Intraindividual variability, gait and falls in old age

Jack Graveson

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Abstract

Falls and gait impairment in older populations present a major challenge to healthcare systems and reduce quality of later life. There is evidence that cognitive decline contributes to falls and gait impairment in older adults and may, therefore, serve as a marker for persons at risk. Intraindividual variability (IIV; trial-to-trial fluctuations in response time across a neurocognitive task) may have screening potential in this respect as this measure is thought to capture unique information about cognitive function not captured by other neuropsychological metrics. The present research, therefore, examined relationships between IIV, gait and falls in cognitively intact older adults. The extent to which relationships varied according to age and the demands placed on the individual when assessing IIV and gait, was also investigated. Finally, a mediational approach identified potential mechanisms underpinning these relationships. Systematic reviews of published research were followed by cross-sectional experimental studies and a longitudinal investigation. The findings provided mixed evidence of a link between IIV and falls. There was strong cross-sectional evidence that greater IIV was associated with poorer gait performance, and that this relationship strengthened with increasing age. Variability better predicted gait outcomes when gait was assessed under more demanding dual-task conditions, and when IIV measures were derived from tasks with higher executive demands. Tests of mediation suggested that processing speed underpinned relationships between IIV and less demanding single-task gait, whereas executive function played a greater role in more demanding gait conditions. Together, the outcomes suggest that IIV measures have potential as an early screening tool for gait impairment, and also falls. Importantly, general slowing accounts of cognitive ageing explained findings when IIV and gait were assessed under lower demand conditions, whereas frontal lobe/executive control perspectives provided a better account when demands were greater.

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Chapter 1

A review of existing theory and research

Section A: Broad issues related to ageing

The ageing population

The last 100 years has seen an unprecedented rise in life expectancy. According to the UN Department of Economics and Social Affairs, the number of adults aged 60 and over around the world tripled between the years 1950 and 2000 (Inzitari, 2010). During the first half of this century the proportion of over 60s is expected to continue to grow exponentially, reaching approximately two billion by the year 2050. Similarly, estimates from the UK Parliament (2011) suggest that the number of adults aged 80 and over in this country is expected to quadruple to around eight million in the same timeframe. This sharp rise in the population of older adults has led to a pressing need to investigate changes that occur as we get older. In healthy individuals, there is a decline in physical (e.g., arthritis, osteoporosis) and sensory (e.g., hearing and vision impairment) functioning that begins in middle adulthood and worsens with increasing age. Later life is also typically associated with an increased risk of chronic disorders such as heart disease, breathing difficulties and high blood pressure (Sigelman & Rider, 2009).

It is important to note that the effects of ageing vary greatly between individuals and can be affected by a number of extraneous factors such as the amount of exercise taken (e.g., Vita et al., 1998) and the level of education attained (e.g., Snowdon, 2002). However, the majority of older individuals experience some combination of changes to their health, wellness and functioning. Such changes often prevent these individuals from maintaining social interactions which can lead to depression (e.g., Simonsick et al., 1998), and can also restrict the performance of daily activities that allow independent living (Haley et al., 2002). The work in this thesis will explore two consequences of ageing that affect many adults at some point in their later lives: falling and gait impairment. Both have been linked to a number of deleterious outcomes and are thought to significantly reduce quality of life in older persons.

Falls in the older population

Falls represent one of the biggest problems facing the older community. It has been estimated that a third of adults over the age of 65 fall every year, with a further 50% of these experiencing recurrent falls (Tinetti, 2003). One study conducted in the UK reported that approximately 650,000 adults over the age of 60 were taken to the accident and emergency ward as a result of a fall over the space of just one year (Scuffham et al., 2003). Furthermore, it is thought that the number of hospital admissions caused by falls increases exponentially with age (Hartholt et al., 2010). This high prevalence of falls in the older community places a significant burden on healthcare providers around the world. A recent review revealed the cost of falls and falls-related injuries in the USA to be around 23 billion dollars each year (Davis et al., 2010) and these expenditures are expected to grow to approximately 55 billion dollars by the year 2020 (U.S. Centers for Disease Control and Prevention, 2016). The same review study suggested that the annual cost of treating falls in the UK is around 1.6 billion dollars, although more recent estimates suggest that over 2 billion pounds is spent treating falls-related hip fractures alone (Age U.K., 2013).

Although it is important to consider the financial consequences of falls, the human costs have also been shown to be substantial. It has been estimated that accidental falls are the third leading cause of disability in older adults (Murray & Lopez, 1996) and the fifth leading cause of death (US Centres for Disease Control and Prevention, 2010). Approximately 30-50% of all falls lead to minor injuries such as bruising and lacerations whereas 5-10% result in major injuries such as traumatic brain injury and hip fractures (Goldacre et al., 2002; Rubenstein & Josephson, 2002). Hip fractures are a particularly serious consequence of falling as, in the year following injury, it has been estimated that 50% of patients suffer a decline in their ability to perform daily activities, whereas 22% are relocated to a nursing home and 25% die (Adelhafiz & Austin, 2003; March et al., 1999). In addition to impact injuries, older adults who fall sometimes have trouble getting up and subsequently remain on the ground for long periods of time. These periods of immobility can subsequently lead to rhabdomyolysis, pressure sores and pneumonia (Fleming et al., 2008). After experiencing a fall it is also common for individuals to develop a fear of falling and, as a result, they may restrict their activities in order to avoid future falls. The resulting loss of confidence and self-efficacy can lead to a cycle of decline in physical fitness, social isolation, depression (Zijlstra et al., 2007) and a significant reduction in quality of life (Chamberlin et al., 2005). To summarise, falls are a major burden to worldwide healthcare systems and a persistent threat to the older community, resulting in a number of adverse physical and emotional consequences, and seriously impacting the daily lives of those who experience them. In the literature, a fall is commonly defined as “an event which results in a person coming to rest unintentionally on the ground or lower level, not as a result of a major intrinsic event (such as a stroke) or overwhelming hazard” (Tinetti et al., 1988, p.1702). Identifying the conditions under which falls most commonly occur is an important first step towards preventing future occurrences of these events. Risk factors for falls are generally classified as being either intrinsic or extrinsic. Intrinsic factors are specific to the individual and include chronic disease, muscle weakness and vision problems, whereas extrinsic factors are those found in the individual’s environment (e.g., low lighting, slippery floors, trip hazards). It has been estimated that around 85% of all falls in older persons can be attributed to intrinsic factors (Tinetti et al., 1988) and guidelines for falls prevention often focus on these factors as they are the most amenable to change (National Institute for Health and Care Excellence, 2013). Mobility problems have been consistently identified as one of the most reliable risk factors for future falls. In a review of 12 retrospective falls studies, Rubenstein and colleagues (2006) attributed 17% of the 3,628 total falls as being due to gait and balance disorders. Furthermore, a meta-analysis on eight prospective studies found that those with an abnormal walking pattern were at higher risk of experiencing single (OR = 2.06) or multiple (OR = 2.16) falls (Deandrea et al., 2010).

Gait in the older population

The evidence presented above suggests that gait dysfunction may be associated with a higher risk of falling in older persons. Gait, which can be broadly referred to as “the pattern of movement of the body during locomotion” (Rosso et al., 2013, p. 2), has itself been shown to be particularly susceptible to the effects of ageing. Population based studies in the US and Europe have estimated that approximately 35% of adults over the age of 70 have some form of gait impairment and this increases to 61% for adults in their late eighties (Verghese et al., 2006; Bloem et al., 1992). Age can affect an individual’s ability to walk in various ways but common features of age-related gait deficits have been identified. The Baltimore Longitudinal Study of Aging compared the gait characteristics of middle-aged (32-57 years), old-aged (58-78 years) and oldest-aged (79-93 years) adults and found slowing in preferred walking speed, reduction in stride length and a greater tendency to land flat-footedly to be associated with increasing age (Ko et al., 2009). These factors, in combination with poorer postural control and body-oriented reflexes, may impair the ability of older adults to avoid a fall when they unexpectedly trip or slip. A reduction in walking speed may be a particularly important consequence of old age. For example, it has been shown that a large proportion of older persons walk slower than 1.2 m/s, the minimum speed needed to safely use the average pedestrian crossing in the UK (Asher et al., 2012). Furthermore, walking speed is one of the most widely used measures of gait in the ageing literature due to the ease with which it can be administered. As a result, there has been considerable interest in studying the links between gait speed and a variety of other ageing effects.

Unsurprisingly, a slower walking speed has been associated with a number of adverse outcomes in old age. As previously mentioned, broadly classified impairments in mobility are a reliable risk factor for falls but a number of studies have identified gait speed measured over 10 metres or less as an independent predictor of future falls (Chu et al., 2005; Montero-Odasso et al., 2005; Biderman et al., 2002) and falls-related fractures (Dargent-Molina et al., 1996). A slower walk also been linked to later difficulties with performing everyday activities (e.g., Onder et al., 2005), a dependency on others to maintain normal functioning (Shinkai et al., 2000) and mobility disability (Ostir et al., 1998). In more severe cases, simple measures of gait speed have been shown to independently predict hospitalisation (Montero-Odasso et al., 2005) and institutionalisation (Woo et al., 1999). One such examination of hospital inpatients reported that a walking speed of 0.15 m/s distinguished those who required long-term care from those who were mobile enough to be discharged (Friedman et al., 1988). Finally, there is considerable evidence in the ageing literature that gait speed may be a reliable indicator of mortality. A pooled analysis of nine cohort studies found that a 0.10 m/s increase in gait speed was associated with significantly higher survival rates over the following 5 or 10 years (Studenski et al., 2011).

While the work described above looked at gait speed as a continuous variable, cut-off points are often used to categorize older adults and identify those who are most at risk of harmful outcomes. Although a number of cut-off points have been proposed in the literature, 1.0 m/s is thought to be a ‘clinically meaningful’ boundary (Cesari et al., 2005) that has been previously used to define normal gait speed in healthy older adults (e.g., Bohannon, 1997; Bendall et al., 1989). In line with the findings presented early, older adults who walk more slowly than 1.0 m/s are more likely to experience difficulties when performing daily activities such as bathing, dressing and using public transport (Verghese et al., 2011). One study found that a cut-off of 1.0 m/s was able to predict declines in global health status, hospitalisation and new difficulties in personal care during the following year (Studenski et al., 2003). A gait speed slower than 1.0 m/s has also been associated with an increased risk of major health outcomes (e.g., Cesari et al., 2005), disability (e.g., Rosano et al., 2008) and death (e.g., Cesari et al., 2009). Taken together these findings suggest that this cut-off point may be useful in distinguishing older adults who walk at a normal speed and are generally healthy and functional, from those who are more prone to issues which may affect their health, mobility and ability to live independently.

Identifying risk factors for gait impairment and falls

In the latest guidelines set out by the National Institute for Health and Care Excellence, it is recommended that older adults at a high risk of falling should be considered for an individualised multifactorial intervention (National Institute for Health and Care Excellence, 2013). These interventions have been shown to be effective, with one systematic review reporting a relative risk reduction of 27% in randomly selected community-dwelling adults (Gillespie et al., 2003). Such efforts to prevent falls are most effective when targeted at at-risk populations that have been identified at an early stage compared to those who already have an established history of falls. The ability of current falls prevention guidelines to identify these populations is limited (Muir et al., 2010) and so there is a pressing need for simple screening tools that can be incorporated into assessments of fall risk. It is this theme that provides the motivation for the present research. Given that age-associated changes in gait (such as a reduced walking speed) have been shown to precede falls, it follows that detecting individuals at risk of these changes may contribute to the prevention of future falls and other adverse outcomes that such changes have been linked to.

Measures of cognition may have considerable potential as an early screening tool as there is substantial evidence linking cognitive function with both gait and falls. It has long been known that falls are more prevalent in older adults who have been clinically diagnosed with dementia (e.g., Buchner & Larson, 1987). The annual incidence of falls in this population has been estimated to be between 60 and 80% which is approximately twice the rate of cognitively intact individuals (Tinetti et al., 1988). The consequences of falling are also more serious in dementia patients with one study reporting a three-fold increase in falls-related fractures and hospitalisation after a fall compared with cognitively intact fallers (Morris et al., 1987). Gait abnormalities are also more common in cognitively impaired individuals. In the Canadian Study of Health and

Aging it was reported that 25 to 30% of healthy older adults were suffering from some form of gait or postural impairment compared to 46 to 53% of those who were cognitively impaired (Camicioli et al., 2007). Compared to their cognitively healthy counterparts, older persons with dementia have been found to have slower walking speed, greater variability in their stepping pattern, larger postural sway paths and a higher likelihood of colliding with obstacles in their path (Alexander et al., 1995; Visser, 1983). Age-associated decline in cognitive function can be thought of as a continuum with one end representing what is expected in healthy ageing and the other representing what is seen in dementia patients. There is also an intermediate stage commonly referred to as Mild Cognitive Impairment (MCI) which is characterised by dysfunction in one or more cognitive domains but without interference in daily living activities (Petersen et al., 1999). More recent work has shown that older adults diagnosed with MCI are also more likely to experience falls (e.g., Delbaere et al., 2012) and problems with their gait (e.g., Verghese et al., 2008).

Taken together, these findings strongly suggest a link between cognitive function, gait and falls in cases where a clinical diagnosis of impairment has been made. But what about in individuals thought to be ageing normally? Following the work that was carried out on MCI and dementia patients, there has been an increasing interest in examining these relationships in healthy older persons. This research provides substantial evidence that cognitive processes may be heavily involved in walking performance, and also contributing significantly to older falls. A full review of this work will be presented later in the chapter. However, against the background that cognition plays a role in both gait and falls, it is relevant to first consider broader changes in cognitive function that occur during normal ageing, and the theories that have been proposed to explain them.

Age-related changes in cognition

Various stereotypes are associated with the cognitive changes that occur during later life, some of which are negative (e.g., older adults are slower and more forgetful) and some of which are positive (e.g., older adults are wiser and more knowledgeable about the world). Indeed, behavioural studies carried out over the past 50 years have shown that some cognitive processes exhibit considerable decline in old age whereas others are relatively well preserved. These processes can be broadly conceptualised in line with Horn & Cattel’s (1967) theory that intelligence is made up of fluid and crystallised abilities which interact and work together to produce general intelligence. Fluid abilities are those which allow an individual to learn new information, solve problems and attend to their environment. These abilities are independent of education and experience and can include abstract reasoning, attention and working memory capacity (Lezak et al., 2012; Elias & Saucier, 2006). Crystallised abilities, on the other hand, refer to the skills and knowledge which have been obtained over the course of an individual's lifespan. These abilities are typically assessed using tests of vocabulary.

Almost all fluid abilities are thought to be adversely affected by the ageing process. More specifically, the speed at which we process information and perform mental operations declines (Salthouse, 1996) and the capacity of working memory available to us is greatly reduced (Craik, 1990). It also becomes more difficult to ignore distracting or irrelevant stimuli (Hasher & Zacks, 1988), recall previously experienced events (Ronnlund et al., 2005) and remember the context in which information was presented (McIntyre & Craik, 1987). By contrast, crystallized abilities such as reading comprehension and memories for learned activities (e.g., tying your shoes) remain relatively stable and even show signs of improvement with age (e.g., Salthouse, 2009). In line with these findings, one study collected multiple measures across several cognitive domains from a sample of adults aged 20 to 95 (Park et al., 2002). The findings provided strong evidence for a consistent decline from decade-to-decade in speed of processing, working memory, short-term memory and long-term memory. Verbal knowledge on the other hand, which was assessed with measures of vocabulary, remained relatively stable across the lifespan.

Theories of cognitive ageing

Having established which cognitive processes are compromised with increasing age and which ones are relatively preserved, researchers have devoted considerable time to examining the underlying causes of age-related differences in cognition. It is important to remember that many factors contribute to between-person differences in cognitive performance, but cognitive ageing research is only concerned with explaining the variance in performance that is attributable to age. A number of theories have been put forward to explain these ageing effects, all of which suggest that decline in particular cognitive or biological mechanisms underlie broader age-related changes in cognition. Four perspectives have been proposed that are relevant in the present context and will be described in the next section: Processing speed, inhibitory deficits, frontal lobe atrophy, and neural noise.

Processing speed

One of the most influential accounts of cognitive ageing relates to speed of processing. This theory states that the mechanism underlying age-related decline in cognitive performance is a generalised slowing of information processing (Salthouse, 1996, 1985). Reflecting on earlier observations that older adults take longer to perform almost any task, Birren and Renner (1977, p. 28) noted that “one of the most clearly established phenomena of aging is the tendency towards slowness of perceptual, motor and cognitive processes”. Building on this, Salthouse (1985) conducted a review of 39 studies that used a reaction time (RT) paradigm to assess age-differences in the time taken to respond to a simple stimulus. Although the age ranges varied considerably from study to study, the average correlation between RT and chronological age was found to be 0.45 (ranging from 0.15 to 0.64). A number of possible suggestions were put forward to explain this age-related slowing in processing such as strategic differences (e.g., an inefficient use of stimulus information), hardware differences involving increased neural noise (see below) and greater concurrent processing demands (Salthouse, 1985).

Salthouse went on to suggest that changes in response speed could be used to account for changes in many other cognitive tasks. In support of this notion, he provided considerable evidence that nearly all age-related variance on many cognitive tasks can be explained by performance on perceptual speed tasks such as the digit-symbol substitution test (Salthouse, 1996). This was even found to be the case for more complex measures of episodic memory and visuospatial reasoning that were lacking an obvious speed component. Two important mechanisms have been proposed to explain the effect of processing speed on cognitive performance (Salthouse, 1996). The *limited time mechanism* captures the notion that there may be less time available to perform the later operations of a cognitive task due to the excess time spent on the earlier operations. Additionally, the *simultaneity mechanism* is centred on the idea that the products of early cognitive operations may be lost by the time the later operations are processed. Therefore, older adults with slower rates of processing may display worse performance because they take too long to complete the early steps of a cognitive task, or they take too long to complete the later steps and thereby lose access to earlier information. Furthermore, it was proposed that greater age-differences in performance would be seen on complex tasks as older adults are more likely to engage in different processes to compensate for their slower processing speed.

Inhibitory deficits

According to the inhibitory deficits hypothesis, the variation in cognitive performance that is attributable to age occurs largely as a result of a decline in the ability to ignore irrelevant information (Hasher & Zacks, 1988). Many decades earlier, James (1890, p. 445) remarked that "the inhibition of irrelevant movements and ideas" is "always present" and Rabbitt (1965) was among the first to empirically identify that this ability might be affected by age. Here, older subjects (aged 65-74) took considerably longer than younger subjects (aged 17-24) to complete a card sorting task which involved discriminating between relevant and irrelevant letters of the alphabet. Across the lifespan, it has been demonstrated that inhibitory control improves during childhood and worsens during late adulthood (Carver et al., 2001; Spieler et al., 1996). Hasher and Zacks (1988) suggested that inhibitory deficits reduce an individual's ability to stop irrelevant information from entering working memory and potentially displacing relevant information. Therefore, older adults possessing such inhibitory deficits are likely to be easily distracted, make inappropriate responses and take longer to complete certain cognitive tasks. They additionally suggested that if interfering stimuli are reduced and environmental support is available, older adults will display similar performance to younger adults on most cognitive measures.

Changes in inhibitory function across the lifespan has been attributed to concomitant changes in the structure and function of the prefrontal cortex, an area of the brain that is thought to control inhibitory processes (e.g., Durston et al., 2002). In support of the inhibitory deficits theory that they put forward, Hasher and Zacks (1988) provided evidence that older adults are more likely than younger adults to unintentionally store information that they heard previously, and that this information has a negative effect on subsequent cognitive performance. Furthermore, a follow-up study using a negative priming paradigm showed that older adults responded quicker when a response that should have been inhibited on an early trial becomes the target for a later trial (Hasher et al., 1991). A criticism of this perspective, however, is that these latter findings have often been difficult to replicate as many studies have shown the effect of negative priming to be relatively stable across the lifespan (McDowd, 1997). Despite these criticisms, the inhibitory deficits hypothesis may be useful for understanding the everyday behaviour of older adults. For example, they may be particularly susceptible to distractions when presented with several sources of information but need to pay attention to only one, such as when using a busy pedestrian crossing.

Frontal lobe atrophy

Theoretical explanations for age differences in cognitive performance also include neuropsychological perspectives that focus on the effect of age on the brain. The frontal lobe hypothesis put forward by West (2000; 1996) is one such example and perhaps the most influential neuropsychological theory in the field. He proposed that age-related cognitive decline is due to localised changes in the frontal lobes and the cognitive processes that are controlled by this region. The theory was founded on complementary sources of evidence from a number of disciplines. First, post-mortem studies and more recent work using brain imaging techniques have demonstrated that the frontal lobes are one of the first areas of the brain to undergo changes related to age (e.g., Raz, 2000; Albert, 1993; Albert & Kaplan, 1980). These changes are thought to involve reductions in the volume of grey and white matter, reductions in metabolic activity and neuronal density, and neurochemical modulation by neurotransmitters such as dopamine (Raz, 2000). Second, neuropsychological studies have reported similarities in the cognitive deficits shown by healthy older adults and younger adults suffering frontal lobe damage (Perfect, 1997; Moscovitch & Winocur, 1992). Third, age group comparisons in healthy populations have demonstrated that older adults perform considerably worse than younger adults on measures devised to detect frontal lobe dysfunction in clinical patients (e.g., Brink & McDowd, 1999; Salthouse & Fristoe, 1995; Kramer et al., 1994).

These measures are thought to capture a set of higher-order cognitive processes collectively referred to as executive function. Although the use of this term varies within and across disciplines, it is generally agreed that executive function refers to the control of higher-order cognitive processes and the regulation of behaviour, and is strategically responsible for behaviours such as planning, assembling, sequencing and co-ordination (Hofer & Alwin, 2008). There is a great deal of evidence to suggest that the neural correlates of executive processes lie in the frontal cortex (e.g., Stuss & Benson, 1986) and individuals who sustain damage to this area of the brain have a similar cognitive profile to that associated with executive impairment (Eslinger et al., 1995). Some researchers have argued that executive control is a general strategic mechanism while others have proposed that it is made up of a number of distinct but interrelated components (Verhaeghen & Cerella, 2002). One such model was proposed by Miyake and colleagues (2000) who provided evidence for three related but clearly separable executive processes: mental set shifting (switching), information updating and monitoring (updating) and inhibition of prepotent responses (inhibition). In support of this model, older adults have been shown to exhibit much poorer performance than younger adults on numerous tasks designed to assess these abilities (Park, 2000; Zacks et al., 2000).

West’s theory suggests that decrements in these processes resulting from age-related atrophy of the frontal lobes can account for many of the observed age differences in cognitive performance. In support of this notion, it has been suggested that the memory impairment shown by patients with pre-frontal damage is resulting from deficits in executive control processes (Shimamura, 1995). In a review of 18 studies, D’Esposito and Postle (1999) provided evidence that lesions to the pre-frontal cortex disrupted performance on delayed response tasks, which rely heavily on executive processes such as attention and inhibition, but not simple tests of memory span. Furthermore, transcranial magnetic stimulation studies have shown that interfering with cortical activity in frontal areas during the delay period of such tasks also leads to a reduction in memory performance (e.g., Brandt et al., 1998; Muri et al., 1996). Finally, more recent work using advanced statistical methods such as structural equation modelling have demonstrated that controlling for executive abilities can eliminate age-differences on tests of episodic memory (McCabe et al., 2010). Despite heavily influencing the way we think about cognitive ageing, several researchers have questioned this perspective and the evidence used to support it. For example, it has often been demonstrated that correlations among different versions of executive tasks are small, suggesting that they are not “process-pure” and other non-executive abilities may be contributing to performance (e.g., Salthouse et al., 2003; Rabbitt, 1997). Furthermore, numerous studies have shown that some age effects on executive tasks are significantly reduced when the variance associated with more basic processes such as psychomotor speed are removed (e.g., Verhaeghen et al., 1998; Fristoe et al., 1997; Salthouse, 1991).

Neural noise

The neural noise hypothesis (Welford, 1981, 1965) was originally proposed to explain the underlying causes of age-related slowing in cognitive processing. Early accounts of slower processing (e.g., Birren, 1965) suggested it was due to dysfunction in the central nervous system (CNS; the brain and spinal cord), rather than the peripheral nervous system (PNS; all nerves and nerve cells outside the CNS). Welford proposed that increasing age is associated with an increase in the amount of random neural fluctuations (i.e. neural noise) that interfere with the transmission of information within the CNS (Welford, 1965). This increased noise may be caused by a variety of factors such as cortical cell loss, weaker input signals and greater spontaneous background activity. Regardless of the cause, a CNS with a lower ratio of signal-to-noise will tend to be slower and more variable in processing information, which may lead to a decrement in performance on many cognitive tasks. One study tested Welford's theory by administering RT tasks with varying levels of distortion and extraneous noise to a small sample of young adults (Salthouse & Lichty, 1985). Consistent with the theory, they found that manipulating the intactness of the stimuli or the amount of background noise led to longer reaction times and lower thresholds of tolerance for distortion and noise that are similar to the effects of ageing.

The neural noise hypothesis has been important to cognitive ageing research and particularly to the present perspective. For example, it has been proposed that variability in the transmission of signals in the CNS may manifest itself at the behavioural level as inconsistency in performance on response time tasks (Hendrickson, 1982). More recently, Li and Lindenberger (1999) suggested that the signal-to-noise ratio of information processing in the CNS may be regulated by the functioning of catecholaminergic neurotransmitters and in particular dopamine. Age-related deficiencies in the dopamine system have been closely linked to decline in cognitive performance (Backman et al., 2000) and animal studies have also demonstrated a link between the catecholaminergic system and both speed and variability in performance (Macrae et al., 1988). Finally, computational models of age-related deficits in information processing have demonstrated that simulated reductions in dopamine neuromodulation lead to less distinct cortical representations and an increase in neural noise (Li et al., 2000). Therefore, it is possible that age-related inconsistency in neurological functioning could be partly responsible for age-related declines in cognition, and in particular increased variability in performance. Such performance variability is central to the present work as it may reflect the neurobiological and cognitive functioning of an individual. Furthermore, increases in variability due to age have been found to be associated with, and often predictive of, a number of adverse outcomes in later life. A full review of this evidence will be presented in a later section.

