialised cognitive functions. These fundamental processes include attention and concentration, speed of information processing, and a range of functions that fall broadly under the term 'executive function' [77]. They underlie most behaviour [78]. They are dependent on the integrity of widespread neural networks involving frontal-subcortical structures, cerebral cortex, brain-stem, the basal ganglia, the cerebellum and the cortico-subcortical white matter tracts [79-81]. The networks involved may be more vulnerable to age-related declines because they are very susceptible to white matter lesions that occur in the frontal regions of the brain. Several types of structural brain changes such as periventricular white matter abnormalities, brain infarcts and generalised brain atrophy may disconnect these networks leading to impaired executive function, attention and processing speed [82, 83], and poorer motor control [84].

Executive function / attention

The executive functions are those capacities that enable people to undertake independent, purposeful and self-directed behaviours successfully [75]. They include initiation, planning, hypothesis generating, flexibility, decision making, regulation, judgement and feed-back regulation [85]. They comprise many subordinate cognitive processes, one of which is working memory – the temporary storage of information connected to current cognitive processes like reading and problem-solving [86, 87].

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Attention refers to many different capacities that together determine how receptive to stimuli a person is and how incoming or already attended-to information is processed [75].

Provided these executive functions are intact, a person can still function independently, productively and in a self-directed manner even under substantial loss in other cognitive functions [75]. However, if these executive functions become impaired, a person may no longer be able to independently self-care or maintain normal social relationships. Impairments can lead to compromised strategies to approaching, organising, and solving tasks [75].

The frontal lobe, linked to executive function, is one of the most susceptible areas to neuronal loss – a common side effect of ageing [75]. The prefrontal areas sustain significant reduction in cerebral blood flow with ageing [75]. Executive function / attention has also been shown to predict falls independently of age and functional motor ability [69]. The effects of ageing on attentional capacities vary with the difficulty of the task or situation. Simple attention span is thought to remain relatively unchanged until the ninth decade of life whereas the capacity to divide attention between two tasks, and distractibility are markedly affected by the ageing process [75].

Processing speed

Processing speed is the rate at which mental activity is performed and is measured with timed tests of cognitive function [75]. There are different types of processing speed including decision speed, psychomotor speed, reaction time and perceptual speed [88]. Decision speed is measured by the time taken to respond to moderately complex content in a cognitive test. Psychomotor speed is usually assessed by timing simple tasks such as repetitive finger tapping. The most frequently used reaction time assessment involves visual stimuli and manual button pressing responses. Perceptual speed, the form of processing speed assessed in this thesis, is assessed by the speed of response to simple tasks that could be completed perfectly if there was no time limit. These tasks often involve comparison of two groups of symbols, searching for one symbol in a group of symbols or substitution of a symbol for a number, with the total number correctly identified in a limited time used as an individual's score [88].

Diseases of subcortical structures, and the frontal-subcortical pathways, often result in slowing of mental processing speed [75]. It has been shown that both the median

processing speed and variability between individuals markedly increases with advancing age [88].

Instrumental cognitive functions

Instrumental functions involve the storage and processing of content, and involve language, spatial abilities and memory. These functions are moderated by the neocortex, with the temporal, parietal and occipital regions contributing significantly to full function [77], though language is also served by frontal neocortex. Language will not be discussed further because it is unlikely to be primarily involved in falling or gait disorders.

Memory

Memory involves a complex process of registration, retainment, and retrieval of information. The process of retrieving information relies on both explicit and implicit memory [85]. Explicit (or declarative) memory involves intentional recollection of information (for example recognition or recall of a memory) whereas implicit memory refers to skill learning, or habit formation as a result of skills acquired previously [85]. All of the memory tests used in the studies described in this thesis deal with explicit memories.

Explicit memory can be divided in to three stages: two stages of short-term memory, and a stage of long-term storage [75]. The first stage is a brief storage for large amounts of incoming information. This sensory stage is thought not to be a memory function strictly, but instead it is a perception function and is not included in classifications of memory that prescribe a two stage system. The second stage is the immediate memory stage when information is temporarily held for registration. This stage may be equated with a simple immediate attention span. The third stage is long term memory when information is stored or consolidated [75].

Damage to the temporal-limbic system is thought to disrupt the formation and retrieval of new explicit information, without damage to previously stored implicit memories. Explicit, but not implicit, memories are regulated by the hippocampus and other mesial temporal structures such as the entorhinal and perirhinal cortices [85] and memory disorders are also linked to cognitive deficits of the basal ganglia [75]. Memory disorders such as Alzheimer's disease and other dementias have been linked

to gait, with abnormal gait reported to be associated with risk of progression to dementia over a three year period [89, 90].

Simple retention of information is the most resistant to ageing [75]. Regardless of a person's age, less information is recalled as the amount of information required to be remembered gets larger. Also, all memory systems become particularly vulnerable to ageing when a person is faced with remembering information whilst attempting to complete another non-related task [75].

Visuospatial ability

Visuospatial ability is the capacity of an individual to perceive their location in relation to their environment and the relative position of proximal objects. Visuospatial skills are used in aiming at targets, reading maps and navigating through the environment. It is the cognitive function least studied with respect to falls.

Visuospatial ability is compromised by lesions in the parieto-occipital region or in some parts of the frontal lobe [75]. Frontal lobe damage disturbs an individual's ability to program an approach to a task, whereas an individual with parieto-occipital lesions would have difficulty assessing the spatial organisation of the environment they are in [75]. Visuospatial disorders are the most common when there is impairment in the right parietal lobe [75] and deficits have also been seen in patients with impaired cerebellar function, either after the removal of left cerebellar hemisphere tumours or after left superior cerebellar artery territory infarction [91-93]. In monkeys, parieto-preoccipital lesions have been shown to produce a variety of visuospatial deficits [94].

Numerous tests of visuospatial abilities have been developed, aimed at detecting disorders of spatial recognition, orientation, visual neglect, many forms of agnosia as well as visual perception [85].

Visuospatial ability is of interest in falls research because it has been shown that postural control requires considerable visuospatial processing [95, 96]. It has also been suggested that secondary tasks involving spatial challenges will be more difficult when performing postural tasks [40, 95, 96].

1.5   Gait as a risk factor for falls

Definitions of gait, gait variability and gait initiation

The following definitions are used throughout this thesis to describe an individual's motion of walking:

Gait – the pattern of walking.

Gait variability – the variation between each step in the gait cycle.

Gait initiation – the time taken to achieve a cyclical gait pattern from standstill.

Gait and gait variability

Gait impairments are frequent in older people as a result of ageing and disease [13, 14, 97, 98] and have been shown to predict falls [8, 9]. An individual's gait can be described quantitatively or qualitatively. Qualitative assessments include descriptions such as slow or fast or shuffling. Quantitative assessments involve measurement of gait to enable the assessment of changes over time and the level of function. This thesis utilises quantitative measures of gait collected by a computerised walkway.

The gait cycle

The most commonly assessed gait measure is gait speed, the distance walked divided by the time taken to walk that distance. Gait speed can be calculated using step time (the time from contact of one foot to contact of the other foot) and step length (the distance along the line of progression between the heel of one foot and the heel of the other foot). Other gait measures include support base (the perpendicular distance from the heel of one footfall to the line of progression of the other foot), swing phase, stance phase, and single and double support phase (the period when both feet are in contact with the ground). These measures are all related within the gait cycle.

The gait cycle is the two step process from first contact with the ground of one foot to when that same foot makes contact with the ground again. The gait cycle can be broken into phases according to time or percentage of the cycle. Stance phase is the period when one foot is in contact with the ground and swing phase is the period

when that foot is not in contact with the ground. Approximately 60% of the gait cycle is spent in stance phase and the other 40% is spent is swing phase. The combination of double support phase and single support phase make up the total stance phase. Double support phase is the period when both feet are simultaneously in contact with the ground. The gait cycle and its components are shown in **Figure 1-1.** A single step in the gait cycle, as measured by the first contact with the ground of one foot to the first contact with the ground of the other foot, can be described in terms of distance (length) or time or by the distance between the feet (support base).
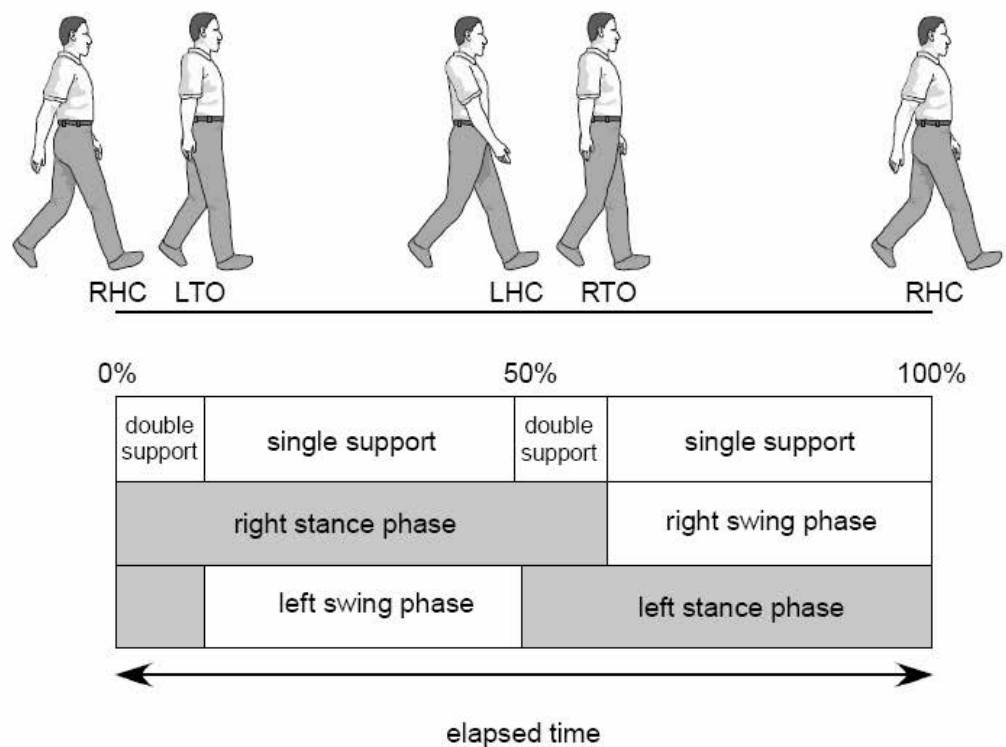
Figure 1-1: Time dimensions of the gait cycle.

RHC: right heel contact; LTO: left toe off; LHC: left heel contact; RTO: right toe off. Used with permission from A/Prof H. Menz, La Trobe University, Melbourne, Australia

In a clinical setting, multiple gait cycles are measured in an individual's recorded walk, and the gait measures are usually averaged across the multiple gait cycles for that individual. The average measures smooth the natural fluctuations between the individual steps. For example, the same average measure of step time could occur with large step-by-step variation in time to execute or with almost no variation at all. These fluctuations are known as gait variability. It is thought that gait variability may be a more sensitive indicator of falls-risk than the average measures of gait [99]. The variability measures detailed in this thesis are of step time, step length, support base and double support phase.

Gait initiation

One phase of gait during which falls happen frequently is the commencement of movement referred to as gait initiation (GI) [100]. GI time is the time taken to go from standing still to the establishment of a recurring pattern of walking. It is a part of everyday activity and its quick and correct execution is crucial. To do that requires modulation of ground reaction forces and joint movements to achieve the right angle and lift of the limb to clear the toe from the ground [101]. Older adults, and especially people with Parkinson's disease or frontal gait apraxia (where the feet stick to the ground), may not achieve that angle and lift, and thus initiate gait poorly. Poor initiation of gait may result in a fall [101].

GI is usually measured with a force platform as the time from stimulus to the release of pressure on the standing foot as the leading foot makes, or prepares to make, contact with an adjacent surface. This measure is commonly divided into smaller components: time to first lateral movement (FLM), transfer time and swing time [102]. These components can be detected on a force platform by a shift in centre of pressure or by a change in velocity. Due to expected large baseline sway in older adults, the change in velocity method is used in this thesis. Time to first lateral movement is the time from stimulus (for example, an auditory cue) to the first detectable lateral change in velocity. Transfer time is the time from FLM to the change in velocity associated with lifting the toe from the leading foot off the force platform (toe off). Swing time is the time from toe off to the change in velocity as a result of the heel of the leading foot making contact with the ground.

Whilst gait initiation is commonly divided into these components [40, 100-107], the relationships between the components have not been investigated. Much of the research on gait initiation has actually measured step initiation [40, 102, 104] rather than GI. Initiation of the gait cycle is more analogous to the everyday performance of commencement of walking – the phase of the gait cycle during which falls are relatively frequent – than is the initiation of the first step. The relationships between the components and other factors such as cognitive function, gait and sensorimotor measures has not been investigated either. Much of the research conducted to date has focused on comparisons between groups of people (for example younger versus older, or healthy versus diseased) [102].

A disadvantage of measuring GI using a force platform is that the platforms are expensive, and technologically somewhat complex to use. A potential alternative is the *GaitRite* walkway, which is increasingly used for clinical and research purposes. The *GaitRite* walkway can be placed on any flat surface and is easily portable. It cannot detect a shift in the centre of pressure as a force platform does, but it can be used to measure GI as the time from stimulus to contact of the leading foot. If the *GaitRite* walkway can be used as an alternative, it would mean that gait researchers would only need to acquire one piece of equipment to measure gait, gait variability and gait initiation. The appropriateness of the *GaitRite* walkway as an alternative to the force platform is investigated in **Chapter 3**.

An issue in GI research is choosing how many trials to conduct. Previous researchers [100-102, 108] have chosen to use up to five trials to obtain an overview of an individual's GI. Melzer and Oddsson [102] report a learning trend across the 3 trials they conducted for each step direction. The relationships between the three components, their associations with cognitive function and their individual contributions to falls-risk are investigated in **Chapter 5**.

1.6 Brain function and gait

Until recently, most research into the brain regions controlling gait has been undertaken in primates [109]. However, with advances in technology, the issue of brain control in human gait has become an increasing field of study. It is now well recognised that specific regions of the brain play an important role in the initiation, planning, execution and maintenance of gait. These regions are the frontal motor, prefrontal and parietal cortices, the basal ganglia and the cerebellum [81].

Walking has been shown to rely on the interaction between the supplementary motor cortex and the basal ganglia [110] and gait speed is thought to be maintained by the supplementary motor and sensorimotor cortices as well as the left prefrontal cortex [111]. In addition, the lateral premotor, cingulate cortices and the dorsal brainstem have been shown to be important in the attentional control of gait [112]. These regions serve as a neural network that most likely work together to produce a "normal" gait cycle.

Allowing this neural network to function properly, the motor cortices are connected by the projection and association of white matter fibers in conjunction with the basal ganglia, parietal cortex and the cerebellum [113-115]. As such, not only is the integrity of the gray matter structures important, but also the connectivity of these white matter networks are crucial to central control of gait.

Gray matter loss, known to happen with age [116], has been shown to occur in the frontal lobe [117] and also perhaps in the basal ganglia, hippocampus and the cerebellum [118]. The loss of cerebral gray matter in these areas with age has consequences for gait control. Further, lesions of the primary motor cortex have been shown to disrupt initiation and the rhythm of walking.

The quality and quantity of white matter is also known to decrease with age but at a later age, and in an accelerated fashion, compared to gray matter loss [116]. The corpus callosum is the primary white matter fiber bundle that connects the two hemispheres of the brain and has been shown to be involved in bimanual coordination [116]. White matter lesions impact on gait speed, the rhythmic pattern and the variability of gait independently of brain atrophy [84, 119, 120]. This impact also increases with increasing age [81].

1.7   Cognitive function and gait

It is well established that gait impairments, caused by ageing or disease, commonly arise in older people [13, 14, 97, 98] and predict falls [8, 9]. Decline in cognitive function, specifically executive function [121], attention [5, 6] and processing speed [5], may also be an important indicator of increased falls-risk in older people [5, 12] but data from population-based studies are scarce. The link between cognitive function and gait in their associations with falls is an important one [55] but is poorly understood. Studying these relationships may provide further insights into the neural substrates of gait control in ageing. Previous research has focused on investigations of the relationships of cognitive function with gait speed [122-131], or gait variability [132-135]. There are no population-based studies, to our knowledge, that have investigated the effects of cognitive function on gait speed, other average gait variables and gait variability together.

They have also mainly focused on the role of global cognitive function [136, 137], executive function and/or attention in gait [132, 135, 138-140], or that of divided attention in gait control [141-144]. Very few studies have examined the effects of other key cognitive domains such as memory or visuospatial ability, particularly in a population-based setting [128, 145]. Inconsistent associations have been described for memory, with one study reporting adverse effects on gait speed [145], while no associations were observed in another [128]. Furthermore, there is a paucity of studies examining cognitive associations with intra-individual gait variability which may be a better indicator of balance and the risk of falls [146]. The results for gait variability are varied, with some researchers finding no associations between cognitive function and gait variability [122, 125, 132], and some reporting increased stance time variability [132], and stride time variability [126] to be associated with poorer cognitive function. Moreover, most studies in this field have been conducted in highly selected clinical samples or in small samples of volunteers, with limited data from the general population [128, 132, 140, 145, 147].

The presence of neurological conditions such as Alzheimer's and Parkinson's disease, with symptoms that include gait abnormalities and a predisposition to falls, indicates that cognitive function and gait are strongly associated. The direction of causality has not been investigated in research conducted to date. On the one hand, gait is known to involve a combination of motor and cognitive factors including

attention, planning and possibly memory [148, 149]. On the other hand, gait disorders may also be associated with declines in cognitive functioning that increase the future risk of dementia [55, 89]. Even though the direction of association between cognitive function and gait has not been established, there are several studies showing the impact on falls of each. One line of research has shown that walking and talking concurrently is associated with poorer balance and an increased risk of falls [142, 150-152].

The links between gait and cognitive function may be through their shared neuro-anatomical substrates. It is thought that white matter lesions may lead to the disruption of axonal connections between subcortical structures and the cortex, and that this may lead to disorders of both cognitive function and mobility, including gait [77]. The relationships between these two important risk factors for falls are investigated in **Chapter 4**.

1.8 Summary

Falls are a significant public health problem in older people. There are major costs and consequences of falls including injury, institutionalisation, morbidity and mortality. Because the number of surviving older adults is increasing over time, the costs and consequences of falls will have greater future impact on society. There is an increasing research imperative to identify risk factors for falls, and to use this information to design interventions to prevent falls.

Cognitive function and gait are two important risk factors for falls. Declines and impairments in general cognitive functioning and gait have been shown to predict falls in older adults independently of many other factors including balance and medication. Investigation of the contributions of specific cognitive functions to falls, and of the inter-relationships of gait and specific cognitive functions in the causation of falls, is at an early stage. Increased understanding of which specific cognitive functions impact on falls may help in the design of therapies for prevention. Understanding of the inter-play between cognitive function and gait may provide markers of rapidly declining function and enable the earlier detection of people likely to fall.

1.9 Research aims and objectives

General aim

The general aim of this thesis was to investigate the relationships between gait, cognitive function and falls in an older population-based sample of residents of southern Tasmania.

Specific objectives

The specific aims of the investigations reported in this thesis were:

i. To study the associations between a range of cognitive functions, gait and gait variability;

ii. To study the associations between a range of cognitive functions and the risk of:

    a. Falling using a surrogate measures of falls-risk,

    b. A single fall,

    c. Multiple falls;

iii. To provide empirical evidence to support the rational choice of an appropriate measure of gait initiation.

General hypotheses

That cognitive function is associated with gait, gait variability and the risk of falling.

More specifically, that the instrumental functions of memory and visuospatial ability are associated with gait and gait variability independently of the fundamental cognitive function of executive function and processing speed.

That multiple measurements of three components of time to GI can be represented by summary statistics that account for learning effects and have greater construct and predictive validity than overall measurements of time to GI.

Study population

The study population for this thesis is that of southern Tasmania in Australia (**Figure 1-2**). In 2004, Tasmania – an island state of Australia located at 42 - 43 degrees latitude south – had a population of 482,200 people, with 42% of those people residing in Hobart. Compared to the national average of 12.7%, 14.0% of Tasmanians were older than 65 years of age in 2004 (ABS 2005, Series B projection) [153]. That percentage is expected to rise over time, with about one third of the Tasmanian population projected to be aged 65 years or older in 2051, and making it the state with the oldest population in Australia. This makes southern Tasmania an ideal setting for this population-based study. The region, southern Tasmania, is that identified in **Figure 1-2** as Hobart and Southern Tasmania – a geographical region defined by postcodes.

Figure 1-2: Map of Australia and Tasmania.

(Used with permission from Oxford Cartographers www.oxfordcartographers.com)

1.10 Thesis outline

In brief, the structure of the thesis is as follows:

Chapter 2: Methods. This chapter presents the study sample and methods of data collection for the subsequent analyses in this thesis.

Chapter 3: Can we use the *GaitRite* walkway to accurately measure gait initiation? This chapter presents results from an investigation of the suitability of the *GaitRite* walkway, as an alternative device to the gold standard force platform, to measure gait initiation in a sample of 28 participants aged 60-86 years.

Chapter 4: Cognitive function, gait and gait variability in older people: a population-based study. This chapter details the results from a cross-sectional analysis of the associations between gait, gait variability and cognitive function in a population-based sample of 416 community-dwelling older people aged 60-86 years. At the time of submission of this thesis, the contents of this chapter had been submitted as a manuscript to the Journal of Gerontology.

Chapter 5: Time to first lateral movement may be the most appropriate measure of gait initiation in older people. This chapter presents results from an investigation in to the statistical characteristics of the components of gait initiation, their inter-relationships and associations with sensorimotor variables, and the effect of cognitive loading on these relationships. The investigation was conducted in a population-based sample of 128 community-dwelling older people aged 60-86 years. At the time of submission of this thesis, the contents of this chapter, other than the appendix, chapter have been published in a peer-reviewed journal [154].

Chapter 6: Visuospatial ability and memory are associated with falls-risk in older people: a population-based study. This chapter details findings from a cross-sectional analysis of the associations between cognitive function and a sensorimotor measure of falls-risk in a population-based sample of 300 community-dwelling older people aged 60-86 years. The contents of this chapter have been published in a peer-reviewed journal [155].

Chapter 7: Cognitive function modifies the effect of sensorimotor function on the risk of multiple falls – a population based study. This chapter reports findings from a study of whether poorer cognitive function predicts the risk of single and multiple falls in a population-based sample of 416 older people aged 60-86 years. At the time of submission of this thesis, the contents of this chapter were under review by a peer-reviewed journal (Journal of Gerontology).

Chapter 8: Summary. This chapter draws together the major findings and conclusions, summarises the collective contribution of the thesis, and presents recommendations for future research.

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Chapter 2:   Methods

2.1   Preface

The aims of this thesis are to investigate the relationships between gait, cognitive function and falls in an older population-based sample. This chapter provides details on the study sample and study factors investigated in the chapters that follow. It also details how these study factors were measured. The data obtained using the methods in this chapter are analysed in subsequent chapters.

2.2   The Tasmanian Study of Cognition and Gait (TASCOG)

The research reported in this thesis was conducted as a part of the Tasmanian Study of Cognition and Gait (TASCOG) conducted during the period 2006 to 2007 at the Menzies Research Institute in Hobart, Tasmania, Australia. Clare Munro and Shalee Richardson recruited the participants. They also participated in data collection assisted by other TASCOG research staff and volunteers (including doctors, neuropsychologists, psychologists and trained PhD students). These people who assisted were: Kate Butorac, Georgie Boon, Jan Stacey, Charlotte McKercher, Clair Storr, Tye Dawson, Laurence Hurst, Stella Foley, Michele Callisaya, Bob Uren, Marilyn Uren, and Tim Albion.