Summary

Cognitive ageing appears to be inevitable. There is a progressive decline in almost all cognitive abilities that begins in early to middle adulthood and continues until death (e.g., Park et al., 2002). Theories of cognitive ageing have proposed that the majority of age-related variance in cognitive performance can be explained by distinct cognitive and neurobiological mechanisms. Evidence in favour of one mechanism does not rule out the possibility that others are also playing an important role. Indeed, there are noticeable overlaps between each of the theories. For example, neurobiological changes in the frontal lobe are likely to cause deficits in executive function, and the ability to inhibit responses has been proposed as a major component of this system (e.g., Miyake et al., 2000). There is also evidence to suggest that a reduction in processing speed may account for some of the age-related variability in performance on executive tasks (e.g., Verhaeghen et al., 1998). Similarly, an increase in the amount of random neural activity (at a neurobiological level) and processing of irrelevant stimuli (at a behavioural level) may reduce the speed at which information is transferred, subsequently leading to slower and less accurate responding on a cognitive task. It seems likely then that related deficits in the mechanisms outlined above contribute to age-associated cognitive decline and are responsible for the performance differences between younger and older adults. This is applicable to laboratory testing where specific cognitive tasks are administered, and also to real-life situations where older adults might have more difficulty completing complex everyday activities such as calculating their finances and managing their medication. The contribution of individual cognitive abilities such as processing speed, inhibitory control and executive processes are likely to vary but the evidence presented here suggests they may all may lend themselves as possible factors that mediate the effects of age on performance.

Section B: The role of cognition in gait and falls

The contribution of higher-order cognitive processes to gait

In the previous section there was a brief outline of the age-related changes that occur in both cognitive abilities and walking performance in the healthy population. Here, the link between the two will be explored, and there will be a review of theoretical and empirical evidence suggesting that cognitive function is playing an important role in gait and, relatedly, falls. Traditional accounts of walking have proposed that it is a simple and automatic motor activity requiring relatively little cognitive input. Consequently, much of the early research looking at the effects of cognition on gait focused on patients diagnosed with neurological disorders such as dementia. As mentioned earlier, gait abnormalities are considerably more prevalent in this population relative to groups of cognitively intact older persons (Camicioli et al., 2007; Alexander et al., 1995). However, in recent decades, increasing evidence has emerged that this view of gait is overly simplistic and higher-order cognitive processes are, in fact, making a significant contribution to successful walking. For example, one study examined the performance of older adults on three tasks: 1) a walking task with no distractions, 2) a simple finger tapping task, and 3) a more complex catching task (which draws on executive processes such as planning, monitoring and real-time adjustment). They found that slower walking speed and greater stride-to-stride variability was significantly associated with poorer catching performance but not slower finger tapping (Hausdorff et al., 2005).

Findings from neurological work also support the notion that cognitive processes are implicated in the control of gait. For example, in a series of studies, Rosano and colleagues (2012; 2008; 2007) investigated gait performance of older adults in relation to grey matter volume of several brain areas (measured with structural magnetic resonance imaging; MRI). They reported that reduced grey matter volume in the prefrontal cortex, which is implicated in the control of executive processes, was associated with slower walking speed and shorter stride length. Relatedly, there is substantial evidence linking white matter lesions and white matter hyperintensities (WMHs; microscopic lesions that manifest as high signal intensities on T2-weighted MRI) in the brain to a number of outcomes related to gait, mobility and balance impairment (Holtzer et al., 2014b; Zheng et al., 2011). These lesions are commonly detected in areas such as the periventricular region (e.g., Srikanth et al., 2009; Silbert et al., 2008) but have been shown to influence frontal lobe processes regardless of their location in the brain (Tullberg et al., 2004). Furthermore, functional magnetic resonance imaging (fMRI) work has identified associations between neural activity in certain brain areas and walking. Although actual walking cannot be assessed with this type of imaging, a number of studies have demonstrated increased activation of frontal areas when observing walking from a third person perspective (Iseki et al., 2008), imagining walking with closed eyes (Bakker et al., 2008) and electrically stimulating the effects of walking (Francis et al., 2009). Finally, modern imaging techniques such as functional near-infrared spectroscopy have allowed researchers to study activity in the brain while walking on a treadmill. One such investigation observed a greater increase of cortical oxygenated haemoglobin in the left pre-frontal cortex when walking at faster speeds (Harada et al., 2009).

Insights from dual-task assessments of gait

With regards to behavioural research, there is a long history of using dual-task paradigms to demonstrate the cognitive demands placed on older adults by walking. Unlike single-task (ST) assessments where individuals walk with no distractions, dual-task (DT) assessments typically involve walking while simultaneously performing a secondary task. These tasks are often cognitive in nature and may include, for example, counting backwards in multiples of 3 (e.g., Srygley et al., 2009; Beauchet et al., 2007) or naming unique words beginning with a certain letter of the alphabet (e.g., Nascimbeni et al., 2015; Hall et al., 2011). Interference in either the walking or cognitive task (often termed the dual-task cost) will subsequently occur when the combined demands exceed the attentional resources that are available the individual (Lajoie et al., 1993; Abernethy, 1988). Using this paradigm, researchers have demonstrated that individuals who engage in attention-demanding activities while walking suffer decrements in gait performance, often slowing down or becoming less stable (e.g., Hamacher et al., 2015; Dubost et al., 2006). Furthermore, previous work has demonstrated that these decrements become more pronounced if the secondary task is made more difficult (e.g., Hall et al., 2011). Taken together, these findings provide strong evidence that walking draws highly on cognitive resources, especially when the attentional demands of the situation are increased but also when individuals walk under the simplest conditions.

A number of researchers have investigated whether gait costs associated with dual-tasking are subject to age differences. Beurskens and Bock (2012) conducted a review of 11 such studies and found that seven of these reported higher decrements in gait performance for older adults relative to younger adults. Furthermore, two of the studies that reported non-significant results used a simple reaction test as the secondary task (Sparrow et al., 2006; Lajoie et al., 1996) and this may not have been sufficiently demanding to interfere with gait performance. Indeed, the average DT cost (i.e., the difference in gait speed between the ST and DT conditions) was less than 5% for both age groups and these figures were considerably lower than those in the other studies that were reviewed. This suggests that older adults may be more adversely affected in dual-tasking situations but only when the attentional demands of the secondary task are sufficiently high. Of particular relevance to the current work, an inability to maintain gait performance while dual-tasking has also been identified as a reliable risk factor for falls. In their seminal investigation, Lundin-Olsson and colleagues (1997) reported that 83% of older adults that stopped walking while talking went on to experience a fall in the following six months. Since then, a great deal of empirical work has demonstrated that individuals who exhibit reduced gait performance in response to a range of secondary tasks are more at risk of experiencing future falls than those who are able to maintain performance (Muir-Hunter & Wittwer, 2016; Hsu et al., 2012; Beauchet et al., 2009).

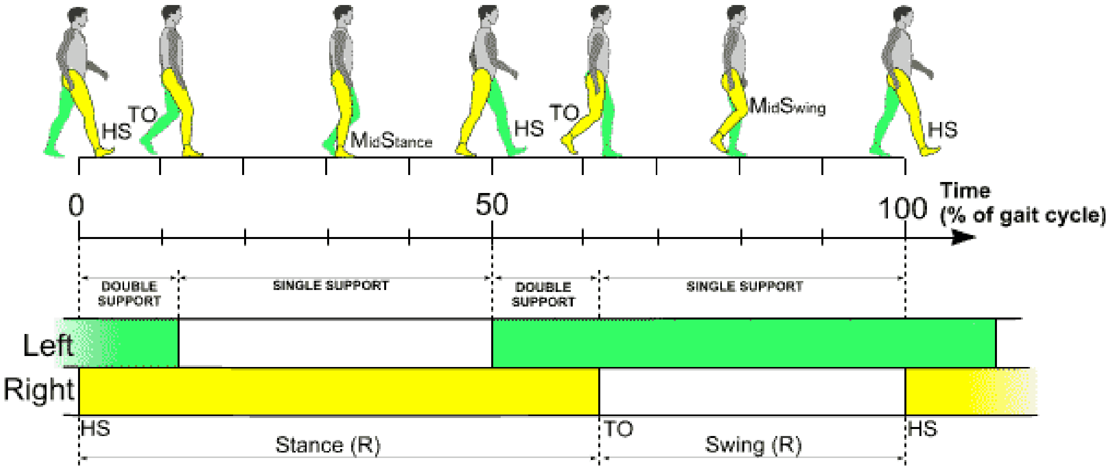
Dual-task walking assessments may also serve as a proxy for everyday walking as this can often involve navigating through complex environments while performing several activities. For example, when crossing a busy street, in addition to walking individuals may also be required to scan for obstacles, read street signs, ensure no traffic is approaching and calculate how long it will take them to cross. Higher-order executive processes are thought to be important in these complex situations as they ensure the appropriate allocation of attentional resources to multiple tasks (Ble et al., 2005) and the inhibition of distracting information while performing these tasks (Plummer-D'Amato et al., 2011). Furthermore, increasing age is accompanied by a deterioration in the sensory and motor processes that control postural and balance responses (Li et al., 2001; Shumway-Cook & Woollacott, 1995). It is thought that older adults attempt to compensate for age-related deficits in these systems by allocating more attentional resources to their walk in complex situations (Yogev-Seligmann et al., 2008). This has been referred to as a “posture-first” strategy (Woollacott & Shumway-Cook, 2002). Deterioration of the prefrontal regions of the brain and associated deficits in executive function may impair the ability of older adults to do this. As a result, they may lack the attentional resources needed to maintain a safe and steady walk, making them potentially vulnerable to a fall. In support of this notion, it has been demonstrated that older fallers are more likely to improve performance on the cognitive task under DT compared to ST conditions, indicating the use of an inappropriate “posture-second” strategy when dual-tasking (Beauchet et al., 2007).

Associations between cognition and gait

The work described above demonstrates that walking is an activity that requires input from higher-order cognitive processes, more specifically, that executive function may be directly contributing to gait performance. There will be now be a brief review of the empirical work that has directly investigated this link. The majority of this comes from longitudinal studies that have examined the extent to which cognitive measures may be useful markers for future gait impairment. For example, several studies reported that baseline assessments of global cognitive function (e.g., Mini Mental State Examination; MMSE) were able to detect individuals who went on to develop severe mobility difficulties or reduce their walking speed between one and six years later (Atkinson et al., 2010; Rivera et al., 2008; Atkinson et al., 2007). Examinations of more specific cognitive abilities have demonstrated that lower scores on executive measures such as the 15-item executive interview (EXIT 15) are associated with a decline in gait speed during follow-up periods of three to five years (Watson et al., 2010; Soumare et al., 2009; Atkinson et al., 2007). Poor performance in other cognitive domains such as perceptual speed, attention, memory and visuospatial ability have also been shown to predict future mobility impairment (Buchman et al., 2011; Inzitari et al., 2007a).

Cross-sectional work examining the relationship between cognitive function and dual-task gait outcomes in older adults has also highlighted the role of executive function and, relatedly, attention. A number of studies have reported that lower scores on single or combined tests of these domains is associated with a slower gait speed (Persad et al., 2008; Rochester et al., 2008; Verghese et al., 2006) and increased stride-to-stride variability in several gait parameters (Holtzer et al., 2012; van Iersel et al., 2008b; Yogev et al., 2005). This is not surprising given that DT walking is thought to place additional demands on attentional resources and executive function is important in the allocation of these resources. Finally, a factor analytical approach has been used to examine the link between specific components of cognition and gait. The sequence of movements we go through when walking, commonly referred to as the gait cycle, is made up of a number of spatial and temporal characteristics (see Figure 1.1). This approach groups these characteristics into distinct domains such as pace (e.g., stride length and velocity), rhythm (e.g., average time spent in the stance phase) and variability (e.g., variability in the time spent in the stance phase between strides). The pace component of gait has been found to be highly correlated with measures of attention and processing speed whereas the variability component has been more strongly linked to executive function (Lord et al., 2013; Ikram et al., 2012). Such work demonstrates that gait is not a unitary construct and that there are numerous cognitive inputs that contribute to maintaining performance across the different components.

Figure 1.1: Phases that make up the gait cycle. Abbreviations: HS = heel strike, TO = toe off. Source: University of Glasgow



Associations between cognition and falls

Empirical findings appear to support the theoretical link between cognition and gait, and there is evidence to suggest that measures of cognition, and particularly executive function, may be useful for identifying those at risk of future gait problems. Given the evidence presented earlier that identified gait impairment as a reliable risk factor for falls, similar links between cognitive function and falls may also be expected. Once again, the majority of evidence here comes from longitudinal work where cognitive measures have been employed as potential screening tools to detect future falls. Muir and colleagues (2012) reviewed 27 such studies and reported that measures of global cognition (such as the MMSE) were significant predictors of single falls, recurrent falls, and falls resulting in serious injuries in all studies involving community-dwelling older adults. Of note, one investigation reported that a one point decrease in MMSE score at baseline was equivalent to a 20% increase in the risk of experiencing a fall over the following year (Gleason et al., 2009). Other empirical studies have examined the link between specific cognitive abilities and falls in old age, with deficits in a variety of cognitive domains found to predict later falls or an increased risk of falls. These domains include processing speed (Anstey et al., 2006), visuospatial ability (Martin et al., 2009) and sustained attention (O'Halloran et al., 2011). However, the majority of past work has predominantly focused on the relationship between executive function and falls.

A review article by Kearney and colleagues (2013) identified 11 prospective studies that examined this relationship, with nine reporting that baseline levels of executive function were associated with falls outcomes between one and 15 years later. Five of these studies found that poor performance on the Trailmaking task (Army Individual Test Battery, 1944), a widely recognised measure of executive function, was associated with more single falls, recurrent falls and injurious falls over the following one or two years. Of particular interest, in one of these investigations, older adults who reported a first time fall during the follow-up period performed much worse on these baseline tests than other fallers and non-fallers (Herman et al., 2010). The other four studies employed various executive measures (e.g., Raven’s coloured progressive matrices) but also found that those with poorer baseline performance were more likely to fall and suffer falls-related injuries during follow-up. Following the publication of this review, subsequent studies have continued to provide evidence for a link between executive function and falls. For example, one study that also measured gait under ST and DT conditions concluded that older adults with more intact executive abilities were better able to deal with and react to challenging walking situations, and that this subsequently reduced the risk of experiencing a fall (Mirelman et al., 2012).

Summary

To summarise, it is well established that gait impairment and falls are more prevalent in older adults diagnosed with cognitive impairment. More recently it has been shown that measures of cognition, and particularly executive function, may be useful in predicting future gait impairment and falls. This is line with theoretical suggestions that everyday walking requires input from higher-order cognitive processes, deficits in which may affect the speed and stability of gait, and predispose an individual to falling. The evidence presented here suggests a pathway may exist between cognition, gait and falls in which falls are preceded by age-associated changes in gait and these changes, in turn, are preceded by age-associated decline in certain cognitive abilities. If this is the case, it is reasonable to assume that older adults displaying early signs of cognitive decline may be at risk of developing mobility problems and experiencing falls in the future.

As mentioned previously, the need for simple screening tools to identify at-risk populations at the earliest possible time is a major thrust behind the current series of studies. Cognitive measures may prove useful in this respect if they are capturing subtle age-related changes in cognitive function that may indicate vulnerability to future falls and gait impairment. In the earlier section that considered theoretical perspectives of cognitive ageing, it was suggested that there is an increased inconsistency in central nervous system functioning in later life that stems from a reduced ability to inhibit random neural activity. This may manifest itself behaviourally as increased inconsistency in performance on a range of cognitive tasks. Damage to the frontal lobes may also contribute to this inconsistency by restricting the ability to maintain attention and, relatedly, to inhibit distracting information while performing a task. Therefore, it could be that the increasingly inconsistent behaviour observed in later life is an important marker of an individual’s underlying cognitive and neurobiological processes. Indeed, after being initially considered as just ‘noise’ in earlier perspectives, the last 20 years or so has produced an increasing amount of research looking at within-person inconsistency in cognitive performance. A review of this work will follow in the next section and evidence will be presented in favour of considering performance inconsistency in relation to falls and gait outcomes in older age.

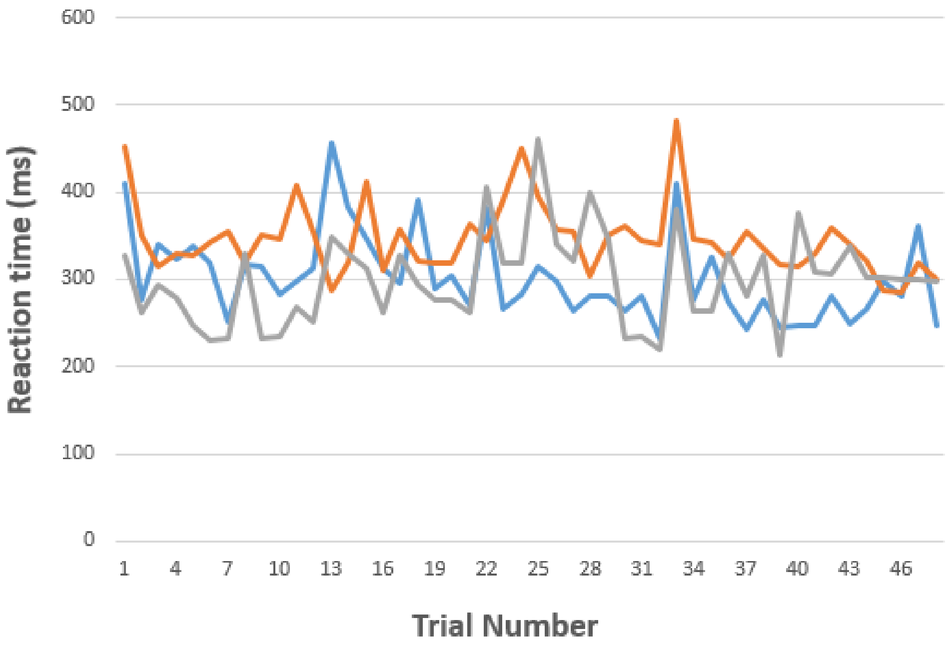
Section C: Intraindividual variability, gait and falls

What is intraindividual variability?

Researchers in the field of cognitive ageing have typically used measures of central tendency to examine cognitive function under the assumption that they capture true level of performance. Reaction time (RT) paradigms, where individuals respond as quickly and accurately as possible to the presentation of stimuli, have been used for this purpose for over a century. Indeed, it was at the end of the nineteenth century when Galton first proposed that differences in general mental ability are captured by differences in the time taken to respond to visual or auditory cues (Jensen, 2006). In addition to studying differences in the average response time, otherwise known as mean RT, the use of such paradigms also allows for variability in cognitive performance to be examined. This variability can be classified in a number of ways. First, it is possible to examine individual differences in performance on a single task performed on one occasion; this is commonly referred to as *diversity* (Hale et al., 1988). Second, it is possible to examine how the performance of one individual differs across a number of tasks performed on one occasion; this can be thought of as *dispersion* (Christensen et al., 1999). However, an individual’s average level of performance on any given task is likely to fluctuate over time due to systematic (e.g., arousal levels, time of day effects) and unsystematic influences (Nesselroade, 1991). This represents a third kind of variability in performance that can be studied by measuring the performance of a single individual on a single task across multiple occasions; this is often called *inconsistency* (Hultsch et al., 2000). Inconsistency can be observed across long intervals, for example by measuring week-to-week performance changes in story recall (e.g., Hertzog et al., 1992). It can also be observed across very short intervals, for example by examining the fluctuations in response time across different trials of a particular cognitive task (see Figure 1.2 for an example). This type of inconsistency, which will henceforth be referred to as intraindividual variability (IIV), cognitive variability or simply variability, will be the focus of the present research.

Although several prominent theorists have suggested that variability may be important for understanding human behaviour (Cattell, 1957; Woodrow, 1932), it has received relatively little attention in the literature compared to average measures of performance. For a number of decades, variation in an individual's RT was considered to be nothing more than random error or noise, or the product of unreliable measurement. However, there is now strong evidence to suggest that IIV is a relatively

Figure 1.2: Intraindividual variability on a two-choice reaction time task with 48 trials for three healthy older adults aged 60-65. Actual data collected from a subsample of participants in the first experimental study of this thesis.



stable characteristic that differs between individuals and can be reliably measured (Jensen, 1992). For example, individuals displaying higher IIV levels on one RT task are also more variable on other RT tasks (e.g., Hultsch et al., 2002), as well as on cognitive tasks measured across longer intervals (e.g., Hultsch et al., 2000). Furthermore, average performance indicators (e.g., mean RT) may not adequately represent the performance characteristics of an individual as a major portion of variance usually attributed to between-person differences is actually caused by within-person fluctuations (Nesselroade & Salthouse, 2004). Therefore, measures of IIV may provide unique and valuable information about systematic variation in cognitive function that cannot be derived from measures of mean RT.

What are the mechanisms underlying IIV?

IIV has received more attention in the literature recently and, as a result, researchers have devoted time to understanding the mechanisms that underlie moment-to-moment fluctuations in cognitive performance. As discussed in the theories of cognitive ageing section above, inconsistent reaction times may be caused at the neurobiological level by increased neural noise in the transmission of signals in the CNS (Hendrickson, 1982). This has led researchers to suggest that IIV at the behavioural level may be a useful indicator of CNS integrity and neurobiological functioning. In support of this notion, several studies have demonstrated that cognitive variability increases in conditions that affect the functioning of the CNS. The most compelling evidence for this notion comes from the study of patients with brain damage. Almost a century ago, Head (1926, p. 145) noted that “an inconsistent response is one of the most striking results produced by a lesion of the cerebral cortex”. In the years that followed, higher levels of IIV have been consistently reported in patients suffering brain lesions regardless of their origin, severity or location (e.g., Stuss et al., 1989; Bruhn & Parsons, 1971).

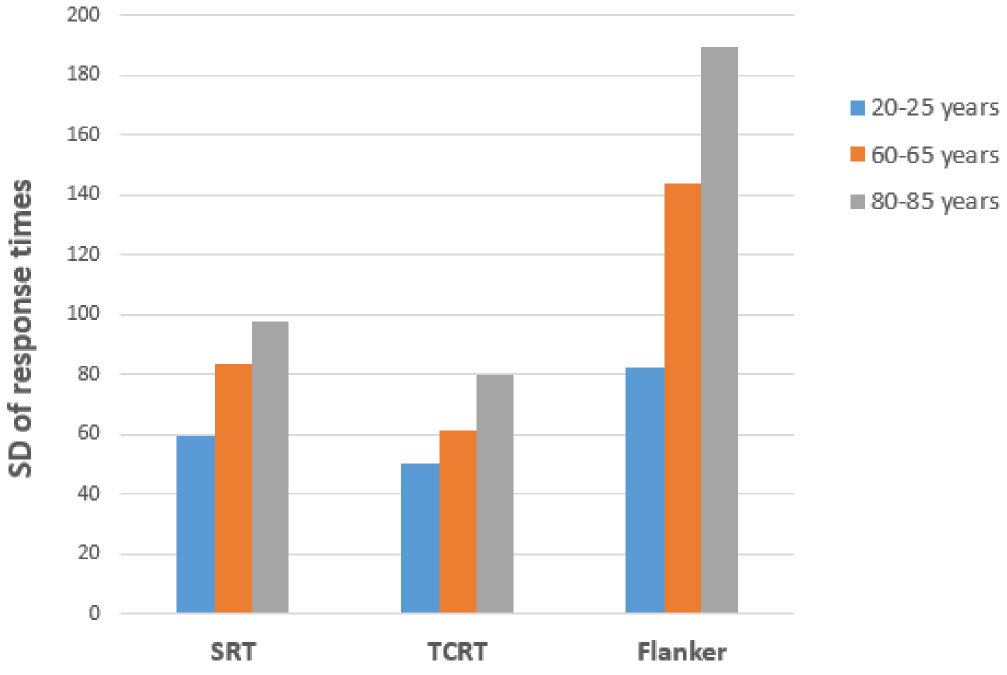
Relatedly, a link has been made between greater IIV and localised lesions that are specific to the frontal areas of the brain (e.g., Stuss et al., 2003). One study using functional magnetic resonance imaging (fMRI) also demonstrated that brain activation in the pre-frontal cortex (PFC) was positively correlated with variability levels on a Go-NoGo task (Bellgrove et al., 2004). Furthermore, West and colleagues (2002) suggested that age-related deficits in the PFC might have a detrimental effect on executive processes, thereby leading to greater IIV. A number of researchers have examined the shape of the response time distribution using ex-Gaussian analysis in order to identify the cognitive mechanisms underlying IIV. In older adults relative to younger adults, these distributions tend to be more positively skewed suggesting that increasing age is associated with an increasing number of very slow responses rather than a general slowing across the distribution (Haynes et al., 2016; West et al., 2002; Spieler et al., 1996). These intermittent longer RTs have been attributed to lapses of attention and intention, both of which are thought to be the result of age-related fluctuations in the efficiency of executive control processes (Bunce et al., 2004; West et al., 2002; Bunce et al., 1993). Momentary variation in attention indicated by slow responses have also been shown to cause decreases in the inhibition of irrelevant stimuli and in the successful processing of relevant stimuli (Weissman et al., 2009).

IIV and healthy ageing

In the cognitive ageing literature, there has been an increasing interest in IIV as it is thought that it may be linked to a number of adverse outcomes in later life. In some cases, it has been shown that IIV is a better predictor of these outcomes than average performance measures such as mean RT. However, before discussing the links between IIV and other consequences of ageing, it is first important to establish how IIV changes across the lifespan. One investigation of this topic examined IIV on a choice RT task in a sample of individuals aged 6-81 years old (Williams et al., 2005). Here, IIV levels were found to decrease rapidly from childhood to young adulthood and then increase gradually from middle to late adulthood. In line with these findings, Dykiert and colleagues (2012) conducted a meta-analysis of 29 studies that investigated age differences in IIV on simple or choice RT tasks. They concluded that older adults (aged 60 and above) had higher IIV than younger adults (aged 20-39) and, to a lesser extent, middle-aged adults (aged 40-59) and that these differences were more pronounced when more demanding choice RT tasks were used. An example of the age differences observed in the present work can be seen in Figure 1.3. Here, IIV levels on three cognitive tasks are displayed for a small group of young adults (20-25 years), old adults (60-65 years) and very old adults (80-85 years).

The demonstration of cross-sectional age differences is consistent with longitudinal work that has looked at changes in IIV levels over a number of years. One such investigation administered a simple and a choice RT task to a group of middle-aged (36 years) and older (56 years) adults during two sessions eight years apart. Both age groups exhibited increased variability on the choice RT task over eight years but only

Figure 1.3: A bar graph demonstrating variability levels for three age groups on a Simple Reaction Time (SRT) task, a Two Choice Reaction Time (TCRT) task and the Flanker task. The standard deviation of response times was calculated as a measure of IIV. Actual data collected from a subsample of participants in the first experimental study of this thesis.



the older group showed increased variability on the simple RT task (Deary & Der, 2005). In another longitudinal study, a sample of 446 adults were divided according to age (young-old = 55-64 years, mid-old = 65-74 years, old-old = 75-94 years) and asked to complete four RT tasks three times over the course of six years. Longitudinal increases in IIV were observed on three of the four tasks for the oldest group but not for the two younger groups (MacDonald et al., 2003). Another study of this cohort administered a number of basic and complex RT tasks to adults aged 64-92 during annual sessions over a period of four years. They found that, although the average 75 year old only exhibited small increases in IIV on the most basic RT task, greater longitudinal changes in IIV levels on all tasks could be seen for each yearly increase after 75 (Bielak et al., 2010b). Finally, one longitudinal investigation administered a simple and choice RT task three times over the course of eight years to a group of older (60-64 years at baseline) and middle-aged adults (40-44 years at baseline). While both groups increased their variability over time on the choice RT task, only the older group did so for the simple RT task (Bielak et al., 2014). Taken together these findings provide evidence for age-related increases in IIV, but also suggest that other factors such as baseline age and the demands of the task used to derive variability measures may be influencing this relationship.

IIV and neuropathological ageing

Further to the work that has examined older adults considered to be ageing normally, IIV has also been extensively studied in relation to neuropathological ageing. Such research has provided strong evidence that neurobiological disorders are characterised by greater levels of variability. For example, one investigation demonstrated that older adults diagnosed with mild dementia were approximately twice as variable as their healthy counterparts on four RT tasks of varying difficulty, even after equivalent measures of mean RT were taken into account (Hultsch et al., 2000). In a more recent study, greater IIV on a complex choice RT task was found to be associated with an increased risk of developing incident dementia over the next four years (Kochan et al., 2016). Another investigation demonstrated that baseline IIV levels on four RT tasks distinguished between individuals who maintained or transitioned into cognitive impairment without a diagnosis of dementia and those who did not over the course of 5 years (Bielak et al., 2010a). Cognitive variability is also thought to be higher in cases of Mild Cognitive Impairment (MCI), an intermediate stage between typical cognitive decline and dementia. For example, IIV on a simple and choice RT task was found to distinguish between healthy older adults and those with mild or moderate MCI after accounting for mean RT on the same task (Dixon et al., 2007). Furthermore, measures of IIV on simple and choice RT tasks have been shown to predict the transition from healthy ageing to MCI in a group of adults aged 60-64 at baseline (Cherbuin et al., 2010). Finally, higher levels of IIV have additionally been observed in individuals with Parkinson’s disease. In one study, both Alzheimer’s and Parkinson’s patients were found to have higher IIV on simple and choice RT tasks compared to healthy controls (Burton et al., 2006) whereas another investigation demonstrated that Parkinson’s patients had higher IIV levels but only on more demanding choice RT tasks (de Frias et al., 2007).

IIV and behavioural outcomes

A great deal of empirical work has been carried out examining the extent to which variability measures are related to other measures of cognitive function. For example, in a series of investigations, Jensen (1992, 1987; 1982) consistently reported that individuals with higher IIV performed more poorly on tests of general intelligence. Furthermore, associations involving IIV were found to be stronger than associations involving equivalent measures of mean RT. In line with these findings, later empirical work demonstrated that IIV levels were also predictive of performance on other intelligence batteries such as the Culture Fair Intelligence Test (Rabbitt et al., 2001) and the Armed Services Vocational Aptitude Battery (Larson & Alderton, 1990). There is also evidence that greater variability is associated with deficits in specific cognitive abilities. For example, one investigation found that IIV measures derived from four RT tasks of varying difficulty predicted performance on measures of perceptual speed, episodic memory, working memory and crystallized intelligence (Hultsch et al., 2002). Furthermore, Bunce and colleagues (Bunce et al., 2008) found that higher levels of variability on a 2-choice and 4-choice RT task were associated with impairments in task switching, updating the contents of working memory and response inhibition. These findings provide further support for the notion that variability is closely tied to higher-order executive processes.

Cross-sectional associations between IIV and cognitive performance are informative but, perhaps more importantly, there has been an increasing interest in studying the extent to which IIV measures may be predictive of future cognitive changes (Haynes et al., 2017). For example, one study reported that baseline IIV on two verbal and two non-verbal RT tasks was significantly associated with changes in multiple cognitive abilities over the following six years (MacDonald et al., 2003). Other empirical work has demonstrated that more variable individuals are more likely to display performance decrements on measures of processing speed, verbal fluency and memory during short term (3 years) or long term (13 years) follow-ups (Bielak et al., 2010b; Lovden et al., 2007). In a more recent investigation, baseline IIV on a four choice RT task moderated cognitive change over six years on measures of word recall and vocabulary, whereas baseline IIV on a four choice RT task with a 1-back condition did so only for word recall (Grand et al., 2016). Finally, in an alternative analysis of the same dataset, higher scores on a “basic” composite measure of variability were associated with a greater decline in word recall over a six year follow-up (Yao et al., 2016). Furthermore, a “complex” composite measure comprising IIV on a four choice 1-back RT task and a switching task was found to predict changes in both word recall and the time taken to complete the Trailmaking B test of executive function. Taken together these findings suggest that IIV may be an important early marker for broader cognitive decline and also decline in specific cognitive processes.

In addition to looking at the links between IIV and cognitive function, previous research has also examined IIV in relation to daily living activities in old age. One such study found that greater IIV was associated with lower scores on the Everyday Problems Test (Burton et al., 2006). This test involves problem solving across a variety of domains that are likely to be encountered on a daily basis such as shopping, telephone use and financial management. Another investigation, which assessed the driving performance of older adults, found that IIV on a version of the Stroop task was correlated with variability in “headway” (i.e., maintaining a safe distance from the vehicle in front) (Bunce et al., 2012). Finally, there is considerable evidence in the literature suggesting that higher variability levels may be a marker for impending death (Haynes et al., 2017). For example, a one SD increase in simple and choice IIV has been associated with a respective 29% and 17% increased chance of being deceased 14 years later (Deary & Der, 2005). Similarly, another study found that individuals with higher IIV on simple and choice RT tasks at baseline were less likely to be alive after a 19 year follow-up (Shipley et al., 2006). Higher levels of baseline IIV on a lexical and semantic decision task also predicted future mortality and, importantly, was a better predictor than mean RT measures (MacDonald et al., 2003). A significant association was also found between IIV on a simple RT task and the likelihood of survival over the next 17 years whereas mean RT derived from the same task was not (Batterham et al., 2014). Finally, in a recent study, baseline levels on a composite IIV measure derived from a simple and choice RT task predicted survival time over the next eight years, but an equivalent mean RT measure did not (Kochan et al., 2017).

To summarise, intraindividual variability appears to be a more important construct than first thought as evidenced by the last few decades of work where it has been examined in a number of contexts. In normally ageing populations, there appears to be a progressive decline in IIV that begins in middle age and continues into very old age. In populations exhibiting neuropathology, there is evidence that IIV is elevated in conditions characterised by neurological dysfunction (e.g., dementia) and may have potential utility when it comes to the early identification of, as yet, undetected conditions. As well as being a marker for neurobiological integrity, IIV also appears to be an indicator of cognitive function as measured with tests that capture general intelligence as well as more specific cognitive abilities such as executive function. There is evidence to suggest that IIV may be a sensitive predictor of impending declines in cognitive performance and also, longer-term outcomes such as death. Furthermore, a number of studies have found IIV to be a stronger predictor of outcome than equivalent measures of mean RT, or found that it captures unique information after mean RT has been controlled for. This suggests that IIV may be detecting elements of cognitive function that are untapped by more widely-used measures of average performance and highlights the importance of including these measures in investigations related to cognitive ageing.

Measuring intraindividual variability

IIV can be quantified in a number of ways depending on the exact objectives of the research being carried out. This section briefly overviews the variability measures that have been most frequently used and some of the methodological considerations that accompany them. The simplest representation of an individual's IIV is given by computing the *raw intraindividual standard deviation* (raw SD) of their RTs across all trials of a particular cognitive task. When taking this approach it is often common to apply minimum and maximum boundaries to the RT data and exclude any trials that fall outside of these boundaries. For example, a number of authors have recommended a minimum boundary of 150 milliseconds and a maximum boundary of the intraindividual mean plus three intraindividual standard deviations (MacDonald et al., 2006; Hultsch et al., 2002). These cut-offs eliminate fast trials that are likely due to accidental or anticipatory responses, and reduces the effect of unusually slow outliers when calculating the raw intraindividual SD. Although commonly used and intuitively understandable, there are several limitations associated with using this measure and this has led researchers to employ other metrics in empirical investigations.

Although much of the work examining IIV has shown that it may provide information beyond that provided by the mean RT, more variable individuals also tend to have slower responses. For example, a number of studies have provided evidence that mean RT and variability of RT have a linear relationship (e.g., Myerson & Hale, 1993) and that the correlation between the two is usually high (Deary & Der, 2005). Therefore, greater IIV may simply be a mathematical function of slower mean RT which points to a generalised slowing in responses. Many researchers have suggested that changes in mean RT may actually be responsible for changes in IIV (e.g., Flehmig et al., 2007). By contrast, it has been argued that "the average speed of RT can be seen as a consequence of variability of RT more easily than the reverse relationship" (Jensen, 1982, p. 103). Regardless of the causal direction, the overlap between these two constructs highlights the importance of controlling for response speed when calculating IIV, particularly if variability measures are to have any practical significance. The simplest way to do this is by computing the *coefficient of variation* (CV), a measure obtained by dividing each individual's raw SD by their mean RT. In effect, this produces a variability measure that has adjusted for individual differences in mean RT.

A major limitation of both the raw SD and CV metrics is that they do not account for systematic factors that can influence IIV such as group differences, learning effects and fatigue over time. A number of authors have advocated the use of regression methods that statistically remove these influences (e.g., Hultsch et al., 2002). This approach regresses individual RTs onto potential confounding variables (e.g., age, gender, trial number), then uses the resulting residual values to calculate the *intraindividual standard deviation* (ISD). Effectively, this procedure partials out within- and between-subject sources of variance. Despite the noted advantages of using the ISD, a higher knowledge of sophisticated statistics is required for its calculation relative to other measures and, as a result, this makes it more difficult to use in applied contexts. Another limitation of ISD measures is that their computation does not fully control for mean RT and, thus, any effects that are identified using these metrics may not be independent of the effects of slower responding. A final approach to calculating variability worth noting is analysis of the whole RT distribution, often employed by researchers interested in examining the mechanisms underlying IIV. Here, it is common to fit a convolution of the normal distribution and exponential distribution, known as an ex-Gaussian function, to the reaction time data (e.g., McAuley et al., 2006; West et al., 2002). This produces three parameters that are thought to reflect the speed of response (μ), the variability of response (σ) and the exponentially distributed tail of the distribution (τ). These measures, though potentially insightful, have been studied much less in relation to ageing outcomes compared to the raw SD, the CV and the ISD.

In addition to the way that IIV measures are calculated, the cognitive demands of the RT task used to derive these measures may also contribute to overall variability levels. This was highlighted earlier in the section where evidence was provided that longitudinal increases in IIV levels are more pronounced when measured with a choice RT task rather than a simple RT task (Bielak et al., 2014; Deary & Der, 2005). Similarly, a meta-analysis of 29 studies comparing IIV levels across three age groups found that effect sizes for older relative to younger and middle-aged adults were greater when derived from choice RT tasks compared to simple RT tasks (Dykiert et al., 2012). Another study investigated age differences in IIV on a simple RT task, a choice RT task and a 1-back choice task. Variability was found to be higher in older adults on all three tasks but this difference was especially pronounced on the 1-back task which places higher demands on executive abilities (Dixon et al., 2007).

In conclusion, a number of metrics have been used to represent IIV in the cognitive ageing literature. The most suitable measure to use in any given situation is likely to depend on the aims of the research being carried out and the resources that are available. As previously mentioned, the development of simple screening tools that may provide predictive information about gait and falls over and above that provided by existing neuropsychological assessments is a central theme of the work in this thesis. To that end, the CV measure is likely to be the most suitable given that it is easy to calculate, and it is thought to be the only measure that completely controls for mean RT on the same task in its computation. In addition, the evidence provided here suggests that the task used to derive measures of variability may affect its relationship with outcome. Previous findings have suggested that more demanding RT tasks, and particularly those that place a higher demand on executive function, may produce stronger effects than simple RT tasks. Against this background, it is reasonable to expect that more demanding tasks would offer greater utility in detecting subtle cognitive changes that may contribute to adverse outcomes such as falls and gait impairment. However, where possible, experimental studies would benefit from administering RT tasks with varying demands as this would lead to a better understanding of the conditions under which IIV is most strongly predictive of outcome.

Evidence for a link between IIV, gait and falls

Up to this point, this review has focused separately on IIV, gait and falls. Each of these constructs has been considered in terms of how they are affected by age, their underlying cognitive mechanisms, and their associations with other age-related outcomes. However, the following section will outline considerations in favour of examining the inter-relations between these constructs. Of particular relevance to the current research, there is evidence to suggest that variability measures may be useful in the prediction of future falls and gait outcomes.

The first consideration concerns executive function and attention. Past empirical work has suggested that increased IIV in older age can be attributed to less efficient executive control processes (West et al., 2002) and, relatedly, momentary reductions in levels of attention (Bunce et al., 2004; Bunce et al., 1993). Likewise, earlier in the chapter it was proposed that age-related decline in executive and attentional processes contribute significantly to walking problems in later life and, subsequently, make older adults more vulnerable to falling. This notion is supported by longitudinal findings where deficits in executive function, and to a lesser extent attention, have been linked to falls outcomes or gait impairment several years later (Kearney et al., 2013). Furthermore, in cross-sectional investigations, measures of executive function and attention predict gait performance in demanding situations such as when individuals walk while performing a secondary cognitive task (Persad et al., 2008; Rochester et al., 2008; Verghese et al., 2006). Given that age-related increases in IIV are likely to reflect impaired executive processes, it follows that more variable individuals would be at a greater risk of developing gait problems or experiencing a fall in the future. Relatedly, these individuals may also struggle to maintain high levels of attention for long periods of time. When faced with complex walking situations, such as dual-tasking, this could compromise their ability to maintain a safe and steady walking motion. As a result, this may lead to decrements in gait performance and, in turn, increase the likelihood of a fall.

The second consideration relates to cognitive impairment. It has previously been mentioned that IIV levels are higher in older adults who have been diagnosed with dementia or MCI (Dixon et al., 2007; Hultsch et al., 2000). IIV measures have also been shown to identify those most at risk of developing these disorders (Kochan et al., 2016; Cherbuin et al., 2010) as well those who remain or transition to cognitive impairment without a diagnosis (Bielak et al., 2010a). Similarly, the prevalence of gait abnormalities and falls has been found to be much higher in adults diagnosed with dementia or MCI compared to healthy older adults (Camicioli et al., 2007; Tinetti et al., 1988). Longitudinal work has also demonstrated that measures of walking speed can be used to predict future changes in global cognition (as indicated by MMSE scores) up to 8 years later (Deshpande et al., 2009; Alfaro-Acha et al., 2007). Taken together, this evidence suggests that higher levels of cognitive impairment, in populations with or without a clinical diagnosis, are associated with increased IIV, abnormal gait and falling. Against this background, it is expected that measures of variability would correlate highly with gait and falls outcomes. This is particularly likely given the evidence presented earlier that IIV may serve as a marker for cognitive function, deficits in which have been shown to contribute to these outcomes.

The final consideration concerns neurobiological functioning. Earlier in the chapter, evidence was presented suggesting that IIV may be an indicator for the integrity of the central nervous system (CNS). In further support of this notion, previous research has shown that IIV across the lifespan is characterised by an inverted U-shape function (Williams et al., 2005). This parallels changes in brain white matter and grey matter volume that is observed from childhood to old age (MacDonald et al., 2006). Reductions in grey matter volume, particularly in the pre-frontal cortex, have also been shown to be greater in those with impaired gait (Rosano et al., 2008) and in fallers (Makizako et al., 2013). This suggests that the age-related changes in gait that may predispose an individual to falls are at least partially attributable to deterioration in certain brain regions. Indeed, Rosso and colleagues (2013) reviewed evidence from a number of clinical and epidemiological studies and concluded that the CNS is making important contributions to gait control in the healthy older population. Therefore, age-related deficits in CNS functioning are likely to manifest as both increased variability and reduced gait control, providing good reason to expect a strong association between measures of these constructs.

Similarly, past empirical work has linked the integrity of brain white matter to IIV, gait and falls. Researchers have been particularly interested in the behavioural correlates of white matter hyperintensities (WMHs). A review paper identified 15 studies that had examined WMHs in relation to gait and stepping, 13 of which (six longitudinal) reported that greater volume of WMHs was associated with poor performance on gait measures (Zheng et al., 2011). Furthermore, six studies looking at WMHs in relation to falls were also identified, with all six (four longitudinal) finding that WMH burden was greater in fallers compared to non-fallers. There is also considerable evidence that white matter integrity, particularly in the frontal region of the brain, is more compromised in older adults that exhibit higher levels of IIV. One study reported that the volume of superior frontal WMHs was significantly correlated with an IIV composite score derived from performance on three RT tasks (Jackson et al., 2012). An investigation by Bunce and colleagues (2007) found that the burden of WMHs in the frontal lobe, but not in other brain regions, was related to IIV levels on a choice RT task but not to other cognitive measures. The same group also demonstrated that IIV measures on a choice RT task with as few as 20 trials were able to reliably predict frontal WMH volume in a group of 44-48 year old adults (Bunce et al., 2013). Taken together, these findings suggest that compromised white matter integrity may be risk factor for gait impairment and future falls, and IIV measures may be useful in detecting this.

Why study IIV in relation to gait and falls?

These converging lines of evidence suggest that, in healthy older populations, variability levels are likely to be associated with performance on various gait parameters and the likelihood of experiencing a fall. An important question that remains to be answered is: Why study IIV in relation to these outcomes as opposed to traditional measures of cognitive performance? It has already been demonstrated that assessments of executive function based on average performance are effective in the prediction of gait speed decline and future falls (Kearney et al., 2013). However, there are good reasons to expect that assessments of variability might have additional utility here. For example, IIV metrics are thought to provide unique information about cognitive functioning, over and above that provided by measures of central tendency such as the mean RT (Jensen, 1992). Furthermore, IIV levels are predictive of or related to a number of age-related outcomes after controlling for mean RT. It could be that IIV is able to explain additional age-related variance in gait and falls outcomes over and above that which is explained by average measures of performance.

In addition, there is also evidence that IIV may be a marker for future decline in cognitive function. A handful of longitudinal studies have found higher IIV at baseline assessment to be associated with performance decrements in cognition several years later (e.g., Bielak et al., 2010b; Lovden et al., 2007). It could be that IIV measures are detecting subtle differences in the cognitive abilities that contribute to gait and falls earlier than traditional neuropsychological tests. Finally, the RT tasks from which IIV measures are derived are quick to complete and can be administered by individuals with little training or experience of neuropsychological assessment. Additionally, they contain minimal linguistic content which means they can be administered to a variety of individuals from different backgrounds, unlike other neuropsychological tests. This also makes them potentially suitable for use in screening assessments in clinical settings. In summary, IIV measures are quick and simple tools that may be particularly useful in the early identification of individuals at risk of developing gait problems and falling. They may provide unique information about cognitive function that is not captured by existing neuropsychological tests and, as such, they may serve as a useful addition to current screening batteries.

In addition to investigating whether IIV measures may be useful in the prediction of future gait and falls outcomes, it is also important to investigate the underlying mechanisms that may be responsible for these associations. One way this can be achieved is by using a mediational approach to determine whether differences in particular cognitive or physiological abilities account for the initial relationships where they are found (Preacher & Hayes, 2004; Salthouse, 1992; Baron & Kenny, 1986). This approach was central to Salthouse’s theory of cognitive ageing as he discovered that many of the age-related differences in cognitive abilities that had been observed could be explained by differences in simple measures of processing speed (Salthouse, 1996). Other work using this approach has provided evidence that measures of sensory function (e.g., vision, hearing) may be equivalent to measures of processing speed when it comes to explaining age-differences in cognition (e.g., Anstey et al., 2001; Lindenberger & Baltes, 1994). However, very few studies to date have attempted to apply this mediational approach to investigations of IIV, gait and falls and, as a result, it remains an important goal for future research in this area.

Overview of the present work

The current series of studies will closely examine the relationship between IIV, gait and falls in the healthy older population. The following two chapters will provide a comprehensive review of empirical work that has already been carried out in this area. To date, seven studies have examined cross-sectional or longitudinal associations between IIV and falls whereas five studies have looked at the relationship between IIV and gait performance. Chapter 2 (Study 1) will describe a qualitative systematic review of this work that updates a previous publication conducted by members of our research group (Graveson et al., 2016). Chapter 3 (Study 2) will provide an additional quantitative review of this work using meta-analytic procedures.

Chapters 4 to 7 will build on the outcomes of these reviews and address any issues that have been identified by previous work. Chapter 4 (Study 3) will investigate the cross-sectional links between IIV, gait and falls; primarily focusing on the utility of IIV measures as predictors of single-task gait speed and falls status over the previous two years. The extent to which these relationships vary according to age will also be investigated. A battery of five RT tasks will be administered to participants that vary according to the demands they place on the cognitive resources of the individual. As a result, it will be possible to examine whether relationships between IIV measures and outcome are affected by the demands of the task used to derive these measures. Finally, a mediational approach will be used to examine whether measures of cognitive (e.g., executive processes) or physiological (e.g., visual acuity) function are accounting for relationships between IIV and gait, and IIV and falls, where they are observed. This approach is will also be used in Study 4 and Study 5.

Chapter 5 (Study 4) will develop this empirical work further by incorporating a more detailed assessment of gait performance. This will make it possible to investigate whether IIV measures are better predictors of dual-task gait and gait variability, as opposed to single-task gait speed. Chapter 6 (Study 5) will take a closer look at dual-task gait performance in order to identify whether measures of IIV are more strongly associated with DT gait outcomes when the demands of the gait condition are increased. This chapter will also incorporate measures that assess individual components of IIV (i.e., motor time and decision time) and executive function (i.e., switching, updating, response inhibition). As a result, it will be possible to examine the size of associations between different variability components and outcome. The extent to which different components of executive function are attenuating associations involving IIV where they are observed will also be tested. In both of these chapters, the extent to which relationships involving IIV vary according to age and cognitive task demands will also continue to be explored.

Chapter 7 (Study 6) will investigate longitudinal associations between IIV, gait speed and falls using a combination of the data collected across the three cross-sectional studies. This longitudinal data will make it possible to address some of the aims most central to the work in this thesis. Of particular importance, the extent to which baseline measures of IIV are able to identify persons at risk of future falls and gait decline several years later will be examined. This chapter will also look at whether these longitudinal relationships are being influenced by age and the demands of the task used to derive measures of variability. Finally, Chapter 8 will provide a general discussion of this empirical work and how it relates to the broader theoretical and empirical literature. By way of a brief preview, this chapter will conclude that there is indeed evidence to suggest that variability measures have potential in the early detection of persons at risk of gait impairment and, to a lesser extent, falls in old age.

Chapter 2

Study 1: A systematic review of past research that has examined IIV in relation to gait and falls

2.1 Introduction

In the previous chapter, a review of existing theory and research identified both falling and gait impairment as serious health concerns in older populations. As well as being a leading case of major injury and disability, they also compromise quality of life and independence, and place a major burden on healthcare systems around the world. Identifying the risk factors associated with these outcomes continues to be an important aim for researchers and, particularly, there is a pressing need for early screening tools to detect groups that are most vulnerable. The review additionally highlighted that measures of cognitive function may have potential in this respect since cognition is thought to be closely linked to both gait and falls in later life. More specifically, several lines of evidence were presented supporting the notion that older adults with higher levels of intraindividual variability (IIV) may be at-risk of falls or gait problems in the future. Therefore, incorporating measures of IIV into screening assessment may prove to be particularly useful in the early detection of these outcomes.