 TASCOG is a study of the neural correlates of cognition, gait and falls in 431 participants. Eligible subjects were residents of Southern Tasmania, a geographical region defined by postcodes (7000 – 7199), who were aged between 60 and 85 years inclusive. They were selected by stratified random sampling without replacement from the Tasmanian Electoral Roll, with stratification by sex and 5-year age groups. Subjects were excluded from the study if they lived in residential care, were unable to walk without a gait aid, or had any contraindications to magnetic resonance imaging (MRI) – a requirement of the TASCOG study investigating the neural correlates of gait and cognitive function. Eligible subjects who did not wish to participate in the study were asked about their medical history and history of falls in the previous 12 months to enable comparisons between participants and those who declined to participate. The response proportion for TASCOG was 52% (431/822).

2.3   Study sample

In the subsequent chapters, analyses have been conducted on sub-samples of the 431 eligible participants (**Figure 2-1**). The sub-samples in each case comprised to reflect the total number of participants who, at that time, had completed assessment of the study factors involved.
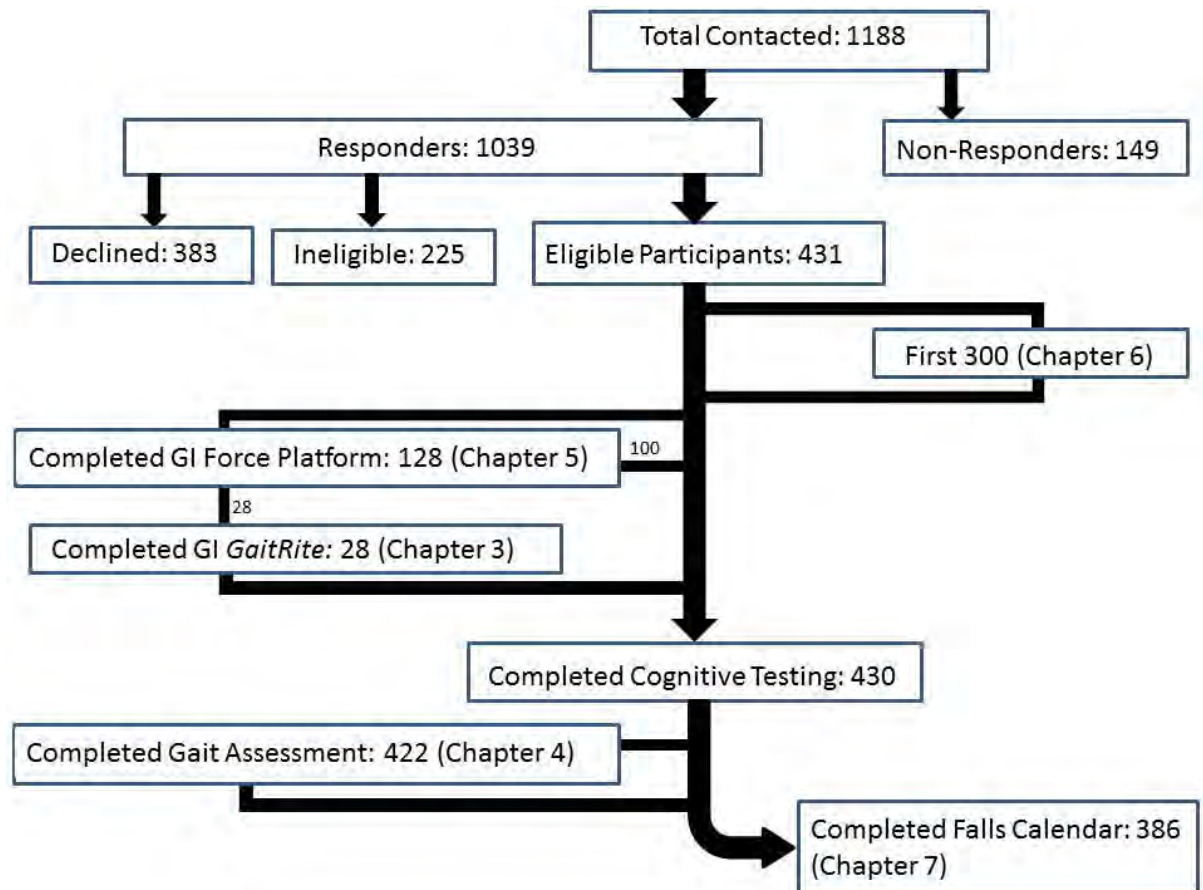
Figure 2-1: The study sample size for TASCOG

The samples for the study reported in each chapter is as follows:

Chapter 3: The 28 consecutive participants who completed gait initiation assessment on both the GaitRite walkway and the force platform;

Chapter 4: All 422 participants, from the full sample, who completed both cognitive function and gait assessment;

Chapter 5: All 128 consecutive participants who completed gait initiation assessment on the force platform;

Chapter 6: The first 300 participants to complete cognitive testing and falls-risk assessment based on sensorimotor function;

<u>Chapter 7</u>: All 386 participants, from the full sample, who either completed the 12 months falls calendar or part thereof and had recorded a fall in that time (these people could be classified as having fallen even though they had not completed the falls calendar).

2.4   Study factors

Cognitive function: fundamental cognitive abilities

The following tests were used to measure fundamental cognitive abilities:

Executive function / attention

Executive function / attention was measured using the Controlled Word Association Test (COWAT – FAS and category fluency) [1], the Victoria Stroop test [2] and the Digit Span subtest of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) [3].

The COWAT comprises two sections which test verbal fluency. The first section involves three tasks. The participant is asked to list as many words as possible beginning with F, A and S without repetition, use of proper nouns or more than one conjugation or declension of a word (examples are fish, fishing and fisherman). The second section involves listing as many animals as possible without repetition. Each task is run for 1 minute. Testing verbal fluency, with tests such as the COWAT's FAS component, has proven to be a sensitive indicator of frontal lobe dysfunction [1, 2]. Test-retest reliability scores for the COWAT tests are high (intraclass correlation coefficient, ICC = 0.70) and studies investigating the concurrent validity show that there is better validity for the letters (F,A,S) than for the categories. Higher scores on the COWAT tests indicate better function.

The Victoria Stroop test measures the ability to shift perception in response to changing demands and suppress a habitual response in favour of another more unusual one [2]. Slow performance on the Stroop test has been associated with frontal lobe lesions, particularly on the left side [1]. The test involves three different white cards each containing 4 rows of 6 items that assess selective attention and cognitive flexibility. The first card contains coloured dots, the second coloured words (for example, car, hat, dog), and the third has colour names in a different coloured font (for example, the word red typed in blue ink). Each time the participant is asked

to read the colour of the font. Time to completion is recorded for the three separate parts [1]. Higher scores on all tests indicate poorer function. The three components of the Stroop test are included in **Appendix 2A.**

The Digit Span comprises two tasks. Lists of numbers are read out loud and the participant is asked to repeat them in the same order. The lists start with two numbers and increase in difficulty until the lists include nine numbers. This test assesses the capacity to maintain auditory attention [4]. This test is sensitive to left hemispheric damage and scores may be decreased in those with frontal lobe lesions [1]. Then the participant is read lists containing two to eight numbers and asked to repeat them backwards [1]. The digit span test has moderate-to-high test-retest reliability (ICC = 0.66 – 0.89 [2]. Higher scores on the Digit span indicate better function.

Processing Speed

Processing Speed was measured using the Symbol Search and Digit Symbol Coding subtests of the Wechsler Adult Intelligence Scale-III (WAIS-III) [3].

The Symbol Search and Digit Symbol Coding tests from the WAIS-III were performed to test processing speed. They are highly sensitive tests of psychomotor performance that are relatively unaffected by intellect, memory and learning [1, 2].

These tests are sensitive to brain damage, with scoring that can be diminished by the slightest impairment. Locating the impairment using these tests alone is difficult, however, because these tests assess the integrity of the cortex and the interconnections of the cortices overall [1].

In the digit symbol coding test, the participant is given nine symbols with a number from one to nine uniquely associated with each one. They are then given a random list of numbers and asked to identify which symbol is associated with each number. They are given two minutes to complete as many as possible, and the number of correct responses is recorded [1]. A copy of the digit symbol coding test is shown in **Appendix 2B**. In the symbol search, the participant is shown two symbols and asked to identify whether either of them were in a group of five symbols. This process is repeated for two minutes and the number of correct responses in that time is recorded.

Both the symbol search and the digit symbol coding tests have high test-retest reliability (ICC > 0.88) and there is substantial correlation (r = 0.5 – 0.8) between

these and other intelligence measures [2]. Higher scores on these tests indicate better function. The symbol search is shown in **Appendix 2C**.

Cognitive function: instrumental cognitive abilities

The following tests were used to measure instrumental cognitive abilities:

Spatial Ability

Spatial ability was measured using the initial copy of the Rey Complex [1].The Rey Complex Figure Test primarily investigates perceptual or constructional organisation and is a highly sensitive measure of parietal lobe function [5]. It also incorporates planning, organisation and problem-solving strategies, and therefore is also an indirect measure of executive/frontal lobe function. The participant is first asked to copy the Rey figure. This is a complex figure formed from lines, circles and dots. It is given to the participant with the figure rotated by 90° (as shown in **Appendix 2D**). The paper on which they are to draw the copy is also placed in this fashion. The participant is not allowed to rotate either piece of paper during the test. This enables the investigator to see if there are difficulties in working with the unrotated material [1]. The figure and the copy are removed once the participant has completed the copy to the best of his/her ability.

For scoring, the figure is broken in to 18 separate units and marks are awarded for the accuracy of the reproduction of each unit and the relative positioning within the whole design. An accurate unit placed correctly is given two marks. One mark is given to an accurate unit poorly placed or a distorted or incomplete unit placed properly. A half mark is given if the item is poorly placed and distorted or incomplete but still recognizable. The participant is given a total score out of 36 for each task [1]. Higher scores indicate better visuospatial ability.

Memory

Memory was measured using the Hopkins Verbal Learning Test – Revised to generate scores for total immediate recall, delayed recall, and recognition memory [1] and a 20 minute delayed reproduction of the Rey Complex Figure test.

The Hopkins Verbal Learning Test – Revised™ (HVLTR) is a brief test for assessment of immediate, delayed and recognition memory. The recall tasks are sensitive to frontal lobe defects and all three conditions are sensitive to basal ganglia

disorders [1]. It comprises three tasks. A list of twelve words is read to the participant. Each participant is tested on their immediate recall three times and once on their delayed recall ability after 20 minutes. To test recognition skills, they are read a list of twenty-four words and asked to identify whether each word was in the list of twelve [1]. Higher scores on all three components of the HVLTR indicate better function. The HVLTR has been shown to have acceptable test-retest reliability across all components (ICC = 0.41 – 0.74) [6] and to be a valid instrument for neuropsychological assessment with elderly patients [7].

Twenty-five minutes after the initial copy of the Rey Complex Figure (**Appendix 2D**), and without prior warning, the participant is asked to reproduce the figure from memory. The delayed recall of this figure is thought to be a sensitive indicator of the presence of various memory deficits that retard the retention of information over time [2]. Test-retest reliabilities of both the immediate and this delayed reproduction are moderate (ICC = 0.47 – 0.59) [2].

Average measures of gait

Gait variables – speed, step time, step length, support base and double support phase (DSP) – were measured using the 4.6m GAITRite system (CIR Systems, PA, USA) at usual walking pace. The *GaitRite* walkway is a portable carpet with embedded sensors that captures information on gait electronically whilst the participants walk along it. Data are captured at a rate of 80Hz on an active area of 366cm long by 61cm wide, containing 288 rows of 48 sensors. Participants were required to complete 6 walks and start and finish walking 2m before and after the mat to allow a constant speed to be maintained during the period of data capture. These 6 walks were combined to provide average measures of a participant's gait.

For use in subsequent chapters, the gait variables are defined as follows:

Gait speed – how quickly the participant covers the 3.66m by walking in a straight line, derived from the distance travelled divided by time taken to walk that distance.

Step time – the time from contact of one foot to contact of the next.

Step length – the distance along the line of progression between the heel of one footfall to the heel of the next footfall.

Support base –   the perpendicular distance from the heel of one footfall to the line of
progression of the other foot.

Double support phase – the time (msec), or percentage of total time, elapsed over the
whole gait cycle when both feet are in contact with the ground.

Intra-class correlations ranged from 0.92 to 0.97 for re-measurement of gait one
week later [8]. Declining function is indicated by slower gait speed and step time,
smaller step length, a wider support base and a longer double support phase.

Gait variability

Intra-person variability in step time, step length, support base and double support
phase was calculated as the standard deviation [9-12] of the measure across all steps
for all 6 walks. Intra-class correlations ranged from 0.22 to 0.59 for re-measurement
of gait variability one week later [8]. Poorer function is marked by increased intra-
individual variability.

Gait initiation

Gait initiation (GI) was measured with a force platform and with a computerised
walkway.

GI on the force platform

Gait initiation was measured using a 200Hz AccuGait force platform and Advanced
Mechanical Technology Inc. (AMTI)-NetForce software. Participants were required
to stand with bare feet in a standardised stance with heels separated by 6cm and with
approximately a 10° angle between the feet [13]. In response to an auditory cue, they
were required to start walking forward a few steps onto an adjacent surface at the
same height as the force platform. Twelve trials were conducted for each participant,
alternating between a state of no cognitive interference (single task, 6 trials) and
cognitive interference (dual task, 6 trials). The dual task was to initiate gait in
response to the auditory stimulus whilst counting backwards in threes from a
designated number (the initial number was varied for each trial). Overall GI time was
recorded as the time from stimulus to the release of pressure on the standing foot as
the leading foot makes, or prepares to make, contact with an adjacent surface. This
measure was divided into three components: time from stimulus to first lateral
movement (FLM); FLM to toe off of the leading foot (transfer time); and time from

toe off to foot contact (swing time). Previous research on the reliability and validity of the force platform has focused on posture, balance and stance [14, 15] and not on the measurement of GI in predicting falls.

GI on the GaitRite walkway

Gait initiation was also measured using the 4.6m GAITRite system (CIR Systems, PA, USA). The *GaitRite* walkway is a portable carpet with embedded sensors that captures information on gait electronically whilst the participant walks on it. Data were captured at a rate of 80Hz on an active area of 366cm long by 61cm wide, containing 288 rows of 48 sensors. Participants were instructed to stand upright on the active part of the mat and, in response to an auditory cue, were required to start walking forward a few steps along the mat. Three trials were conducted per participant. Overall GI time was recorded as the time from stimulus to contact of the leading foot.

Sensorimotor measures of falls-risk

Falls risk was assessed in accordance with the protocols of the short form of the Physiological Profile Assessment (PPA) [16]. The PPA consists of the following measurements:

(1) Edge contrast sensitivity was assessed using the Melbourne Edge Test chart that has 20 circles containing edges with reducing contrast. The objective is to identify the orientation of the edge in each circle. The orientation can be horizontal, vertical, diagonally left or diagonally right. The lowest correctly identified edge contrast was recorded in decibel (dB) units.
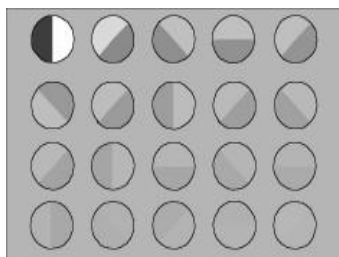
Figure 2-2: PPA - Edge Contrast Sensitivity

(2) Proprioception was assessed using a lower-limb matching task. Participants were asked to sit in a chair with their eyes closed and to align their feet either side of a

perspex sheet with lines depicting angles from the horizontal drawn on it. The degree of displacement between the two big toes was measured.

Figure 2-3: PPA - Proprioception

(3) Knee extension strength (kg) was measured using a spring gauge attached to the subject's dominant leg. The gauge is also fixed to a crossbar behind the subject. Whilst seated, the subject is asked to pull against the strap with maximum force three times. The greatest force in kilograms is recorded as the knee extension strength. The average of three attempts was recorded.

Figure 2-4: PPA - Knee extension strength

(4) Simple reaction time, in seconds, was measured as the time to depression of a switch by the finger in response to a light stimulus. It was recorded as the average of 10 trials.
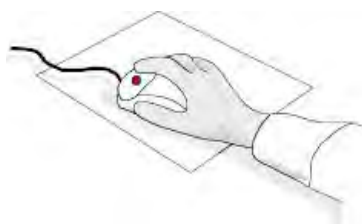
Figure 2-5: PPA - Reaction time

(5) Postural sway was measured using a sway meter that recorded displacements (mm) of the body at waist height while subjects stood on a medium-density foam rubber mat with eyes open and closed. The sway metre consists of a 40cm pole with a vertically mounted pencil attached to the end. The other end of the pole is attached to the back of the subject's waist with a band. While the subject attempts to stand as still as possible for 30 seconds, the pencil marks the subject's sway on graph paper. The subject's total sway is the total number of millimetre squares that the pencil crosses.
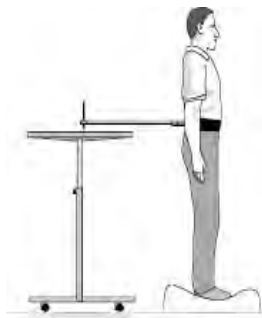
Figure 2-6: PPA - Postural sway

Summary measure of Falls-Risk

Using an established algorithm [16], a standardised falls-risk z-score was then computed as a summary of weighted scores from the above individual tests with higher falls-risk z-scores indicating a greater falls risk. In a prospective study of community-dwelling older women, the falls-risk z-score has been shown to predict those at risk of multiple incident falls compared with non-multiple falls with75% predictive accuracy [17]. In a prospective study of older adults, the PPA distinguished those at risk of multiple falls from those not at risk with 79% predictive accuracy [18].

The PPA was used as a measure of falls-risk because it is easily conducted, provides a quantitative assessment, is reliable and has been shown to discriminate between fallers and non-fallers (including distinguishing between single and multiple fallers) [16-19]. In addition, the individual factors within the test – vision, proprioception, strength, reaction time and sway – are potentially modifiable or amenable to treatment [16].

Intra-class correlation (ICC) coefficients for the test-retest reliability of the PPA tests range from 0.50 to 0.97 for older adults re-measured two weeks apart [16]. The test of proprioception had the lowest relative reliability with sway with eyes open the second lowest (ICC = 0.57) meaning that these tests are measured with the greatest random error. The tests for visual contrast sensitivity, sway with eyes closed and knee extension strength all had ICCs greater than 0.80.

Incident falls

A fall, for the purposes of this study, was defined as "coming to rest on a lower level". Participants were advised to include falling to the floor from a standing position and also falling onto a chair or bed (these are surfaces lower than their head in standing position). This is in accordance with the ProFaNE consensus statement [20]. Falls were measured using a self-report 12-month prospective calendar. Information on the number of falls, the reason for each fall and the outcome (whether any injury was sustained) was collected using a reporting form that was completed and returned at two monthly intervals during the 12 months. Follow-up phone calls were made if a participant had not returned their reporting form promptly.

Other study factors

Clinical and demographic information was collected to ascertain age, sex, height, weight and level of education (in years). Self-reported history of falls and arthritis were also recorded. Mood was measured using the 15-Item Geriatric Depression Scale (GDS) [21] with higher scores indicating poorer mood [22]. A detailed list of over-the-counter and prescription medicines was compiled for each participant. Based on this list, participants were classified as taking a psychoactive medication if they were using any of the following: antidepressants, antipsychotics, sedative/hypnotics, antiepileptics or antiparkinsonian drugs. They were also classified according to whether they were taking any blood-pressure medication. Ambulatory activity was assessed using a Yamax Digi-Walker SW-200 pedometer worn on 7 consecutive days. Participants were required to complete a 7-day diary of daily steps, and to report times the pedometer was worn and not worn. Recordings for days on which the pedometer was worn for less than 8 hours were excluded when calculating mean number of steps per day.

2.5   Data analysis

Methods of data analysis for each individual study are reported in the relevant chapters of this thesis that details the conduct and results of that study.

2.6   Ethics

Written consent was obtained from all of the participants. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved this study.

2.7   Postscript

This chapter provides detailed information on the methods for collecting data on cognitive function, gait (including variability and initiation), sensorimotor measures of falls-risk and incidence falls. It discussed the force platform as a device to measure the gait initiation of older adults. This device is the gold standard measurement device but it is expensive and elaborate to set-up. In the next chapter, the *GaitRite* walkway is assessed as a potential alternative device with which to measure gait initiation in older people. This devices is more portable and therefore better suited to large scale field work.

2.8   References

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Appendix 2A: Victoria Stroop test
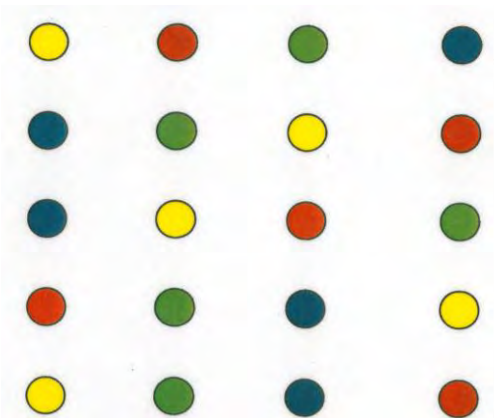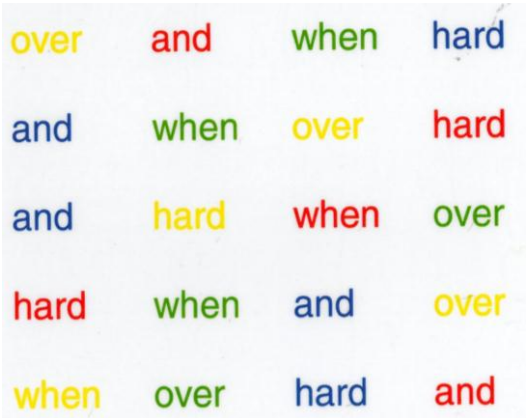
Stroop Words   **Stroop Dots**

Stroop Colours

Appendix 2B: WAIS-III digit symbol coding

Digit Symbol—Coding

1	2	3	4	5	6	7	8	9
—	⊥	⊐	∟	⊔	○	∧	✕	=

Sample Items

2	1	3	7	2	4	8	2	1	3	2	1	4	2	3	5	2	3	1	4

5	6	3	1	4	1	5	4	2	7	6	3	5	7	2	8	5	4	6	3

7	2	8	1	9	5	8	4	7	3	6	2	5	1	9	2	8	3	7	4

6	5	9	4	8	3	7	2	6	1	5	4	6	3	7	9	2	8	1	7

9	4	6	8	5	9	7	1	8	5	2	9	4	8	6	3	7	9	8	6

2	7	3	6	5	1	9	8	4	5	7	3	1	4	8	7	9	1	4	5

7	1	8	2	9	3	6	7	2	8	5	2	3	1	4	8	4	2	7	6

Appendix 2C: WAIS-III symbol search

Sample Items

Practice Items

Appendix 2D: Rey Complex Figure
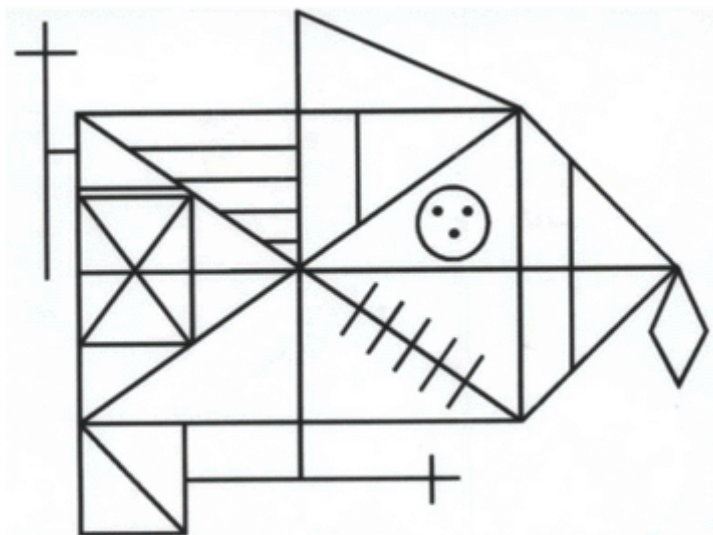
Chapter 3: Can we use the *GaitRite* walkway to accurately measure gait initiation?