Regarding the link between cognition, falls and gait, it is well established that cognitively impaired older populations (e.g., those diagnosed with dementia) are more likely to experience a fall (e.g., Tinetti et al., 1988) or problems with their gait (e.g., Camicioli et al., 2007). Neuropsychological work has also demonstrated that disruption to the frontal areas of the brain, which are thought to be implicated in higher-order executive processes, is greater in fallers and those with mobility limitations (e.g., Holtzer et al., 2014b; Zheng et al., 2011). Furthermore, dual-task assessments of gait have provided evidence that walking is attentionally demanding and, in complex situations, input from executive processes is required in order to maintain speed and stability (e.g., Hamacher et al., 2015). Older adults that struggle to maintain performance while completing a secondary cognitive task have been consistently shown to be at a higher risk of falling (e.g., Beauchet et al., 2009). In longitudinal investigations, measures of global cognition have been shown to predict those who went on to fall or experience gait difficulties several years later (e.g., Clouston et al., 2013; Muir et al., 2012). More specifically, deficits in executive function have been identified as a strong risk factor for both falls and gait outcomes in a recent review (Kearney et al., 2013).

This systematic research review focuses on a particular aspect of cognitive function, intraindividual variability (IIV). IIV refers to fluctuations in reaction time (RT) observed across trials for a given cognitive task. As noted in the previous chapter, it has been suggested that IIV may be a marker for neurobiological disturbance as a number of studies have demonstrated greater variability in patients with brain damage (e.g., Stuss et al., 1989). Researchers have also proposed that IIV reflects fluctuations in the efficiency of executive and attentional control processes (e.g., Bunce et al., 2004; West et al., 2002; Bunce et al., 1993). Despite frequently being overlooked as random error or noise, IIV is now thought to represent a stable characteristic that may provide unique information about cognitive functioning not provided by average performance measures such as the mean RT (e.g., Jensen, 1992). As a result, there has been an increased interest in the study of IIV in relation to a variety of age-related outcomes in recent decades.

For example, IIV increases in healthy ageing (e.g., Hultsch et al., 2002) and is greater in the presence of neuropathological disorders such as mild cognitive impairment or dementia (e.g., Hultsch et al., 2000). Furthermore, IIV measures are effective in detecting those most at risk of developing these conditions (e.g., Kochan et al., 2016; Cherbuin et al., 2010). Greater levels of IIV are associated with lower scores on general intelligence measures as well as tests of more specific cognitive abilities such as perceptual speed, episodic memory and executive function (e.g., Hultsch et al., 2002). In longitudinal investigations, baseline IIV has been found to predict future changes in multiple cognitive abilities (e.g., Bielak et al., 2010b), suggesting that it may be a marker for early cognitive decline. Researchers have also demonstrated that higher IIV is associated with poorer performance of everyday activities such as problem solving (e.g., Burton et al., 2006) and driving (e.g., Bunce et al., 2012). Furthermore, a large body of empirical work has also provided evidence for a link between IIV and mortality (e.g., Kochan et al., 2017; Batterham et al., 2014).

There are a number of reasons to expect that IIV might be associated with both gait and falls in older adults. First, theoretical accounts suggest variability is closely tied to both executive function and attention, measures of which have been shown to be useful in the prediction of future falls and gait impairment. Therefore, it is expected that more variable individuals would be more likely to have deficits in these processes that may contribute to later gait problems and, subsequently, increasing their risk of a fall. Second, IIV levels tend to be greater in populations that are cognitively impaired such as in those who have been diagnosed with dementia or mild cognitive impairment. The prevalence of gait abnormalities and falls is also much higher in these populations relative to healthy older adults. Therefore, It is reasonable to expect that measures of IIV would correlate highly with measures of falls and gait outcomes. Finally, age-related changes in grey matter volume have been linked to greater IIV (e.g., Williams et al., 2005), gait problems (e.g., Rosano et al., 2008) and falls (e.g., Makizako et al., 2013) in later life. IIV measures have also been found to predict the volume of frontal white matter hyperintensities (e.g., Bunce et al., 2013) while other work has demonstrated that WMH burden is greater in fallers and those with gait impairment (Zheng et al., 2011). These findings suggest that deterioration in grey and white matter may be a risk factor for gait problems and falls, and increased IIV may serve as a behavioural marker for this.

To date, only a small amount of empirical work has examined the link between IIV and either gait or falls in old age. Some of these more recent studies specifically set out to test this relationship whereas others only did so in addition to a number of other research objectives. The present chapter provides a systematic review of this work that is based on a recent publication (Graveson et al., 2016)[1]. Here, the literature search has been updated to include several studies that became available since that initial review. The first aim of the chapter is to assess the extent to which IIV is associated with both falls and gait outcomes in cognitively intact older adults. Against the evidence that was presented earlier, it is anticipated that higher IIV will be associated with more falls and poorer gait performance (e.g., slower speed, greater variability) in both cross-sectional and longitudinal investigations.

A second aim of the review is to investigate whether these relationships vary according to the methods used to assess IIV. A number of metrics can be used to represent trial-to-trial variability on a cognitive RT task, the most basic of which is the raw standard deviation of RTs (raw SD). There are also other metrics available that control for differences in mean RT (e.g., coefficient of variation; CV) and systematic factors such

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[1] The present chapter is an updated version of a systematic research review that was recently published. The full reference for this publication is as follows: Graveson, J., Bauermeister, S., McKeown, D. & Bunce, D. (2016). Intraindividual Reaction Time Variability, Falls, and Gait in Old Age: A Systematic Review. Journals of Gerontology, Series B: Psychological Sciences and Social Sciences, 71, 857-864.

as learning effects (e.g., intraindividual standard deviation; ISD). It could be that more sophisticated IIV measures that control for such confounds produce stronger associations with gait or falls than basic calculations. Finally, IIV measures can be obtained from a variety of RT tasks and these can differ greatly according to the cognitive demands they place on the individual. Previous research has shown that age-differences in IIV are more pronounced when more complex RT tasks are administered relative to simple tests of psychomotor speed (e.g., Dykiert et al., 2012). Therefore, it is expected that variability will be a better predictor of gait performance, and falls, when IIV is derived from tasks with higher cognitive demands.

2.2 Methods

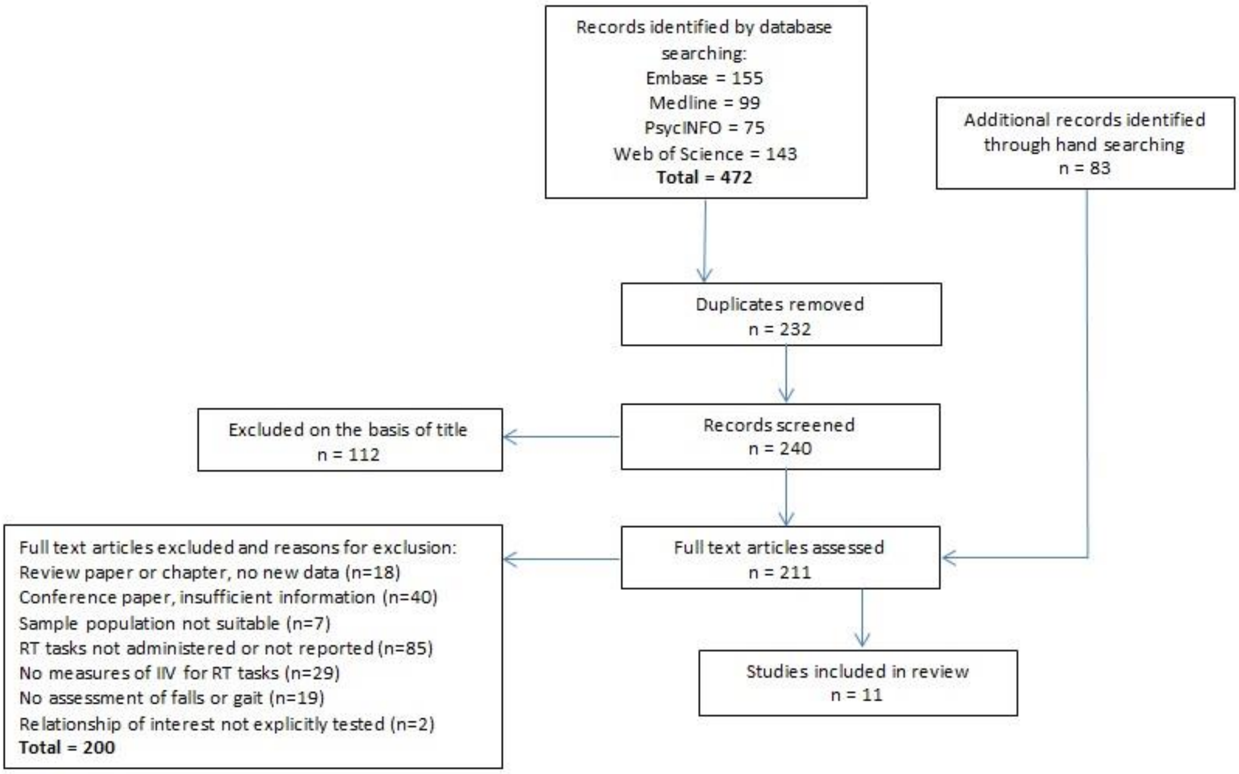
Eligibility criteria

In order to be included in the systematic review, potential studies had to fulfil a number of criteria. First, they must have reported at least one cross-sectional or longitudinal association between IIV and either falls or gait. Studies that only reported the mean RT, the number of errors or the percentage of correct responses for a given cognitive task, were excluded. Second, only investigations of older adults that were healthy and cognitively intact were included, while studies that focused solely on clinical groups diagnosed with a neurological condition (e.g., mild cognitive impairment, dementia, traumatic brain injury) were excluded. The exception was investigations of Parkinson’s disease patients as gait abnormalities are a key characteristic of the disorder and, thus, makes this group particularly vulnerable to falls. Finally, studies were only included if the mean age of the sample was over 65 years old. This is consistent with other systematic reviews which have recently been published in the area (Kearney et al., 2013; Beauchet et al., 2009). Studies that stratified the sample according to age were also included but only subgroups with a mean age of over 65 years were considered.

Study selection

The electronic databases Embase, Medline, PsycINFO and Web of Science were used to identify relevant literature until 31st August 2016. The search was conducted by combining any of the following terms (fall*, gait, walk*, mobility) with the term IIV and any of its known variations (intraindividual variability, cognitive variability, neurocognitive variability, reaction time variability, response time variability, RT variability, reaction time inconsistency, response time inconsistency, RT inconsistency). A number of terms were added later as further variations of IIV (attentional variability, sustained attention, impaired attention). Following the electronic search, the identified works were subjected to backward and forward searches. This involved examining the reference list of each article and identifying any work that had cited the study since it was published. Finally, key articles and review papers in the area were also examined in order to identify any studies that had been overlooked by the electronic and hand searches. A flow diagram of the study selection process, including the number of excluded studies and reasons for their exclusion, is presented in Figure 2.1.

Figure 2.1: Flow diagram of the study selection process



2.3 Results

Study details

The initial electronic and hand searches identified a total of 555 studies and, of these, 211 full-text articles were obtained for detailed analysis. Two hundred of these articles did not meet the inclusion criteria (e.g., they did not administer RT tasks or did not measure IIV on these tasks) and were excluded. This left a total of 11 studies, seven of which looked at IIV in relation to falls (Table 2.1). Five of these studies examined IIV in relation to gait (Table 2.2) and this included one study that additionally looked at IIV and falls (Bauermeister et al., 2017). These studies assessed a total of 2,923 older adults, the majority of whom were healthy and resided in the local community (n = 2,618). The remainder of the population was made up of Parkinson's disease patients (n = 214) and hospital outpatients (n = 91).

The majority of studies used an age cut-off of 60 years or higher, although two of the 11 studies recruited participants as young as 50 (Bauermeister et al., 2017; O'Halloran et al., 2014). One of these studies (O'Halloran et al., 2014) stratified their sample by age to create a subgroup of young-old (50-65 years) and old-old (65+ years) adults. Only associations for the older subgroup are considered here. As a result, the mean age of all samples included in the review was 70 years old or higher. All but one study (Allcock et al., 2009) screened participants for clinically significant cognitive impairment, defined in most cases using cut-off scores on the Mini Mental State Examination (MMSE; Folstein et al., 1975). Two of the 11 studies screened for cognitive impairment using other recognised diagnostic criteria (Bunce et al., 2016b; Holtzer et al., 2014b) whereas another study used cut-off scores on the Repeatable Battery for the Assessment of Neuropsychological Status (Sukits et al., 2014).The majority of investigations excluded individuals demonstrating cognitive impairment, however, one study (Bunce et al., 2016b) created a subgroup of healthy older adults and mild cognitive impairment patients. Only associations from the cognitively intact group will be considered here.

Of the seven studies that examined associations between IIV and falls, all seven recorded falls history over a period of either 12 months or 24 months. Three studies additionally collected follow-up falls data over a period of 12 months (Bunce et al., 2016b; Allcock et al., 2009) or 66 months (Mirelman et al., 2012). The way in which fallers were classified also varied across studies with some requiring individuals to have fallen more than once during the assessment period (e.g., Hausdorff et al., 2006) or to have experienced an injurious fall (e.g., Bauermeister et al., 2017). Of the five studies examining associations between IIV and gait, four of these included gait speed as a primary outcome measure with the remaining study recording various parameters of gait variability (Sukits et al., 2014).

Table 2.1: Summary of studies investigating IIV in relation to falls that were included in the review

Author (year)	Sample	IIV measure(s)	How were falls classified/measured?	Main findings
Hausdorff et al. (2006)	Community-dwelling fallers ($n = 18$), non-fallers ($n = 25$) and PD patients ($n = 30$)	Raw SD for Go-NoGo, Stroop no interference and Stroop interference	Two falls in the 12 months prior to study and one in the last 6 months	IIV on each task was significantly higher for fallers compared to non-fallers (all $p < .05$)
Allcock et al. (2009)	PD patients ($n = 164$)	Composite CV for SRT, 2-CRT and Digit Vigilance	Fall frequency over the 12 months following the study	The composite CV measure significantly predicted fall frequency, even after correcting for the severity of PD (RR = 4.54, 95% CI 1.18-17.5, $p < .05$)
Reelick et al. (2011)	Geriatric outpatients classified as recurrent ($n = 38$) or non-recurrent fallers ($n = 22$)	CV for 5-CRT	Two falls in the 12 months prior to study	IIV was significantly higher for recurrent fallers compared to non-recurrent fallers ($p < .05$)
O'Halloran et al. (2011)	Community dwelling fallers ($n = 261$) and non-fallers ($n = 197$)	Raw SD, SFV and FFV for SART	One fall in the 12 months prior to study	FFV was significantly associated with falls status (OR 1.14, 95% CI 1.03-1.26, $p < .01$) but Raw SD and SFV were not
Mirelman et al. (2012)	Community dwelling older adults ($n = 256$)	Raw SD for Go-NoGo	Fall frequency over the 66 months following the study	IIV was a strong predictor of fall frequency (RR = 1.19, 95% CI 1.07-1.34, $p < .01$)
Bunce et al. (2016)	Community-dwelling fallers ($n = 91$) and non-fallers ($n = 180$)	Raw SD for SRT and 2-CRT	Two falls or one injurious fall in the 12 months following the study	IIV on the SRT and 2-CRT was not significantly associated with future falls
Bauermeister et al. (2016)	Older adults and hospital outpatients classified as fallers ($n = 42$) or non-fallers ($n = 66$)	CV for SRT, 2-CRT, Flanker, Stroop and Simple Visual Search	Two falls or one injurious fall in the 24 months prior to study	IIV on the 2-CRT, Flanker and Stroop tasks was significantly associated with fall status (all $p < .05$) but IIV on the other tasks was not

Notes: 2-CRT = 2-choice reaction time; 5-CRT = 5-choice reaction time; CV = coefficient of variation; FFV = fast frequency variability; PD = Parkinson's disease; Raw SD = raw standard deviation; SART = sustained attention to response task; SFV = slow frequency variability; SRT = simple reaction time

Table 2.2: Summary of studies investigating IIV in relation to gait measures that were included in the review

Author (year)	Sample	IIV measure(s)	Gait measures	Main findings
de Frias et al. (2011)	Community-dwelling older adults (n = 48) and PD patients (n = 50)	ISD for SRT, 2-CRT, 4-CRT and 8-CRT	Average time taken to complete two 30ft trials and cadence score (steps per second)	No significant associations were found between IIV on all four tasks and any of the gait measures
O’Halloran et al. (2014)	Community-dwelling adults over the age of 65 (n = 1,426)	Raw SD, SFV and FFV for SART	Average gait speed over two 16ft trials; cut-offs used to define low gait speed	FFV was a significant predictor of low gait speed (OR 1.31, 95% CI 1.08-1.59, $p < .01$) but Raw SD and SFV was not
Holtzer et al. (2014)	Community-dwelling older adults (n = 234)	CV for Flanker	Gait speed over one 8.5m trial under both single and dual-task conditions	IIV correlated highly with ST and DT gait speed ($p < .01$) but only the association with DT gait was significant in a fully adjusted model ($p < .01$)
Sukits et al. (2014)	Community-dwelling older adults (n = 71)	Raw SD for Response Conflict and Perceptual Conflict	Four measures of gait variability (stance time, double support time, step time, step length)	No significant associations were found between IIV on either task and any of the gait variability measures
Bauermeister et al. (2016)	Community-dwelling older adults and hospital outpatients classified as fallers (n = 42) or non-fallers (n = 66)	CV for SRT, 2-CRT, Flanker, Stroop and Simple Visual Search	Average time taken to complete three 4m trials	Walking time correlated highly with IIV on the 2-CRT, Flanker, Stroop and Simple Visual Search tasks (all $p < .01$) but not on the SRT task

Notes: 2-CRT = 2-choice reaction time; 4-CRT = 5-choice reaction time; 8-CRT = 8-choice reaction time; CV = coefficient of variation; FFV = fast frequency variability; PD = Parkinson’s disease; Raw SD = raw standard deviation; SART = sustained attention to response task; SFV = slow frequency variability; SRT = simple reaction time

All studies included at least one measure of IIV although there was great variation in the RT tasks from which these measures were derived. Some studies used simple assessments of psychomotor speed (e.g., Simple Reaction Time task) whereas others used tasks that placed a higher demand on executive function (e.g., Flanker task). There was also variation in the way that measures of variability were computed. Six of the 11 studies calculated the raw standard deviation of RTs (raw SD), with five studies using the coefficient of variation (CV) and the remaining study using the intraindividual standard deviation (ISD). In addition to these three measures, which are described in more detail in the previous chapter, two studies (O'Halloran et al., 2014; O'Halloran et al., 2011) additionally analysed the RT data using a fast Fourier transformation (e.g., Johnson et al., 2007). This produced two further measures of variability: Slow frequency variability (SFV; thought to reflect a continuous slowing down of the RT over the course of the task) and fast frequency variability (FFV; thought to capture moment-to-moment changes in RT during the task).

Associations between IIV and falls

Six of the seven studies that measured falls reported a significant association with at least one measure of IIV (see Table 2.1). One study (Hausdorff et al., 2006) compared the performance of healthy older adults and older fallers on three cognitive tasks: a Go-NoGo task, a Stroop task and a Stroop interference task. The raw SD of response times on all tasks was significantly higher for fallers after controlling for age, gender, education and computer experience. In another study (Reelick et al., 2011), IIV on a 5-choice RT task was significantly higher in a group of recurrent fallers compared to a group of non-recurrent fallers. One investigation (O'Halloran et al., 2011) calculated several measures of IIV from a sustained attention task, although not all were found to be associated with falls. While the raw SD and fast frequency variability (FFV) distinguished between non-fallers, single fallers and recurrent fallers, the slow frequency variability (SFV) measure did not. Furthermore, the results of a multivariate linear regression adjusting for age and gender showed that FFV was the only measure significantly associated with fall status.

The remaining four studies also used regression analyses to determine whether IIV was a potential risk factor for falls. One study (Bauermeister et al., 2017) compared the performance of older fallers and non-fallers on a battery of five RT tasks. Logistic regression adjusting for a measure of estimated full-scale IQ demonstrated that IIV on the 2-CRT, Flanker and Stroop tasks, but not on a simple RT or visual search task, was associated with fall status. In one of the three prospective studies (Bunce et al., 2016b), baseline IIV on simple and choice RT tasks was not significantly associated with fall status over the following 12 months in healthy older adults after accounting for education and gender. In another longitudinal investigation of PD patients (Allcock et al., 2009), a composite CV measure was calculated comprising performance on a simple RT, 2-choice RT and digit vigilance task. Negative binomial regression indicated that this measure predicted fall frequency over the following 12 months, even after controlling for scores on the Unified Parkinson's Disease Rating Scale. In the final prospective study (Mirelman et al., 2012), raw SD on a Go-NoGo task was significantly associated with fall frequency during a 66 month follow-up period after controlling for age, gender, education, body mass index, history of falls and grip force.

Associations between IIV and gait

Three of the five studies that assessed gait reported a significant association with at least one measure of IIV (see Table 2.2). One investigation (Bauermeister et al., 2017) examined correlations between the CV on five RT tasks and the average time taken to complete a four metre walk. Strong, positive correlations were reported between IIV on four of the five RT tasks (2-CRT, Flanker, Stroop, Simple Visual Search) and gait performance. Another study (Sukits et al., 2014) examined correlations between IIV on a response conflict and perceptual conflict task and several gait variability parameters: Stance time, double support time, step time and step length. However, no significant associations between IIV and gait variability were reported having adjusted for gait speed and mean RT on the same task. In another investigation (Holtzer et al., 2014b), IIV on the Flanker task was correlated with both single-task and dual-task gait speed. However, in a multivariate linear regression analysis that controlled for age, gender, education, disease comorbidity and gait abnormalities, IIV was only associated with dual-task gait speed.

In a large-scale investigation of 1,426 older adults (O'Halloran et al., 2014), a binary logistic regression analysis was used to determine associations between IIV measures derived from a sustained attention task and low gait speed defined using age and height cut-offs. Here, fast frequency variability (FFV), but not raw SD or slow frequency variability (SFV), distinguished between those with low and normal gait speed after adjusting for age, gender, processing speed, executive function, chronic conditions and medication use. Finally, one study (de Frias et al., 2007) examined IIV on a series of simple and choice RT tasks in relation to three measures of gait speed: Average time taken to complete two trials, average number of steps and cadence score (number of steps per second). However, a multivariate regression analysis did not identify any significant associations between IIV and gait in either healthy older adults or a group of older Parkinson's disease patients.

2.4 Discussion

The present systematic review considered research that had examined the relationship between IIV and either gait or falls in the older population. A total of 11 relevant works were identified after updating the literature search of a recent publication (Graveson et al., 2016). Six studies investigated IIV in relation to falls, four in relation to gait, and one in relation to both. Of the seven studies that assessed falls, six found evidence of a relationship with at least one measure of IIV after adjusting for a range of variables including age, gender and years in education (see Table 2.1). Specifically, more individuals with higher IIV levels were more likely to experience a future fall in longitudinal investigations or have a history of falls in cross-sectional work. By contrast, of the five studies that assessed gait performance, only three of these reported an association with IIV (see Table 2.2). In all three of these studies, greater cognitive variability was associated with a slower walking speed.

This review provides clear evidence for an association between IIV and falls in older adults, and suggests that higher variability may indicate a greater risk of falling in the future. This finding makes sense since IIV is thought to reflect the efficiency of executive and attentional control processes (e.g., Bunce et al., 2004; West et al., 2002; Bunce et al., 1993), deficits in which have been shown to be a risk factor for falls (e.g., Kearney et al., 2013). Previous work has also demonstrated that both IIV and the prevalence of falls increase in cognitively impaired populations such as those diagnosed with dementia (e.g., Hultsch et al., 2000; Tinetti et al., 1988). Furthermore, a number of studies have reported a link between frontal brain integrity, indicated by the presence of white matter hyperintensities, and both IIV and falls (e.g., Bunce et al., 2013; Zheng et al., 2011). Against this background, the association between IIV and falls is completely in line with prior expectations. One of the three prospective studies, however, did not find evidence for this association (Bunce et al., 2016b) even though it was comparable in terms of size and the characteristics of the sample. These non-significant findings could have been due to the low demands of the SRT and 2-CRT tasks used to assess variability. Indeed, neither task produced significant differences in variability levels between fallers and non-fallers in a group of healthy older adults or a group of individuals diagnosed with mild cognitive impairment. It is worth noting, however, that variability on a choice-stepping RT task, which involved stepping on one of four panels when they became illuminated, did predict falls in the impaired group. Nevertheless, the influence of task demands on relationships involving IIV is an important consideration and will be revisited in more detail later in the discussion.

The present findings provided mixed evidence for an association between IIV and gait performance. This is somewhat surprising given that even simple walking tasks have been shown to involve a mix of frontally mediated cognitive and motor processes (e.g., Holtzer et al., 2014b). A number of studies have also provided direct evidence that measures of executive function and attention are associated with gait performance (e.g., Kearney et al., 2013; Lord et al., 2013). It is possible that methodological differences between the five studies that measured gait outcomes were partially responsible for these inconsistent findings. For example, sample sizes were smaller in the two investigations that reported non-significant associations between IIV and gait (Sukits et al., 2014) and, additionally, one of these studies set alpha conservatively at the $p<.01$ level (de Frias et al., 2007). Therefore, it is possible that low statistical power was contributing to the mixed findings regarding gait that were reported here. Furthermore, one of these two studies examined IIV in relation to measures of gait variability (Sukits et al., 2014) rather than measures of gait speed, which were the focus of the other studies. As mentioned in the previous chapter, there is evidence that cognitive processes such as processing speed and executive function are differentially related to different components of gait (e.g., Verlinden et al., 2013). This may also be the case for cognitive variability. Specifically, it could be that IIV is more strongly associated with the “pace” component of gait relative to the “variability” component. Additionally, correlations between cognitive and gait variability in this study controlled for both gait speed and mean RT on the same task from which the IIV measure was derived. This may have weakened the associations that were produced.

An important goal of the present work is establishing whether IIV measures explain additional variance about outcome that is not explained by average performance indicators from the same task (e.g., mean RT). Although not described in the results section, the majority of the reviewed studies additionally reported associations between mean RT and either falls or gait. A number of studies provided evidence that, when mean RT and IIV were measured on the same task, only IIV was significantly associated with falls or gait impairment (Holtzer et al., 2014b; O'Halloran et al., 2014; Reelick et al., 2011; Allcock et al., 2009; Hausdorff et al., 2006). Similarly, the three studies that reported nonsignificant associations between IIV and either falls or gait also reported nonsignificant associations for equivalent measures of mean RT (Bunce et al., 2016b; Sukits et al., 2014; de Frias et al., 2007). Finally, two studies found that both IIV and mean RT derived from the same task was a significant predictor of falls (Mirelman et al., 2012; O'Halloran et al., 2011). Taken together these results suggest that, under certain circumstances, IIV measures may be capturing information about falls and gait that is not captured by mean RT. However, this finding was not consistent across all studies and more work is needed to determine the conditions under which IIV measures are making unique predictions about these outcomes.

Across the 11 reviewed studies, the way that IIV was assessed varied considerably. For example, a total of five IIV metrics were used: Raw SD, CV, ISD, slow frequency variability (SFV) and fast frequency variability (FFV). In the six studies that included the raw SD, the most basic measure of variability, only two found reported a significant association with either falls or gait. By contrast, all four of the studies that used the CV measure, which adjusts for the intraindividual mean RT, found IIV to be a significant predictor of outcome. This suggests that the more sophisticated CV measure may possess greater sensitivity in detecting effects where they exist. This is possibly due to the potential confounds that have been controlled for when computing this measure (e.g., general age-related slowing as captured by mean RT). In addition, two studies by O’Halloran and colleagues (2014; 2011) used a fast Fourier transformation to calculate slow frequency variability (SFV) and fast frequency variability (FFV) measures of variability. They found that FFV on a sustained attention task was associated with both falls and gait speed but SFV on the same task was not. Previous research has suggested that greater FFV may reflect fluctuations in top-down attentional control whereas greater SFV may signal deteriorating brain arousal levels (e.g., Johnson et al., 2007). Therefore, these findings suggest that greater variability in top-down attentional processes may contribute to gait problems and falls in older persons, supporting previous suggestions that IIV is closely tied to attentional processes (Bunce et al., 1993).

A total of 13 RT tasks were administered to participants across the 11 studies and these varied according to the demands they placed on the individual. Some of these tasks can be thought of as simple tests of psychomotor ability (e.g., simple and choice

RT) whereas others rely more on higher-order executive processes such as response inhibition (e.g., Flanker) or information updating (e.g., SART). A total of 11 associations were examined between IIV on a simple or choice RT task and either falls or gait, with only two of these found to be statistically significant. By contrast, of the 11 associations where IIV was derived from tasks that placed higher demands on executive abilities (Go-NoGo, Flanker, Stroop, SART), all 11 of these were statistically significant. These results suggest that the demands of the task used to derive variability measures is influencing relationships involving these measures. Specifically, tasks with higher executive demands seem to be producing the strongest associations between IIV and outcome. This is consistent with previous research demonstrating more pronounced age differences in IIV when measures are derived from, for example, a 4-CRT task with a 1-back condition relative to a simple RT task (Dixon et al., 2007).

To summarise, this review of intraindividual variability, falls and gait considered a total of 11 studies. Six investigations looked at IIV in relation to falls, with five of these finding evidence that greater IIV was associated with an increased risk of falling. Although there are theoretical reasons to expect that IIV would also be related to gait, only three of the five studies that examined this link reported a positive association. However, it is possible that methodological differences between studies were responsible for these inconsistent results. There was evidence that IIV measures were more highly associated with falls and gait than mean RT measures obtained from the same task suggesting that IIV may be capturing unique information about these outcomes. The results also suggested that demands of the task used to assess IIV is important, with evidence suggesting that tasks with higher executive demands were producing stronger associations with gait and falls. While the present study provided a qualitative review of the literature, a further quantitative assessment would allow for the associations involving IIV to be empirically tested. It may also help to elucidate a number of outstanding issues that have been raised in this discussion. Therefore, Study 2, reported in the following chapter, will describe a meta-analysis of the same works covered in this review. In addition to building on the present study, the meta-analysis will have two main aims. First, there will be an empirical comparison of associations involving mean RT and IIV obtained from the same task, thereby providing information about the unique predictive utility of variability measures. Second, there will be a comparison of associations involving IIV derived from tasks with lower and higher executive demands. This will enable a more comprehensive investigation of the effects of task demands on these relationships.

Chapter 3

Study 2: A meta-analysis of past research that has examined IIV in relation to gait and falls

3.1 Introduction

In the opening chapter of this thesis, a review of existing theory and research highlighted the serious physical, emotional and financial costs associated with gait impairment and falling in the older community. Evidence suggests that cognitive decline may be linked to both gait problems (e.g., slower walking) and falls in later life and, therefore, cognitive assessments may have potential for detecting at-risk populations. More specifically, several arguments were presented in support of the notion that measures of intraindividual variability (IIV) may be a useful early screening tool. There are several reasons for this view as Chapter 1 highlighted. First, IIV is thought to reflect fluctuations in the efficiency of executive function and attention, deficits in which are a risk factor for gait impairment and falls. Second, variability levels are higher in cognitively impaired individuals (such as those diagnosed with dementia) whereas the prevalence of gait abnormalities and falls is also higher in these populations. Finally, IIV measures have been found to predict the burden of frontal white matter hyperintensities, which is also greater in fallers and persons suffering from gait impairment.

The previous chapter provided a qualitative review of 11 studies that have examined variability in relation to either falls or gait in old age. This review provided strong evidence that higher IIV was associated with a history of falls in cross-sectional investigations and an increased likelihood of future falls in longitudinal investigations. By contrast, there was mixed evidence of an association between IIV and gait performance, though it was suggested that differences in the methodologies of these studies was contributing to these inconsistent results. The qualitative review also demonstrated that, in some cases, IIV was a better predictor of gait and falls than mean RT derived from the same task. This suggests that variability measures may capture unique information about outcome, although this finding was not consistent across all studies. Finally, there was evidence that the demands of the task used to assess variability was influencing the strength of associations between these measures and either falls or gait. Specifically, IIV metrics derived from tasks placing higher demands on executive control were producing the strongest associations with outcome.

The present chapter will describe a quantitative review of the same 11 studies using meta-analytic procedures. This will allow the strength of relationships involving IIV to be empirically tested. Using these procedures, it will also be possible address a number of methodological concerns that were raised in the previous chapter. For example, it was suggested that low statistical power may have affected the results of the systematic review as some of the studies that measured gait had small sample sizes (Sukits et al., 2014) or set alpha conservatively at the $p < .01$ level (de Frias et al., 2007). In the current work, the number of individuals in each sample will be taken into account statistically and an average effect size across all studies will be produced. Relatedly, some studies included in the review reported associations between IIV and outcome that were adjusted for other variables such as mean RT or gait speed (Sukits et al., 2014). Such adjustments may have weakened associations and potentially prevented them from reaching statistical significance. The present study, therefore, will analyse effect sizes that have been derived from unadjusted associations, thereby eliminating the influence of potentially confounding variables.

A meta-analysis will enable further investigation of two other issues that are central to the work in this thesis. First, the extent to which variability measures are capturing unique information about outcome will be assessed. The qualitative review identified several examples where IIV, but not mean RT on the same task, was significantly associated with either falls or gait speed. However, some studies reported that equivalent measures of IIV and mean RT were equally strong in the prediction of falls (Mirelman et al., 2012; O'Halloran et al., 2011). Therefore, the unique predictive utility of IIV metrics in relation to detecting falls and gait impairment remains unclear. A meta-analysis will empirically test associations involving IIV and mean RT derived from the same task. The resulting summary statistics will provide an indication of the relative strength of each performance measure in relation to outcome.

Second, the extent to which associations between IIV and falls, and IIV and gait, vary according to the demands of the task used to measure variability will be examined. Previous work has demonstrated that age differences in variability are more pronounced when IIV is assessed using tasks that place a high demand on executive function (e.g.,Dixon et al., 2007). In line with these findings, the qualitative review provided evidence that IIV metrics derived from higher demand tasks (e.g., Flanker, Stroop) were the strongest predictors of falls and gait. By contrast, studies that derived these measures from tasks with lower executive demands (e.g., SRT, 2-CRT) tended to report non-significant associations with outcome. The present study will aim to provide further evidence for this trend by conducting separate analyses on effect sizes derived from tasks that place either low or high demands on executive abilities. The resulting summary statistics will reveal the extent to which task demands influence associations between IIV and both falls and gait.

To summarise, the present study will quantitatively review the 11 studies that were examined in the previous chapter. The main aim of this review is to build on Study 1 by empirically testing the strength with which IIV is related to falls and gait speed across these investigations. The use of meta-analytic procedures will make it possible to address outstanding issues from the previous study such as the effect of low statistical power and the influence of confounding variables on relationships involving IIV. This study will also examine measures of mean RT obtained from the same task in relation to falls and gait speed, thereby providing a better indication of the unique predictive utility of IIV measures. Finally, the effect of task demands on relationships involving IIV will be examined by comparing how well variability measures predict outcome when derived from tasks placing either lower or higher demands on executive function.

3.2 Methods

Eligibility criteria and study selection

For details of the criteria that studies had to fulfil to be included in this review, please see the Methods section of Study 1. Information about the selection process used to identify studies can also be found there.

Calculation of effect sizes

As falls data are typically dichotomous (i.e., yes or no) and gait speed data are typically continuous (i.e., measured in seconds), different procedures were used to calculate effect sizes for these outcomes. For falls data, effect sizes in each study were calculated by subtracting the average IIV for the non-fallers group from the average IIV for the fallers group, then dividing this value by the pooled standard deviation. This standardised mean difference, Cohen's *d,* was then transformed to an unbiased estimate, Hedges' *g*, as the former measure is thought to overestimate effect sizes in small samples (Rustenbach, 2003). For gait data, the correlation coefficient *r* between IIV and gait speed can serve as an effect size index that is both standardized and intuitive to interpret. However, as the variance of the effect size depends heavily on the correlation itself, *r* was converted using the Fisher's *z* scale and all analyses were performed using these transformed values.

The successful calculation of effect sizes depends on the availability of information such as the sample size, average IIV values for faller and non-faller groups, and their standard deviations. If this information was not reported in the published article, authors were contacted to obtain the relevant data. Several studies that examined IIV in relation to falls also recorded measures of gait speed. Although associations between IIV and gait speed were not explicitly reported in these investigations, authors from three of the studies (Bunce et al., 2016a; Mirelman et al., 2012; Reelick et al., 2011) provided data that enabled these effect sizes to be calculated. In order to meet the assumption of statistical independence between effects, only one effect size was permitted per study. Where a study reported more than one association between IIV and either falls or gait speed (e.g., they administered several RT tasks), an average of the multiple effect sizes was taken and this value was used in subsequent analyses. Finally, effect sizes were recoded where necessary to ensure they were all in the same direction. For example, when examining effects relating to gait speed, a negative value for Pearson's *r* indicated that lower values of mean RT or IIV (indicating faster or less variable responses) were associated with higher values of gait speed (indicating a faster walk).

Statistical analysis

Meta-analysis of the falls data was carried out first. To begin, study-level effect sizes for associations between IIV on all tasks and falls were assessed. This was done by performing *z*-tests on the Hedges' *g* estimate from each study to determine if it significantly differed from zero. If a study had more than one Hedges' *g* (i.e., they administered more than one RT task), the average of all these values was calculated. A fixed-effects meta-analysis was then performed on these study-level effect sizes using R version 3.3.0 (R Core Team, 2016). This was done twice so that IIV and mean RT could be examined separately in relation to falls. In each meta-analysis, individual effect sizes were pooled together to produce an average effect size that was weighted across studies. *Z*-tests were then performed on the average effect sizes to determine if they significantly differed from zero.

To assess the validity of each meta-analytic model, a chi square statistic, *Q*, was calculated to test for homogeneity among effect sizes. A non-significant *Q* indicates that the observed studies are likely to have come from the same population and, thus, a single effect size is a good descriptor of the data. However, this test has been found to have low statistical power in meta-analyses with a small number of studies (Hardy & Thompson, 1998). As a result, the I^2 index was also calculated to assess the degree of inconsistency in findings across studies. This index represents the percentage of variance across studies that is not attributable to chance alone and is calculated using the formula:

$$\frac{Q-df}{Q} \text{ x } 100 \tag{1}$$

Heterogeneity in study findings is considered to be low when I^2 is 25%, moderate when I^2 is 50%, and high when I^2 is 75% (Higgins et al., 2003).

The next stage of the analysis investigated whether IIV and mean RT measures were more highly associated with outcome when derived from tasks with either low or high executive demands. Hence, the RT tasks used in each study were classified into two categories: psychomotor and executive. Tasks were classified as psychomotor if they predominantly assessed the speed of an individual's response to a stimulus (e.g., simple and choice RT tasks). Tasks were classified as executive if they primarily placed demands on at least one of the three components of executive function described by Miyake and colleagues (Miyake et al., 2000). These components are task switching, response inhibition or information updating and monitoring. A total of 23 tasks were used across the 11 studies included in the meta-analysis. Tasks were classified by the present author and a colleague, resulting in agreement for 22 of the 23 classifications (interrater reliability, Cohen's κ = .916, p < .001). The one classification for which there was a disagreement was referred to a third colleague. Of the 23 tasks, 12 were classified as psychomotor and 11 as executive.

Study-level effect sizes for associations between IIV on psychomotor or executive tasks and falls were then assessed. Here, z-tests were performed on Hedges' g estimates that were averaged across all psychomotor tasks and all executive tasks in each study. This was then repeated for associations involving mean RT. Fixed-effects meta analyses were then performed on study-level effect sizes derived from either psychomotor or executive tasks. This produced an additional four average weighted effect sizes that were then subjected to z-tests. For one of the seven studies that measured falls (Allcock et al., 2009), it was not possible to calculate task-specific effect sizes using the available data. Consequently, this study was excluded from this part of the analysis.

Meta-analysis of the gait data was then carried out following the same procedures that were described for the falls data. Study-level effect sizes between either mean RT or IIV on all tasks and gait speed were examined first. This was done by converting the untransformed correlation coefficients *r* for each study into *t*-values using the following formula:

$$\frac{r}{\sqrt{(1-r^2)/(N-2)}} \tag{2}$$

Critical values of *t* were then consulted to determine the statistical significance of each study-level effect. Following this, fixed-effects meta-analyses were conducted and *z*-tests were performed on the average weighted effect sizes that were produced. These steps were then repeated for study-level effect sizes derived from either psychomotor or executive tasks. A further four meta-analyses were carried out at this stage, producing a total of 12 meta-analyses across both the falls and gait data.

3.3 Results

A total of 11 studies were identified by the literature search. Six of these examined IIV in relation to falls, four in relation to gait, and one in relation to both. Descriptive information for these studies, including the age and background of the sample and the methods used to assess each of the key variables, can be found in the Results section of Study 1 (see Tables 2.1 and 2.2). Authors of three of the studies that measured falls provided additional data via email correspondence that enabled effect sizes describing the relationship between IIV and gait speed to be calculated. This resulted in a total of seven studies for which associations between IIV and falls could be analysed (n = 4 with at least one psychomotor task, n =4 with at least one executive task). For IIV and gait speed there was a total of eight studies (n = 5 with at least one psychomotor task, n = 5 with at least one executive task).

Variability, mean RT and falls

All task estimates: Study-level effect sizes averaged across all RT tasks for the relationship between IIV and falls, or mean RT and falls, are presented in Table 3.1. Positive values of Hedges' *g* indicate that fallers had slower reaction times or more variable responses on the given task(s). Effect sizes for each study ranged from 0.18 to 1.03 for mean RT, and 0.14 to 1.05 for IIV. After conducting z-tests on these values, study-level effects for both IIV and mean RT were found to be significantly different than zero in four of the seven studies (Bauermeister et al., 2017; Mirelman et al., 2012; O'Halloran et al., 2011; Hausdorff et al., 2006). Fixed-effects meta-analyses were than carried out to test the association between mean RT and falls, and IIV and falls. For each meta-analysis, forest plots were generated displaying the effect size (with 95% confidence intervals) and weight (indicated by the size of the black square) for each individual study, and the weighted average effect size across all studies (Figures 3.1). The weighted average effect size for associations between IIV and falls was 0.34 (Figure 3.1a) and this was found to significantly differ from zero at the $p < .05$ level. The weighted average effect size for associations between mean RT and falls was 0.32 (Figure 3.1b) and this also differed from zero at the $p < .05$ level. Tests for heterogeneity among effect sizes were non-significant for both IIV and mean RT (Q = 2.35 - 2.40) whereas inconsistency in study findings was found to be low for both models ($I^2 = 0.0\%$). This suggested that a fixed-effects estimate was a good descriptor of the data.

Psychomotor task estimates: Study-level effect sizes averaged across psychomotor tasks for associations between either IIV or mean RT and falls can be seen in Table 3.2. Effect sizes for each study ranged from 0.18 to 1.08 for mean RT predicting falls, and 0.14 to 1.42 for IIV predicting falls. After conducting z-tests on these values, study-level effects for both IIV and mean RT significantly differed from zero in two of the four studies (Bauermeister et al., 2017; Hausdorff et al., 2006). As shown in Figure 3.1c, the weighted average effect size for associations between IIV and falls was 0.47 and this significantly differed from zero ($p < .05$). For associations between mean RT and falls, this value was 0.42 (Figure 3.1d) which did not significantly differ from zero. Tests for heterogeneity among effect sizes were non-significant for both IIV and mean RT (Q =

Table 3.1: Study-level effect sizes for IIV or mean RT predicting falls averaged across all tasks

Study	**RT task(s) used in calculation**	**mRT - Hedges' *g* (95% CI)**	**IIV - Hedges' *g* (95% CI)**
Allcock et al. (2009)	SRT, 2-CRT, Digit vigilance	.182 (-.14/.50)	.251 (-.07/.57)
Bauermeister et al. (2016)	SRT, 2-CRT, Flanker, Stroop, Visual search	.579 (.19/.97)**	.622 (.23/1.02)**
Bunce et al. (2016)	SRT, 2-CRT	.181 (-.07/.43)	.140 (-.11/.39)
Hausdorff et al. (2006)	Go-NoGo, Stroop interference, Stroop no interference	1.03 (.40/1.67)**	1.05 (.41/1.68)**
Mirelman et al. (2012)	Go-NoGo, Stroop	.188 (-.08/.46)	.340 (.07/.61)*
O'Halloran et al. (2011)	SART	.315 (.13/.50)**	.250 (.06/.44)**
Reelick et al. (2011)	5-CRT	.206 (-.31/.73)	.269 (-.25/.79)

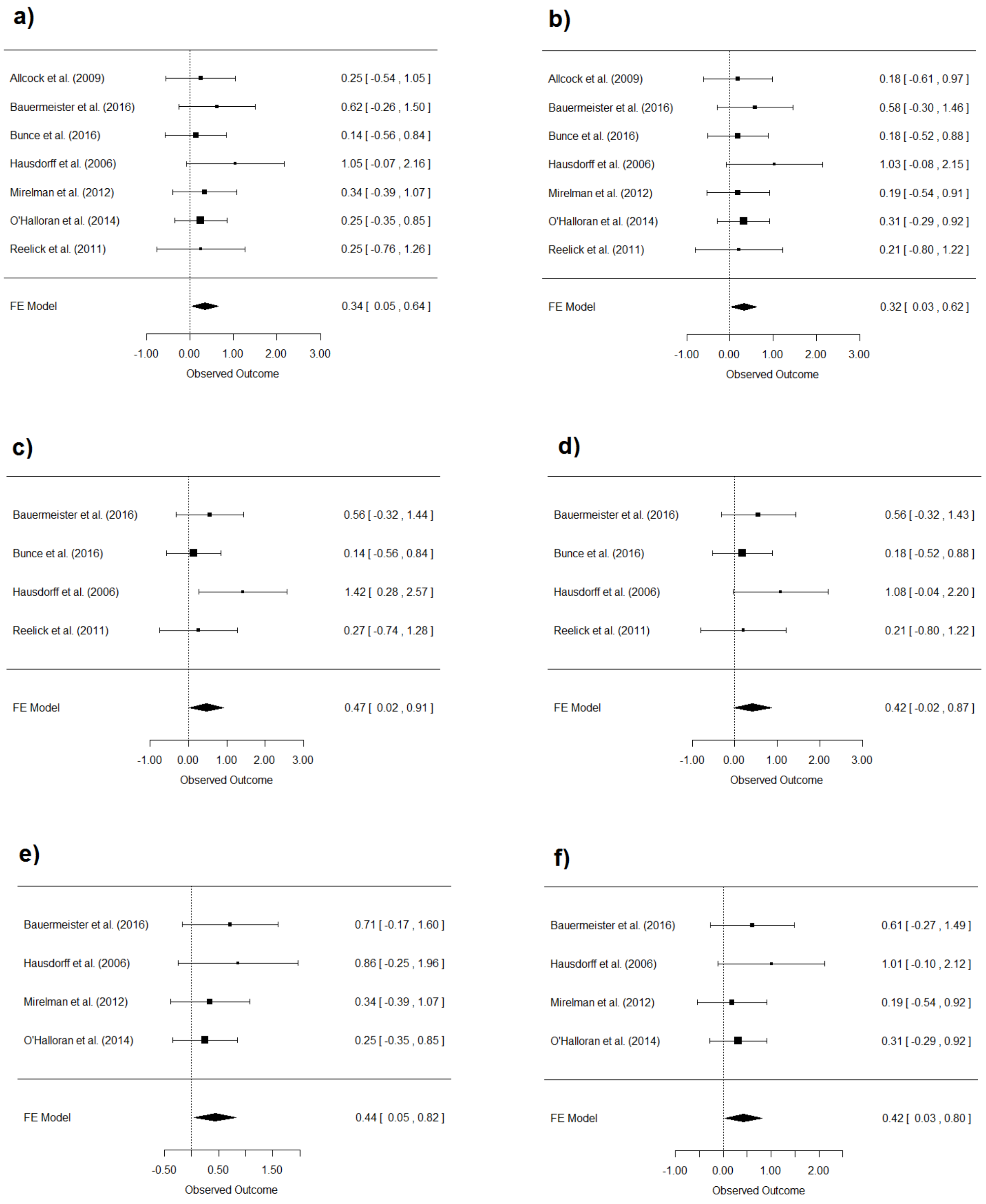
Notes: * p < .05 ** p < .01
2-CRT = 2-choice reaction time; 5-CRT = 5-choice reaction time; SART = sustained attention to response task; SRT = simple reaction time

Table 3.2: Study-level effect sizes for IIV or mean RT predicting falls averaged across either psychomotor or executive tasks

Study	**Task classification**	**RT task(s) used**	**mRT - Hedges' *g* (95% CI)**	**IIV - Hedges' *g* (95% CI)**
Bauermeister et al. (2016)	Psychomotor	SRT, 2-CRT, Visual search	.558 (.17/.95)**	.561 (.17/.95)**
Bauermeister et al. (2016)	Executive	Flanker, Stroop	.610 (.22/1.00)**	.714 (.32/1.11)**
Bunce et al. (2016)	Psychomotor	SRT, 2-CRT	.181 (-.07/.43)	.140 (-.11/.39)
Hausdorff et al. (2006)	Psychomotor	Stroop no interference	1.08 (.44/1.72)**	1.42 (.76/2.09)**
Hausdorff et al. (2006)	Executive	Go-NoGo, Stroop interference	1.01 (.38/1.64)**	.858 (.23/1.48)**
Mirelman et al. (2012)	Executive	Go-NoGo, Stroop	.188 (-.08/.46)	.340 (.07/.61)*
O'Halloran et al. (2011)	Executive	SART	.315 (.13/.50)**	.250 (.06/.44)**
Reelick et al. (2011)	Psychomotor	5-CRT	.206 (-.31/.73)	.269 (-.25/.79)

Notes: * p < .05 ** p < .01
2-CRT = 2-choice reaction time; 5-CRT = 5-choice reaction time; SART = sustained attention to response task; SRT = simple reaction time

Figure 3.1: Forest plots displaying the study-level and average weighted effect sizes for the following predictors of falls: a) IIV on all tasks, b) mean RT on all tasks, c) IIV on psychomotor tasks, d) mean RT on psychomotor tasks, e) IIV on executive tasks, f) mean RT on executive tasks



2.05 – 3.76) whereas inconsistency in study findings was found to be low for both models (I^2 = 0.0 – 20.1%).

Executive task estimates: Study-level effect sizes averaged across executive tasks ranged from 0.19 to 1.01 for mean RT predicting falls, and 0.25 to 1.42 for IIV predicting falls (Table 3.2). Z-tests revealed that study-level effects for both mean RT and IIV were significantly different from zero in three of the four studies (Bauermeister et al., 2017; O'Halloran et al., 2011; Hausdorff et al., 2006). One additional study also produced an effect for IIV that significantly differed from zero (Mirelman et al., 2012). The weighted average effect size was 0.44 for associations between IIV and falls (Figure 3.1e), and 0.42 for associations between mean RT and falls (Figure 3.1f). Both average effects were found to significantly differ from zero (ps < .05). Tests for heterogeneity among effect sizes were non-significant for both IIV and mean RT (Q = 2.13 - 2.23) whereas inconsistency in study findings was found to be low for both models (I^2 = 0.0%).

Variability, mean RT and gait speed

All task estimates: Study-level effect sizes averaged across all RT tasks for the relationship between IIV and gait speed, or mean RT and gait speed, are shown in Table 3.3. Effect sizes for each study ranged from -0.49 to 0.06 for mean RT predicting gait speed, and -0.39 to 0 for IIV predicting gait speed. After converting these correlation coefficients to *t*-values, study-level effects in three studies were statistically significant for both mean RT and IIV (Bauermeister et al., 2017; Holtzer et al., 2014b; O'Halloran et al., 2014). A further two studies were found to have significant effects for just mean RT (Reelick et al., 2011; de Frias et al., 2007). In all cases, quicker or less variable responding was associated with better walking performance. Fixed-effects meta-analyses indicated that the average weighted effect size for associations between IIV and gait speed was -0.29 (Figure 3.2a), and for associations between mean RT and gait speed was -0.34 (Figure 3.2b). Z-tests revealed that both average effects significantly differed from zero at the p < .05 level. Tests for heterogeneity among effect sizes were non-significant for both IIV and mean RT (Q = 2.90 - 6.35) whereas inconsistency in study findings was found to be low for both models (I^2 = 0.0%).