3.1 Preface

In the previous chapter, information on the sample of participants and the materials and methods that were used to measure cognitive function, gait (including variability and initiation) and falls in the studies were reported.

In this chapter, I assess the suitability of the 80Hz, 4.8metre *GaitRite* walkway as a potential alternative to the gold standard force platform for measurement of gait initiation in older people. This work is important because the *GaitRite* walkway is portable, cheaper than the force platform, and is increasingly being used in gait research. If it could also be used to accurately measure gait initiation, one piece of equipment could capture data on gait, gait variability and gait initiation.

3.2 Introduction

Impairments in gait are common in older people [1-4] and are known to predict falls [5, 6]. Falls occur frequently during gait initiation (GI) [7]. This is the commencement of movement, and it is measured as the time elapsed between standing still and taking the first step in a recurring pattern of walking. GI is a widely investigated phase of gait. It is usually measured with force platforms [7-9] as the time elapsed from a stimulus until the release of pressure on the standing foot as the leading foot makes or prepares to make contact with an adjacent surface. Using a force platform either requires the platform to be embedded in the ground or placed on the ground and surrounded by surfaces of the same height (for example, by surrounding it with a raised surface constructed from wooden planks).

A disadvantage of measuring GI using a force platform is that the platforms are expensive, and technologically somewhat complex to use. The *GaitRite* walkway, which is increasingly being used for clinical and research purposes, may provide a cheaper but untested alternative method of measuring GI. The *GaitRite* walkway is a portable carpet with embedded pressure sensors that captures information on gait electronically whilst the participant walks on it. It can be placed on any flat surface

and is easily portable. It cannot detect a shift in the centre of pressure as a force platform does, but it can be used to measure GI as the time from stimulus to contact of the leading foot.

Our aim, therefore, was to investigate the comparative validity of measurements of GI made with the *GaitRite* walkway as an alternative for measurements of GI made with the force platform.

3.3   Methods

Subjects

The sample consisted of 28 subjects from the Tasmanian Study of Cognition and Gait (TASCOG) that was conducted at the Menzies Research Institute in Hobart, Tasmania, Australia during the period from 2006 to 2007. Eligible TASCOG participants were residents of Southern Tasmania, a geographical region defined by postcodes (7000 – 7199), and were aged between 60 and 85 years inclusive. They were selected by stratified random sampling without replacement from the Tasmanian Electoral Roll, with stratification by sex and age in 5 year groups. The Electoral Roll of registered voters is a comprehensive population listing. Potential subjects were excluded from the study if they lived in residential care, were unable to walk without a gait aid, or if they had any contraindications to magnetic resonance imaging – a requirement of the overall study. The 28 participants in this study were consecutive TASCOG subjects who were asked to complete GI measurements on both the force platform and the *GaitRite* walkway.

Measurements

Gait initiation (GI)
GI was measured using the *GaitRite* walkway and a force platform.

GI on the force platform
GI was measured using a 200Hz AccuGait force platform and Advanced Mechanical Technology Inc. (AMTI)-NetForce software. Participants were required to stand with bare feet in a standardised stance with heels separated by 6cm and with approximately a 10° angle between the feet [10]. In response to an auditory cue, they were required to start walking forward a few steps onto an adjacent surface at

the same height as the force platform. Six trials were conducted for each participant. Overall GI was recorded as the time from stimulus to the release of pressure on the standing foot as the leading foot makes, or prepares to make, contact with an adjacent surface. This overall measure can be divided into three components: time from stimulus to first lateral movement (FLM); FLM to toe off of the leading foot (transfer time); and time from toe off to foot contact (swing time). We do not make use of these individual components in this analysis because they are not measured by the *GaitRite* walkway, and hence no comparisons are possible.

GI on the *GaitRite* walkway

Gait initiation was also measured using the 4.6m GAITRite system (CIR Systems, PA, USA). The *GaitRite* walkway is a portable carpet with embedded sensors that captures information on gait electronically whilst the participant walks on it. Data were captured at a rate of 80Hz on an active area of 366cm long by 61cm wide, containing 48*288 sensors. Participants were instructed to stand upright on the active part of the mat and, in response to an auditory cue, were required to start walking forward a few steps along the mat. Three trials were conducted per participant. Overall GI was recorded as the average of the three measures of time from stimulus to contact of the leading foot.

Other Measures

The *GaitRite* walkway was also used to capture other information on the participant's gait. Participants were required to complete 6 walks and to start and finish walking two metres before and after the mat respectively to allow a constant speed to be attained. Measurements were made of step time and step length (both used to derive gait speed), support base and double support phase (DSP) [11]. These gait measures are described in greater detail in **Chapter 2**.

Sensorimotor function related to stability and gait was measured using the short form of the Physiological Profile Assessment (PPA) [12]. The PPA measures include visual edge contrast sensitivity, lower limb proprioception, knee extension strength, reaction time, postural sway and a standardized falls-risk score that is computed as a summary of weighted scores from the above individual tests [13-15]. These PPA measures are described in greater detail elsewhere [16] (**Chapter 2**).

Data analysis

Reliability analysis

T-tests were used to assess the mean difference between the measurements of GI made with the force platform and the *GaitRite*. To assess the clinical significance of the mean difference, the falls risk z-score was regressed on measurements of GI by the force platform. This allowed us to assess the proportion of subjects that might be misclassified by measurements of GI made with the *GaitRite* walkway. Specifically, we estimated the change in z-score associated with the observed mean difference in GI, and calculated the proportion of the distribution of a standard normal variable that this range of z-scores represents. This proportion varies at different values of the z-score, and is greatest at the median ($z = 0$).

To assess the relative agreement between the two devices, scatter plots and Bland-Altman plots were used to inspect the data, and Spearman rank correlations and intra-class correlation (ICC) coefficients were used to quantify the reliability. As a concept of reliability, we had in mind the ratio of between-subject variability to total variability that is comprised of error variance in addition to between-subject variability [17]:

$$reliability = \frac{\text{between-subject variability}}{\text{between-subject variability} + \text{error variance}}. \qquad (1)$$

This reliability coefficient is quantified by various forms of the ICC as described by Shrout and Fleiss [18]. Using this terminology for an inter-method comparison study, let x_{ij} denote the rating of the ith ($i=1,2,…,k$) judge on the jth ($j=1,2,…,n$) target. A simple measurement error model is the linear model:

$$x_{ij} = \mu + a_i + b_j + e_{ij} \qquad (2)$$

where μ denotes the overall population mean of the ratings, a_i denotes the difference from μ of the mean of the ratings of the ith judge, b_j denotes the difference from μ of the "true" score for the jth target, $(ab)_{ij}$ denotes the difference of the rating of the ith judge for the jth target from the mean of the ratings of the ith judge, and e_{ij} denotes the random error in the ith judge's scoring of the jth target. In this study, the targets

are the 28 subjects, the judges are the two devices (the force platform and the *GaitRite* walkway), and the ratings are the measurements of GI.

When each target is rated by each of the same *k* judges who are the only judges of interest, as was the case in this study where each of the 28 subjects was measured using each of the *k* = 2 methods (force platform and *GaitRite* walkway) that are the only two methods of measuring GI, the reliability coefficient takes the form:

$$reliability = \frac{\sigma_T^2 - \sigma_I^2/(k-1)}{\sigma_T^2 + \sigma_I^2 + \sigma_e^2} \tag{3}$$

where σ_T^2 denotes the variance of the b_j (the variance of the "true" value for each subject about the overall population mean), σ_I^2 denotes the variance of the $(ab)_{ij}$ (the variance of the measurements by each device for each subject about the mean of the measurements of each device), and σ_e^2 denotes the variance of random error. This reliability coefficient is estimated consistently but with bias by *ICC(3,1)*.

$$ICC(3,1) = \frac{BMS - EMS}{BMS + (k-1)EMS} \tag{4}$$

where *BMS* denotes the between-subject mean square and *EMS* denotes the residual mean square from a one-way analysis of variance, and *k* is the number of replications (here $k = 2$, being the two devices of interest).

The formula (4) for the reliability coefficient does not include σ_S^2, the variance of the a_i. Hence *ICC(3,1)* does not include variance of systematic error due to the different measurement devices, and as a result it is closely approximated by the Pearson product moment correlation coefficient *r* [19, 20].

Other analyses

Linear regression was used to estimate associations between the difference between the measurements of GI made with the *GaitRite* walkway and the force platform with factors that might have contributed to the difference. Spearman rank correlations were used to assess the associations of GI measured by both devices with step length and with the PPA measures. To investigate whether it was possible to improve the predictive validity of the *GaitRite* walkway measurements by correcting the *GaitRite*

walkway measurements to have the same mean as the force platform measurements at each level of the force platform measurements, a correction factor was calculated by regressing the *GaitRite* walkway (G) measurements on the force platform (F) measurements. Denote the fitted regression line for subject *j* (j=1,2,…,*n*) as:

$$\hat{G}_j = \hat{a} + \hat{b}F_j \tag{5}$$

where $\hat{a}$ and $\hat{b}$ are the estimated coefficients. The regression errors are:

$$\hat{e}_j = G_j - \hat{G}_j = G_j - \hat{a} - \hat{b}F_j. \tag{6}$$

By adding the regression errors to the force platform measurements, the mean-corrected *GaitRite* measurements ($\hat{\hat{G}}$) were calculated as:

$$\hat{\hat{G}}_j = F_j + \hat{e}. \tag{7}$$

Note that this correction differs from statistical calibration, which involves use of the estimated relationship to make estimates of the independent variable (*F*) from new observations of the dependent variable (*G*). This would be done using the relation:

$$\hat{F}_j = -\frac{\hat{a}}{\hat{b}} + \frac{1}{\hat{b}}G. \tag{8}$$

It was not done in this study because the simple correlation coefficient is invariant to a linear transformation of either marginal distribution – the correlation between $\hat{F}$ (the calibrated value of *G*) and *F* is identical to the correlation between *G* and *F*.

3.4   Results

The mean age of the sample was 71.8 (SD = 6.4) years and the sample comprised 16 males (57%) and 12 females (43%). The mean and standard deviation of measurements of time to GI for both the *GaitRite* walkway and the force platform, together with mean and standard error of the difference between the two measurements, are presented in **Table 3-1.** Overall, the measurements of time to GI by the force platform exceeded those made by the *GaitRite* walkway, but that difference was not statistically significant in this sample size (p = 0.16). If these data are representative of the population values, the difference would have

been statistically significant ($p < 0.05$) in a sample just two times larger. This was confirmed by repeating the test in a dataset ($n = 56$) with each observation replicated once.

Table 3-1: Times to gait initiation on the force platform and the *GaitRite* walkway.

	Mean	SD*	Difference	SE†	P-value (diff)
Force platform	1.089	(0.140)	0.048	(0.033)	0.159
GaitRite walkway	1.040	(0.179)			

* SD – standard deviation; † SE – standard error

To assess the clinical significance of a difference of 0.048ms, the falls-risk z-score was regressed on the measurements of GI by the force platform to find that a difference of 0.048ms in GI predicted a difference in falls-risk z-score of 0.02 units. At the median z-score ($z = 0$), a difference of 0.02 units would misclassify around 1% of subjects. It can therefore be concluded that a difference of 0.048ms in GI would classify fewer than 1% of subjects overall. To identify factors associated with the difference, the difference was regressed on covariates representing possible factors in a dataset replicated 6 times ($n = 196$). A larger difference between the two devices (force platform recording longer times than the *GaitRite* walkway) was associated with being older, shorter in stature, shorter step length, lighter in weight, having greater sway with eyes closed, poorer vision, worse proprioception and a higher falls-risk z-score (all $p < 0.01$). To better understand these associations, the associations between these factors and double support phase (DSP) were investigated. In the full TASCOG dataset ($n = 412$) from which this sample was drawn, age ($r = 0.14$), height ($r = –0.010$), vision ($r = –0.12$) and falls-risk z-score ($r = 0.26$) were associated with DSP.

The correlation between GI on the force platform and the *GaitRite* walkway was $r = 0.41$. Upon inspection of the data (**Figure 3-1),** one influential observation was conspicuous at far right. This outsider was an older woman who walked slowly and was generally frail. Removing this person reduced the correlation coefficient to $r = 0.36$.
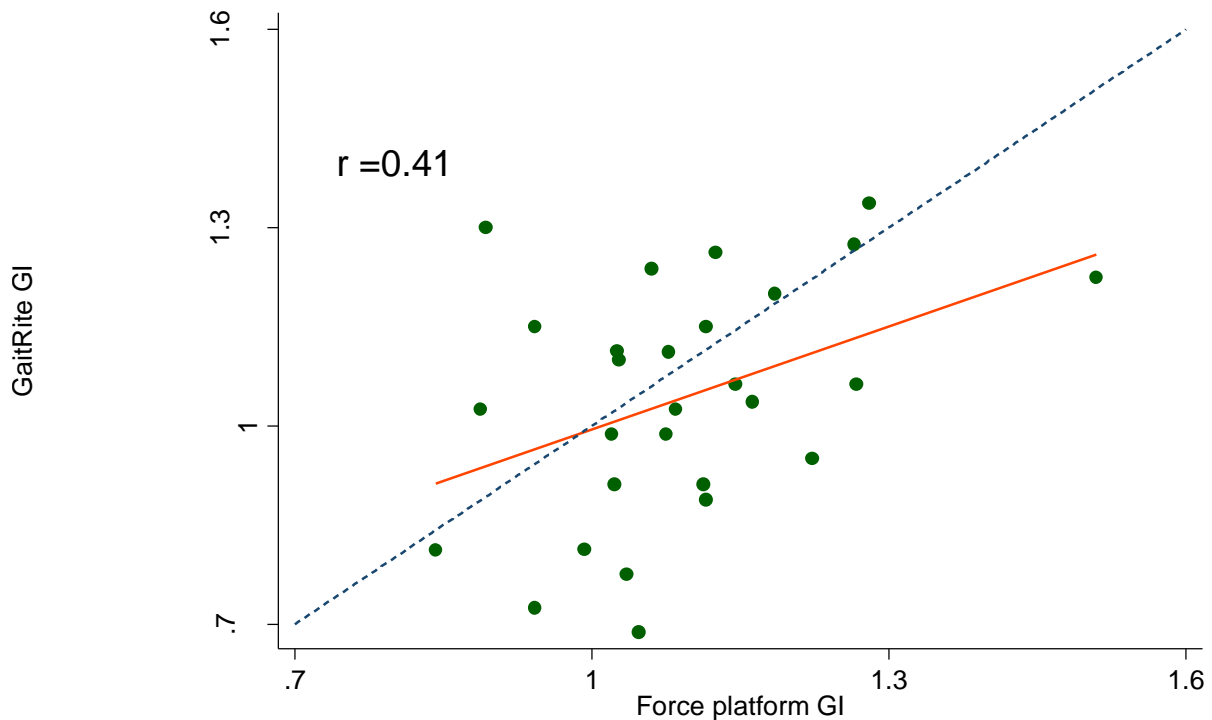
Figure 3-1: Gait initiation time measured by the *GaitRite* walkway plotted against gait initiation time measured by the force platform (line of best fit in red).

The line of best fit on which the correlation coefficient is based is less steeply sloping than the 45° line in **Figure 3-1**. This shows firstly that the correlation coefficient is not a measure of agreement (agreement is indicated by the 45° line), and secondly that time to GI measured by the *GaitRite* walkway exceeds time to GI measured by the force platform for fast initiators (those with smallest GI times), but the reverse is the case for slow initiators (those with greatest GI times).

The intraclass correlation coefficient (ICC) is more closely aligned to the theoretical construct of relative reliability than is the Pearson product-moment correlation coefficient, but the *ICC(3,1)* is expected to be little different to the Pearson statistic. For these data, the ICC was *ICC(3,1)* = 0.39 or *ICC(3,1)* = 0.33 with the influential observation excluded.

A Bland-Altman plot of the difference in time to GI against the average of the times measured by the two devices is presented in **Figure 3-2**. It also shows that the *GaitRite* walkway records a greater time elapsed than the force platform for faster initiators, but a lesser time elapsed than the force platform for slower initiators.
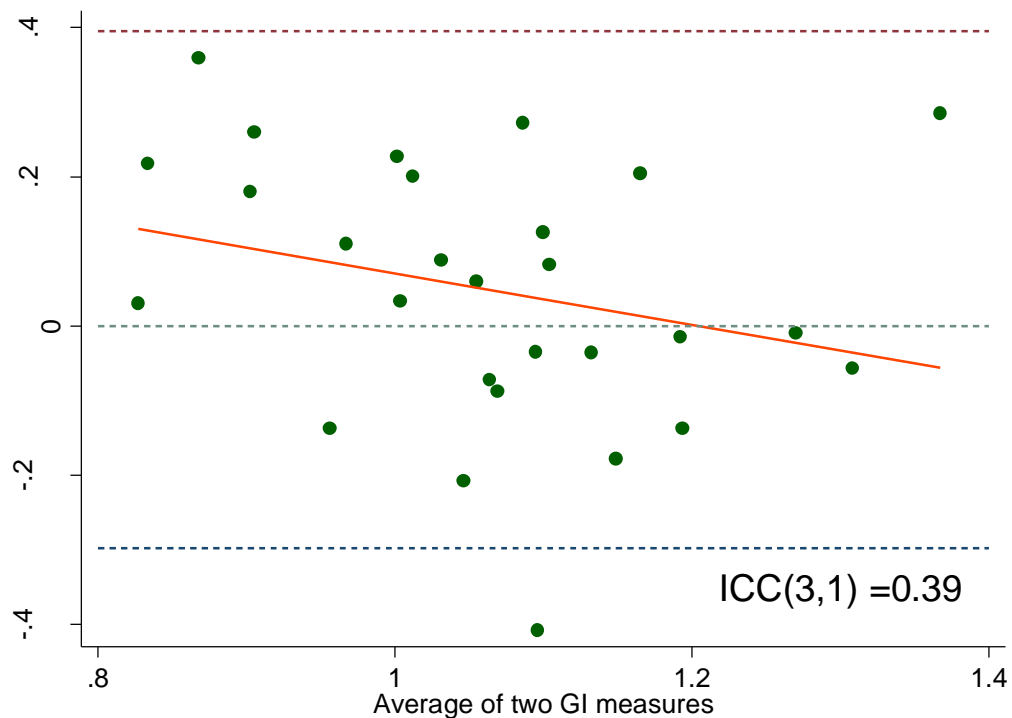
Figure 3-2: Difference of gait initiation time plotted against the average of the two gait initiation measures (line of best fit in red).

The 95% limits of agreement are shown on the plot. With 28 sets of readings, one of them would be expected to exceed these limits if the data are normally distributed, and this was the case. The data for this person were investigated nonetheless, but no explanation was found of why this man had much longer time to GI when measured by the *GaitRite* walkway than when measured by the force platform. The person at the top left of the plot was also investigated but without any distinguishing characteristics being indentified that might explain why time to GI was greater when measured by the force platform than when measured by the *GaitRite* walkway.

Also shown in **Figure 3-2** is the line of best fit. The downward slope was not statistically significant over the 28 observations (slope = –0.34, p = 0.179) but it would have been in a sample three times larger if this sample is representative of all data. This was confirmed by repeating the test in a dataset (n = 84) with each observation replicated twice. Removing the previously identified influential observation (far right) increased the negative slope and it became statistically significant (slope = –0.62, p = 0.02) in the original dataset (n =28).

Table 3-2: Correlations of time to gait initiation on two different devices with sensorimotor measures.

	Time to gait initiation measured by:		
	Force platform	*GaitRite* walkway	Corrected *GaitRite*
Proprioception	0.54†	–0.08	0.09
Reaction time	0.18	0.05	0.08
Balance (eyes open)	0.33	0.20	0.27
Balance (eyes closed)	0.09	–0.32	–0.29
Leg strength	–0.19	–0.12	–0.15
Vision	–0.20	0.14	0.04
Falls-risk z-score	0.51†	0.16	0.29

$^{*}p<.001$; $^{\dagger}p<.01$; $^{\ddagger}p<.05$

Correlations between measurements of time to GI and with sensorimotor measures of falls-risk are presented in **Table 3-2**. Longer times to GI as measured by the force platform were moderately correlated with the sensorimotor measures of falls-risk, and most strongly with worse proprioception and a higher falls-risk z-score, whereas the correlations of times to GI as measured by the *GaitRite* walkway were uniformly weaker. Once the measurements from the *GaitRite* walkway were corrected in accordance with the estimated relationship between the force plate and the *GaitRite* walkway measurements (see Methods), the correlation coefficients became stronger and more like those of the force platform correlation coefficients but lesser in magnitude.

3.5 Discussion

In this comparison of measurements of GI made using a 4.6m, 80Hz *GaitRite* walkway and a 200Hz force platform, there was only a minor difference in the mean values of the measurements made with each device. This difference would have been statistically significant in a dataset twice as large (56 observation rather than 28), but it was too small to have practical significance in terms of prediction of the falls-risk score. The minor overall difference masked systematic error, however. The *GaitRite* walkway tended to over-estimate GI time for fast initiators (those with smallest GI

times) but underestimate GI time for slow initiators (those with greatest GI times). Thus despite high absolute reliability overall, relative reliability was only moderate because slow and fast initiators were ranked differently by the *GaitRite* walkway and the force platform. This was confirmed in the analyses of predictive validity. GI measured by force platform was more strongly correlated with sensorimotor factors of falls-risk, and with the summary z-score, than was GI measured by the *GaitRite* walkway. Correcting the *GaitRite* walkway measurements, by reducing the values of faster initiators and increasing the values of slower initiators, improved the strength of the correlations with the falls-risk indicators but without removing the difference altogether.

The assessments of absolute and relative reliability produced somewhat different findings. Assessment of absolute reliability requires examination of whether the two devices yield the same measurements on average. The difference in the measures, however minor, should then be interpreted in a clinical context to determine what that difference means. In our study, the two devices yielded very similar average measures of time to GI and the difference between them, when expressed in terms of the falls-risk z-score, translated in to less than 1% of older adults being misclassified at the median fall-risk z-score. Older age, shorter step length and declines in sensorimotor function were associated with recording longer GI times on the force platform than the *GaitRite* walkway. We suppose that, in order to accommodate for poorer function and especially poorer balance, the oldest subjects in our sample were be taking shorter steps and contacting the surface with their leading foot before transferring their weight, and thus registering on the *GaitRite* walkway before the force platform.

Assessment of relative reliability requires examination of how alike the two devices are over the range of measurements – for example, do individuals who record high scores on one device also record high scores on the other device, and vice versa. In our study, there was only a moderate correlation between measurements made with the two devices and it became clear that this was due to subjects with fast or slow GI being misclassified by the *GaitRite* walkway. For this reason also, the predictive validity of the *GaitRite* measurements – in terms of the strength of associations with sensorimotor factors of falls-risk – was inferior to that of the force platform measurements. GI is known to be a phase of walking where falls are likely to occur

[7] and as such the PPA is a suitable measure to assess the predictive validity of the *GaitRite* walkway in comparison to the force platform.

Whilst the *GaitRite* walkway is portable and more cost effective for researchers already using it in gait research, our results suggest that it does not match the force platform in terms of accuracy in measuring time to GI. We hypothesise that the very nature of the way the data is captured (foot contact as opposed to shift in pressure), and the fact that it is made from an electronic "carpet" rather than a solid surface, each contribute the discrepancies between the measurements at the instrument level. The force platform stops measuring GI when weight is transferred from the standing, but the *GaitRite* walkway continues until the leading foot contacts the mat. Whilst these two events are very similar, some differences in timing are to be expected. What was unexpected was that these differences would vary systematically with GI time. Due to this systematic variation, we discount the possibility that the differences in times to GI could be due to the difference in frequency of capture between the *GaitRite* walkway (80Hz) and the force platform (200Hz).