Table 3.3: Study-level effect sizes for IIV or mean RT predicting gait speed averaged across all tasks

Study	**RT task(s) used in calculation**	**mRT – Pearson's *r***	**IIV – Pearson's *r***
Bauermeister et al. (2016)	SRT, 2-CRT, Flanker, Stroop, Visual search	-0.492**	-0.391**
Bunce et al. (2016)	SRT, 2-CRT	0.057	-0.002
de Frias et al. (2007)	SRT, 2-CRT, 4-CRT, 8-CRT	-0.222*	-0.039
Holtzer et al. (2014)	Flanker	-0.163*	-0.216**
Mirelman et al. (2012)	Go-NoGo, Stroop	-0.105	-0.085
O'Halloran et al. (2014)	SART	-0.174**	-0.216**
Reelick et al. (2011)	5-CRT	-0.438**	-0.095
Sukits et al. (2014)	Choice response, Perceptual conflict, Response conflict	-0.061	0

Notes: * p < .05 ** p < .01
2-CRT = 2-choice reaction time; 5-CRT = 5-choice reaction time; SART = sustained attention to response task; SRT = simple reaction time

Psychomotor task estimates: Study-level effect sizes averaged across psychomotor tasks for associations between either IIV or mean RT and gait speed can be seen in Table 3.4. Effect sizes for each study ranged from -0.47 to 0.06 for mean RT predicting gait speed, and -0.32 to 0.04 for IIV predicting gait speed. In three of the five studies, a significant effect was found for mean RT (Bauermeister et al., 2017; Reelick et al., 2011; de Frias et al., 2007) whereas only one of these reported a significant effect for IIV (Bauermeister et al., 2017). The average weighted effect size for associations between IIV and gait speed was -0.15 (Figure 3.2c), and for associations between mean RT and gait speed was -0.41 (Figure 3.2d). Neither of these average effects were found to significantly differ from zero. Tests of heterogeneity among effect sizes were non-significant for both IIV and mean RT (Q = 1.88 – 5.43). Inconsistency in study findings was found to be low for the model where IIV was the predictor (I^2 = 0.0%) and low-to-moderate for the model where mean RT was the predictor (I^2 = 26.3%).

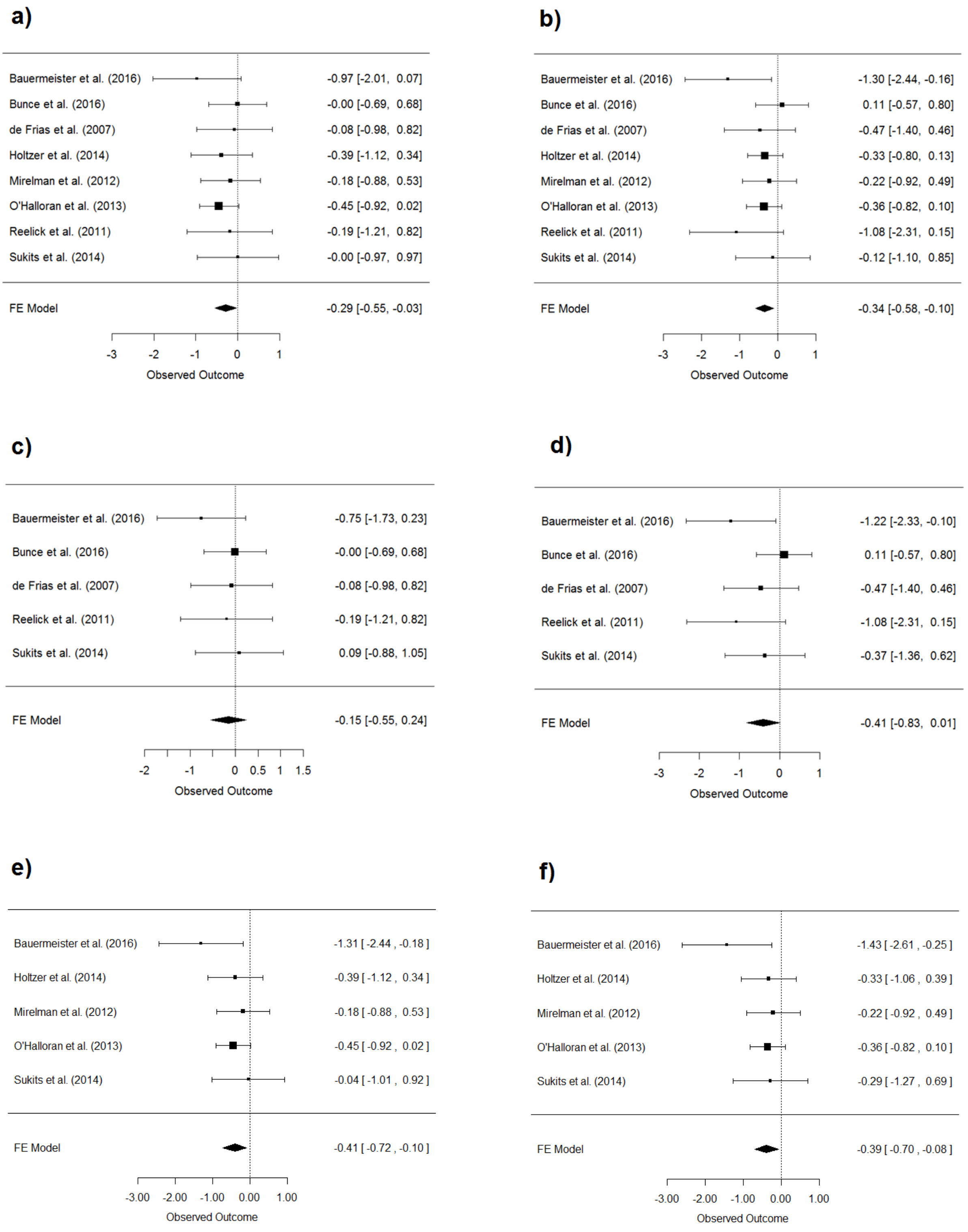
Table 3.4: Study-level effect sizes for IIV or mean RT predicting gait speed averaged across either psychomotor or executive tasks

Study	**Task classification**	**RT task(s) used**	**mRT – Pearson's *r***	**IIV – Pearson's *r***
Bauermeister et al. (2016)	Psychomotor	SRT, 2-CRT, Visual search	-0.471**	-0.320**
Bauermeister et al. (2016)	Executive	Flanker, Stroop	-0.523**	-0.498**
Bunce et al. (2016)	Psychomotor	SRT, 2-CRT	0.057	-0.002
de Frias et al. (2007)	Psychomotor	SRT, 2-CRT, 4-CRT, 8-CRT	-0.222*	-0.039
Holtzer et al. (2014)	Executive	Flanker	-0.163*	-0.216**
Mirelman et al. (2012)	Executive	Go-NoGo, Stroop	-0.105	-0.085
O'Halloran et al. (2014)	Executive	SART	-0.174**	-0.216**
Reelick et al. (2011)	Psychomotor	5-CRT	-0.438**	-0.095
Sukits et al. (2014)	Psychomotor	Choice response	-0.179	0.044
Sukits et al. (2014)	Executive	Perceptual conflict, Response conflict	-0.001	-0.022

Notes: * p < .05 ** p < .01
2-CRT = 2-choice reaction time; 5-CRT = 5-choice reaction time; SART = sustained attention to response task; SRT = simple reaction time

Executive task estimates: Study-level effect sizes averaged across executive tasks ranged from -0.52 to 0 for mean RT predicting gait speed, and -0.5 to -0.02 for IIV predicting gait speed (Table 3.4). Three of the five studies reported significant study-level effects for both mean RT and IIV (Bauermeister et al., 2017; Holtzer et al., 2014b; O'Halloran et al., 2014). The average weighted effect size for associations between IIV and gait speed was -0.41 (Figure 3.2e), and for associations between mean RT and gait speed was -0.39 (Figure 3.2f). Both average effects significantly differed from zero at the p < .05 level. Tests for heterogeneity among effect sizes were non-significant for both IIV and mean RT (Q = 3.41 – 3.83) whereas inconsistency in study findings was found to be low for both models (I^2 = 0.0%).

Figure 3.2: Forest plots displaying the study-level and average weighted effect sizes for the following predictors of gait speed: a) IIV on all tasks, b) mean RT on all tasks, c) IIV on psychomotor tasks, d) mean RT on psychomotor tasks, e) IIV on executive tasks, f) mean RT on executive tasks



3.4 Discussion

In the present study, a meta-analysis was performed on seven studies examining IIV and mean RT in relation to falls in older adults, and eight studies examining them in relation to gait. Both measures significantly predicted fall status and gait speed when averaged across all cognitive tasks. However, there was considerable variation in the effect sizes between studies. Separate analyses were carried out to assess the influence of task demands on these relationships. When effect sizes were derived from tasks with low executive demands (i.e., psychomotor tasks), IIV but not mean RT was significantly associated with falls. Corresponding models for gait speed did not identify IIV or mean RT as significant predictors. When effect sizes were derived from tasks with high executive demands (i.e., executive tasks), IIV and mean RT were found to be associated with both falls and gait speed. However, while almost all study-level effects relating to falls were significant, this was only the case for some of the studies that examined gait. Finally, heterogeneity among effect sizes and inconsistency in findings between studies was low throughout, indicating that fixed-effects estimates provided a good description of the data.

Variability, mean RT and falls

A strong association between IIV and falls is in line with the findings from the qualitative review, as well as the theoretical arguments presented in Chapter 1. This finding was consistent across analyses that considered all RT tasks, as well as analyses that considered psychomotor or executive tasks separately. This suggests that the demands of the task did not heavily influence associations between IIV and falls, contrary to prior expectations. However, inspection of the task-specific effect sizes within each study indicated that IIV was more consistently associated with falls when measures were derived from executive tasks (4 out of 4 studies) relative to psychomotor tasks (2 out of 4 studies). This inconsistency in outcomes could be partly due to the particularly large effect that one study (Hausdorff et al., 2006) produced for the psychomotor task (Hedges' $g = 1.42$). This may have caused the average effect size across all studies to be overestimated. If this were the case, one might infer that IIV measures are actually a better predictor of falls when derived from tasks that place high demands on executive abilities as the findings from Study 1 suggested. However, further research is needed to better understand whether certain types of RT task produce stronger relationships between IIV and falls than others.

Mean RT measures also predicted falls in two of the three analyses, partially supporting previous work that has demonstrated associations between processing speed and falls outcomes (e.g., Sosnoff et al., 2013; Anstey et al., 2006). However, a non-significant relationship between mean RT and falls was reported when effect sizes were derived only from psychomotor tasks. It could be that response time latencies on tasks with low cognitive demands (e.g., SRT task) are not useful in distinguishing between fallers and non-fallers, perhaps as they capture deficits in motor function rather than deficits in higher-order cognitive abilities (e.g., executive function) that may be contributing to falls. By contrast, IIV measures derived from psychomotor tasks did significantly predict fall status. It should also be noted that average effects for IIV predicting falls were marginally higher than those for mean RT predicting falls in all three meta-analyses. These findings provide support for the notion that IIV measures may be capturing unique information about falls that is not picked up by measures of mean RT. However, the small size of these differences suggests that the two are closely linked, and highlights the difficulty of distinguishing the effects of greater variability from those of slower responding.

Variability, mean RT and gait speed

The present findings provided evidence that higher IIV levels were associated with slower walking speed in older persons. This is in line with prior expectations and the theoretical linkage between IIV and gait presented in previous chapters. For example, IIV is thought to reflect fluctuations in executive control mechanisms and measures of executive function have been shown to be good predictors of future gait performance (e.g., Watson et al., 2010; Atkinson et al., 2007). Investigating the influence of task demands on the relationship between IIV and gait revealed that variability was a greater predictor of outcome when derived from tasks with higher relative to lower executive demands. This finding supports observations in the qualitative review as well as previous work reporting greater age differences in variability when derived from tasks with higher executive demands relative to simple psychomotor tasks (Dixon et al., 2007). Similarly, a significant association between mean RT and gait speed was observed when effect sizes were derived from executive tasks but not psychomotor tasks. Taken together, these findings suggest both IIV and mean RT are more highly associated with gait when assessed with tasks that place a higher demand on executive abilities. This is in line with expectations given that more demanding tasks are likely to produce greater between-person variation in these measures, thereby increasing their ability to detect effects where they exist.

In contrast to the work examining IIV and falls, there was no evidence that IIV measures were capturing unique predictive information about gait performance. In fact, for analyses where effects were averaged across all tasks and only psychomotor tasks, mean RT was more strongly associated with gait than variability. One possible explanation for this finding is that response speed measures derived from psychomotor tasks may be better at detecting differences in gait performance when walking is not attentionally-demanding (i.e., under ST conditions). This is likely since both tasks rely heavily on related motor processes, but do not place a great demand on higher-order cognitive abilities. Finally, as with the falls data, there was considerable variation in the size of study-level effects. This may be due to between-study differences in the individuals who were assessed. For example, the two investigations that produced the largest correlations between IIV and gait both included hospital outpatients in their sample (Bauermeister et al., 2017; Reelick et al., 2011). It is likely that gait impairment and other limitations related to physical function are more common in these groups. Previous research has demonstrated that older adults with deficits in sensory and motor processes rely heavily on cognitive abilities, and particularly executive function, to maintain a safe and steady walk (e.g., Yogev-Seligmann et al., 2008). Given that IIV is thought to reflect fluctuations in executive control, a stronger association between variability and gait performance in groups that have been admitted to hospitals is to be expected.

Conclusion

The present work develops the qualitative review carried out in Study 1 in several ways. First, the meta-analytic procedures employed made it possible to evaluate weighted associations averaged across a number of studies. This provided an empirical and more precise estimation of the strength with which IIV was related to both falls and gait. Second, the results of this study were not influenced by potentially confounding variables or reduced statistical power, both of which were identified as limitations that may have affected the results of the previous review. Third, mean RT measures obtained from the same task were additionally examined in relation to both falls and gait speed, thereby providing a better understanding of the unique predictive utility of IIV in relation to these outcomes. Finally, IIV metrics derived solely from tasks with either low or high executive demands were independently tested. This made it possible to examine the effect that task demands were having on relationships between IIV and outcome.

Taken together, the results of the qualitative and quantitative reviews provide strong evidence of a link between variability and falls in old age, and slightly less compelling evidence in favour of a link with gait performance. Both studies found that the strength of these relationships varied according to the way that IIV was assessed, with tasks placing a higher demand on executive abilities producing consistently stronger associations. Both reviews also provided evidence that variability was significantly predicting fall status when mean RT from the same task was not. These findings suggest that IIV measures may be capturing unique information about falls outcomes. This was not the case for studies examining gait, however, as mean RT proved to be just as strong in the prediction of these outcomes as variability.

Future directions

Due to the small number of studies reviewed in the present work, further investigation of the relationship between IIV, gait and falls in older adults is warranted. One objective of future empirical work is to provide further evidence that higher variability levels are a reliable risk factor for future falls and gait impairment. Establishing the extent to which IIV measures are making unique predictions about falls and gait outcomes also remains a pressing matter. This is particularly the case for investigations of gait as the evidence provided by empirical work to date has been mixed. To that end, future research would benefit from the use of IIV metrics that control for mean RT on the same task (e.g., coefficient of variation) to ensure that effects due to more variable responding are not confounded by the speed of the response. Finally, the previous chapters provided evidence that IIV is a better predictor of both falls and gait performance when derived from tasks that place a greater demand on executive function. In order to better understand the importance of task demands in these relationships and to ensure that potentially significant effects do not go undetected, future work should aim to measure variability using tasks with both high and low executive demands.

In addition to investigating IIV in relation to both falls and gait, there is also good reason to examine whether these relationships vary according to age. Previous work has demonstrated that both cognitive and motor functions undergo age-related changes. For example, between early and later old age there is a marked decline in cognitive ability across multiple cognitive domains (e.g., Buckner, 2004) as well as in levels of variability (e.g., Lovden et al., 2007). This transition from early to later old age is also associated with deleterious changes in gait performance such as reduced speed and reduced stability (e.g., Ko et al., 2009) which are likely to increase an individual's risk of falling. There is also evidence that age may moderate the relationship between cognitive and motor processes. For example, one study showed that the association between these domains strengthens with age as a result of the higher demands that motor processes place on attentional resources (Voelcker-Rehage & Alberts, 2007). Furthermore, as previously mentioned, the role that higher-order cognitive processes play in maintaining gait performance has been shown to increase during later life (e.g., Yogev-Seligmann et al., 2008). Given the link between variability and executive function, one might expect IIV measures to better predict both gait and falls outcomes in later old age. Since no studies to date have investigated how relationships between IIV, gait and falls vary according to age, this is an important aim for empirical work going forward.

Future research would also benefit from investigating mechanisms that are underlying the effects that IIV is having on both gait and falls. This issue has received little attention in experimental work to date. Elsewhere in cognitive ageing research, however, mechanisms underpinning the age-related differences in cognitive function have been tested using mediator models (Salthouse, 1994, 1992). This approach involves introducing potential explanatory variables into models where predictor and outcome variables have been found to be associated. Then, the strength of this association is examined after these variables have been statistically taken into account (Preacher & Hayes, 2004; Salthouse, 1992; Baron & Kenny, 1986). Only one study has attempted to apply this approach to investigations of IIV and falls in older adults. Here, motor function but not higher-order executive abilities was found to be playing an important role in this relationship (Bauermeister et al., 2017). This is surprising given that IIV is thought to reflect levels of executive control, deficits in which have been identified as a risk factor for future falls (Kearney et al., 2013). Further research is therefore needed to examine the extent to which different cognitive and physiological processes are underlying associations involving IIV. Such work would better elucidate the pathways through which variability is contributing to falls and gait performance.

The following chapter will describe the first of four experimental studies that were carried out. Study 3 will build on the findings of the two review chapters by examining cross-sectional associations between IIV, gait and falls in a group of cognitively intact older adults. Variability will be assessed with a battery of RT tasks that vary according to the executive demands placed on the individual, and using a metric that controls for mean RT derived from the same task. Gait performance will be assessed with a simple walking speed test that has been widely used in clinical geriatric settings. The speed of individuals will be measured continuously (i.e., in seconds) as well as dichotomously (i.e., slow and fast) using a threshold that has previously been linked to multiple adverse outcomes. Finally, a mediational approach will be used to investigate whether differences in cognitive (e.g., executive function, processing speed) or physiological (e.g., vision, grip strength) function are underlying relationships between IIV and falls, and IIV and gait, where they are observed.

Chapter 4

Study 3: An empirical investigation of the association between variability, gait and falls

4.1 Introduction

The previous two chapters reviewed existing research that has examined intraindividual variability (IIV) in relation to either falling or gait impairment in older adults. These reviews provided strong evidence that IIV measures were associated with falls, and slightly weaker evidence for a link with gait performance. For investigations of both gait and falls, effect sizes varied greatly between studies and it was suggested that this was due to methodological differences relating to the sample and the way in which variability was assessed. Indeed, IIV metrics were found to be stronger predictors of both falls and gait when derived from tasks that placed higher demands on executive abilities. The two reviews also investigated the unique predictive utility of variability measures relative to mean RT measures derived from the same task. For falls, the findings suggested that IIV was capturing unique information about outcome, however, there was less evidence that this was the case for gait.

The present experimental study will build on the work described in these reviews by examining relationships between IIV, gait and falls in a population of cognitively intact older adults. As discussed in Chapter 1, gait impairment has been identified as a reliable risk factor for future falls (Deandrea et al., 2010). Additionally, previous research has linked decline in cognitive abilities such as executive function to reductions in gait performance (e.g., Watson et al., 2010). Given that age-associated changes in gait are likely to precede falls, it follows that detecting subtle cognitive changes which may contribute to gait impairment may also be useful in the early detection of potential fallers. It is this possibility that motivates the present study as IIV measures have been shown to predict future deficits in a range of cognitive abilities including executive function (e.g., Yao et al., 2016; Bielak et al., 2010b). Despite clear linkage between gait problems and falls in old age, and evidence suggesting that IIV measures might be useful in the prediction of these outcomes, only a handful of studies have explored how these three constructs are related. In one study that took place in our laboratory, motor function captured by measures of lower and higher extremity muscle strength, gait and balance was shown to mediate the associated between IIV and falls (Bauermeister et al., 2017). Another investigation from members of our research group demonstrated that the association between IIV on a choice stepping RT task and falls varied according to whether individuals exhibited normal or abnormal gait (Bunce et al., 2016a).

These findings provide some evidence that gait may be playing a role in the relationship between variability and falls. However, the populations that were sampled in the aforementioned studies consisted partly of clinical falls patients (Bauermeister et al., 2017) or individuals diagnosed with Mild Cognitive Impairment (Bunce et al., 2016a). Furthermore, the latter of these two studies administered a choice stepping RT task that required specialised equipment to record the responses participants made with their feet. Clearly then, more research is needed to examine the role that gait is playing in this relationship in healthy older populations, and also using hand-administered tasks that can be easily applied in a variety of contexts. With this in mind, the work in the following chapters aims to establish a framework that connects subtle age-related deficits in cognition (represented by higher IIV), early changes in physical mobility (represented by a slowing in gait) and an increased risk of falling. This approach will hopefully shed more light on the mechanisms by which cognitive decline contributes to both gait problems and falls in old age.

Another important question that has not been comprehensively addressed by previous research is how the relationship between IIV, gait and falls varies according to age. This is a notable omission as both cognitive and motor functions undergo changes with increasing age. For example, cognitive performance across a number of domains is fairly well maintained between the ages of 50 and 70 but declines substantially in the 20 years that follow (Buckner, 2004). There is also evidence of a similar trend in variability levels. Although within-person increases in IIV are detectable even in middle-aged adults (Bielak et al., 2014), these changes are considerably greater in persons over the age of 70 (Lovden et al., 2007; MacDonald et al., 2003). As mentioned in Chapter 1, ageing is associated with a deterioration in physical and sensory functioning that begins in middle adulthood and worsens during later life (Sigelman & Rider, 2009). Such deterioration has been linked to alterations in posture and balance (Li et al., 2001; Shumway-Cook & Woollacott, 1995) that may cause an individual’s gait to become less stable, thereby increasing their risk of falling. It has been suggested that older adults direct more attentional resources towards walking in order to compensate for these age-related changes (Yogev-Seligmann et al., 2008; Woollacott & Shumway-Cook, 2002). Given that higher-order executive abilities are implicated in the allocation of attentional resources (e.g., Ble et al., 2005), it is not surprising that an increased reliance on executive function has been found in later life in order to maintain walking performance (Yogev-Seligmann et al., 2008).

Taken together, these findings suggest that age may influence both cognitive and motor performance in older persons. However, there is also evidence that age may moderate the relationship between the two. For example, research has demonstrated that the association between cognitive and motor abilities strengthens with age as a result of the higher demands that motor processes place on attentional resources (Voelcker-Rehage & Alberts, 2007). Based on this evidence, there is good reason to investigate associations between IIV, gait and falls in both the younger and older age ranges. It was noted earlier that executive function and attention play a greater role in gait with increasing age, and also that variability is thought to reflect fluctuations in executive and attentional control. Against this background, it is expected that IIV measures would be stronger predictors of both gait and falls outcomes in later old age relative to early and middle old age. This hypothesis will be tested here.

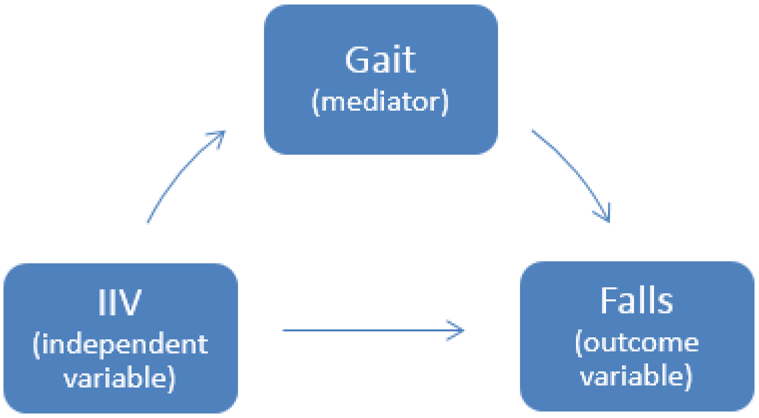
In the present work, gait performance will be assessed over a distance of four metres, with the average time taken to complete three trials used as a measure of walking speed. This measure has been widely used in clinical geriatric settings (Studenski et al., 2003) and has been recommended for assessing a range of conditions characterised by poor mobility such as frailty (WGFOCL, 2008) and “dismobility” (Cummings et al., 2014). Although gait speed is most commonly measured as a continuous variable, the present research will additionally use a cut-off of 1.0 m/s to separate older adults with “slow” or “normal” walking speed. This cut-off represents a clinically meaningful boundary as individuals who walk slower than 1.0 m/s have been shown to be more at risk of a range of adverse outcomes (Studenski et al., 2011; Verghese et al., 2011; Rosano et al., 2008). The present study will be the first to examine variability in relation to a specific cut-off for walking speed, which will help provide insights into whether such measures are useful in distinguishing between older adults who are healthy and functional, and those who are not.