This is the first study to investigate the potential of the *GaitRite* walkway as a cheaper alternative with which to measure GI. The devices used in this study were sophisticated – the force platform is the gold standard for measuring GI and the *GaitRite* walkway is increasingly being used in clinical settings. Further, all measurements were made under standardised protocols with the express intention of minimising random error.

The limitations of this study need to be borne in mind. The sample size was small but fortunately, this did not obscure plausible associations between measurements of GI made by the force platform and sensorimotor measures of falls-risk. There were some differences in protocols for the two devices, with the force platform capturing data on 6 trials when only 3 trials were captured on the *GaitRite* walkway and these may have contributed in unknown ways to the difference observed. Furthermore, whilst ideally we would have assessed test re-test reliability by asking the participants to repeat the test at a later point in time, replication was not attempted because the demands on the participants were already onerous. This meant that we were not able to observe the stability of the measurements over time.

3.6   Conclusions

The 4.6m, 80Hz *GaitRite* walkway, whilst recording only minor differences overall in average measures of time to GI, over-estimates time to GI for fast initiators and under-estimates time to GI for slow initiators, and has inferior predictive validity for falls risk than does the force platform. Advances in technology may enable this to occur in later models of the *GaitRite*, but their validity will require testing.

3.7   Postscript

In this chapter, I have reported that the 4.6m, 80Hz *GaitRite* walkway, because of systematic errors in its measurements of GI and their inferior predictive validity for falls risk, is not a good alternative to the 200Hz force platform. This finding had consequence for the investigation of gait initiation reported in **Chapter** 5, because it compelled that investigation to be conducted in the subsample of subjects with measurements of gait initiation by the force platform.

In the following chapter, data on gait and gait variability measures captured with the *GaitRite* walkway – for which the walkway is a valid and reliable measurement device – are utilised to investigate the associations between gait and cognitive function. This is of importance as impairments in both gait and cognitive function are associated with an increased risk of falls, but their inter-relationships are not well understood.

3.8   References

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Chapter 4: Cognitive function, gait and gait variability in older people – a population-based study.

4.1 Preface

The previous chapter provided information on the reliability and predictive validity of the *GaitRite* walkway as a device to measure gait initiation. Whilst the *GaitRite* walkway was not a good alternative to the force platform for measurement of gait initiation, it remains a valuable tool in gait research for the measurement of gait and gait variability.

Gait and cognitive function are important risk factors for falls in older adults, but there has been little research into the relationships between them. The cognitive constructs of processing speed and executive function in relation to gait have received attention but less is understood about the effects of other cognitive functions on gait or intra-individual gait variability. In this chapter the associations between a range of cognitive functions, gait and gait variability are investigated in a population-based sample of older people.

The text that follows is included in a manuscript that has been submitted for review by the Journal of Gerontology.

4.2 Introduction

Gait and cognitive impairments, caused by ageing or disease, commonly occur in older people [1-3] and have been shown to predict falls [4-6]. However, the interrelationships between cognitive function and gait are relatively poorly understood. Studying these relationships may provide further insights into the neural substrates of gait control in ageing. Previous research has focused on investigations of the relationships of cognitive function with gait speed [7-16], or gait variability [17-20]. There are no population-based studies, to our knowledge, that have investigated the effects of cognitive function on gait speed, other gait variables and gait variability together.

They have also mainly focused on the role of global cognitive function [21, 22], executive function and/or attention in gait [17, 20, 23-25], or that of divided attention

in gait control [26-29]. Very few studies have examined the effects of other key cognitive domains such as memory or visuospatial ability, particularly in a population-based setting [13, 30]. Inconsistent associations have been described for memory, with one study reporting adverse effects on gait speed [30], while no associations were observed in another [13]. Furthermore, there is a paucity of studies examining cognitive associations with intra-individual gait variability which may be a better indicator of balance and the risk of falls [31]. The results for gait variability are varied, with some researchers finding no associations between cognitive function and gait variability [7, 10, 17], and some reporting increased stance time variability [17], and stride time variability [11] to be associated with poorer cognitive function. Moreover, most studies in this field have been conducted in highly selected clinical samples or in small samples of volunteers, with limited data from the general population [13, 17, 25, 30, 32]. We examined the associations between a range of cognitive functions, gait and gait variability in a population-based sample of older people.

4.3 Methods

Subjects

The sample consisted of 422 participants in the Tasmanian Study of Cognition and Gait (TASCOG) conducted in Hobart, Tasmania, Australia. Eligible participants were aged 60-85 years inclusive, were residents of the region of southern Tasmania that is defined by postcodes 7000 – 7199, and were randomly selected from the Tasmanian Electoral Roll. They were excluded if they lived in residential care, were unable to walk without a gait aid, or if they had any contraindications to magnetic resonance imaging (MRI) that was a requirement of the overall study. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved this study.

Measurements

Gait and gait variability

Absolute gait measures were obtained using the 4.6m GAITRite system (CIR Systems, PA, USA) at usual walking pace. Participants were required to complete 6 walks and to start and finish walking 2m before and after the mat to allow a constant speed to be captured. Variables collected were step time and step length (both used to derive gait speed), support base and double support phase (DSP) [33]. Gait speed is how quickly a person can walk in a straight line, derived from the distance travelled and the time taken to walk that distance.. Step time is the time elapsed from contact of one foot to contact of the next. Step length is the perpendicular distance between the heel of one footfall to the heel of the next footfall. Support base is the perpendicular distance from the heel of one footfall to the line of progression of the other foot. DSP is measured in two ways: the time (msec) elapsed during DSP, or the percentage of DSP of the whole gait cycle when both feet are in contact with the ground.

Intra-person variability in step time, step length, support base and double support phase was calculated using the standard deviation [17, 31] of the measure across all steps for all 6 walks

Cognitive function

A battery of cognitive tests was conducted to assess the following cognitive domains: (1) *Executive function / attention* using the Controlled Word Association Test (COWAT, using the letters F, A, and S) [34], Category Fluency (animals) [34], the Victoria Stroop test – comprised of three subtests a) coloured dots, b) coloured everyday words and c) coloured colour-names (e.g. the word blue written in red ink) [35] and the Digit Span subtest of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) [36]; (2) *Processing speed* using the Symbol Search and Digit Symbol Coding subtests of the WAIS-III [36]; (3) *Visuospatial ability* using the Rey Complex Figure copy task [34]; and (4) *Verbal memory* using the Hopkins Verbal Learning Test (HVLT) – Revised generating scores for total immediate recall, delayed recall, and recognition memory [34] and *Visual memory* using a delayed reproduction after 20 minutes of the Rey Complex Figure [34].

Other measurements

Ambulatory activity was measured using a Yamax Digi-Walker SW-200 pedometer worn over 7 consecutive days. Participants were required to complete a 7-day diary of daily steps, times worn and times not worn. Recordings for days on which the pedometer was worn for less than 8 hours were excluded when calculating mean number of steps per day. Mood was measured using the 15-Item Geriatric Depression Scale (GDS) [37]. Over the counter and prescription medicines were recorded, and participants were classified as taking a psychoactive medication if they were using any of the following: antidepressants, antipsychotics, sedative/hypnotics, antiepileptics or antiparkinsonian agents. They were also classified as either using or not using blood pressure lowering drugs.

Data analysis

Similar to our previous work [38] (shown in **Table 6-2)**, the raw scores of cognitive tests were grouped into the specific cognitive domains of executive function / attention, processing speed and memory, and then subjected to data reduction using principal components analysis. A summary cognitive component score was used to represent each of these domains. Regression scores were generated for each of these components using Thomson's method [39] and were then used as variables in further analysis. The Rey Complex Figure Copy task was the sole test of visuospatial ability and hence only its raw score was used in analyses.

Univariable regressions were first performed to examine associations of cognitive factors with gait and gait variability. Multivariable linear regression was then used to examine associations adjusting for age, sex, physical activity, medication use, mood and years of education. In the case of analyses for memory and visuospatial ability, additional adjustment was made for speed and executive function / attention because the former functions may be governed by the latter. Gait speed was assessed for its potential role as a confounder or an intermediate in the relationship between cognitive function and gait variability, and was adjusted for accordingly. If adding gait speed into the regression model changed the coefficients for both cognitive function and gait speed more than 10%, gait speed was deemed a confounder. Based on this, regressions of step time variability and support base variability were thus additionally adjusted for gait speed. Fractional polynomials were used to assess the scale of the covariates.

4.4 Results

The mean age of the sample (n = 422) was 72.0 years (SD = 7.0) with 238 men (56.4%) and 184 women (43.6%). The sample response proportion was 51% with non-responders generally older (p < 0.01) and with a higher self-reported incidence of hypertension (p = 0.03). Demographic, gait, and cognitive test characteristics are shown in **Table 4-1**.

Loadings of cognitive tests on the cognitive components derived from the PCA were very similar to our previously reported analyses [38] and are shown in **Table 6-2**. Unadjusted correlations between the cognitive components and the gait measures and variability measures are shown in **Table 4-2**. Poorer executive function / attention, processing speed and memory were associated with poorer performance on all of the absolute gait measures (all p< 0.01), whereas poorer visuospatial ability was associated only with slower gait speed, shorter step length and smaller DSP as a percentage of the gait cycle (all p < 0.05). Poorer executive function / attention and processing speed were associated with greater variability in all gait measures (all p < 0.05). Poorer memory was only associated with greater step time variability and poorer visuospatial ability was associated with greater variability in all measures except support base variability (all p< 0.001).

Multivariable regressions between cognitive function and the gait and gait variability measures are shown in **Table 4-3** adjusting for age, sex, mood, medications, physical activity and education. Processing speed remained independently associated with all average gait measures (all p < 0.05). Executive function / attention was associated with all average gait measures (p < 0.05) except step time and support base. Memory was only associated with DSP (%), but this association disappeared after further adjusting for executive function / attention and processing speed. Visuospatial ability was not associated with any of the absolute gait measures. With respect to variability (**Table 4-3**), executive function / attention was independently associated with step time and DSP variability, whereas processing speed was only associated with DSP variability. Memory was not associated with any gait variability measure, whereas visuospatial ability was independently associated with greater DSP variability (p = 0.04), even after adjusting for executive function / attention or processing speed.

Table 4-1: Participant characteristics (n = 422)

Variable	Mean	(SD/%)
Age (years)	72.0	(7.0)
Male sex (n / %)	238	(56)
Geriatric Depression Scale score	2.05	(2.3)
Number taking psychoactive drugs (n / %)	88	(20.9)
Average gait measures		
Gait speed (cms^{-1})	113.5	(21.6)
Step time (ms)	548.67	(53.7)
Step length (cm)	61.5	(9.4)
Support base (cm)	9.99	(2.9)
Double support phase (DSP, ms)	255.91	(59.1)
DSP (% of gait cycle)	23.2	(3.9)
Gait variability measures		
Step time variability (ms)	22.4	(13.8)
Step length variability (cm)	2.73	(0.93)
Support base variability (cm)	2.12	(0.69)
DSP variability (ms)	20.9	(11.2)
Cognitive tests		
Digit span	15.8	(3.8)
Category fluency	17.05	4.99
COWAT	35.9	(13.3)
Stroop dot (sec)	16.1	(5.3)
Stroop words (sec)	22.0	(10.6)
Stroop colours (sec)	39.2	(22.7)
Digit symbol coding	49.8	(15.3)
Symbol search	22.7	(7.6)
Rey Complex Figure copy	32.1	(4.7)
Rey Complex Figure delay	14.8	(7.0)
Hopkins immediate recall	22.0	(6.3)
Hopkins delayed recall	7.5	(3.1)
Hopkins recognition	21.6	(2.9)

SD – Standard deviation; COWAT – Controlled Oral Word Association Test;

DSP – Double support phase;

Table 4-2: Unadjusted correlations between cognitive components and gait measures.

Gait measures	Executive / attention	Processing speed	Memory	Visuospatial ability
Gait speed (cms^{-1})	–0.34*	0.40*	0.21*	0.20*
Step time (ms)	0.24*	–0.24*	–0.24*	–0.03
Step length (cm)	–0.28*	0.36*	0.11‡	0.26*
Support base (cm)	0.16†	–0.19*	–0.18*	–0.01
DSP (ms)	0.30*	–0.29*	–0.24*	–0.09
DSP (%)	0.23*	–0.24*	–0.19*	–0.10‡
Gait variability measures				
Step time (ms)	0.29*	–0.31*	–0.16†	–0.19*
Step length (cm)	0.13‡	–0.17*	–0.07	–0.21*
Support base (cm)	0.10‡	–0.12‡	–0.03	–0.06
DSP (ms)	0.24*	–0.28*	–0.07	–0.24*

$^*p<.001$; $^†p<.01$; $^‡p<.05$; DSP – Double support phase; SD – Standard deviation; Higher scores in executive / attention reflect worse function, whereas higher scores on the other cognitive components reflect better function.

Table 4-3: Adjusted linear regression of gait variables with cognitive components

Gait measures	Regression coefficient (β), 95% confidence interval			
	Executive / attention	**Processing speed**	**Memory**	**Visuospatial ability**
Gait speed (cms^{-1})	−1.57 (−2.67,−0.47)†	2.42 (0.78,4.06)†	0.94 (−0.44,2.32)	0.28 (−0.16,0.71)
Step time (ms)	2.57 (−0.41,5.55)	−4.95 (−9.36,−0.55)‡	0.24 (−3.44,3.93)	−0.08 (−1.25,1.08)
Step length (cm)	−0.60 (−1.04,−0.16)†	0.82 (0.16,1.47)‡	0.41 (−0.14,0.96)	0.16 (0.01,0.33)
Support base (cm)	0.14 (−0.03,0.30)	−0.27 (−0.52,−0.29)‡	−0.04 (−0.25,0.16)	−0.04 (−0.10,0.03)
DSP (ms)	3.73 (0.49,6.98)‡	−5.68 (−10.52,−0.84)‡	−3.10 (−7.15,0.95)	0.15 (−1.13,1.43)
DSP (%)	0.25 (0.05,0.46)‡	−0.31 (−0.62,−0.004)‡	−0.33 (−0.59,−0.08)†	−0.02 (−0.07,0.10)
Gait variability				
Step time (ms)	0.78 (0.05,1.51)‡	−0.69 (−1.78,0.40)	0.54 (−0.36,1.44)	−0.28 (−0.56,0.0004)‡
Step length (cm)	0.004 (−0.05,0.05)	−0.04 (−0.12,0.04)	0.07 (0.0005,0.13)	−0.01 (−0.03,0.01)
Support base (cm)	0.03 (−0.01,0.07)	−0.04 (−0.10,0.02)	0.02 (−0.03,0.07)	−0.004 (−0.02,0.01)
DSP (ms)	0.78 (0.13,1.44)‡	−1.13 (−2.10,−0.15)‡	0.55 (−0.27,1.37)	−0.34 (−0.60 ,−0.09)†

$^{*}p<.001$; $^{†}p<.01$; $^{‡}p<.05$; DSP – Double support phase; Higher scores in executive / attention reflect worse function, whereas higher scores on the other factors reflect better function. All models adjusted for age, sex, medications, mood, physical activity, years of education; and step time variability & support base variability additionally adjusted for gait speed.

4.5 Discussion

To our knowledge, this is the first population-based study to examine the relationships between a wide range of cognitive functions gait and gait variability in older people. Executive function / attention and processing speed were associated with poorer performance on most absolute gait measures. Memory and visuospatial ability had no independent effects on absolute gait measures after taking into account the effects of executive function and processing speed. Executive function / attention, processing speed and visuospatial ability, but not memory, were independently associated with DSP or step-time variability, with effects being most consistent for DSP variability. The consistent associations found across the range of related variables adds to conviction that they reflect true relationships.

Consistent with most previous research [25, 30, 40, 41], we showed that poorer executive function / attention and processing speed were associated with slower gait speed, which was explained by their associations with step length rather than step time. A possible logical explanation for this association may be that neural substrates that serve these cognitive functions are shared with those for step length, particularly the connections between the frontal cortex and basal ganglia [34, 35].

In contrast to previous research showing decline in gait speed in patients with Alzheimer's disease [42, 43], but consistent with other work [13], we found that neither memory nor visuospatial ability were independently associated with any of the absolute gait measures. This suggests that temporal and parietal structures that serve these cognitive functions may not play a primary role in gait control. An alternative explanation for the lack of associations may be that the tests used to measure these domains may not have been sufficiently sensitive to capture associations. However, the HVLT and Rey Complex Figure task are robust tests of these functions with high validity [35], making it less likely that measurement error may have been responsible for the lack of associations. Another explanation may be that the sample in our study was on average relatively cognitively healthy, with 75% of participants achieving high raw scores (> 30) on the Rey Complex Figure copy test. We may have thus underestimated the true magnitude of associations by excluding frail older people in residential care and because of non-response bias.

Our results, like other studies, showed that poorer cognitive function is associated with increased gait variability. We found associations for step time variability and DSP variability, but not for step length or support base variability. This is consistent with previous findings in younger people of increased stride time variability, but not stride length variability, under dual-task cognitive interference [9]. The finding of associations between poorer executive function / attention and step time variability is supported by previous studies using the Stroop test [11] or divided attention tasks [7, 13, 18]. The role of executive function in step-time variability has also been emphasized in people with Parkinson's or Huntington's disease, in whom loss of gait variability may occur due to disease of the basal ganglia [44].

Our findings of no association for memory add to the work by Hausdorff et al. [11] who showed that stride time variability was not associated with memory. A novel finding in our study was that visuospatial function, the representation of objects in a spatial array (a person in relation to their environment for example, or the relative position of a table in a room), was independently associated with DSP variability. This parietal lobe-driven function is known to play a significant role in navigation [45] and falls-risk [38]. DSP is also a marker of dynamic balance control during walking [46], and may well mediate some of the effect of visuospatial function on falls risk, and hence it would be interesting to examine this theory prospectively.

The major strength of this study is its use of a large population-based sample to examine, for the first time, the associations of a range of cognitive tests with several gait measures, including the intra-individual variability in those measures. The study response proportion was moderate, and because non-responders were older, we may have underestimated associations. The gait walkway used was relatively short but we accounted for acceleration and deceleration by allowing the participants two meters either side of the walkway to reach a rhythmic "usual" pace at the time the sensors were activated. Another possible issue with a short mat was that gait variability was calculated from a minimum of 24 strides. However, Hollman et al. [47] reported that measurements based on fewer than 20 strides showed a moderate test-retest reliability in gait variability. Because this is a cross-sectional study, it is uncertain from these results whether the associations reflect the cognitive control of gait, or an impact of gait on cognition, or whether there is simply a shared neural substrate between the two functions and impaired cognition is a marker for poor gait (or vice

versa). A causal relationship between declining cognition and gait is best studied in a longitudinal fashion.

4.6 Conclusions

In relatively cognitively healthy community-dwelling older people, executive function / attention and processing speed, but not memory or visuospatial ability, were associated with poorer performance on absolute gait measures. Poorer executive function / attention, processing speed and visuospatial ability, but not memory, were associated with increased gait variability. Poorer cognitive function seems to have the greatest impact on DSP variability, an important factor in balance control during walking.

4.7 Postscript

In this chapter I have shown that in community-dwelling older people, visuospatial ability may play a role in gait control in addition to executive function and processing speed. For gait variability, the effects of poorer cognitive function were most consistently seen for DSP, a measure of balance during walking.

Establishing balance is important in gait initiation, which is a phase of gait during which falls occur frequently. In the next chapter I investigate gait initiation, and its associations with cognitive function and sensorimotor measures of falls-risk and the inter-relationships of its component measures.

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Chapter 5: Gait initiation in older people – time to first lateral movement may be the measure of choice.

5.1 Preface

In the previous chapter, the inter-relationships between gait and cognitive function were investigated in a population-based sample of 422 older adults. Poorer executive function / attention and processing speed were associated with poorer performance in gait measures and increased variability in those measures (particularly in respect of double support phase, which is important in balance control). Poorer visuospatial ability was associated with increased gait variability, and memory had the least influence.

Gait initiation (GI) is a phase of walking where falls are likely to occur whilst balance is being established, and thus the associations of GI and cognitive function should be assessed. As a precursor to a detailed examination of cognitive associations with GI, this chapter reports on an investigation of the statistical characteristics of the components of gait initiation (GI), their inter-relationships and associations with sensorimotor variables, and the effect of cognitive loading on these relationships.

The material presented here has been published in a peer-reviewed journal [1]. Additional analyses not included in the manuscript are included in **Appendix 5A**.

5.2 Introduction

Gait impairments are frequent in older people [2-5] and predict falls [6, 7]. Falls occur frequently during gait initiation (GI) [8], the time taken to go from standing still to a recurring pattern of walking. GI is usually measured with force-platforms as the time elapsed from stimulus until the leading foot makes contact with an adjacent surface. This measure has three components [9]. The first is the time taken from the stimulus to the first lateral movement (FLM) detected. The second, transfer time, is from FLM to when the leading foot leaves the platform. The last, swing time, is from the foot leaving the platform to the contact of that foot with the adjacent surface. While all these component measures are used commonly in research, it has not yet

been established whether they have more predictive ability than the overall measure and, if so, which components are most appropriate.

To reduce random error from intra-individual variation, it is common to collect data over multiple trials to derive a single summary statistic representing the data for each subject [8-11]. The arithmetic mean, which is most frequently used, may not be the best summary statistic if the data are unevenly distributed. Previous researchers [8, 9] have found evidence of learning effects during multiple measurements. This suggests uncertainty as to which summary statistic may be appropriate to deal with such distribution and learning effects.

The inter-relationships between the components of GI have not been investigated. It is important to understand how they relate to each other and to see whether people who are slow over one component are slow over all components. Whilst Melzer and Oddsson [9] showed that GI was slower under divided attention caused by a concurrent cognitive task, it is unknown whether the GI components are differentially responsive to dual-tasking.

We investigated the statistical characteristics of the GI components, their inter-relationships and associations with sensorimotor measures of falls-risk, and the effect of cognitive loading on these relationships in a randomly selected sample of older people.

5.3   Methods

Subjects

The sample consisted of 128 consecutive participants in the Tasmanian Study of Cognition and Gait (TASCOG) conducted in Hobart, Tasmania, Australia. Eligible participants were residents of Southern Tasmania, a geographical region defined by postcodes (7000 – 7199), and aged between 60 and 85 years inclusive. They were randomly selected using age- and sex-stratified sampling from the Tasmanian Electoral Roll. They were excluded if they lived in residential care, were unable to walk without a gait aid, or if they had any contraindications to magnetic resonance imaging (MRI) which was a requirement of the overall study. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved this study.

Measurements

GI was measured using a 200Hz AccuGait force-platform and Advanced Mechanical Technology Inc. (AMTI)-NetForce software. Participants were required to stand with bare feet in a standardized stance with heels separated by 6cm, with an approximately 10° angle between feet [12]. In response to an auditory cue, they were required to start walking forward a few steps onto an adjacent surface at the same height as the force-platform. Twelve trials were conducted for each participant, alternating between a state of no cognitive interference (single-task, 6 trials) and cognitive interference (dual-task, 6 trials). The dual-task was to initiate gait in response to the auditory stimulus whilst counting backwards in threes from a designated number (varied for each trial). Overall GI was recorded as the time from stimulus to contact of the leading foot with the adjacent surface. This measure was divided into three components: time from stimulus to first lateral movement (FLM); FLM to toe off of the leading foot (transfer time); and time from toe off to foot contact (swing time).

Sensorimotor function related to stability and gait was measured using the short form of the physiological profile assessment (PPA, described in detail in a previous paper) [13]. The PPA measures include *visual edge contrast sensitivity* (decibels, dB), *lower limb proprioception* (degrees), *knee extension strength* (kg), *simple reaction time* (seconds), *postural sway* (mm) and a standardized *falls-risk score*, computed as a summary of weighted scores from the above individual tests [14-16]. The Digit Symbol Search and Symbol Search subtests from the Wechsler Adult Intelligence Scale – Third Edition [17] were used to measure cognitive processing speed which is closely related to gait in older people [18, 19].

Data analysis

Eleven single-task values by 10 participants and 21 dual-task values by 18 participants were excluded due to errors in data collection, leaving 757 single-task measurements and 747 dual-task measurements by the 128 subjects for analysis.

For both single- and dual-tasking for each individual, the mean of the 6 measurements was first calculated. Measurements were deemed to be discrepant if the effect of deleting them was to change the mean of the remaining 5 by more than

15%. This criterion was chosen because, on inspection of the data, it resulted in the identification of obvious outliers.

To summarize the trial data, six candidate indices of central tendency were investigated. These were (i) the arithmetic mean, calculated as $\bar{x} = \sum_{i=1}^{n} x_i / n$ where x_i denotes the measurement on a given trial and n is the number of trials (here $n = 6$), (ii) the arithmetic mean with discrepant values excluded, (iii) the trimmed mean calculated as the arithmetic mean of the middle observations with the smallest and the largest measurements excluded, (iv) the geometric mean calculated as $\bar{x} = \sqrt[n]{\prod_{i=1}^{n} x_i}$, (v) the harmonic mean calculated as $\bar{x} = n / \sum_{i=1}^{n} 1/x_i$, and (vi) the median.

To determine the best candidate index, the median (50th percentile, p_{50}) of the summary statistics (n= 128) produced by each index was compared with the median (P_{50}) of all measurements (single-task N= 757, dual-task N= 747) using the absolute difference $D = (P_{50} - p_{50})$ as the criterion. The index consistently with the smallest D was considered to be the best index.

Large outlying summary values ("outsiders") were identified from box-and-whisker plots of the data. Values were deemed as "outsiders" if they were above the upper fence (1.5 interquartile ranges above the 75th percentile) or below the lower fence (1.5 interquartile ranges below the 25th percentile) of the box-and-whisker plot. To further examine the characteristics of these outsiders, log binomial regression was used to ascertain factors such as age, sex, height and weight that predicted persons with large summary values.

Overall GI and the components were regressed on trial number to investigate potential learning effects. The square of trial number was included as a covariate to model non-linearity. Linear regression techniques were used to test for sex differences in the component and overall measures, and to assess the predictive capacity of the component and overall measures in regard to the falls-risk z-score. Spearman rank correlations were used to assess the inter-relationships between the three GI components, and their associations with demographic, sensorimotor and cognitive variables under single- and dual-tasking. The difference in time between

dual- and single-tasks per subject was used with regression techniques to assess the relationships between cognitive interference, processing speed and GI.

5.4   Results

Sample characteristics are provided in **Table 5-1**. The mean age of the sample was 70.9 years (SD = 6.9), and it comprised 75 men (58.6%) and 53 women.

Choice of summary measure

Summary data on all measurements of GI and its components under single- and dual-task conditions are shown in **Table 5-2.** Among all trials, there were 102 discrepant values among the component measurements. Nearly all (91/102) were large. Most (72/102) of the component discrepant values occurred for FLM. Of those, most (42/72) occurred under dual-tasking and most of those (22/42) arose on the first of 6 trials. Removing discrepant values reduced but did not eliminate the right-skewness in the data.

A comparison of the median of each of the 6 candidate indices is shown in the right-most columns of **Table 5-2**. For all three components under each task, the median summary measure had the least absolute difference (D) from the median of all the measurements. Interestingly, the most commonly used measure, the arithmetic mean, was second worst. In what follows, we use the median to summarise the measurements from the 6 trials. Median time to GI was increased under dual-tasking primarily because time to FLM was increased.

Figure 5-1 depicts the distribution of the n= 128 summary measures for each component under the two task conditions. For time to FLM but not transfer time or swing time, dual-tasking resulted in an increase in the median (p< 0.001) and interquartile range, and greater dispersion of the outsiders (the values above the upper fence of the boxplot). An analysis of the outsiders revealed that female sex (p < 0.001) and greater age (p = 0.036) were independent predictors of persons with very large summary values of time to FLM, transfer time and swing time. These values were considered plausible and were not excluded from analysis.

Table 5-1: Participant characteristics.

	Mean / n	(SD) / (%)
Age	70.9	(6.9)
Sex (males)	75	(58.6%)
Height (cm)	167.8	(9.8)
Weight (kg)	80.4	(16.4)
Self-reported history:		
Hypertension	60	(47%)
Arthritis	55	(43%)
Diabetes	14	(11%)
PPA measures:		
Edge contrast sensitivity (db)	21.1	(1.8)
Reaction time (ms)	226.4	(32.9)
Proprioception (degrees)	1.9	(1.3)
Sway (eyes open) (mm)	18.2	(8.2)
Sway (eyes closed) (mm)	39.7	(20.8)
Knee extension strength (kg)	32.7	(13.3)
Cognitive measures		
Digit symbol search	51.1	(14.4)
Symbol search	23.5	(7.2)

SD – standard deviation

Learning effects

Under single-tasking, transfer time ($p < 0.001$) and swing time ($p < 0.001$) decreased in a linear fashion with each successive trial. Time to FLM decreased also, but the trend was not significant ($p = 0.39$). Under dual-tasking, the pattern was not linear with greater reductions in earlier trials and improvements confined to the first four or five trials (time to FLM $p = 0.005$, transfer time $p = 0.08$, swing time $p = 0.03$). To summarise, these trends are shown for time to FLM in **Figure 5-2**.

Associations between gait initiation components

The three components of GI were moderately correlated (r= 0.28 to 0.33) with each other under single-tasking, but the correlations between the components and swing time were markedly diminished under dual-tasking (both r= 0.09).

Associations of gait initiation with other study factors

Time to FLM was associated with age, height, weight, the sensorimotor factors other than proprioception, the falls-risk z-score and cognitive speed **Table 5-3.** The associations with age, knee extension strength and the cognitive tests were stronger (age p< 0.001, strength p= 0.02, cognitive tests p< 0.001) under dual-tasking. Those with height and weight were secondary to that for knee extension strength, which was moderately correlated with height (r= 0.57) and weight (r= 0.39). Transfer time was associated only with simple reaction time, knee extension strength and the falls-risk z-score. Cognitive processing speed and dual-tasking were independently associated with time to FLM. Swing time was only associated with the cognitive tests of processing speed under single-tasking. These associations were much weaker under dual-tasking, suggesting that dual-tasking is more likely to be an intermediate of the relationship between processing speed and swing time.

Under single-tasking, a one standard deviation change in time to FLM was associated with a 0.23unit change in the falls-risk z-score, whereas a one standard deviation change in overall GI was associated with a 0.31unit change in the falls-risk z-score.

Table 5-2: Summary statistics for gait initiation component measures.

	All measurements (N=757 single task, N=747 dual task)					Subject-specific summary measures (n=128)						
			Discrepant values (DV)[†]									
Measure*	**Median**	**Range**	**Small**	**Large**	**Total**	**Arithmetic mean (DV incl.)**	**Arithmetic mean (DV excl.)**	**Trimmed mean**[‡]	**Geometric mean**	**Harmonic mean**	**Median**	**Range**
Time to FLM												
Single task (ms)	220	(70, 3465)	3	27	30/757	233	225	225	227	222	218	(138, 593)
Dual task (ms)	330	(105, 2895)	5	37	42/747	340	332	339	332	310	330	(168, 1600)
Transfer Time												
Single task (ms)	480	(165, 995)	0	1	1/757	483	483	485	476	470	483	(233, 778)
Dual task (ms)	465	(145, 1445)	0	3	3/747	466	466	467	460	457	465	(268, 925)
Swing Time												
Single task (ms)	350	(130, 2270)	3	10	13/757	351	351	350	349	347	348	(220, 630)
Dual task (ms)	345	(160, 1305)	0	13	13/747	347	340	347	342	337	344	(245, 930)
Overall												
Single task (ms)	1060	(635, 4490)	0	10	10/757	1054	1051	1056	1051	1050	1050	(738, 1938)
Dual task (ms)	1158	(700, 3575)	0	2	2/747	1177	1172	1183	1173	1156	1161	(835, 2490)

* Time to FLM = stimulus to first lateral movement, Transfer Time = FLM to toe off, Swing Time = toe off to foot contact
† Number of measurements so distant from the mean of its set of 6 measurements that removing them changed the mean by more than 15%.
‡ Trimmed mean calculated by removing the smallest and largest values from each set of 6 measurements before calculating the arithmetic mean.
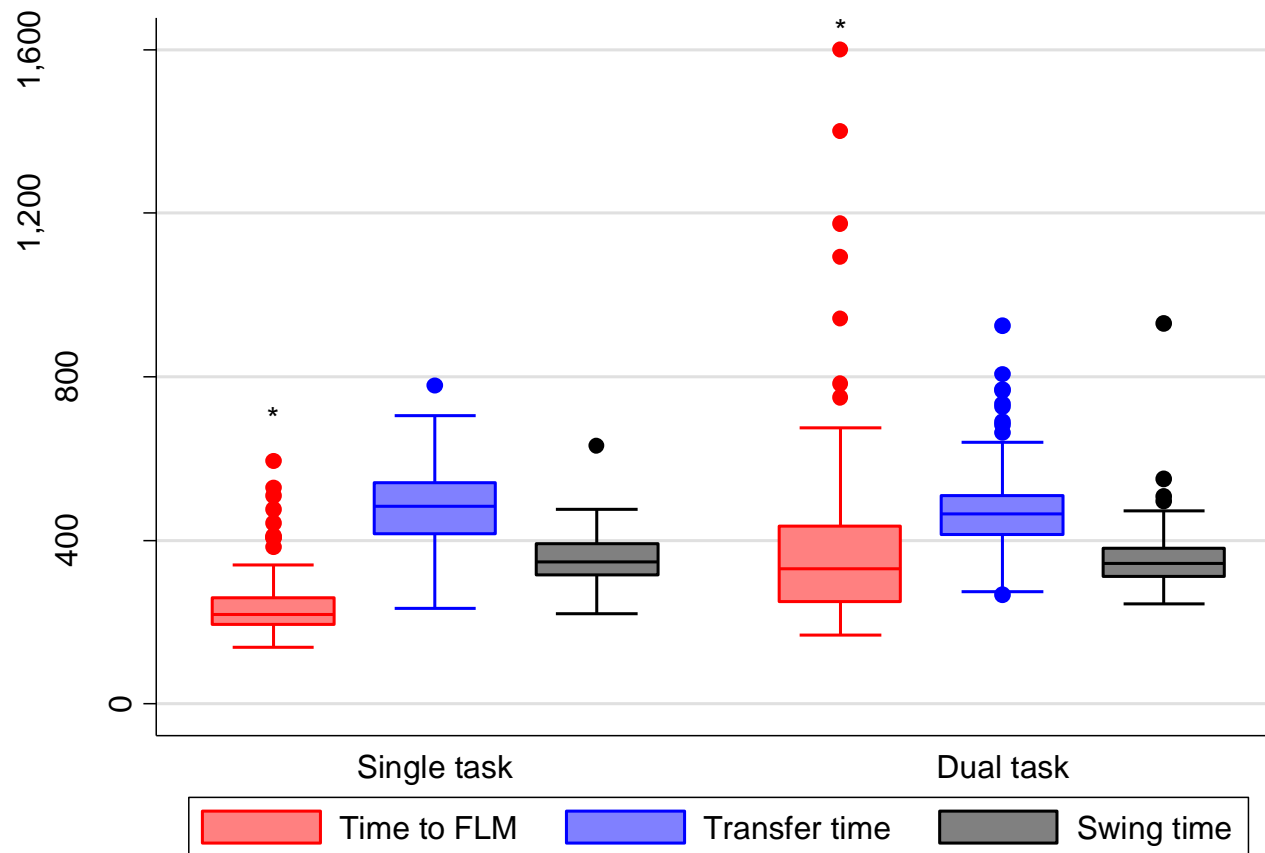
Time to FLM = stimulus to first lateral movement, Transfer Time = FLM to toe off, Swing Time = toe off to foot contact.
* p<0.001; for the comparison of time to FLM under single and dual-task conditions.
Figure 5-1: Distributions of the three gait initiation components under single and dual-task conditions.
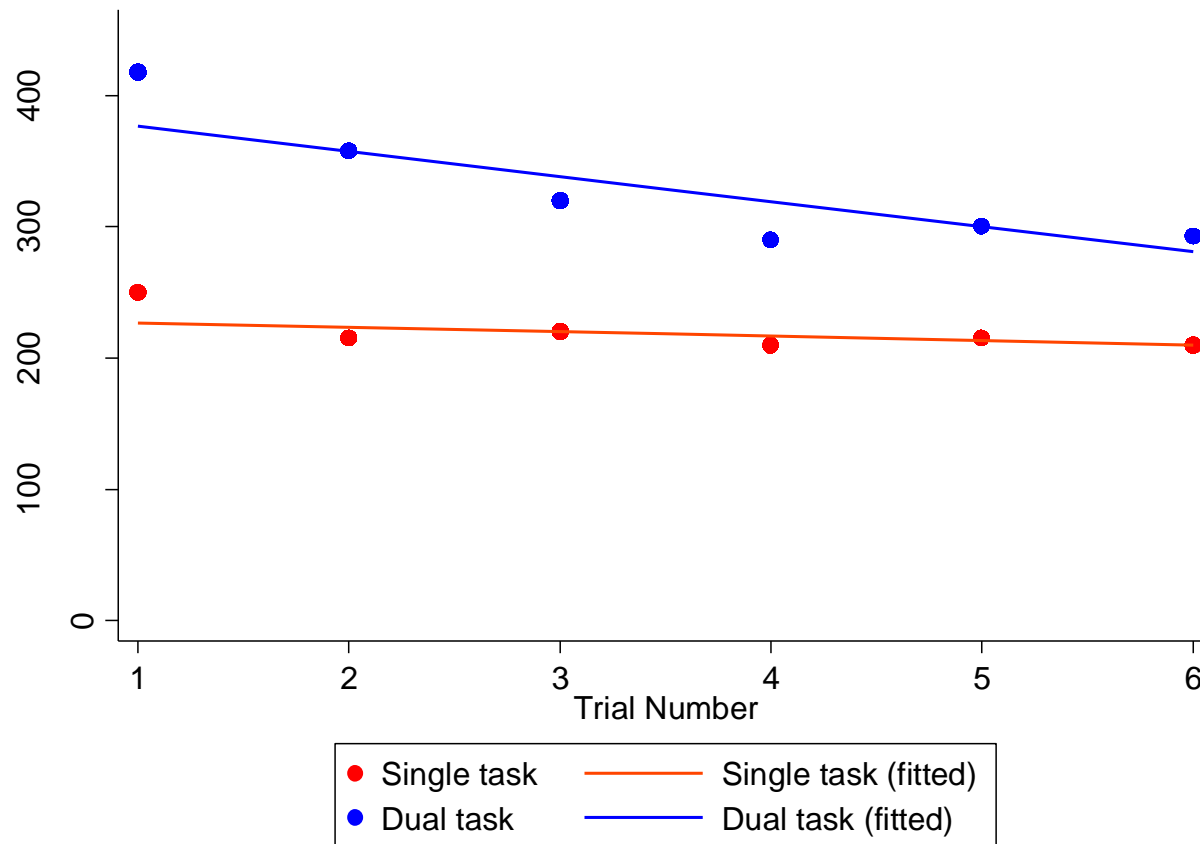
Time elapsed decreased with each successive trial in a linear pattern (p = 0.39) under single task conditions and in a non-linear pattern (p < 0.005) under dual task conditions.

Figure 5-2: Time to first lateral movement (FLM) by trial number under single and dual-task conditions.

Table 5-3: Rank correlations between gait initiation and other study factors.

Measure*	Age	Height	Weight	Knee Extension Strength	Hand Reaction Time	Proprioception	Edge Contrast Sensitivity	Balance (Eyes Open)	Balance (Eyes Closed)	Digit Symbol Search	Symbol Search
Time to FLM											
Single task (ms)	0.17	−0.10	−0.09	−0.18§	0.35†	0.02	−0.16	0.20§	0.16	−0.30†	−0.26‡
Dual task (ms)	0.33†	−0.23§	−0.21§	−0.30†	0.26‡	0.05	−0.11	0.19§	0.12	−0.37†	−0.40†
Transfer Time											
Single task (ms)	−0.09	−0.11	0.13	−0.19§	0.27‡	0.08	−0.03	0.09	−0.01	−0.09	−0.11
Dual task (ms)	−0.06	−0.11	0.13	−0.20§	0.16	0.09	−0.07	0.16	−0.04	−0.05	−0.08
Swing Time											
Single task (ms)	0.03	0.16	0.02	0.03	0.15	0.03	−0.06	0.07	−0.06	−0.27†	−0.20‡
Dual task (ms)	−0.001	0.10	0.01	0.06	0.06	−0.02	0.03	−0.05	−0.08	−0.12	−0.10
Overall											
Single task (ms)	0.02	−0.07	0.02	−0.19§	0.32†	0.08	−0.12	0.23§	0.07	−0.25‡	−0.25‡
Dual task (ms)	0.20§	−0.16	−0.11	−0.28‡	0.26‡	0.08	−0.11	0.24‡	0.04	−0.31†	−0.34†

* Time to FLM = stimulus to first lateral movement, Transfer Time = FLM to toe off, Swing Time = toe off to foot contact
† $p<.001$; ‡ $p<.01$; § $p<.05$

5.5   Discussion

In this population-based sample of older people, we found that time to FLM is the most informative component of GI given its association with a wide range of demographic and clinical variables and responsiveness to cognitive interference. However, in terms of the strength of associations, the advantages of studying time to FLM, rather than overall time to GI, were not substantial. Overall time to GI has stronger predictive performance in relation to falls-risk.

When measuring GI, we recommend using multiple trials to elucidate learning effects and to summarize trials using the median. Investigators should be aware that discrepant values will arise and may need to be taken into account. This problem is pronounced when GI is divided in to its components. In this study, five to 10% of the component values were identified as being discrepant in the sense of strongly influencing the mean for an individual. Faced with this variability, investigators may prefer to use a summary of the multiple measurements as the unit of analysis. For the component measures, we found that the median of multiple measurements provided the best choice of summary index. If overall GI was used instead of the component measures, the discrepant values were less problematic.

Another issue is choosing how many trials to conduct. Previous researchers [8, 9, 11, 20] have chosen to use up to five trials to obtain an overview of an individual's GI. Melzer and Oddsson [9] report a learning trend across the 3 trials they conducted for each step direction. We expanded the number of trials, conducting 6 trials per task condition to better understand how repetition of the task affects GI. We found marked reductions in time taken over the first three or four trials under dual-tasking. The first trial provides an indication of GI in novel circumstances. Performance on trials five and 6 might be a better reflection of how subjects initiate gait under customary or learned circumstances. We also found evidence of continued improvement over all 6 trials under single-tasking but the improvements were minor. The continued improvements suggest that 6 trials under each task condition on a force-platform are manageable by typical 60-86 year old subjects, without undue fatigue. We would recommend at least 6 trials per task condition per subject to provide flexibility in characterization of GI.

When investigating GI, most researchers [8, 9, 11, 21-26] have used one or more of the components (all three when available) in their analyses. Our results for this older sample show that the three components are moderately correlated under single-tasking. Under dual-tasking, time to FLM was increased by about 50 percent. Those with longer time to FLM tended to have longer transfer times but not longer swing times. Combined with the fact that time to FLM has the strongest correlation with other factors including age and body size, this component appears to be the key contributor to overall GI.

Little is known about how GI and its components are associated with factors such as muscle strength and balance that may predict falls-risk. Our results show that younger members of this sample had faster times to FLM particularly under dual-tasking, and increased strength in the knees, less weight, faster motor reactions and better balance were associated with having a faster GI.

The measurements made in this study using the cognitive tests (digit symbol search and symbol search) provided us with the opportunity to study the combined effects of processing speed and divided attention under dual-tasking. We found that processing speed markedly increased time to FLM and that the inverse association became more pronounced under dual-tasking. Processing speed and ability to divide attention were positively correlated and independently associated with time to FLM. Dual-tasking slightly reduced swing time, however, and the inverse associations between GI and the cognitive test results were reduced under dual-tasking. Whilst it is possible that processing speed and handling of divided attention are independent contributors to swing time, these results suggest that attention is more proximal than processing speed in the control of the swing of the leg to complete the first step.

Although using a small sample, this is the first population-based investigation of GI in older people. Previous studies have focused on step initiation [9, 21, 23] rather than GI. Initiation of the gait cycle, as examined in our study, is more analogous to the everyday performance of commencement of walking – the phase of the gait cycle during which falls are relatively frequent – than is the initiation of the first step. A further strength of this study is that we measured GI over 6 trials, which enabled us to investigate possible learning effects. Previous studies have generally used a smaller number of trials.

A possible limitation of this study was that we used a force-platform that measured movement at 200Hz when other studies have had sampling rates of up to 400Hz. Against this, however, we captured information on time to FLM (the shortest component) with adequate discrimination to reveal moderate associations with age, body size, sensorimotor variables and cognitive factors. A further possible limitation lies in the arithmetic nature of the dual-task. We did not assess the numeracy of our participants, and it is possible some with weaker arithmetic skills struggled with the dual-task. This may mean that their times to GI were slower than people who did not struggle with the arithmetic nature of the task.

5.6   Conclusions

Dividing time to GI into its three components provides additional information that may be important. If the GI components are to be measured, multiple trials are recommended to elucidate possible learning effects and to reduce the influence of discrepant values. It is best to use the median to summarise the multiple measurements of the components. The strengths of associations with time to FLM far outweigh the other components but are also greater than the overall GI time. Time to FLM appears to be the key component of GI with cognitive processing speed and ability to handle divided attention both playing a role in its regulation.

5.7   Postscript

Reported in the body of this chapter is an investigation of the statistical properties of the components of GI, their inter-relationships and associations with sensorimotor variables, and the effect of cognitive loading on those relationships. It was found that slow processing speed markedly increased time to FLM and the inverse association became more pronounced under handling of divided attention. Time to FLM appears to be the key component of gait initiation due to its association with the other study factors and its susceptibility to dual-tasking. Due to learning effects particularly when attention is divided, 6 trials per task are recommended. Learning effects are plausible if it is the cognitive interference task that is slowing GI.

Reported in the text and more fully in an appendix to the chapter (**Appendix 5A**) is an investigation of cognitive associations with GI. There, it is shown that GI time is

associated with the fundamental functions of executive function / attention and processing speed, and with visuospatial ability under conditions of cognitive interference.

Having provided evidence of cognitive links with gait and gait variability (**Chapter 4**) and with gait initiation (**Chapter 5**) the next step was to investigate whether cognitive functioning is associated with risk of falling. A report of this investigation is provided in the next chapter.

5.8   References

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Appendix 5A: The relationships between gait initiation and cognitive function in older people

A5A.1   Introduction

Gait and cognitive impairments, caused by ageing or disease, commonly occur in older people [1-3] and have been shown to predict falls [4-6]. Gait initiation (GI) is one phase of gait where falls are likely to occur [7]. GI is the commencement of movement, and is measured as the time elapsed between standing still and taking the first step in a recurring pattern of walking. GI is a widely investigated phase of gait, but the interrelationships between cognitive function and gait initiation are relatively poorly understood. Studying these relationships may provide further insights into the neural substrates of gait initiation in ageing. The aim was to investigate the relationships between cognitive function and gait initiation, two very important risk factors for falls.

A5A.2   Methods

Sample

The sample consisted of 128 subjects from the Tasmanian Study of Cognition and Gait (TASCOG) that was conducted at the Menzies Research Institute in Hobart. Eligible TASCOG participants were residents of Southern Tasmania, a geographical region defined by postcodes (7000 – 7199), who were aged between 60 and 85 years inclusive. They were selected by age- and sex-stratified random sampling without replacement, from the Tasmanian Electoral Roll (a comprehensive population listing). Potential subjects were excluded from the study if they lived in residential care, were unable to walk without a gait aid, or if they had any contraindications to magnetic resonance imaging (MRI) – a requirement of the overall study.