As previously discussed in the first chapter, IIV can be assessed with several metrics that vary in their sophistication and the extent to which they take confounding influences into account. The importance of distinguishing variability measures from average performance measures obtained from the same cognitive task has already been emphasised. Accordingly, IIV in the present study will be assessed using the coefficient of variation (CV) as this metric adjusts for individual differences in mean RT in its calculation. A further advantage of this measure is that it is quick and easy to compute, making it suitable for use in a wide range of clinical and applied settings. Another important issue identified in the review chapters was the influence that cognitive task demands may be having on associations between IIV and outcome. There was clear evidence that tasks placing higher demands on executive abilities produced stronger associations with both gait and falls than tasks with low executive demands. In the present study a battery of five RT tasks will be administered and these tasks will vary according to the demands they place on executive function. Variability on each of the tasks will then be examined in relation to both gait speed and falls, allowing for the influence of task demands on these relationships to be assessed

In addition to examining relationships between IIV, gait and falls, another important goal of the present research is to identify mechanisms that may be underlying these relationships. One way that researchers have previously attempted to do this is by using a mediational approach (Preacher & Hayes, 2004; Salthouse, 1992; Baron & Kenny, 1986). In this approach, potential explanatory variables, or mediators, are introduced into models where predictor and outcome variables have been found to be associated. In order to better understand what is meant by the term mediator, a path diagram has been created depicting the hypothesised relationship between IIV, gait and falls (see Figure 4.1). Here, IIV (predictor variable) and gait (mediator) both causally predict falls (outcome variable) whereas IIV also predicts gait. In order for gait to mediate the relationship between IIV and falls, three criteria need to be satisfied: 1) changes in IIV need to be associated with changes in gait, 2) changes in gait need to be associated with changes in falls, and 3) after statistically controlling for gait, the association between IIV and falls needs to be substantially attenuated. If the relationship between IIV and falls was fully mediated, this would provide evidence that gait is a major mechanism underlying this relationship. However, as there are likely to be multiple constructs having direct and indirect effects, a more practical way to identify possible mediators is to look for meaningful reductions in the strength of the association between predictor and outcome.

The mediational approach has previously been applied to investigations of cognitive ageing, notably by Salthouse who demonstrated that age differences in cognitive ability were often majorly attenuated after controlling for performance on simple tests of processing speed (Salthouse, 1994, 1992). However, there are few examples of experimental work that has applied the mediational approach to investigations of IIV,

Figure 4.1: Path diagram depicting the hypothesised relationship between IIV, gait and falls



gait and falls. As mentioned earlier, one study carried out in our laboratory found that a composite measure of motor function mediated the association between variability and falls (Bauermeister et al., 2017). A composite measure of executive function was also tested as a potential mediator but was not found to be having a significant effect. This is a somewhat surprising result given that IIV is thought to be closely tied to executive control processes and deficits in these processes have been identified as a risk factor for future falls. Consequently, there is a need for more research to examine the neurocognitive and physiological factors underlying the relationships between IIV and falls, and IIV and gait impairment.

The present work will add to this research by examining the influence that a number of variables have on the strength of these associations. One possible mechanism through which IIV might be affecting gait and falls is the physiological systems that contribute to maintaining stability. Lord and colleagues (2003) outlined a number of these in their Physiological Profile Approach to falls and, based on this approach, the current study will assess several aspects of physical performance that have previously been linked to falls. Specifically, tests of both higher extremity (i.e., hand grip) and lower extremity (i.e., leg resistance) muscle strength will be included as these have both been found to be compromised in fallers (e.g., Wickham et al., 1989; Whipple et al., 1987). Two tests of vision will also be included as older adults with sight problems are more likely to fall compared to those who are fully sighted (e.g., Legood et al., 2002). With regards to cognitive function, there is evidence that deficits in executive control are linked to both slower walking speed and falls (Kearney et al., 2013). Furthermore, previous work has demonstrated that older persons with slower cognitive processing are also more prone to falling (e.g., Holtzer et al., 2007). Therefore, executive function and processing speed will both be tested as potential mediators in this study.

To summarise, the current research will investigate relationships between variability, gait speed and falls in cognitively intact older adults. This work will address a number of aims. First, the extent to which measures of IIV and gait speed are able to predict fall status will be examined. Second, this study will determine how whether IIV measures are significantly associated with gait speed measured continuously and also using a cut-off point of 1.0 m/s that distinguishes between slow and normal walkers. Third, the extent to which relationships between IIV, gait speed and falls vary according to age will be examined. Fourth, the current research will assess the effect that cognitive task demands are having on associations between IIV and falls, and IIV and gait speed. Finally, this work will investigate potential mechanisms underlying these relationships. This will involve introducing several cognitive and physiological variables into any significant associations that are found and measuring subsequent changes in the strength of these associations.

4.2 Methods

Data were collected as part of a larger study[2] carried out in the School of Psychology at the University of Leeds and St James's University Hospital in Leeds. Here, only data from the University of Leeds portion of the study will be used as this was conducted with older adults living in the community. A recent publication (Bauermeister et al., 2017) additionally used data from the St James's University Hospital portion of the study in which clinical falls patients were tested. The main aim of the broader study was to identify cognitive and physical risk factors for falling in older persons.

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[2] The data analysed in the present study were also used in a recent publication in addition to data that were collected from a clinical falls population. The full reference of this publication is as follows: Bauermeister, S., Sutton, G., Mon-Williams, M., Wilkie, R., Graveson, J., Cracknell, A., Wilkinson, C., Holt, R., & Bunce, D. (2016). Intraindividual variability and falls in older adults. Neuropsychology, 31, 20-27.

Participants

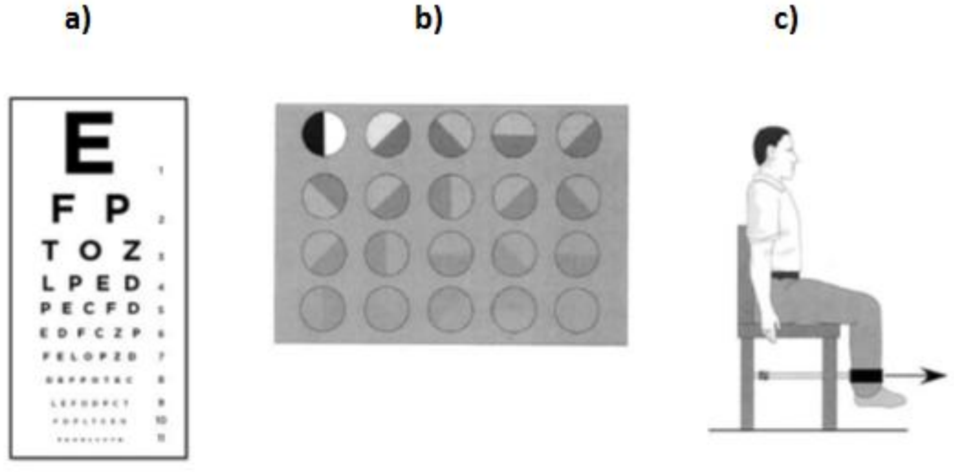
A total of 69 older adults from the local community took part in the study. Potential recruits were identified using an existing panel of volunteers who were interested in our research and through local organisations (e.g., community centres) where the study was advertised. Participants were screened for cognitive impairment using a cut off score of 26 or lower on the Mini Mental State Examination (MMSE; Folstein et al., 1975) with no individuals excluded on this basis. However, two individuals were unable to complete the battery of cognitive tasks and were therefore excluded from the study. The remaining sample of 67 adults had a mean age of 69.6 years (range: 53-86), had spent an average of 15 years in full time education and included 55 women (82%). Participants also completed the National Adult Reading Test (NART; Nelson, 1982) to determine their predicted full-scale IQ. Five of the 69 adults who took part were from a non-English speaking background and so an alternative formula was used to compute their predicted IQ. The two formulas are based on regression equations that have been calculated previously (Sullivan et al., 2000) and can be seen in Appendix 1A.

Physical Measures

*Vision tests: V*isual acuity was assessed using a Snellen chart (Figure 4.2a) which participants read from a distance of 3m. Acuity score, which range from 1 to 11, were calculated according to the lowest line at which the participant could correctly identify more than 50% of the letters on that line. Contrast sensitivity was assessed using the Melbourne Edge Test (Verbaken & Johnston, 1986), a chart containing 20 circles that gradually reduce in contrast (Figure 4.2b). Participants were required to identify the orientation of each circle, with the last correctly identified circle used to give a contrast sensitivity score between 1 and 25.

Muscle force tests: Hand grip strength was measured using a handheld dynamometer which participants were instructed to grip with one hand and apply the maximum force possible for 3 seconds. A total of 6 trials was administered, alternating between the left and right hand, and the average force (in kilograms) was recorded. Leg resistance strength was measured using a spring gauge attached to the participant's dominant leg with a strap and Velcro fastener. Participants were tested while sitting in a chair with their hip and knee joints positioned at 90 degree angles (Figure 4.2c). They were instructed to exert the maximum force possible with their dominant leg by extending

Figure 4.2: Physical measures: a) Snellen chart, b) Melbourne Edge Test, c) Leg resistance strength test



away from the chair and holding for 3 seconds. This was done for 3 trials and the average force (in kilograms) was recorded.

Gait test: Walking speed was measured using a 4m walkway along which participants were instructed to walk at their usual pace from a standing start. The walk was timed using a stopwatch and the average time taken to complete three trials (in seconds) was recorded. Average gait speed (in cm/s) was calculated using the following formula:

$$\frac{4}{Average\ time} \text{ x } 100 \tag{3}$$

Falls History

A falls questionnaire (Appendix 1B) was administered to participants in a semi-structured interview style in order to establish a comprehensive falls history for the previous two years. Participants were first asked if they had experienced a fall which was defined as “an unexpected event in which the person comes to rest on the ground, floor, or lower level” (Lamb et al., 2005). Participants were then asked to provide details about when and where each fall occurred, the cause, and whether or not they required medical treatment afterwards. Based on classifications in previous work (e.g., Talbot et al., 2005), causes of falls were classified as one of the following: (1) ice and snow, (2) an object, (3) uneven surface, (4) wet/slippery surface, (5) unknown or (6) other.

Cognitive Measures

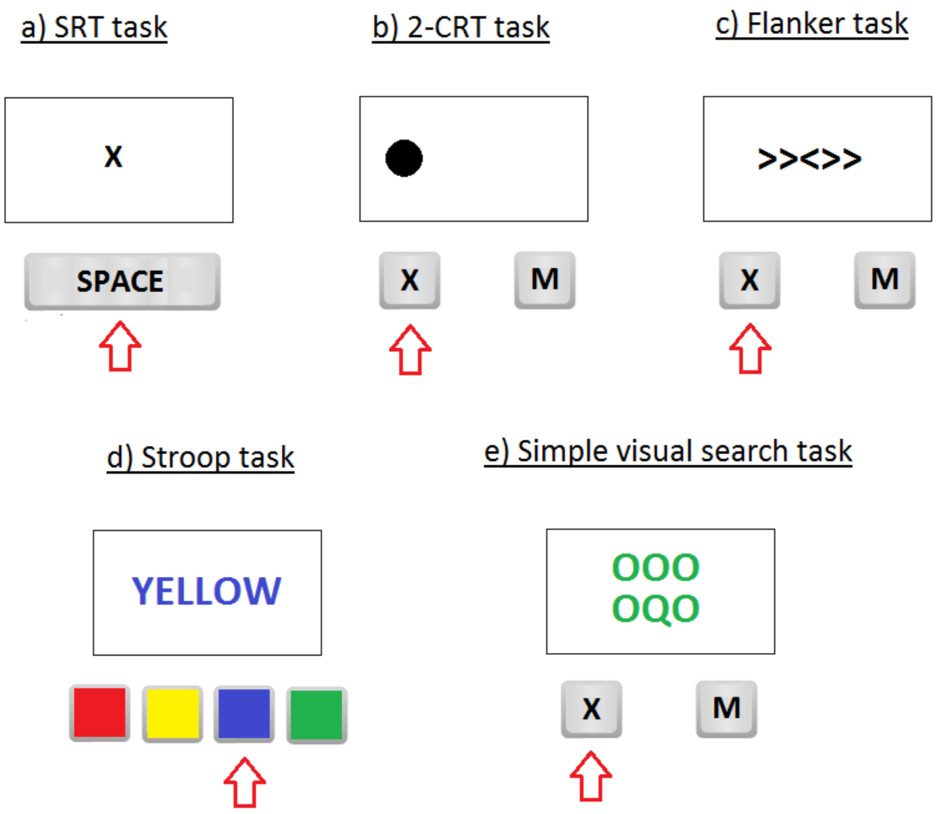
Cognitive RT tasks: Participants were asked to complete five RT tasks, all of which have been used previously by members of this research group (e.g., Bauermeister & Bunce, 2016; Bauermeister & Bunce, 2015; Bunce et al., 2008). These were administered on a computer using E-Prime version 2.0 (Psychology Software Tools, 2012) with trials presented pseudo randomly and practice trials given for each task. Written instructions were presented before the beginning of each task, with participants asked to respond as quickly and as accurately as possible.

Psychomotor speed tasks: In the Simple Reaction Time (SRT) task, the letter ‘X’ appeared on a computer screen at random intervals between 300 and 1000 milliseconds (see Figure 4.3a). Participants were instructed to press the spacebar key in response to stimuli for 48 test trials. In a 2-Choice (2-CRT) version of the task, a black circle with a diameter of 25mm was presented to either the left or right side of the screen at intervals of 500 milliseconds (see Figure 4.3b). Participants were instructed to press the ‘X’ key or ‘M’ key if stimuli appeared to the left or right, respectively for 48 test trials.

Response inhibition tasks: In a version of the Flanker task (Eriksen & Schultz, 1979), a series of arrows were presented on the computer screen, one central target arrow and two distractor arrows on either side, at intervals of 500 milliseconds (See Figure 4.3c). Participants were required to respond to the direction of the central arrow with either the ‘X’ key for left or the ‘M’ key for right. This was done for 64 test trials, half of which were congruent (all arrows pointed in the same direction) and half incongruent (the middle arrow pointed in the opposite direction to the distractors). In a version of the Stroop task, a series of words (red, blue, yellow or green) were presented on the screen at intervals of 500 milliseconds (see Figure 4.3d). Participants were instructed to ignore the written word and respond only to the ink colour of the word (also red, blue, yellow or green) using the appropriately coloured response key on the keyboard. This task consisted of 96 test trials, half of which were congruent (the word and ink colour matched) and half incongruent (they did not match).

Visual Search task: In the Simple Visual Search task, a 6 x 6 array of green letter ‘O’s was presented on the screen at intervals of 500 milliseconds (see Figure 4.2e). For half of the trials, a green letter 'Q' was embedded randomly within the array. Participants

Figure 4.3: Examples of stimuli used in cognitive tasks: (a) Simple RT task, (b) Two-choice RT task, (c) Flanker task, (d) Stroop task, (e) Simple Visual Search task.



were instructed to indicate the presence or absence of a Q using the ‘X key’ or ‘M’ key, respectively. This task consisted of 64 test trials, half of which were control trials (the Q was not present) and half of which were target trials (the Q was present).

Other cognitive tasks: In addition to the battery of RT tasks, a verbal task (Animal Country) and two written tasks (Trailmaking A and B) were also administered. Animal Country is an alternate category task (Parkin et al., 1995) where participants must alternate between verbally naming different animals and countries. The number of novel animal/country pairs named in 60 seconds was recorded as a measure of executive function. The Trailmaking tasks (Army Individual Test Battery, 1944) involve joining together circles to create a complete trail. In Part A the circles contain the numbers 1 to 25 and in Part B they contain the numbers 1 to 12 as well as the letters A to L. Both the numbers and the letters must be joined in ascending order but participants are required to alternate between the two (i.e., 1-A-2-B-3-C…) in Part B. In the case of an error, participants were instructed to return to the last circle that was correctly joined and proceed from there. The time taken to complete Part A was recorded as a measure of processing speed. The difference in the time taken to complete Parts A and B, also known as the Delta TMT (ΔTMT) score, was used as a measure of executive function as this is thought to isolate the switching component of the task (Kearney et al., 2013).

Procedure

Basic demographic information such as age, gender and years in full-time education was first collected from participants. This was followed by a short medical questionnaire which recorded information on a range of past conditions and current medication usage. The NART, MMSE and a questionnaire to determine details of any falls that may have been experienced in the previous two years were then administered. This was followed by the battery of physical measures which included the Snellen test, Melbourne Edge Test, tests of grip strength and leg resistance, and the gait speed assessment. Participants then completed the battery of cognitive RT tasks including the SRT, 2-CRT, Flanker, Stroop and Visual Search tasks which were counterbalanced according to subject ID. Finally, participants completed the Animal Country and Trailmaking tasks (Part A and B) which were also counterbalanced. The entire testing session lasted approximately 60 minutes. Ethical approval for this part of the study was obtained from the School of Psychology Research Ethics Committee and testing began in October 2013.

Data Processing

Calculation of IIV measures: After removing practice trials and incorrect responses, the coefficient of variation (CV) measure of variability was computed for the five RT tasks. Computation of the CV involved first calculating the mean RT and standard deviation of RTs for each individual on each task, then dividing the SD by the mean. CV measures were later converted to z-scores for use in the regression analyses in order to aid with interpreting the results. As the Flanker and Stroop tasks were used to assess the effect that greater task demands had on the relationship between IIV and outcome, only the incongruent trials involving response inhibition contributed to the assessment of IIV on these tasks. In line with previous work (Hultsch et al., 2002), the RT data for each cognitive task were inspected for extremely slow or fast responses. A lower boundary of 150ms and an upper boundary of the individual mean RT + 3 SD was set, beyond which trials were excluded. Eliminated RTs were replaced at the individual data level using the mean RT for that particular individual on that particular task. Table 4.1 shows the percentage of trials removed from each task during the different stages of data processing.

Missing data: Missing data across the dataset were rare and replaced by imputing new values at the aggregate sample level. This was done in SPSS using the expectation maximisation algorithm (Schafer & Graham, 2002). This procedure provides the best estimate for a missing value having taken into account all other variables available in the dataset for that individual. Missing data frequencies ranged from 1.5% to 4.5% and did not exceed the 5% threshold under which it has been deemed acceptable to use this algorithm (Schafer & Graham, 2002).

Table 4.1: Number of trials removed and replaced at each stage of data processing for the five RT tasks

Task	Incorrect responses removed (%)	Trials < 150ms removed (%)	Trials > Mean + 3SD replaced (%)
SRT	0	22 (0.69%)	51 (1.62%)
2-CRT	57 (1.78%)	1 (0.03%)	50 (1.58%)
Flanker (congruent)	25 (1.18%)	1 (0.05%)	38 (1.82%)
Flanker (incongruent)	103 (4.88%)	0	40 (1.99%)
Stroop (congruent)	28 (0.88%)	0	46 (1.46%)
Stroop (incongruent)	215 (6.79%)	0	38 (1.29%)
VS (control)	72 (3.36%)	0	37 (1.74%)
VS (target)	75 (3.50%)	1 (0.05%)	13 (0.62%)

Notes: 2-CRT = 2-choice reaction time; SD = standard deviation; SRT = simple reaction time; VS = visual search

*Composite measures: T*wo composite measures were computed for use in the statistical analyses: A PPA composite, based on the Physiological Profile Approach to falls risk (Lord et al., 2003), and an executive function composite. The PPA composite consisted of performance on the Melbourne Edge Test, the grip strength test and the leg resistance test. This composite represents the functioning of physiological systems, with higher scores indicating better physiological function. The executive function composite consisted of performance on the Animal Country task and the Trailmaking B task. Performance on Trailmaking B task was measured with the ΔTMT score which is the difference in the time taken to complete Parts A and B of the Trailmaking task. This composite represents the functioning of the executive system, with higher scores indicating better executive control. Both the PPA and executive function composites were computed in SPSS using principal components analysis with varimax rotation. The factor scores from this procedure were then saved.

Statistical Analysis

Analysis of the data proceeded through a number of stages. First, the sample was split according to fall status (fallers vs. non-fallers) and gait speed (slow vs. normal) using a cut off of 1.0m/s. Independent t-tests or chi square tests then identified any significant differences in demographic, physical or cognitive characteristics between fallers and non-fallers, or slow and normal walkers. Second, a correlational analysis provided an overview of bi-variate associations and also determined whether any of the demographic variables (e.g., gender, IQ) were associated with either gait speed or falls. If this was the case, these variables were controlled for in the later regression analyses. Third, a series of logistic regression analyses explored whether measures of IIV or gait speed were significantly associated with fall status. Fourth, a series of linear regression analyses examined the strength of associations between IIV and continuously measured gait speed. Where logistic regressions are reported, the unstandardized coefficient of the intercept (B) and the exponentiation of the B coefficient (OR; the odds ratio) have been included in tables. Where linear regressions are reported, the standardized coefficient of the intercept (β; beta) and the proportion of variance in the dependent variable explained by the independent variables (R^2) have been included. This is consistent for all the experimental work in this thesis.

Fifth, another series of logistic regression analyses determined whether IIV measures could distinguish between those with slow and normal walking speed. Sixth, Age x IIV and Age x Gait interaction terms were additionally examined in all regression analyses to determine the extent to which relationships between IIV, gait and falls varied according to age. In the event that interaction terms were found to be significant predictors after adjusting for the primary effects, the sample was stratified into two subgroups. The median value for age was used as a cut-off point for these groups. The corresponding associations were then retested in both groups to determine if the initial relationships were stronger in early or later old age.

Finally, a series of mediational analyses investigated the mechanisms underlying relationships between IIV, gait and falls where they were found. In these analyses, explanatory variables representing physiological function or cognitive ability were introduced into significant associations. These models were then examined before and after these variables were statistically controlled for. In linear regression models, changes in the variance explained (R^2) were examined. Salthouse’s (1992) formula for calculating mediating effects was used to measure these changes and this is shown below:

$$\frac{R^2 1 - R^2 2}{R^2 1} \text{ x } 100 \tag{4}$$

The resulting metric provides the percentage by which the initial explained variance in outcome is attenuated after controlling for the effect of the explanatory variable. In logistic regression models, changes in the odds ratio were examined using the same formula. In accordance with previous suggestions, attenuations of less than 20% were interpreted as being small, between 20% and 40% as interesting, between 40% and 60% as important, and above 60% as major (Salthouse, 1992). Three explanatory variables were introduced at this stage: 1) a PPA composite representing physiological function, 2) an executive function composite, and 3) processing speed assessed with the Trailmaking A task.

4.3 Results

Pr*edictors of fall status*

Fallers and non-fallers were similar in terms of their demographic, physical and cognitive characteristics with only gait speed found to be significantly different (Table 4.2). Those who had experienced a past fall took 0.45 seconds longer on average to complete the 4m walk compared to non-fallers. A series of hierarchical logistic regressions explored the relationship between IIV and falls, and gait speed and falls, and the effect that age had on these relationships. As none of the demographic variables (e.g., gender, IQ) were correlated with fall status (Table 4.3), these were not included in the models. The results indicated that there were no primary effects of IIV on falls regardless of the task that was used (Table 4.4). However, a positive trend was found between gait speed and falls that approached statistical significance ($p = .059$), indicating that those with a slower walk were more likely to be fallers. The Age x IIV and Age x Gait interaction terms were not found to be predicting falls after accounting

Table 4.2: *D*emographic, physical and cognitive characteristics of fallers and non-fallers and those with normal and functionally slow gait

Variable	**Fallers (n = 18)**	**Non-fallers (n = 49)**	**Slow gait (n = 23)**	**Normal gait (n = 44)**
Age (years)	69.3 (5.53)	69.8 (7.50)	74.2 (7.79)	67.3 (5.21)**
Gender – female (n,%)	16 (88.9)	39 (79.6)	22 (95.7)	33 (75.0)*
NART Predicted IQ	122.0 (6.05)	122.6 (5.78)	119.0 (6.78)	124.2 (4.32)**
Melbourne Edge Test	21.3 (1.64)	21.0 (1.56)	20.6 (1.23)	21.3 (1.68)*
Grip strength (kg)	25.1 (9.27)	26.6 (8.93)	21.4 (6.70)	28.7 (9.06)**
Leg resistance (kg)	17.3 (7.36)	18.9 (7.09)	15.0 (4.69)	20.3 (7.55)**
Gait (s)	4.33 (1.35)	3.88 (0.76)*	4.94 (1.08)	3.51 (0.35)**
SRT CV	0.23 (0.07)	0.26 (0.10)	0.26 (0.09)	0.24 (0.10)
2-CRT CV	0.20 (0.06)	0.19 (0.05)	0.20 (0.06)	0.19 (0.05)
Flanker CV	0.23 (0.11)	0.20 (0.08)	0.26 (0.09)	0.18 (0.07)**
Stroop CV	0.25 (0.06)	0.24 (0.10)	0.29 (0.11)	0.22 (0.07)**
Visual Search CV	0.19 (0.06)	0.20 (0.08)	0.22 (0.10)	0.18 (0.05)
Trailmaking A (s)	36.2 (18.2)	31.8 (10.1)	40.59 (17.2)	29.1 (7.25)**
Trailmaking B (s)	67.7 (29.5)	65.5 (26.1)	82.8 (31.8)	57.3 (19.1)**
Animal/Country	17.6 (7.85)	18.8 (7.02)	15.6 (6.85)	20.0 (6.98)*

Notes: * p<.05 ** p<.01
Continuous variables are expressed as means (SDs) and differences between fallers and non-fallers or those with slow and normal gait were assessed using independent t-tests
Categorical variables are expressed as frequencies (%) and differences between fallers and non-fallers or those with slow and normal gait were assessed using chi square tests

for the primary effects, indicating that age was not having an effect on these initial relationships. As a result, none of the predictors of falls were examined further as a function of age.

Predictors of gait speed

Slow and normal walkers significantly differed in their demographic, physical and cognitive profile. Slower individuals tended to be older, male, had a lower predicted IQ, and poorer performance on tests of vision and grip strength (Table 4.2). They took considerably longer to complete both parts of the Trailmaking task, performed more poorly on the Animal Country task and had higher IIV on the Flanker and Stroop tasks. A series of hierarchical linear regressions explored the association between IIV and gait speed measured continuously, whereas logistic regressions examined how well IIV predicted membership in the slow and normal gait groups. The effect that age was having on these relationships was also investigated. As predicted IQ was found to correlate significantly with gait speed (Table 4.3), this was controlled for in each model.