Measurements

Gait initiation (GI)

GI was measured using a 200Hz AccuGait force platform and Advanced Mechanical Technology Inc. (AMTI)-NetForce software. Participants were required to stand with

bare feet in a standardised stance with heels separated by 6cm and with approximately a 10° angle between the feet [8]. In response to an auditory cue, they were required to start walking forward a few steps onto an adjacent surface at the same height as the force platform. Twelve trials in total were conducted for each participant, alternating between single and dual cognitive tasks. The single task was to initiate gait in response to an auditory stimulus. The dual task was to initiate gait in response to an auditory stimulus whilst counting backwards in threes from a particular number (different numbers were allocated for each trial). Eleven single task values by 10 subjects, and 21 dual task values by 18 subjects, were excluded due to errors in data collection. Overall GI was recorded as the time from stimulus to the release of pressure on the standing foot as the leading foot makes, or prepares to make, contact with an adjacent surface. This measure was divided into three components: time from stimulus to first lateral movement (FLM); FLM to toe off of the leading foot (transfer time); and time from toe off to foot contact (swing time).

Cognitive function

A battery of cognitive tests was conducted to assess the following cognitive domains: (1) *Executive function / attention* using the Controlled Word Association Test (COWAT, using the letters F, A, and S) [9], Category Fluency (animals) [9], the Victoria Stroop test comprised of three subtests a) coloured dots, b) coloured everyday words and c) coloured colour-names (e.g. the word blue written in red ink) [10] and the Digit Span subtest of the Wechsler Adult Intelligence Scale Third Edition (WAIS-III) [11]; (2) *Processing speed* using the Symbol Search and Digit Symbol Coding subtests of the WAIS-III [11]; (3) *Visuospatial ability* using the Rey Complex Figure copy task [9]; and (4) *Verbal memory* using the Hopkins Verbal Learning Test (HVLT) Revised generating scores for total immediate recall, delayed recall, and recognition memory [9] and *Visual memory* using a delayed reproduction after 20 minutes of the Rey Complex Figure [9].

Data analysis

As in previous work **Table 6-2**, the raw scores of cognitive tests were grouped into the specific cognitive domains of executive function / attention, processing speed and memory, and then subjected to data reduction using principal components analysis. A summary cognitive component was thus derived to represent each of these domains. Regression scores were generated for these components using Thomson's method

[12] and these scores were used as variables in further analysis. The Rey Complex Figure Copy task was the sole test of visuospatial ability and hence only its raw score was used in analyses.

Spearman rank correlations were used to assess the relationships between cognitive function and gait initiation under single and dual task conditions.

A5A.3 Results

The mean age of the sample was 70.9 years (SD = 6.9). It contained 75 men (59%). The associations between cognitive function and gait initiation, and its component measures, under single and dual task conditions are presented in **Table 5-4**. Longer times to FLM under both task conditions were associated with poorer cognitive function across all domains, though less so with memory under single task conditions (p = 0.17). Swing time, under single task conditions only, was associated with executive function / attention and processing speed. Transfer time was not associated with any cognitive function. Overall, GI time was associated with executive function and processing speed, and with visuospatial ability under dual-tasking only.

Table 5-4: Correlations between cognitive function and gait initiation under single and dual task conditions.

	Executive function / attention	Processing speed	Memory	Visuospatial ability
Time to FLM				
Single task	0.33^{*}	-0.30^{*}	-0.12	$-0.22^{\ddagger}$
Dual task	0.48^{*}	-0.42^{*}	$-0.26^{\dagger}$	-0.34^{*}
Transfer time				
Single task	0.10	-0.11	0.02	-0.02
Dual task	0.12	-0.06	0.03	-0.07
Swing time				
Single task	$0.18^{\ddagger}$	$-0.26^{\dagger}$	-0.11	-0.14
Dual task	0.05	-0.13	-0.09	0.01
Overall				
Single task	$0.21^{\ddagger}$	$-0.26^{\dagger}$	-0.03	-0.15
Dual task	0.35^{*}	-0.33^{*}	-0.13	$-0.20^{\ddagger}$

$^{*}p<.001; ^{\dagger}p<.01; ^{\ddagger}p<.05$

A5A.4   Discussion

This is the first population-based study, to our knowledge, that has investigated the associations between cognitive function and GI. GI time was found to be associated with the fundamental functions of executive function / attention and processing speed, and with visuospatial ability particularly when there was cognitive interference. Time to GI was not associated with memory. Of the components of time to GI, time to FLM appears to be the most informative given its associations with all of the cognitive functions particularly under dual-tasking.

The findings of associations with executive function and GI add to recent work by Giladi et al. [13] who speculated that the hesitation, or freezing of gait at initiation, as seen in people with Parkinson's disease, may be associated with cognitive initiation (or executive function) problems. They hypothesised that freezing of gait may be related to inabilities to switch between motor programs that may be linked to inabilities in switching cognitive programs. The specific links were not investigated.

In our study, the strongest associations between cognitive function and GI were seen with executive function / attention and processing speed. These associations may be due to the neural substrates that serve these cognitive functions and are shared with those for gait control, particularly the connections between the frontal cortex and basal ganglia [9, 10]. The associations between visuospatial ability and GI (particularly time to FLM) warrant further investigations in respect of the impact of visuospatial skills on GI and the neural substrates that link them. The lack of associations with memory suggests that temporal and parietal structures that serve these memory functions may not play a primary role in gait initiation.

This is the first study to investigate the associations between cognitive function and gait initiation in community-dwelling older adults. Despite the relatively small sample size, strong associations were found between cognitive function and GI. Due to this study's cross-sectional nature, causal links cannot be identified and thus these results require further investigation in a longitudinal setting.

A5A.5   References

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Chapter 6: Visuospatial ability and memory are associated with falls-risk in older people – a population-based study.

6.1 Preface

The previous chapter provided an insight into the statistical characteristics of the components of gait initiation (GI), their inter-relationships and associations with sensorimotor variables, and the effect of cognitive loading on these relationships. We showed that cognitive interference, by dual-tasking, had the most effect on time to FLM, increasing times significantly. Time to FLM was also consistently associated with age, height and weight, sensorimotor variables and cognitive speed. It was also shown (**Appendix 5A**) that GI time is associated with executive function / attention and processing speed, and with visuospatial ability under divided attention.

Having shown that cognitive functioning is associated with gait and gait variability (**Chapter 4**) and with gait initiation (**Chapter 5**), it was time to turn attention to falls as an outcome of the complex interplay of cognition and gait. In this chapter the relationships between cognitive function and a physiological measure of falls-risk are investigated. In particular, I wished to examine whether falls-risk is associated with cognitive functions beyond executive function / attention and processing speed.

The material presented here has been published in a peer-reviewed journal [1].

6.2 Introduction

Falls are a major public health problem in older people [2] and are expected to become a more significant problem as populations become older [3]. They are associated with mortality, injury and disability and early admission to residential care [4, 5]. The annual cost of falls in Australia is currently AUD \$24million [2]. This figure is expected to rise to AUD \$1.3billion by 2051 [3]. The study of factors associated with the risk of falling may assist in the early identification of people at high risk of falls, and permit better targeting of prevention strategies.

Cognitive function may be an important indicator of falls-risk in older people [6, 7]. Previous data show that attention / executive function are associated with the risk of falls [8-11]. Data from population-based studies are scarce, with the few published results suggesting that executive function [9], attention [7, 12] and processing speed [7] may each be associated with falls. Cognitive abilities such as memory and visuospatial ability are dependent on whether fundamental abilities such as attention and executive ability are intact. Their unique contributions to the risk of falls in the general older population have not been firmly established. We hypothesised that the variability in a physiological measure of falls-risk would be explained by key cognitive functions beyond executive function / attention and processing speed.

6.3 Methods

Subjects

The sample consisted of the first 300 participants in the Tasmanian Study of Cognition and Gait (TASCOG) conducted in Hobart, Tasmania, Australia. Eligible participants were residents of Southern Tasmania defined by postcodes (7000 – 7199) and aged between 60 and 85 years inclusive. They were randomly selected using a comprehensive list of residents, the Tasmanian Electoral Roll. Eligible individuals were sent a letter asking them to participate followed up with a phone call. They were excluded if they lived in residential care, were unable to walk without a gait aid, or if they had any contraindications to magnetic resonance imaging (MRI) which was a requirement of the overall study. Those unwilling to participate (non-responders) were asked about their medical history and history of falls in the previous 12 months. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved this study.

Measurements

Falls-risk score

This was determined using a validated instrument, the short form of the physiological profile assessment (PPA) [13]. The PPA measures: (1) Edge contrast sensitivity - using the Melbourne Edge Test chart that has 20 circles containing edges with reducing contrast. The lowest correctly identified edge contrast was recorded in

decibel (dB) units. (2) Proprioception - using a lower-limb matching task. Participants were asked to align their feet either side of a perspex sheet with a protractor drawn in it, keeping their eyes closed. The degree of displacement between the two big toes was measured. (3) Knee extension strength (kg) - measured as an average of three attempts using a spring gauge attached to the subject's dominant leg. (4) Simple reaction time, in seconds, - measured as the time to depression of a switch by the finger in response to a light stimulus averaged over 10 trials. (5) Postural sway - using a sway meter that recorded displacements (mm) of the body at waist height while subjects stood on a medium-density foam rubber mat with eyes open and closed. Using an established algorithm [13], a standardized falls-risk score was then computed as a summary of weighted scores from the above individual tests. The falls-risk score gives an indication of the risk that an individual has of falling (defined as "unintentionally coming to the ground or some lower level …" [14]) relative to the average risk of Australians aged 65 or over [15-17]. A score of zero indicates that the individual's risk is equal to the average risk of Australians aged 65 years or over. A positive score indicates an increased risk of falling and a negative score indicates a decreased risk of falling. This score has at least 75% accuracy in identifying older people at risk of multiple falls [13, 15].

Cognitive function

The following functions were measured: (1) *Executive function / attention* using the Controlled Word Association Test (COWAT, FAS) [18], Category Fluency (animals) [18], the Victoria Stroop test [19] and the Digit Span subtest of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) [20]; (2) *Processing Speed* using the Symbol Search and Digit Symbol Coding subtests of the WAIS-III [20]; (3) *Visuospatial ability* using the Rey Complex Figure copy task [18]; *Verbal Memory* using the Hopkins Verbal Learning Test – Revised generating scores for total immediate recall, delayed recall, and recognition memory [18] and *Visual Memory* using a delayed reproduction after 20 minutes of the Rey Complex Figure[18].

Other measurements

Mood was measured using the 15-item Geriatric Depression Scale (GDS) [21]. All over the counter and prescription medicines were recorded. Based on this list, participants were classified as taking a psychoactive medication if they were on any of the following: antidepressants, antipsychotics, sedative/hypnotics, antiepileptics or antiparkinsonian drugs.

Data analysis

Chi-squared analysis and t-tests were used to compare responders and non-responders. Similar to our previous work [22], cognitive tests were grouped together to represent specific domains based on accepted cognitive theoretical framework [18] (**Table 6-2**). Each group of tests was subjected to data reduction using principal components analysis, generating cognitive components for that particular domain. Regression scores were then generated for each component using Thomson's method [23] and used as variables in further analyses. The Rey Complex Figure Copy was the sole test of visuospatial ability and hence its score was used as such.

Associations of the cognitive components with the individual measures of the PPA and the falls-risk score were first examined using Spearman correlations. Linear regression was used to model the relationship between the individual cognitive components and the falls-risk score. Because the reaction time task of the PPA has an element of cognitive speed combined with motor speed, we were concerned that the association between the falls-risk score and the processing speed cognitive component may become artificially inflated. We sought to avoid this by further adjusting for the PPA reaction time task in that regression. Cognitive abilities such as memory and visuospatial ability may be dependent on more fundamental functions such as executive ability / attention and processing speed. Therefore, to investigate their independent contribution to the falls-risk score, we adjusted for executive ability / attention and processing speed.

Additional adjustment was performed for putative confounders including age, sex, GDS score and the use of psychoactive drugs. Education level and self-reported history of stroke, epilepsy and Parkinson's disease (PD) were also initially considered as potential confounders. However, adjusting for these factors did not

markedly change the coefficients and standard errors of the covariates for the cognitive components, and thus they were left out of the final models.

Statistical interaction between age and the individual cognitive components was assessed by a test of significance of a $(CognitiveComponent \times Age)$ product term. Similar product terms of the individual cognitive component with sex, mood and psychoactive medication use were also tested for significance. We carefully checked for non-linearity in the final models.

Standard regression diagnostics were applied to assess adequacy of the models.

6.4   Results

The sample response proportion was 55.0% (300 responders / 541 eligible). Non-responders were older (p < 0.001) but did not differ from responders with respect to sex (p = 0.17) and self-reported history of hypertension (p = 0.36), stroke (p = 0.53), diabetes mellitus (p = 0.46), ischaemic heart disease (p = 0.61), ever-smoking (p = 0.26) and previous falls (p = 0.89). Participant characteristics are presented in **Table 6-1.** The mean age of the sample was 72.5 years (SD = 7.0) with 162 men (54%). The falls-risk score in our population-based study ranges from −2.32 up to +4.26 with a mean of −0.17 and a standard deviation of 0.91.

The groupings of cognitive tests used to generate each cognitive component, the component loadings and variance proportion explained by each component are shown in **Table 6-2**. Higher regression scores from these components indicate better memory and processing speed and worse executive function / attention. Higher scores on the Rey Complex Figure copy task indicate better visual constructional ability.

Unadjusted correlations between the individual PPA measures, the falls-risk score and the cognitive components are shown in **Table 6-3**. Greater visual edge contrast sensitivity and longer motor reaction times were associated with better function in all cognitive abilities. Greater knee extension strength was associated with better function in all cognitive abilities except memory. Increased sway was associated with poorer processing speed, memory and visuospatial ability. Proprioception was not associated with any cognitive function.

Table 6-1: Participant characteristics (n=300)

Variable	Mean	(SD)	Range
Age (years)	72.5	(7.0)	[61, 86]
Sex (number of males / %)	162	54%	–
Geriatric Depression Scale score	2.07	(2.4)	[0, 12]
Number taking psychoactive drugs (n / %)	47	16%	–
Physiological Profile Assessment (PPA)			
Composite falls-risk score[*]	−0.17	(0.91)	[−2.32, 4.26]
Edge contrast sensitivity (dB)	20.5	(2.3)	[10, 26]
Reaction time (s)	0.23	(0.04)	[123.5, 460.3]
Proprioception (degrees)	1.4	(1.2)	[0.1, 6.6]
Sway (eyes open, mm)	21.3	(8.4)	[3.0, 53.0]
Sway (eyes closed, mm)	37.3	(18.6)	[3.0, 141.0]
Knee extension (kg)	30.9	(12.5)	[2.0, 77.0]
Cognitive tests			
Digit span	15.6	(3.9)	[3, 27]
Category fluency	16.3	(5.1)	[0, 29]
COWAT	36.0	(13.6)	[3, 77]
Stroop dots (sec)	15.9	(5.4)	[7, 50]
Stroop words (sec)	22.1	(10.9)	[10, 129]
Stroop colours (sec)	38.42	(18.8)	[18, 174]
Digit symbol coding	49.34	(15.3)	[0, 89]
Symbol search	22.31	(7.6)	[0, 46]
Rey Complex Figure copy	32.5	(4.8)	[1.5, 36.0]
Rey Complex Figure delay	15.0	(7.1)	[0.0, 30.0]
Hopkins immediate recall	20.9	(6.3)	[0, 36]
Hopkins delayed recall	7.1	(3.2)	[0, 12]
Hopkins recognition	21.3	(3.3)	[0, 24]

SD – standard deviation; dB – decibel units; COWAT – Controlled Oral Word Association Test

[*] The Falls-Risk score is a summary of weighted scores from the individual PPA tests with higher scores indicating a greater risk of falling.

Table 6-2: Principal components analysis of cognitive tests.

Cognitive Test	Executive /attention	Processing speed	Visuospatial ability	Memory
Digit span	−0.29	–	–	–
Category fluency	−0.37	–	–	–
COWAT	−0.39	–	–	–
Stroop dots	0.49	–	–	–
Stroop words	0.50	–	–	–
Stroop colours	0.47	–	–	–
Digit symbol coding	–	0.71	–	–
Symbol search	–	0.71	–	–
Rey Complex Figure (RCF) copy	–	–	1.00*	–
RCF delayed visual recall	–	–	–	0.30
Hopkins immediate recall	–	–	–	0.59
Hopkins delayed recall	–	–	–	0.60
Hopkins recognition	–	–	–	0.45
Percent total variance†	55.5	86.9	100.0	57.2

* No PCA performed for Rey Complex Figure copy task is sole test of visual constructional ability

† Percentage of the total variance of each group of cognitive variables that is explained by first principal component in that grouping

COWAT – Controlled Oral Word Association Test

In univariable analysis, poorer function in all cognitive components was associated with a greater falls-risk score (**Table 6-4).** Visuospatial ability (p<0.01), memory (p <0.05) and executive function / attention (p <0.05) in separate models were each independently associated with the falls-risk score after adjusting for age, Geriatric Depression Scale (GDS) score and the use of psychoactive drugs (**Table 6-4).** The effect of processing speed, however, was not independent of age. Visuospatial ability (β = −0.05, 95% confidence interval [CI] −0.07, −0.02) and memory (β = −0.12, 95% CI −0.21, −0.04) remained associated with the falls-risk score after adjusting for executive function / attention and processing speed. Exploring the association of the memory component further, immediate verbal recall

($\beta = -0.02$, 95% CI -0.04, -0.01), delayed verbal recall ($\beta = -0.04$, 95% CI -0.07, -0.01), and delayed visual recall ($\beta = -0.02$, 95% CI -0.04, -0.01) were each associated with the falls-risk score independently of age, GDS and medications, whereas verbal recognition memory was not ($\beta = -0.001$, 95% CI -0.03, 0.03). Adjustment for sex, presence of self-reported Parkinson's disease or stroke did not change the results. There were no significant interactions observed. In the final multivariable models, visuospatial ability explained the most variation in falls-risk score (partial $R^2 = 0.022$) followed by executive function / attention.

Table 6-3: Correlations between cognitive components and measures of the Physiological Profile Assessment (PPA)

PPA measure	Executive / attention	Processing speed	Visuospatial ability	Memory
Edge contrast sensitivity	$-0.18^{\dagger}$	0.21^{*}	$0.16^{\dagger}$	0.24^{*}
Reaction time	0.25^{*}	-0.26^{*}	$-0.13^{\ddagger}$	-0.20^{*}
Proprioception	0.04	0.01	-0.06	-0.05
Sway (eyes open)	0.05	$-0.19^{\dagger}$	$-0.12^{\ddagger}$	$-0.18^{\dagger}$
Sway (eyes closed)	0.12	$-0.17^{\dagger}$	-0.12	$-0.14^{\ddagger}$
Knee extension	$-0.13^{\ddagger}$	$0.16^{\dagger}$	$0.14^{\ddagger}$	0.06
Composite falls-risk score[§]	0.25^{*}	-0.20^{*}	-0.22^{*}	-0.24^{*}

$^{*}p<.001$; $^{\dagger}p<.01$; $^{\ddagger}p<.05$

[§] The falls-risk score is a summary of weighted scores from the individual PPA tests with higher scores indicating a greater risk of falling.

Higher scores from these components indicate better spatial ability and processing speed and worse executive function / attention.

Table 6-4: Linear regression of composite falls-risk score on cognitive components

	Regression coefficient (β), 95% confidence interval		
Cognitive component	**Unadjusted**	**Model 1**	**Model 2**
Executive / attention	0.14* (0.09, 0.20)	0.10* (0.05, 0.15)	0.07‡ (0.01, 0.12)
Processing speed§	−0.14* (−0.22−0.07)	−0.07 (−0.15, 0.01)	−0.07 (−0.14, 0.01)
Visuospatial ability	−0.06* (−0.08, −0.04)	−0.05* (−0.07, −0.03)	−0.03† (−0.05, −0.01)
Memory	−0.17* (−0.23, −0.10)	−0.11† (−0.17, −0.04)	−0.07‡ (−0.13, −0.00)

$^*p<.001$; $^†p<.01$; $^‡p<.05$

§ Processing speed was adjusted for reaction time

Model 1 – adjusted for age; Model 2 – adjusted for age, Geriatric Depression Scale score and psychoactive medication use.

Higher scores from these components indicate better memory, visuospatial ability and processing speed and worse executive function / attention.

6.5   Discussion

In this population-based sample of relatively independent older people, we found that poorer visuospatial ability, executive function / attention and memory were independently associated with a worse physiological falls-risk score. Verbal and visual memory both contributed to the effect of memory on the falls-risk score. The effect of processing speed on the falls-risk score was confounded by age. The strengths of this study are that it is one of the few population-based studies with a substantial sample size measuring a range of cognitive domains, and carefully adjusting for confounding due to interdependence between cognitive abilities.

Consistent with previous research, we show that executive function / attention are independent factors associated with falls-risk [9-11, 24, 25], although the effect of processing speed was confounded by age. In a population-based sample of people aged ≥ 70 years, Holtzer *et al* [9] showed that attention was strongly related to self-reported falls. Executive function has also been shown to predict falls independently of age and functional motor ability [10]. Such fundamental cognitive abilities are dependent on the integrity of neural networks involving subcortical structures, cerebral cortex, brain-stem and the cerebellum [26]. Structural brain changes such as age-related white matter abnormalities may disconnect these networks leading to impaired executive function / attention [27] and consequent poorer motor control [28].

A novel finding in this study was the association between the Rey Complex Figure copy score and falls-risk. This constructional task is a robust test of visuospatial function, or the representation of objects in a spatial array (e.g. a person in relation to their environment, the relative position of objects in a room) [29]. Although we did not directly measure visual acuity, participants with uncorrected visual problems (n=3) were excluded from the analysis. Thus, visual acuity is unlikely to confound the relationship between visuospatial skills and the falls-risk score. Performance on this test also relies upon the integrity executive function (organisation and planning), raising the possibility that the observed effects could be explained by these functions. However the association remained even after controlling for some aspects of executive function such as set-shifting (Stroop) and word generation (COWAT).

It is, however, possible that the organisation/problem solving skills necessary for the Rey Figure contributed towards explaining the falls-risk score. Ageing has been associated with worse performance on all components of the Rey complex figure test [30]. Older people may have a higher risk of falling if they are unable to navigate effectively between two places by judging distances and avoiding objects. Based on our findings, more detailed examination of the impact of visuospatial skills on falls-risk is warranted. If further research were to confirm our findings, the study of the neuro-anatomical substrate of this association may be of interest, speculating that age-related changes in structures and networks involved in visuospatial function may be important determinants of the risk of falls. We also found that immediate and delayed verbal memory and delayed visual memory were independently associated with the falls-risk score. Van Schoor et al. [12] showed previously that immediate memory was predictive of recurrent falls particularly in people aged ≥ 75 years. Immediate and delayed recall are served principally by mesial temporal structures including the hippocampus. Hippocampal structure and volume are known to decline with age as well as Alzheimer's disease (AD) [31]. Neurodegeneration involving such mesial temporal structures may thus be relevant to the mechanisms underlying falling in older people.

A limitation of this study is the use of the PPA rather than a prospective estimate of actual falls. Although the PPA is an established intermediate measure of the risk of falls [13], it would be important to validate these findings against an estimate of actual falls. The study response rate of 55% means that there could potentially be a non-response bias. However, responders and non-responders differed only in age. Although non-responders were slightly older, there was no in-sample evidence that the associations between the cognitive components and the falls-risk score differed in magnitude or direction by age (data not shown) suggesting that non-response bias due to age alone is unlikely to affect the validity of our results. For this reason, and because our sample did not include frail older people, our results cannot be generalised to the oldest-old. In this respect, our sample was representative of community-dwelling elderly people. It can be argued, however, that it is important to detect the future risk of falling in relatively healthy people in order to institute preventative measures. To this end, our findings point towards the potential use of specific cognitive tests (such as the Rey Complex Figure) in the clinical prediction of falls. However, given that this is a population-based sample, one could expect that a

proportion of the participants may have undiagnosed cognitive impairment or dementia. Hence our sample should not be considered to be a completely healthy population sample. The cross-sectional nature of the study also means that we are unable to show causality in the observed relationships and hence a longitudinal study is required.

6.6   Conclusions

Adding to the known effects of executive function / attention, visuospatial ability and memory were predictors of a composite falls-risk score in this population-based study. The effect of processing speed was confounded by other factors such as mood and age. Confirmation of the association between visuospatial ability and falls risk using additional measures of visuospatial skills is warranted. It would also be important to validate these findings using a prospective estimate of actual falls. Further study of the neuroanatomical substrates underlying these associations may provide useful information regarding the neural mechanisms underlying falls in older people.

6.7   Postscript

In a first step in the investigation of cognitive factors that underlie falls in older adults, attention was turned in this chapter to a physiological measure of falls-risk. Functioning in each of the four cognitive domains studied was shown to be associated with falls-risk in cross-sectional data though each was confounded by age and that with processing speed was no longer statistically significant after adjustment for age. The next step is to determine whether these cognitive functions predict incident falls in a prospective study.

6.8   References

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Chapter 7: Cognitive function modifies the effect of sensorimotor function on the risk of multiple falls – a population based study.

7.1 Preface

The previous chapter provided an insight into the associations between cognitive function and a physiological measure of falls-risk. In a novel finding, visuospatial ability was shown to be a key contributor to risk. Confirming previous results, executive function / attention and memory were shown to be associated with the surrogate measure of falls-risk. Each of the associations was confounded by age, and that of processing speed was no longer statistically significant after adjusting for age.

In this chapter, I turn to a prospective measure of single and multiple falls and investigate the associations with cognitive function in a population-based sample of older adults. With an actual measure of falls used as the outcome, there was now freedom to investigate the inter-relationships of cognitive factors with measures of sensorimotor functioning, and also with gait. In the previous analysis (**Chapter 6**), these sensorimotor variables were used in the assessment of falls-risk outcome.

The text that follows is included in a manuscript that is under review by the Journal of Gerontology.

7.2 Introduction

Falls are a major health problem, occurring in about a third of all people aged over 65 years [1-3], with around half of those having multiple falls over a 12 month period [4, 5]. They lead to injury, hospitalisation or institutionalisation, loss of independence, morbidity and even mortality [6, 7]. The costs of falls to the community are large, with total cost estimated to be US $19 billion per annum [8, 9] in the United States of America and AUD $24 million per annum in Australia [10]. In 2006, 500 million people worldwide were older than 65 years and that figure is estimated to rise to 1 billion people by 2030 [5]. The costs of falls are estimated to double by 2020 [9] and to exceed AUD $1.3 billion in Australia by 2051 [11]. For all

of these reasons, it is important to obtain a good understanding of risk factors for falls to enable identification of targets for intervention and prevention.

Reduced cognitive function has been identified as an important risk factor for falling in specific patient groups [12-22] and more generally in population-based studies [3, 23-25]. Most of this research has focused on general cognitive function as assessed by instruments, such as the Folstein Mini Mental Status Examination (MMSE) [26]. Recently, an emerging focus has been placed on studying the effects of decline in specific cognitive domains such as executive function, attention and memory [22, 24, 25, 27]. The rationale is that decline in cognitive function occurs non-uniformly across domains, and studying levels of and changes in specific cognitive abilities may better elucidate the pathways leading to falls. In addition, declines in sensorimotor function (such as balance, muscle strength, vision and gait speed) are also related to a greater risk of falls [28]. To our knowledge, there are no studies examining potential interactions between cognitive and sensorimotor impairments that contribute to falls risk, or whether such interactions are restricted to specific cognitive functions. Knowledge of such interactions may enable a better understanding of how best to target falls prevention strategies.

We hypothesised that poorer function in a range of cognitive domains, and particularly visuo-spatial abilities, would increase the risk of falls in the general older population, and would do so by modifying the effects of sensorimotor impairments on the risk of falls.

7.3   Methods

Subjects

The sample consisted of 386 participants from the population-based Tasmanian Study of Cognition and Gait (TASCOG) conducted in Hobart, Tasmania, Australia. Subjects were residents of Southern Tasmania, a region defined by postcodes (7000 – 7199). They were aged between 60 and 85 years inclusive and were randomly selected using age- and sex-stratified sampling from the Tasmanian Electoral Roll. Subjects were excluded from the study if they lived in residential care or if they had any contraindications to magnetic resonance imaging (MRI) which was a

requirement of the overall study. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved this study.

Measurements

Cognitive function

Cognitive function was assessed using a range of standardised tests and grouped according to the domains they represented. The tests of *executive function / attention* were the Victoria Stroop tests: colored dots, colored general words (for example truck, fish) and colored color-names (for example the word red written in blue ink) [29], the Digit Span test from the Wechsler Adult Intelligence Scale – Revised Edition (WAIS-III) [30], and the FAS and category fluency tests from the Controlled Oral Word Association Test (COWAT) [31]. The tests of *processing speed* were the digit symbol coding and symbol search subtests of the WAIS-III [30]. The singular test of *visuospatial ability* was the copy format of the Rey Complex Figure test [31]. The tests of *memory* were the Hopkins Verbal Learning Tests - Revised (HVLTR) of immediate, delayed and recognition memory [31] and the delayed reproduction of the Rey Complex Figure test [31]. These tests are described in more detail elsewhere [32].

Other measurements

Mood was assessed using the 15-item Geriatric Depression Scale score (GDS) [33]. Recordings were made of prescription and non-prescription medicines used, and participants were classified as taking a psychoactive medication if they were using any of the following: antidepressants, antipsychotics, sedatives/hypnotics, antiepileptics or antiparkinsonian drugs. They were also classified as either using or not using blood pressure lowering drugs.

Gait speed was measured using the 4.6m GAITRite system (CIR Systems, PA, USA) at usual walking pace. Participants were required to complete 6 walks and start and finish walking two meters before and two meters after the mat to make it possible to reach and maintain a constant speed. Physical activity was measured using a Yamax Digi-Walker SW-200 pedometer worn on 7 consecutive days. Participants were required to complete a 7-day diary of daily steps, and to report times the pedometer was worn and not worn. Recordings for days on which the pedometer was worn for less than 8 hours were excluded when calculating mean number of steps per day.

Sensorimotor measures of falls risk were assessed using the short form of the Physiological Profile Assessment (PPA) as detailed elsewhere [32]. The tests included assessment of body sway, leg strength, visual contrast sensitivity and lower limb proprioception.

Falls

Falls were ascertained using a self-report 12 month prospective calendar. For the purpose of this study, a fall was defined as "an unexpected event in which the person comes to rest on the ground, floor, or lower level" in accordance with the Prevention of Falls Network Europe (ProFaNE) guidelines [34]. Information on the number of falls, the reason for each fall and the outcome (whether any injury was sustained) was collected using a diary that was completed daily, and summarised at two monthly intervals during the 12 months on a reporting form that was returned by post.

Data analysis

The cognitive test variables, other than the Rey Complex Figure copy task, were grouped into the specific cognitive domains of *executive function / attention, processing speed,* and *memory*. Each group of tests was subjected to data reduction using principal components analysis to derive a single score for that cognitive domain. The individual tests loaded on the same components as in our previous analysis using a smaller sample, and the factor loadings were very similar [32]. Summary regression scores were generated for each component using Thomson's method [35]. In order to fully explore the data, analysis of associations between cognition and falls were performed using both individual raw test scores and the summary scores for each domain. The Rey Complex Figure Copy task was the sole test of *visuospatial ability* and hence its raw score was used for that domain.

Participants were divided into non-fallers, single fallers and multiple fallers. Those who did not complete the full 12 months of recordings were treated as missing if they had not reported a fall in their completed recordings, but as single or multiple fallers if one or more falls respectively had been reported. There were 19 participants who did not complete recordings but reported a fall, and could therefore be classified as having had a fall.

One way analysis of variance and chi-squared tests were used to assess difference in study factors between subjects who recorded no falls, a single fall or multiple falls. Spearman rank correlation coefficients were computed as measures of association between scaled explanatory study factors. Log multinomial regression was used to generate estimates of relative risk of single falls and of multiple falls for levels of exposure to study factors other than the reference level [36]. Interaction between cognitive function and sensorimotor factors was assessed by a test of the coefficient of a product term formed from the summary cognitive score for a domain and a sensorimotor factor. Each statistically significant interaction term was then adjusted for the other study factors to assess the independence of the association. Non-linearity in the scale of covariates was assessed by including power transformations of the covariates in the model. The tests of non-linear trend reported in results are the results of tests of significance of the coefficient of the square of the covariate (the memory score and visuospatial ability score).

7.4 Results

The study response proportion was 51.7% (431/834) with non-responders being generally older (p <0.01) than participants. Forty-five participants from the full sample were excluded from this analysis because they had not completed 12 months of recordings and had not recorded a fall in their completed recordings. These participants had slower gait speed (p = 0.02) and poorer memory (p = 0.05) but otherwise did not differ from the remaining participants in the study factors. Characteristics of subjects in the final sample (n=386) are summarized in **Table 7-1** where they are classified as non-fallers, single fallers or multiple fallers. The mean age of the final sample was 72.2 (SD =7.1) years. It comprised 215 men (55.7%).

Overall, 214 (55.4%) participants did not fall during the 12 months of follow-up, 94 (24.4%) had a single fall, and 78 (20.2%) recorded more than one fall. Those who fell were older, more likely to be female, more often were taking psychoactive medications, walked slower and had poorer leg strength, greater sway, slower reaction time, poorer visual contrast sensitivity, and worse function on selected tests of executive function and visuospatial ability (all p <0.05).

Univariable associations between the explanatory study factors are summarised as correlation coefficients in **Table 7-2**. Poorer cognitive summary scores were generally associated with greater age, worse mood, lesser ambulatory activity, slower gait speed and poorer sensorimotor function (all p <0.05).

The associations of cognitive scores with single falls and multiple falls are reported in **Table 7-3** as relative risks per unit of each score. There were no statistically significant associations with the risk of single falls. The composite score for executive function was not significantly associated with the risk of multiple falls in this sample size, but three of the component tests – Stroop dot subtest, Stroop words subtest and category fluency – were, and results for each test pointed to increased risk of multiple falls for subjects with impaired executive function.

The associations with processing speed and memory suggested greater risk of multiple falls for subjects with slower processing speed or poor memory, but they did not reach statistical significance in this sample size. The single test of visuospatial function was significantly associated with risk of multiple falls, with the direction of association indicating reduced risk for those with better function. This association persisted after adjustment for executive function or processing speed, which are known to influence visuospatial ability.

The associations of the memory and visuospatial ability composite scores with the risk of multiple falls were non-linear (both p < 0.05), with greatest risk for those with best or worst function. In each case this was due to a small group of multiple fallers with high memory function and visuospatial ability, respectively, whose falls were not explained by any of the other physiological factors (for example, they did not have weak leg strength or very poor balance).

Restricting analyses to the composite cognitive scores, the associations for memory and visuospatial ability with the risk of multiple falls were non-linear, with greatest risk for those with best or worst function. In each case this was due to a small group of multiple fallers with high memory function and visuospatial ability, respectively, whose falls were not explained by poor scores in any of the other physiological factors (e.g. they did not have weak leg strength, very poor balance or very few steps per day for example).

Table 7-1: Participant characteristics.

	No falls (n = 214)		Single fall (n = 94)		Multiple falls (n= 78)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age (years)	71.3	(6.8)	72.4	(6.3)	74.3	(8.4)[†]
Male sex (% /n)	62.1%	(n= 133)	48.9%	(n= 46)	46.2%	(n= 36)[‡]
Psychoactive medications (% /n)	17.8%	(n= 38)	19.1%	(n= 18)	34.6%	(n= 27)[†]
BP lowering medications (% /n)	52.3%	(n= 112)	59.6%	(n= 56)	57.7%	(n= 45)
Geriatric Depression Scale score	1.47	(1.8)	2.01	(1.79)	3.28	(3.15)[*]
Gait speed (cm/sec)	118.0	(19.4)	112.8	(19.2)	105.8	(27.2)[*]
Ambulatory activity (steps/day)	5959.3	(3148.1)	6204.4	(3002.7)	5489.4	(3499.3)
Sensorimotor measures:						
Sway (mm)	19.5	(7.9)	20.8	(8.0)	22.7	(11.4)[‡]
Vision (dB)	20.8	(2.1)	20.9	(2.1)	20.2	(2.6)[‡]
Leg strength (kg)	92.5	(43.4)	80.5	(38.6)	69.8	(42.7)[*]
Reaction time (ms)	224.5	(29.1)	226.2	(28.2)	244.2	(48.8)[*]
Proprioception (degrees)	1.55	(1.22)	1.48	(1.15)	1.69	(1.33)

Cognitive Tests (number of correct responses)

Stroop dot time	16.0 (5.5)	15.1 (3.9)	17.7 (7.3)[‡]
Stroop word time	22.0 (9.6)	20.3 (6.0)	24.7 (17.7)[‡]
Stroop colour time	39.7 (25.3)	37.1 (19.0)	41.6 (22.7)
COWAT[§]	35.5 (13.2)	37.3 (12.3)	34.7 (14.5)
Category fluency	17.3 (4.8)	17.4 (4.7)	15.4 (6.2)[‡]
Digit span	16.0 (4.1)	15.5 (3.4)	15.4 (4.0)
Digit symbol coding	50.1 (14.8)	50.6 (14.8)	48.2 (17.7)
Symbol search	23.1 (7.9)	22.6 (6.8)	21.6 (8.2)
Hopkins immediate	22.6 (6.0)	22.1 (5.9)	21.0 (7.8)
Hopkins delayed	7.68 (3.03)	7.88 (2.79)	7.11 (3.52)
Hopkins recognition	21.7 (2.3)	21.5 (3.2)	21.6 (3.3)
Rey Complex Figure copy	32.3 (4.3)	32.1 (4.8)	30.4 (7.4)[‡]
Rey Complex Figure delay	15.1 (7.0)	15.1 (6.4)	13.5 (7.3)

SD – standard deviation; BP – blood pressure; * $p<.001$; † $p<.01$; ‡ $p<.05$ (Assessed by ANOVA for continuous variables and Chi-Squared tests for categorical variables); § Controlled Oral Word Association Test

Table 7-2: Correlations between cognitive functions, age, mood, gait speed, ambulatory activity and sensorimotor measures.

	Executive function	Processing speed	Memory	Visuospatial ability	Age	GDS[§]	Gait speed	AA[¶]	Sway	Vision	Leg strength	Reaction time
Executive function	1.00											
Processing speed	−0.70*	1.00										
Memory	−0.54*	0.51*	1.00									
Spatial ability	−0.41*	0.46*	0.34*	1.00								
Age	0.30*	−0.38*	−0.31*	−0.21*	1.00							
GDS[§]	0.10	−0.18†	−0.10	−0.04	0.11	1.00						
Gait speed	−0.34*	0.35*	0.22*	0.16†	−0.30*	−0.29*	1.00					
AA[¶]	−0.22*	0.25*	0.20*	0.11	−0.34*	−0.23*	0.32*	1.00				
Sway	0.06	−0.18†	−0.13‡	−0.11	0.27*	0.04	−0.15‡	−0.14‡	1.00			
Vision	−0.22*	0.30*	0.28*	0.20†	−0.42*	−0.13	0.19†	0.18†	−0.17†	1.00		
Leg strength	−0.14‡	0.24*	−0.03	0.11	−0.30*	−0.12	0.33*	0.11	−0.08	0.05	1.00	
Reaction time	0.24*	−0.21*	−0.13‡	−0.14‡	0.09	0.08	−0.21*	−0.14‡	0.10	−0.14‡	−0.17†	1.00
Proprioception	0.01	−0.04	−0.01	−0.13‡	0.07	0.08	−0.04	−0.06	0.01	−0.03	0.09	−0.04

* $p<.001$; † $p<.01$; ‡ $p<.05$; § Geriatric Depression Scale score; ¶ Ambulatory activity (steps/day).

Table 7-3: Associations of cognitive function measures with the risk of single and multiple falls.

	No falls (n = 214)	Single fall (n = 94)	Multiple falls (n= 78)
	RR	RR {95% CI}	RR {95% CI}
Executive function /attention[§]			
Stroop dot time	1.00	0.961 (0.923, 1.001)	1.032 (1.012, 1.052)[†]
Stroop word time	1.00	0.974 (0.949, 1.000)	1.016 (1.006, 1.025)[†]
Stroop colour time	1.00	0.995 (0.986, 1.005)	1.003 (0.997, 1.009)
COWAT	1.00	1.008 (0.995, 1.021)	0.994 (0.979, 1.009)
Category fluency	1.00	1.019 (0.983, 1.056)	0.943 (0.911, 0.976)[†]
Digit span	1.00	0.983 (0.940, 1.027)	0.979 (0.932, 1.029)
Composite score	1.00	0.935 (0.842, 1.038)	1.062 (0.977, 1.153)
Processing speed[¶]			
Digit symbol coding	1.00	1.003 (0.991, 1.015)	0.992 (0.979, 1.006)
Symbol search	1.00	0.998 (0.977, 1.021)	0.984 (0.959, 1.009)
Composite score	1.00	1.005 (0.881, 1.146)	0.915 (0.787, 1.064)
Memory[¶]			
Hopkins immediate	1.00	1.000 (0.969, 1.027)	0.970 (0.939, 1.001)
Hopkins delayed	1.00	1.030 (0.970, 1.093)	0.949 (0.891, 1.010)

Hopkins recognition	1.00	0.972 (0.911, 1.038)	0.993 (0.915, 1.077)
Rey Complex Delay	1.00	1.007 (0.982, 1.032)	0.973 (0.945, 1.002)
Composite score	1.00	1.000 (0.887, 1.128)	0.918 (0.803,1.050)
Visuospatial ability[¶]	1.00	1.012 (0.973, 1.052)	0.947 (0.919, 0.976)[*]
Other study factors:			
Age	1.00	1.005 (0.980, 1.030)	1.046 (1.017, 1.075)[†]
Sex	1.00	1.312 (0.924, 1.864)	1.467 (0.986, 2.182)
Psychoactive medications	1.00	0.870 (0.553, 1.370)	1.920 (1.289, 2.859)[†]
BP lowering medications	1.00	1.215 (0.845, 1.747)	1.095 (0.733, 1.636)
GDS	1.00	1.008 (0.942, 1.078)	1.135 (1.089, 1.184)[*]
Gait speed (cm/sec)	1.00	0.998 (0.991, 1.006)	0.981 (0.975, 0.987)[*]
AA(1000steps/day)	1.00	1.027 (0.973, 1.083)	0.953 (0.885, 1.026)
Sway (mm)	1.00	1.004 (0.986, 1.024)	1.024 (1.007, 1.041)[†]
Vision (dB)	1.00	1.048 (0.964, 1.140)	0.890 (0.819, 0.968)[†]
Leg strength (kg)	1.00	0.997 (0.993, 1.001)	0.990 (0.984, 0.996)[†]
Reaction time (ms)	1.00	0.998 (0.992, 1.003)	1.011 (1.007, 1.014)[*]
Proprioception (degrees)	1.00	0.946 (0.813, 1.101)	1.082 (0.932, 1.257)

[*] $p<.001$; [†] $p<.01$; [‡] $p<.05$; [§] Higher scores indicate poorer function; [¶] Higher scores indicate better function; GDS – Geriatric Depression Scale score; AA – Ambulatory activity (1000steps/day)

Table 7-4: Risk of multiple falls for cognitive factors in combination with gait speed, ambulatory activity and sensorimotor variables.

	Effect of cognitive function in absence of study factor		Effect of study factor in absence of cognitive function		Effect of cognitive function and study factor combined			Interpretation of interaction term
	β	(SE)*	β	(SE)	β	(SE)	P-value[‡]	Risk of multiple falls increased by:
Executive function								
Sway	−0.596(0.205)		0.027(0.013)		0.0294(0.008)		0.001	greater sway, particularly for worse EF
Reaction time (RT)	−1.777(0.534)		0.013(0.002)		0.0068(0.002)		0.001	slower RT, particularly for worse EF
Processing speed								
Gait speed	−1.101(0.302)		−0.013(0.006)		0.0111(0.003)		<0.001	slower gait speed, particularly for worse PS
AA[†]	−0.278(0.139)		−0.025(0.040)		0.0665(0.021)		0.001	fewer steps, particularly for worse PS
Sway	0.908(0.214)		0.012(0.012)		−0.0438(0.009)		<0.001	greater sway, particularly for worse PS
Reaction time (RT)	2.889(0.593)		0.010(0.002)		−0.0116(0.002)		<0.001	slower RT, particularly for worse PS
Memory								
Gait speed	−0.574(0.264)		−0.016(0.006)		0.0056(0.003)		0.037	slower gait speed, particularly for worse M
Sway	0.383(0.222)		0.023(0.012)		−0.0182(0.008)		0.030	greater sway, particularly for worse M
Reaction time (RT)	0.922(0.436)		0.010(0.003)		−0.0035(0.002)		0.040	slower RT, particularly for worse M

Visuospatial ability

AA[†]	−0.085(0.034)	−0.569(0.246)	0.0178(0.008)	0.020	fewer steps, particularly for worse VA[§]
Sway	0.113(0.053)	0.198(0.055)	−0.0064(0.002)	0.001	greater sway, particularly for worse VA
Vision	−0.710(0.341)	−1.213(0.585)	0.0352(0.018)	0.046	poorer vision, particularly for worse VA
Leg strength	−0.142(0.049)	−0.081(0.027)	0.0021(0.001)	0.009	weaker strength, particularly for worse VA
Reaction time (RT)	0.797(0.287)	0.119(0.038)	−0.0033(0.001)	0.005	slower RT, particularly for worse VA

* β (SE) = regression coefficient (standard error); †Ambulatory activity -units of 1000 steps/day; ‡ P-value for interaction term;

§ – seen only for those with a visuospatial ability score < 31.66 (30% of subjects);

EF – Executive function / attention, PS – Processing speed, M – Memory, VA – Visuospatial ability; All models adjusted for age and sex.
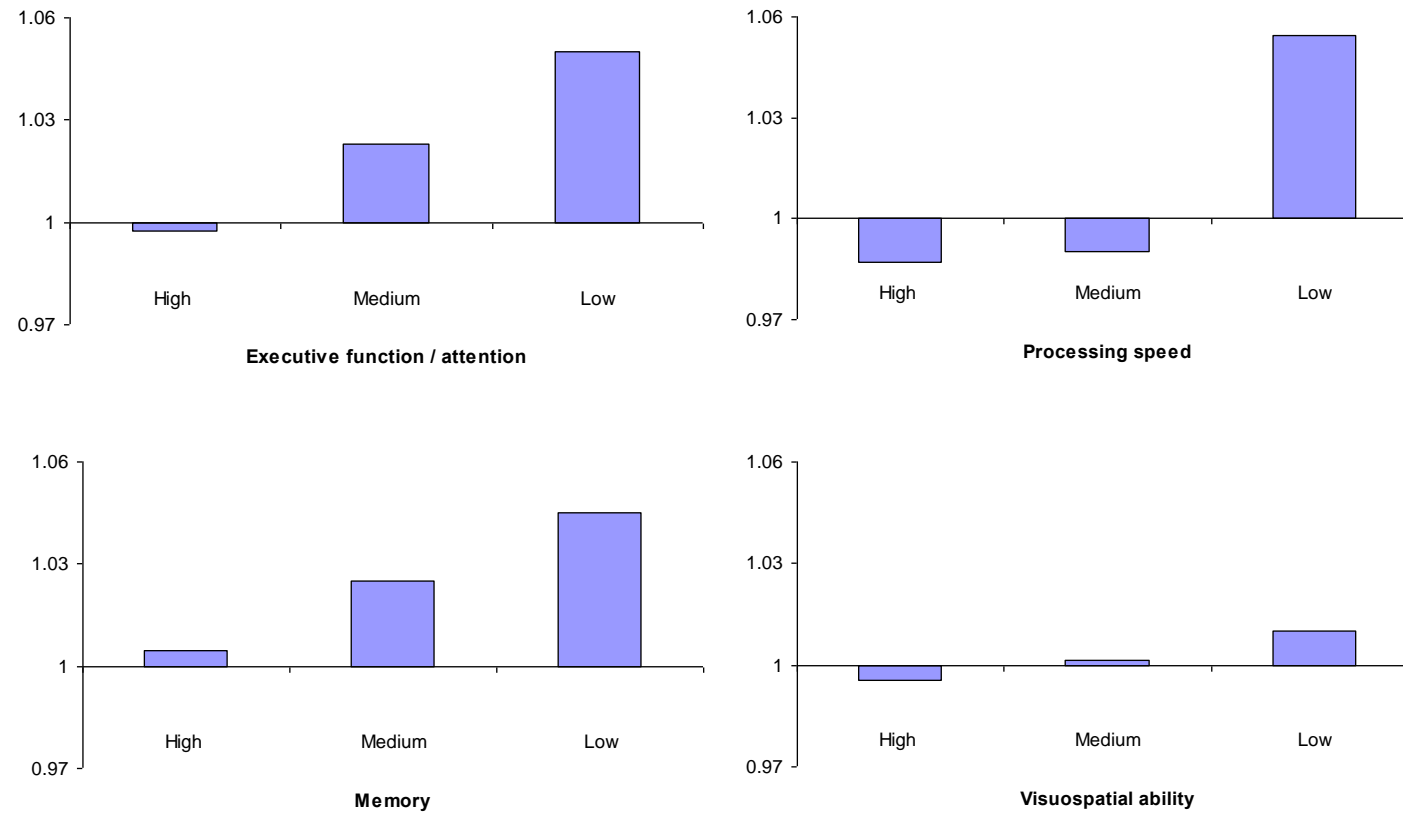
Figure 7-1: Risk of multiple falls per mm of sway at three levels of each of the four cognitive factors.
y-axis is the relative risk per mm of sway, x-axis is tertiles of each cognitive function.

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Also shown in **Table 7-3** are the associations with falls of other study factors including sensorimotor function. As with cognitive function, none of these factors were significantly associated with single falls. Risk of multiple falls was higher for subjects of greater age, poorer mood, poorer leg strength, greater sway, longer reaction time, slower gait speed and poorer visual contrast (all $p < 0.05$). Risk of multiple falls was higher for women than for men ($p = 0.06$).

There were significant and consistent age and sex-adjusted interactions between the cognitive scores and physiological measures in their association with the risk of multiple falls. For brevity, results are reported in **Table 7-4** for the four summary scores. The regression coefficients and standard errors for the cognitive summary score, the physiological factor and their product term are presented. For example, risk of multiple falls was increased by greater sway particularly for those with poorest cognitive function (interaction $p < 0.05$) as assessed for each of the four cognitive domains. These interactions are depicted in **Figure 7-1,** where relative risks of multiple falls per mm of sway are shown for participants categorised by tertile of each cognitive function. When examined in a multivariable model containing all significant interactions, most remained significantly associated with the risk of multiple falls. Only the interactions of processing speed with sway and reaction time, executive function with sway, and memory with gait speed were rendered non-significant (data not shown).

Because significant interactions were also found between age and each of the cognitive summary scores (data not shown) for the risk of multiple falls, we explored whether this could be partly or fully explained by the observed interactions between cognitive and physiological factors. Suggesting that this was the case, the addition of a *cognitive x physiological factor* product term in the model for each cognitive domain substantially attenuated the coefficient of the *cognition x age* product term.

7.5   Discussion

In this population-based sample of older adults, neither cognitive function nor physiological sensorimotor factors were associated with the risk of single falls but, consistent with the findings of previous studies [37, 38], tests of executive function / attention were predictive of multiple incident falls. A novel finding was that poorer visuospatial function was also predictive of multiple falls independent of its

relationship with executive function / attention or processing speed. A further key finding was that poorer cognitive function, irrespective of domain involved, amplified the adverse effect of the physiological sensorimotor factors on the risk of falls, and that these cognitive-sensorimotor interactions appeared to explain other interactions between age and cognitive function in respect to falls risk. These data suggest that targeting of falls prevention strategies may need to be tailored according to whether or not an older person demonstrates any cognitive impairment, and particularly impairment in executive or visuospatial abilities.

Most previous research on cognitive function as a risk factor for falls has broadly examined the influence of general cognitive status using relatively simple cognitive tools such as Folstein's Mini Mental State Examination [12, 13, 22-25, 39, 40]. There are few population-based data explaining the impact of specific cognitive domains (other than executive function / attention) on falls [22, 37, 39]. In this study, a comprehensive battery of cognitive tests was employed with the finding that executive function and visuospatial ability may be the principal cognitive domains contributing to the risk of multiple falls amongst community-dwelling older people.

While the finding in relation to executive function is consistent with previous work [38], the data suggesting that visuospatial ability is an independent contributor to risk are novel. The findings prospectively confirm our previous cross-sectional results linking visuospatial function with surrogate measures of falls-risk [32] in a smaller sample from TASCOG. A further interesting finding was that none of the memory measures used in our study were associated with falls. The mechanisms underlying these relationships are unclear, but age-related loss of cerebral grey or white matter may play a role. If this was the case, it would be debatable whether or not such changes were disease-related. It has been shown that cognitive functions (e.g. visuospatial ability) other than memory exhibit earlier decline during the process of developing Alzheimer's disease (AD) [41]. It has also been proposed that older people with visuospatial loss and increased falls risk may have preclinical AD, suggesting that these phenomena lie on the continuum of neurodegenerative disease [42]. However, such a postulate needs to be confirmed with longitudinal measurement of cognition, falls and possibly brain imaging to tease out the causal relationships involved.

Even though there is an abundance of research on other physiological factors involved in falling, and a growing body of work on cognitive function, there is none to our knowledge that attempt to examine the inter-relationships between them. Consistent with previous research [3, 4, 23, 24, 28, 37, 39, 43-51], we showed that the risk of multiple falls in older people is increased for those with poorer performance in tests of balance, muscle strength, vision, reaction time, gait speed and ambulatory activity. In addition, our results demonstrate that the adverse effects of several physiological factors on the risk of multiple falls are magnified by the presence of poorer cognitive function, and that this is consistently the case across all measured cognitive domains. These interactions tended to explain effect modification by age of cognitive function in explaining falls risk, suggesting that the physiological factors play a more proximal role on the causal pathway leading to multiple falls. This strengthens previous observations that the combination of host factors, rather than individual factors themselves, is important in heightening the risk of potentially injurious falls [48]. Community-dwelling older people with impaired cognitive function, as a function of poorer brain reserve, may be less able to compensate for physical frailty and this may lead to a loss of mechanisms that are protective against falling. Arguably, the physical environment may also play an important role but we did not evaluate its impact on these relationships. One could speculate that there may be complex interactions between host and environmental factors, and it would be interesting to study the effect of environmental hazards, that may also be modified by cognitive function or other physiological factors.

Our results confirm previous findings that there may be different causal mechanisms underlying single and multiple falls [37]. It has been shown that single fallers do not differ from non-fallers in their health status, balance or overall cognitive function [37] and our results support this. Holtzer et al. [39] suggested that the same cognitive processes are at play in both single and multiple falls, but that there is an additional contributing factor to multiple falls. People who fell just the once during the course of our study were slightly older, more likely to be female, walked slower and had poorer muscle strength than non-fallers. They had a greater level of ambulatory activity than non-fallers, however, with no obvious differences seen in average cognitive scores. It is interesting to speculate that some of these people may be on the cusp of suffering further falls, and that this may happen in the event of further cognitive deterioration: a theory that can be tested in further follow-up. It is also

possible that single falls are accidental in highly active people who put themselves in situations of greater risk, and that further falls will not occur in the absence of further or other disease.

A strength of this study is that it is the first population-based study in older adults to assess the inter-relationships between cognitive function across a range of domains and a number of physiological measures – two leading risk factors for falls in the elderly – in their relationship with single and multiple falls. A further strength lies in the comprehensive battery of cognitive tests employed. As part of the range of cognitive tests over several domains, we assessed the contribution of visuospatial ability, an emerging area of interest. We studied incident falls, but there are always limitations of self-reporting when using a two monthly falls questionnaire. Nevertheless, this at present remains the preferred method of collection [54] in large studies. The effect of self-report bias may be by under-reporting of falls in those who are cognitively impaired, and hence this may have resulted in an underestimation of associations. The use of higher-end technology such as accelerometers may in the future overcome this issue. Because our sample was younger than the non-participants in our study, our results may not be generalisable to the oldest of old. Another possible weakness is the sole test of visuospatial ability that was used. However, the Rey Complex Figure is a very robust test of such function with high validity [29] and sensitivity to disease states.

The critical role played by diminished executive function and attention in the causation of falls has been demonstrated in this study and in others [22, 24, 25, 27]. The new information provided here is that visuospatial ability appears to be a key area of interest in the field of falls prevention.

7.6   Conclusions

Poorer executive and visuospatial functions may be most likely to predict risk of multiple falls in community-dwelling older people. The risk of multiple falls is increased by sensorimotor impairments, and those risks are magnified by poorer cognitive function. These data may assist in targeting of falls prevention strategies.

7.7   Postscript

In this chapter, I investigated whether poorer function in a range of cognitive abilities would increase the risk of falls in the general older population, particularly in the setting of age-related sensorimotor impairments. No associations between any of the cognitive functions and the risk of single falls were found but poorer visuospatial ability, and some tests of executive function / attention, predicted an increased risk of multiple falls. Even after adjusting for age and sex, the adverse effects of greater sway, less ambulatory activity, slower reaction time and gait speed, weaker muscle strength and poorer visual contrast on the risk of multiple falls were enhanced in the presence of poorer function in any cognitive domain. Programs to prevent falls by training sensorimotor function of community-dwelling older people may need to be tailored depending on the nature and extent of cognitive impairment, which is a key factor in their inability to compensate for physical decline.

This completes the current series of studies that commenced by comparing alternative methods of measuring time to initiation of gait, proceeded to investigate associations of cognitive factors with gait (including gait variability) and gait initiation, confirmed cognitive involvement in falls-risk, and culminated in the identification of hitherto unsuspected interplay of cognition with sensorimotor factors and gait or ambulatory activity in the occurrence of prospectively-ascertained multiple falls.

In the final chapter, I summarise the work within this thesis and suggest what implications this may have for older community-dwelling adults. I also highlight areas that still need to be investigated.

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Chapter 8:   Summary

8.1   Background and aims of the thesis

Falls are a major health problem for older people. They lead to loss of independence, disability, injury, fractures, and hospitalisation. They cause problems for the individual and their family, and for society as a whole due to the ever-rising costs involved. It is well established that the causes of falls are multi-factorial with age, balance, strength, vision, sensation, physical activity, cognition and gait playing roles. This thesis focuses on the relationships between cognitive function, gait (including gait variability and gait initiation) and the risk of falling.

Impairments in both cognitive function and gait are frequent in older people. Poorer cognitive function and worse gait have each been shown to increase the risk of falls, but there is limited understanding of the interplay between these measures. Previous studies have primarily examined the associations between individual cognitive functions and average measures of gait, and have mainly focused on executive function and gait speed. Little is known about the role of other cognitive functions, including visuospatial ability and memory, and other measures of gait in causation of falls by community-dwelling older adults. In particular, there is little research on the relationships between cognitive function and intra-individual gait variability. It is thought that gait disorders are manifest not only as impaired gait performance, but also as variability in gait performance. Current literature suggests that gait variability may be a more sensitive indicator of walking instability and risk of falls than average measures of gait.

Furthermore, gait initiation – the process of going from standing still to establishing a recurring pattern of walking – is a phase of gait during which falls commonly occur. Gait initiation is not a part of the rhythmical cycle of gait and it is thought that it may be harder for older people to co-ordinate their limbs in order to maintain balance during this phase. The measurement and characteristics of gait initiation are poorly understood, however, and are in need of further elucidation.

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The general aim of this thesis was to investigate the relationships between gait, cognitive function and falls in an older population-based sample. The specific aims of the investigations reported in this thesis were:

i.   To study the associations between a range of cognitive functions, gait and gait variability.

ii.   To study the associations between a range of cognitive functions and the risk of falling using the following outcome measures:

a. A physiological falls-risk assessment

b. Single incident falls

c. Multiple incident falls

iii.   To provide empirical evidence to support the rational choice of an appropriate measure of gait initiation.

8.2   Methods

The data presented in this thesis are from a population-based study during 2006-2007 of older people (TASCOG) examining the neural correlates of cognition and gait. The participants are community-dwelling residents of southern Tasmania, aged between 60 and 86 years inclusive. They were selected from the Tasmanian electoral roll using age- and sex-stratified random sampling.

Cognitive measures were collected using a battery of tests grouped into 4 domains:

 1) E*xecutive function / attention* using the Victoria Stroop tests – coloured dots, coloured general words (truck, fish) and coloured colour-names (the word red written in blue ink) [1], the Digit Span test from the Wechsler Adult Intelligence Scale – Revised Edition (WAIS-III) [2], and the FAS and category fluency tests from the Controlled Oral Word Association Test (COWAT) [1];

2) P*rocessing speed* using the digit symbol coding and symbol search subtests of the WAIS-III [2];

3) M*emory* using the Hopkins Verbal Learning Tests - Revised (HVLTR) of immediate, delayed and recognition memory [1] and the delayed reproduction of the Rey Complex Figure test.

4) V*isuospatial ability using* the copy format of the Rey Complex Figure test [1]; and

Average gait measures and their intra-individual variability were captured using the *GaitRite* walkway. Measurements were made of gait speed, step time and step length, support base and double support phase (DSP). The standard deviation of step time, step length, support base and DSP were used as measures of variability. Gait initiation was measured using a 200Hz AccuGait force platform and Advanced Mechanical Technology Inc. (AMTI)-NetForce software. Each participant was required to initiate gait under two task conditions: no interference (single task) and whilst counting backwards in threes (dual task).

Falls were assessed in two ways. Firstly, sensorimotor variables were collected via the protocols of the Physiological Profile Assessment and used to calculate a weighted z-score as a physiological surrogate measure of falls risk. The variables included in the calculation of the z-score were edge contrast sensitivity, proprioception, knee extension strength, reaction time and postural sway with eyes open and closed. Secondly, incident falls were measured prospectively over 12 months using a falls calendar. Participants provided reports every two months during that year of falls that had occurred in the intervening two months.

8.3   Major findings and implications

Can we use the *GaitRite* walkway to accurately measure gait initiation? (Chapter 3)

Significance

The 4.6m, 80Hz *GaitRite* walkway was investigated as an alternative device with which to measure gait initiation (GI). The accepted gold standard of measuring GI is the force platform, which is costly and not readily transportable. The *GaitRite* walkway is increasingly being used in gait research and its ease of use warranted investigation of its potential as a lower-cost alternative to the force platform.

Findings

There was only moderate correlation between measurements of GI time on the *GaitRite* walkway and the force platform because measurements by the walkway systematically over-estimated GI time by fast initiators and under-estimated GI time by slow initiators. The predictive validity of the *GaitRite* walkway measurements for falls-risk was relatively poor in comparison to that of the force platform.

Implications

This particular type of *GaitRite* walkway cannot be recommended for use in measuring GI, and the investigation of GI that is reported in **Chapter 5** had to be confined in consequence to measurements made with the force platform for a subset (n = 128) of subjects. Advances in technology may enable later models of the *GaitRite* walkway to be used to measure GI, but the validity of the improved measurements will need to be verified before adoption.

Cognitive function, gait and gait variability in older people – a population-based study. (Chapter 4)

Significance

This is the first population-based study to investigate the associations between a range of cognitive tests across multiple domains and a variety of gait measures including the variability of those measures.

Findings

Consistent with previous research, the fundamental functions of executive function / attention and processing speed were found to be independently associated with each of the average gait measures. Results for gait variability showed that double support phase variability – a measure of stability and balance – was the key measure independently associated with cognitive functions, specifically with executive function / attention, processing speed and visuospatial ability. Memory was not independently associated with any gait or gait variability measure.

Implications

Executive function / attention and processing speed, the fundamental cognitive functions that are exercised through frontal-subcortical connections, are associated not only with gait speed but with each phase of the gait cycle. These fundamental

cognitive functions also operate to limit variability in gait, if this is the direction of causation, and particularly in double support phase. There is a hitherto unsuspected role for visuospatial ability in this regard.

Gait initiation in older people – time to first lateral movement may be the measure of choice. (Chapter 5)

Significance

There are few empirical data to guide the choice of a measure of gait initiation (GI) in older people. We investigated the statistical characteristics of the components of GI measured with a force platform, their inter-relationships and associations with sensorimotor variables, and the effect of cognitive loading on these relationships.

Findings

There is considerable intra-individual variation in measurement of GI, and learning effects were observed under both single and dual-task conditions with marked reductions in time taken over the first three or four trials under dual-tasking. Multiple trials are required to capture information on GI in customary circumstances and the median of trials per participant is the best summary measure. Time to first lateral movement (FLM) was most consistently associated with age, height and weight, sensorimotor variables, falls-risk score and cognitive speed, and was most responsive to dual-tasking. This component was strongly related to executive function, processing speed and visuospatial ability, and with memory under dual-tasking. Transfer time and swing time were associated with relatively few other study factors.

Implications

Multiple trials (at least 6 per task condition per subject), summarised by the median, are recommended for GI measurement. Time to FLM may be the GI measure of choice in older people due to its relationship with the other factors and its responsiveness to cognitive loading. Its strong associations with function in each of the four cognitive domains suggest that GI is an important target for future gait research.

Visuospatial ability and memory are associated with falls-risk in older people – a population-based study. (Chapter 6)

Significance

This is one of the few population-based studies to examine the associations of measurements of cognitive ability in a range of cognitive domains with the PPA z-score, a physiological measure of falls risk, allowing for confounding due to age and interdependence between cognitive abilities.

Findings

In addition to the known effects of executive function / attention, visuospatial ability and memory predictors of the composite falls-risk score in this population-based study. Verbal and visual memory both contributed to the effect of memory on the falls-risk score. The associations of falls-risk with each of the cognitive functions were confounded by age, and that with processing speed was no longer statistically significant after adjustment by age.

Implications

In addition to the effects of deficiencies in the executive abilities and memory, older people seem to have a higher risk of falling if they are unable to navigate effectively between two places by judging distances and avoiding objects. Furthermore, structural brain changes – such as age-related white matter abnormalities or neurodegeneration involving mesial temporal structures – may be relevant to the mechanisms underlying falls by older people.

Poorer cognitive function modifies the effect of poorer physiological function on multiple falls. (Chapter 7)

Significance

This is the first population-based study to examine the associations of a wide range of cognitive functions on the risk of single and multiple falls, and to investigate the combined effects of cognitive function and sensorimotor measures on the risk of falls.

Findings

Overall, 24.4% of older adults had a single fall, and 20.2% had multiple falls. Neither cognitive function nor sensorimotor measures predicted the risk of single falls. However, the risk of multiple falls was increased by poorer visuospatial ability and some aspects of executive function. The adverse effects of greater sway, less ambulatory activity, slower reaction time and gait speed, weaker muscle strength and poorer visual contrast on the risk of multiple falls were all greater in the presence of poorer function in any cognitive domain.

Implications

Recurring falls involve a complex interplay of cognitive deficits with deterioration in sensorimotor function. Cognitive function may be less relevant in the causation of a sporadic fall.

8.4   Clinical implications

The results presented in this thesis show that cognitive function plays a very important role in the maintenance of each phase of the gait cycle, suggesting that current targeted interventions to improve gait in older adults, such as balance and strength training, should also take in to account maintenance and possibly strengthening of cognitive abilities.

Cognitive functioning is also very important in falls risk assessment and falls prevention strategies. To date, most falls prevention strategies rely heavily on training to improve physiological capabilities, but this thesis demonstrates the need for combining this with targeted interventions to improve cognitive capacity to undertake those physiological functions. These interventions could include training in performance of cognitively challenging tasks such as dual-tasking and brain training exercises. In particular, tasks that utilise visuospatial abilities should be added to falls risk assessment and interventions. These include training on obstacle courses.

Older adults with gait or sensorimotor problems, who are at a high risk of falling, should undergo cognitive testing because the potential improvements in physiological domains may be hindered by cognitive impairments.

8.5   Recommendations for future research

The work in this thesis has added to and advanced previous knowledge of how cognitive function is associated with mobility and falls. In addition, gait initiation time – and particularly the time to first lateral movement – has been identified as being a critical phase of gait in it association with cognitive function and sensorimotor measures of falls-risk. There are however, remaining gaps in the research paradigm that needs to be filled. If this study were to be replicated, I would advise adding a test of global cognitive function such as the MMSE. This allows participants who may have mild cognitive deficits to be identified and analysed.

These areas for further research are listed below:

o   Future advances in the *GaitRite* walkway software and sample rates may warrant that the *GaitRite* walkway be re-investigated as a surrogate measure of gait initiation in older people. In future, the improved sensitivity of the measurements may increase the predictive validity of the *GaitRite* walkway (**Chapter 3**), and remove systematic error and thereby enable this cheaper, portable device to be used to gather valid and reliable information on gait initiation.

o   Gait initiation is a phase of gait where falls are likely to occur, and it has now been linked with cognitive function (**Chapter 5**). Time to FLM, the key component of GI (**Chapter 5**), should be assessed in relation to its impact on the risk of incident falls. This would confirm whether this component of gait initiation should be targeted in interventions and prevention strategies.

o   Confirmation of the association between visuospatial ability and falls (**Chapter 7**) is warranted. The findings suggest that visuospatial ability is a key cognitive function in its association with falls. This was based on a single, but robust, test. If these results are able to be replicated with other tests of visuospatial ability, it would further highlight the importance of this function in the prevention of falls in older people. It would also provide a further cognitive marker of risk.

o   In addition, the results may provide a basis for investigating the link between dementia and the risk of falling, with the Rey Complex Figure test being a

sensitive test for dementia [1,4]. Further study of the neuroanatomical substrates underlying the associations between visuospatial ability and multiple falls (**Chapter 7**) may provide useful information regarding the neural mechanisms underlying falls in older people.

o The results in this thesis are based on cross-sectional data. Longitudinal analysis of the associations between executive function / attention and processing speed with average measures of gait (**Chapter 4**) would enable the causal pathways to be better examined and the direction of the associations to be determined.

o Confirmation of the associations between double support phase variability and cognitive function (**Chapter 4**), plus investigation of the neuroanatomical substrates underlying those associations, is warranted to ascertain the role that double support phase variability has to play in causing falls by older people.

o The contributions of gait and gait variability to the relationships between cognitive function and multiple falls should be examined in a similar fashion to the analyses of the inter-relationships between cognitive function and sensorimotor measures (**Chapter 7**).

o Neither cognitive function nor sensorimotor measures appear to play a role in predicting the risk of single falls (**Chapter 7**). Further research is needed into the risk factors for single falls.

8.6   Conclusions

The population-based studies reported in this thesis provide new and important information on the relationships between gait, cognitive function and falls in an older population-based sample. The results from each of these studies highlight particular cognitive functions that may be important in targeting interventions and designing programs for prevention of falls by older adults. In accordance with the initial study aims, the following conclusions have been reached:

i)   Poorer executive function / attention and processing speed, but not visuospatial ability or memory, are independently associated with poorer

gait. In respect of gait variability, increased double support phase variability is independently associated with poorer executive function / attention, processing speed and visuospatial ability. Memory is not independently associated with any gait or gait variability measure.

ii)   a) Poorer executive function, memory and visuospatial ability are independently associated with sensorimotor functioning that contributes to falls-risk. Processing speed is not independent of age in its association with falls-risk.

b) Cognitive function is not associated with single falls.

c) Poorer visuospatial ability and some aspects of executive function are associated with an increased risk of multiple falls.

iii)   Time to first lateral movement may be the key component of gait initiation in its association with sensorimotor measures of falls-risk and cognitive function.

8.7   References

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