Table 4.3: Pearson correlation coefficients for associations between key demographic, cognitive and physical characteristics

Variable	**Mean (SD)**	1	2	3	4	5	6	7	8	9	10	11	12
1. Age (years)	69.6 (6.99)	—											
2. Gender – female (n,%)	55 (82.1)	.12	—										
3. Predicted IQ	122.4 (5.81)	-.25*	-.19	—									
4. Fallen in the last 2 years (n,%)	18 (26.8)	-.03	.11	-.05	—								
5. Gait speed (s)	4.00 (0.97)	.47**	.24	-.35**	.21	—							
6. SRT CV	0.25 (0.10)	.40**	.26*	.07	-.15	.19	—						
7. 2-CRT CV	0.19 (0.06)	.25*	.18	-.12	.06	.20	.15	—					
8. Flanker CV	0.21 (0.09)	.37**	.02	-.05	.11	..43**	.02	.37**	—				
9. Stroop CV	0.26 (0.09)	.15	.04	.11	.06	.31*	.17	.16	.44**	—			
10. Visual Search CV	0.19 (0.05)	.32**	-.06	-.01	-.06	.20	.20	.27*	.30*	.05	—		
11. PPA composite	—	-.19	.04	-.13	.07	-.14	-.14	.11	-.14	-.26*	-.14	—	
12. Switching composite	—	-.35**	-.01	-.08	-.02	-.28*	-.17	.02	-.27*	-.30*	-.20*	-.35**	—
13. Trailmaking A	33.0 (12.8)	.49**	.15	-.17	.15	.64**	.17	.39**	.47**	.10	.37**	-.34	.02

Notes: * p < .05 ** p < .01
Gender is coded as 1 for males and 2 for females; Fallers were coded as 1 with non-fallers coded as 0
2-CRT = two-choice reaction time; CV = coefficient of variation; PPA = physiological profile approach; SRT = simple reaction time

Table 4.4: Logistic regression models for age, IIV measures and gait speed predicting falls

	SRT CV		**2-CRT CV**		**Flanker CV**		**Stroop CV**		**VS CV**		**Gait speed**	
Model	B	OR	B	OR	B	OR	B	OR	B	OR	B	OR
Step 1												
Age	.09	1.10	-.10	.90	-.19	.83	-.09	.92	-.09	.92	-.37	.69
Predictor	-.42	.66	.16	1.18	.32	1.38	.14	1.15	.08	1.09	.61^	1.85^
Step 2												
Age x Predictor	-.43	.65	-.10	.90	.43	1.54	-.01	.99	-.42	.66	-.19	.83

Notes: ^ *p < .06*
Fallers were coded as 1 with non-fallers coded as 0; *n* fallers = 18 (27%); Step 1, df = 2; Step 2, df = 3
2-CRT = two-choice reaction time; CV = coefficient of variation; SRT = simple reaction time; VS = visual search

For each of the five linear models, Step 2 was found to significantly add to the variance explained in gait speed (Table 4.5). Inspection of the beta weights indicated a primary effect for IIV on two of the five RT tasks, Flanker and Stroop (ps < .01), with more variable individuals displaying poorer gait performance. In line with these findings, primary effects for IIV on the Flanker (p < .05) and Stroop (p < .01) were also found in the logistic models (Table 4.6). IIV on the Visual Search task was also found to be a significant predictor at the p < .05 level. Inspection of the odds ratios indicated that a 1 SD increase in variability on the Flanker, Stroop and Visual Search tasks was associated with a 60%, 77% and 69% increased likelihood of having a slower walk, respectively. In both the linear and logistic regression models, the Age x IIV interaction terms were found to be non-significant after accounting for the primary effects. This indicated that age was not having an effect on the relationship between IIV and gait speed. Consequently, predictors of gait were not examined further as a function of age.

Testing for potential mediators

After establishing that Flanker IIV and Stroop IIV were significant predictors of gait speed across the whole sample, a mediation analysis was performed on these relationships. The results of this analysis are presented in Table 4.7. First, after entering the PPA composite into the regression models, the variance in gait speed explained by IIV fell by 20% for the Flanker task and 19% for the Stroop task. This suggests a small attenuation and both models remained significant at the $p < .05$ level. Second, after entering the executive function composite into the models, the variance explained fell 17% for the Flanker task and 23% for the Stroop task. Again, this represents a small attenuation with both models remaining statistically significant. Finally, after entering time taken to complete Trailmaking A into the models, a major attenuation of 80% was observed for IIV on the Flanker task which caused the model to become non-significant. However, there was only a weak attenuation of 14% for the Stroop task and this model remained significant at the $p < .01$ level.

Table 4.5: Linear regression models for age and IIV measures predicting gait speed

	SRT CV		**2-CRT CV**		**Flanker CV**		**Stroop CV**		**VS CV**	
Model	β	R^2	β	R^2	β	R^2	β	R^2	β	R^2
Step 1										
NART IQ	-.35**	.13**	-.35	.13**	-.35**	.13**	-.35**	.13**	-.35**	.13**
Step 2										
Age	.39**		.39**		.30*		.36**		.37**	
Predictor	.06	.16**	.07	.16**	.30**	.24**	.29**	.24**	.13	.18**
Step 3										
Age x Predictor	-.03	.00	.17	.03	.20	.04	.17	.03	-.06	.00

Notes: * $p < .05$ ** $p < .01$
Step 1, *df* = 1,65; Step 2, *df* = 3,63; Step 3, *df* = 4,62
2-CRT = two-choice reaction time; CV = coefficient of variation; SRT = simple reaction time; VS = visual search

Table 4.6: Logistic regression models for age and IIV measures predicting slow or normal gait speed

	SRT CV		**2-CRT CV**		**Flanker CV**		**Stroop CV**		**VS CV**	
Model	B	OR	B	OR	B	OR	B	OR	B	OR
Step 1										
NART IQ	.22**	1.25**	.22**	1.25**	.22**	1.25**	.22**	1.25**	.22**	1.25**
Step 2										
Age	-1.06**	.35**	-1.04**	.36**	-.73*	.48*	-.93**	.40**	-.93**	.40**
Predictor	.17	1.18	.18	1.20	-.92*	.40*	-1.47**	.23**	-1.16*	.31*
Step 3										
Age x Predictor	.15	1.16	-.51	.60 .	-.71	.49	-.81	.45	-.30	.74

Notes: * *p* < .05 ** *p* < .01
Slow walkers were coded as 1 with normal walkers coded as 0
n slow walkers = 23 (37%); Step 1, df = 1; Step 2, df = 3; Step 3, df = 4
2-CRT = two-choice reaction time; CV = coefficient of variation; SRT = simple reaction time; VS = visual search

Table 4.7: Explanatory variables entered into linear regression models for IIV measures predicting gait speed that were significant across the whole sample

Predictor	Explanatory variable	R^2 change Before	R^2 change After	% attenuation
Flanker CV	PPA	.079**	.063*	20.3%
	Executive Function	.079**	.076**	16.5%
	Trailmaking A	.079**	.016	79.8%
Stroop CV	PPA	.078**	.063*	19.2%
	Executive Function	.078**	.071*	23.1%
	Trailmaking A	.078**	.067**	14.1%

Notes: * p < .05 ** p < .01
Age and NART IQ were adjusted for at Step 1 (df = 2,64), explanatory variables were entered at Step 2 (df = 3,63) and IIV measures were entered at Step 3 (df = 4,62)
CV = coefficient of variation; PPA = physiological profile approach; ST = single-task

4.4 Discussion

In the present study, cross-sectional associations between IIV, gait speed and falls were examined in a group of healthy, community-dwelling older adults. Nonsignificant associations were found between all IIV measures and a history of falls in the two years prior to testing. However, there was evidence that fallers walked more slowly than non-fallers. Higher IIV on the two cognitive tasks that placed the highest demands on executive abilities, Flanker and Stroop, was associated with a slower gait speed when measured continuously. Variability on the same two tasks also distinguished between individuals who walked more slowly or more quickly than a clinically significant cut-off of 1.0 m/s. None of these effects, however, were found to vary according to age. Mediation analyses were carried out on significant associations between IIV and gait. These associations were largely unaffected after controlling for measures of physiological and executive function. However, adjusting for a measure of processing speed majorly attenuated the association between Flanker IIV and gait speed but not the association between Stroop IIV and gait speed.

The positive trend found between gait speed and falls was in line with previous literature that has identified slow walking as a major risk factor for falls (Deandrea et al., 2010). However, the absence of a relationship between IIV and falls was unexpected, particularly given the evidence provided in the two review chapters that fallers tend to be more variable than non-fallers. There are several factors that could have contributed to these non-significant findings. First, the number of falls observed in the present study was relatively low, with only 27% of the sample reporting a single fall in the two years prior to testing and only 8% reporting two or more falls. In other studies which demonstrated that higher IIV levels were linked to an increased risk of falls, the prevalence of single and recurrent falls was much higher (Mirelman et al., 2012; Reelick et al., 2011; Allcock et al., 2009). Furthermore, falls data in the present study were collected retrospectively using a questionnaire, unlike other studies that have collected data prospectively using monthly falls diaries. Monthly diaries have previously been recommended as the most reliable method for collecting information on falls (Hannan et al., 2010) with one study demonstrating that the self-report method underestimated the number of falls experienced over 12 months by 33% relative to monthly diaries (Garcia et al., 2015). It is possible, therefore, that the number of falls experienced by individuals in the current study was actually higher than the results indicated but this figure may have been underestimated due to, for example, biases in memory during self-reporting. This is likely to have affected the outcomes of the study and, particularly, the ability of IIV measures to distinguish between fallers and non-fallers.

It is also possible that differences in the populations sampled contributed to the low number of falls that were reported. For example, individuals as young as 53 years old took part in the present study compared to previous investigations of IIV and falls in which minimum cut-offs of 65 years and 70 years were used. In the present work, individuals were excluded if they scored 26 or less on the MMSE as this may indicate possible cognitive impairment. By contrast, two other studies that examined IIV in relation to falls did not have exclusion criteria relating to cognitive impairment (Reelick et al., 2011; Allcock et al., 2009), and a further two studies used lower MMSE scores as exclusion criteria (O'Halloran et al., 2011; Hausdorff et al., 2006). Furthermore, the average predicted IQ of participants in the present study (mean = 122) was considerably higher than in previous investigations suggesting that older adults here may have spent longer in full-time education. Taken together, this suggests that individuals in the present study were younger, more highly educated and less likely to display signs of impairment than those sampled in previous work. It is reasonable, therefore, to expect that the majority of falls experienced by these older adults were more likely to be one-off incidents caused by accidental slips and trips, rather than the result of age-related cognitive decline. Indeed, in support of this notion, further examination of the falls data revealed that 14 of the 26 (54%) total falls were attributed to ice or snow, an object or an uneven surface.

The finding that IIV was associated with gait speed supports the reviews carried out in the previous chapters. Given that these associations were produced using an IIV metric that controls for differences in response speed in its calculation, it seems likely that variability measures were capturing differences in gait performance that were not detected by average performance measures. This is line with the findings from two previous studies that looked at gait speed in relation to both mean RT and IIV on the same task, but only reported a significant association with the latter (Holtzer et al., 2014b; O'Halloran et al., 2014). One way the present work developed previous investigations of IIV and gait was by incorporating a clinically meaningful cut-off point of 1.0m/s in order to distinguish between older adults who walk at slow and normal speeds. IIV on several of tasks (Flanker, Stroop, Visual Search) was able to significantly distinguish between individuals in these two groups, producing a similar pattern of results to when continuous gait speed was used. This finding is potentially important as it suggests that measures of variability may be useful in detecting those individuals who are at risk of their walking speed dropping to a point that makes them susceptible to conditions that may affect their health, mobility and ability to live independently.

An important aim of the present work was to determine whether relationships involving IIV vary according to demands of the task used to produce these measures. The current study found that gait speed was related to IIV on the two RT tasks that placed greater demands on executive function, Flanker and Stroop. However, nonsignificant associations were reported between gait speed and IIV on the SRT and 2-CRT tasks. These results are in line with the qualitative and quantitative reviews considered in the previous chapters, as well as other work that has shown age differences in IIV to be more pronounced in the presence of higher task demands (e.g., Dykiert et al., 2012; Dixon et al., 2007). The findings of this study, therefore, give further weight to the notion that IIV on tasks with high executive demands may be a more sensitive predictor of outcomes such as gait performance than IIV measures derived from simple psychomotor tasks. This may also shed some light on the inconsistent findings that have previously been reported concerning variability and gait. For example, one study that reported nonsignificant associations between these constructs assessed IIV using a battery of simple and choice RT tasks (de Frias et al., 2007). It could be that these IIV tasks were not sufficiently demanding to distinguish between individuals with different walking speeds, particularly as this study had a small sample size and set alpha for statistical significance conservatively at $p < .01$.

Another aim of this study was to examine whether relationships between IIV and falls, and IIV and gait, varied according to age. Contrary to expectations, the present findings found no evidence that age was having an effect on these relationships. This is somewhat surprising given that there is thought to be a greater reliance on executive function and attention to maintain walking performance with increasing age (Yogev-Seligmann et al., 2008), and IIV is thought to reflect fluctuations in these processes. As a result, it is reasonable to expect that variability would be more closely related to gait speed in very old groups relative to those in early and middle old age. One possible explanation of these non-significant findings relates to the relatively small size of the sample (n = 67), which may have limited the statistic power of the models that tested Age x IIV interaction effects. Contrary to this notion, another study with a considerably large sample (n = 1,426) also provided evidence that the relationship between IIV and gait is not affected by age (O'Halloran et al., 2014). Here, variability on a sustained attention task significantly distinguished between those with low and normal walking speed in a group of adults aged 50-64 and in an older group aged 65 and above. Clearly then, more research investigating the extent to which associations between IIV and gait, and also IIV and falls, vary according to age is warranted.

A number of potential explanatory variables were entered into models that significantly predicted gait speed to determine if the initial effects would remain after adjusting for certain factors. First, controlling for physiological function (PPA composite) did little to attenuate the effects of Flanker IIV and Stroop IIV on gait. This was in line with prior expectations. Since performance levels on these more demanding tasks are likely to be determined by higher-order cognitive processes rather than the basic sensorimotor responses that were captured by these physiological measures. Second, introducing a measure of executive function also had a negligible effect on the two associations. This finding was contrary to expectations given that variability has previously been shown to be closely tied to executive control processes (Bunce et al., 2008; West et al., 2002). However, it does support the findings of one previous study where controlling for executive function did not attenuate the relationship between IIV and falls (Bauermeister et al., 2017). Both studies used the same switching tasks (Trailmaking B, Animal/Country) to assess executive function and this may partially explain the non-significant findings. As outlined in Chapter 1, one proposed model of executive function suggests that this construct is made up of two other components in addition to task switching: response inhibition and information updating (Miyake et al., 2000). Therefore, it is likely that the measure used in the present study did not completely capture the full range of abilities that contribute to executive function.

Finally, controlling for processing speed (Trailmaking A) majorly attenuated the effects of Flanker IIV, but not Stroop IIV, on gait speed. This finding partially supports earlier demonstrations that associations between prefrontal brain matter volume and walking speed were considerably reduced after processing speed was taken into account (Rosano et al., 2012). More broadly, these results partially support speed of processing theories of cognitive ageing which have suggested that age-deficits in a wide range of cognitive processes can largely be explained by a general slowing in information processing capability (Salthouse, 1996). However, it seems unlikely that the increased IIV levels observed in slower walkers is solely due to these individuals also having slower responses, particularly as the IIV metric used in the present study is thought to control for response time. It is possible that visual-spatial abilities common to both the Trailmaking A and Flanker tasks, such as visual scanning and following a sequence, are partially underlying the effects that were observed. This possibility is supported by the finding that Trailmaking A time was significantly correlated with IIV on the 2-CRT, Flanker and Visual Search tasks, all of which involve a visual-spatial component, but not the SRT and Stroop tasks (see Table 4.3). These results suggest that the extent to which explanatory variables attenuate the relationship between IIV and outcome depends heavily on the type of demand that is placed on individuals by the cognitive task.

Limitations

Several limitations with the present study have already been mentioned, such as the age and status of individuals in the sample, and the retrospective method used to collect falls data. There are, however, additional limitations that may have influenced the results and should therefore be acknowledged. First, as only cross-sectional data were collected, inferences about causality cannot be made when considering associations between variability and gait speed. This is important as there is considerable debate in the literature regarding the temporal direction of the broader relationship between cognition and gait. While some studies have demonstrated that baseline levels of global cognitive function, and also specific cognitive abilities, predict later changes in gait performance (e.g., Buchman et al., 2011; Atkinson et al., 2010; Watson et al., 2010), other work has provided evidence for this relationship in the opposite direction (e.g., Mielke et al., 2013; Inzitari et al., 2007b; Abbott et al., 2004). These contrasting findings suggest more longitudinal investigations are needed to better elucidate the relationship between cognition and gait. Particularly, there is a need to examine longitudinal relationships between IIV and gait as no previous empirical work has been carried out in this area to date. Furthermore, prospective research in this area is important for establishing the utility of IIV measures as predictors of future gait impairment, one of the central themes of the current research.

Second, the 4-metre gait speed test used in the present study is limited in that it only provides information about walking performance under simple conditions. Everyday locomotion, however, often involves more complex walking situations (e.g., crossing a busy street) that require the individual to multitask. Previous research has examined such situations using dual-task (DT) paradigms where individuals are required to walk while simultaneously completing a secondary task. In addition to measuring the speed at which older adults walk under DT conditions, it common to examine how gait performance deteriorates in dual-task relative to single-task walking. These decrements, commonly referred to as dual-task costs, have been found to increase with age (Beurskens & Bock, 2012) and in older fallers relative to their younger counterparts (Muir-Hunter & Wittwer, 2016). Previous work has provided evidence that measures of executive function are better predictors of DT relative to ST gait performance (Killane et al., 2014; Hausdorff et al., 2008). Given the link between variability and executive control, it is possible that this would also be the case for IIV metrics. Evidence of a strong association between IIV and dual-task gait performance would suggest that more variable individuals may be struggling to cope with everyday walking situations that place higher demands on the individual.

Relatedly, the gait assessment used in the present study only enabled the examination of walking speed. As previously mentioned, the temporal and spatial characteristics that make up an individual’s walk have been grouped into a number of distinct components (e.g., Lord et al., 2013). The development of more specialised equipment has made it possible to analyse an individual’s gait in more detail, allowing for components other than speed to be measured. One component that has been increasingly studied in recent years is gait variability; that is, the stride-to-stride fluctuations in an individual’s walking pattern. Previous work has demonstrated that measures of executive function are predictive of stride-to-stride variability in a number of gait parameters (e.g., van Iersel et al., 2008b; Hausdorff et al., 2005). Since IIV is closely tied to executive function, it is possible that measures of cognitive and gait variability would also be highly correlated with each other. Evidence of such associations may have particular importance since increased variability in a number of gait parameters has been linked to an increased risk of falls (e.g., Taylor et al., 2013;

Callisaya et al., 2011). Therefore, the detection of at-risk populations may contribute to the prevention of future falls, as well as to the prevention of gait impairment.

Future directions

The forthcoming chapters will address several considerations that have been raised in this Discussion section. The next chapter (Study 4) will describe an empirical study that builds on the present work by incorporating a more comprehensive assessment of gait performance. As previously mentioned, there is evidence to suggest that measures of executive function may be better able to predict measures of DT gait and gait variability than single-task gait speed. It is possible that this would also be the case for IIV metrics. Study 4 will examine this possibility using a dual-task paradigm where individuals will be asked to walk while simultaneously performing a backwards counting task. The number of single-task gait trials will also be increased making it possible to calculate a measure of variability between trials, as well as a measure of average speed across trials. With these additions to the gait assessment, it will be possible to whether IIV measures are significantly associated with DT gait performance and gait variability. Given that impairment in these gait parameters has been linked to an increased risk of falling, determining the extent to which IIV measures predict these outcomes may also be useful in the prevention of future falls.

Chapter 5

Study 4: Examining IIV in relation to dual-task gait and gait variability

5.1 Introduction

Study 3 empirically tested relations between IIV, gait speed and falls in a group of healthy older adults. The study built on previous investigations by examining how these relationships varied according to age and the demands of the task used to measure variability, while also investigating mechanisms that underpinned these relationships. Contrary to the majority of previous work, IIV measures did not distinguish between fallers and non-fallers though this may have been due to the low number and type of falls (e.g., slipped on ice) reported. Higher variability on the tasks with higher executive demands, Flanker and Stroop, was associated with slower walking speed whereas nonsignificant associations were reported for the three tasks with lower demands. Contrary to prior expectations, there was no evidence that associations between IIV and gait speed, or IIV and falls, varied as a function of age. Finally, a number of explanatory variables were examined as potential mediators of the relationship between IIV and gait. Adjusting for measures of physiological function and executive function did not have any impact on these associations. However, after controlling for processing speed, the association between Flanker IIV and gait was majorly attenuated.

A number of methodological limitations in the previous study were identified and, in particular, it was noted that the assessment of gait was relatively basic. This assessment included a 4-metre gait speed test where participants were timed while completing several walks along a short pathway with no distractions. This can be thought of as single-task (ST) walking. However, everyday situations generally involve more complex walking scenarios where the individual must simultaneously complete other tasks such as avoiding obstacles and route planning. This can be thought of as dual-task (DT) walking. In the ageing literature, DT walking has been extensively examined using dual-task paradigms in which an individual's gait performance is measured while concurrently performing a secondary task (e.g., reciting the alphabet). A number of studies have demonstrated that the addition of a secondary task often results in deleterious changes to gait in older adults such as reduced speed and reduced stability (e.g., Hausdorff et al., 2008; Dubost et al., 2006). This deterioration in performance, often referred to as the DT cost, occurs when the combined demands of both tasks exceed the attentional resources available to the individual, resulting in a decrement in either the walking or the secondary task (Lajoie et al., 1993; Abernethy, 1988; Kahneman, 1973).

Previous research has demonstrated that gait performance is reduced in the presence of a demanding secondary task in both younger and older adults. However, these DT costs have been shown to increase with increasing age (Beurskens & Bock, 2012). Given that older adults may struggle to cope with everyday activities that involve dual-tasking, there is good reason to investigate the factors that may contribute to reduced performance in these situations. This is particularly important as recent work has highlighted that these factors have not yet been fully elucidated (e.g., Vallesi, 2016). Furthermore, a number of reviews have demonstrated that older fallers adjust their gait more in response to a secondary task then older non-fallers (Muir-Hunter & Wittwer, 2016; Hsu et al., 2012; Beauchet et al., 2009). This suggests that individuals with increased DT costs may be particularly vulnerable to falls and, therefore, the early identification of these individuals may be important in preventing future falls.

Theoretically, it is expected that motor functions placing higher demands on executive abilities would be more closely related to IIV than motor functions with lower demands. For example, walking in a straight line with no distractions is not likely to draw on higher-order cognitive processes. However, complex walking scenarios that involve dual-tasking (e.g., crossing a busy street) may draw on executive abilities in order to, for example, inhibit distracting information. In line with this notion, executive measures have been shown to be highly associated with gait speed when measured under DT but not ST conditions (Killane et al., 2014; Coppin et al., 2006). Furthermore, lower scores on these measures predict greater decrements in gait performance in response to a secondary cognitive task (Hausdorff et al., 2008; Sheridan & Hausdorff, 2007). Given that IIV is thought to reflect fluctuations in executive control, it is possible that IIV measures would be a better predictor of walking performance under DT rather than ST conditions. Only one study has previously tested this hypothesis (Holtzer et al., 2014). Here, IIV on a Flanker task was associated with gait speed when individuals were simultaneously performing a backwards counting task, but not when they walked without distraction. The present study will extend these findings by incorporating a dual-task paradigm into the gait assessment, thereby allowing associations between IIV and DT gait to be examined.

In addition to looking at dual-task gait speed, it is also possible to assess other parameters of gait not related to speed. As mentioned in Chapter 1, the various temporal and spatial characteristics that make up an individual's walking pattern can be grouped into distinct components (e.g., Lord et al., 2013). One component that has been increasingly studied is gait variability; that is, the stride-to-stride fluctuations in an individual's walking pattern. Gait variability is relevant to the present work because it has been shown to increase with age (e.g., Kang & Dingwell, 2008; Owings & Grabiner, 2004). Increased gait variability can lead to poor balance and unsteadiness in older adults which, in turn, may increase the risk of a fall. In line with this notion, older fallers have been found to be more variable in a number of gait parameters, and all of these measures were better predictors of fall status than gait speed (Taylor et al., 2013; Callisaya et al., 2011; Verghese et al., 2009; Brach et al., 2005; Hausdorff et al., 2001).This suggests that increases in gait variability may be an important marker for falls risk. Therefore, elucidating the factors associated with these changes may contribute to the detection and prevention of future falls.

As with DT gait, there is a link between gait variability and higher-order cognitive abilities. For example, older adults with reduced white matter integrity in the frontal areas of the brain have more variable gait patterns (e.g., Srikanth et al., 2009; Rosano et al., 2007). In work that has fractionated gait into its constituent components, the "variability" component of gait has been more strongly associated with executive function than components such as "pace" and "rhythm" (Ikram et al., 2012). Furthermore, greater executive deficits have been found to predict higher variability in a number of gait parameters (van Iersel et al., 2008a; Hausdorff et al., 2005). Given the aforementioned link between IIV and executive control, measures of cognitive and gait variability might be expected to correlate highly with one another. Two studies have previously examined this relationship but these works produced contrasting findings (Sukits et al., 2014; Reelick et al., 2010). Subsequently, the present study will incorporate a measure of gait variability into the walking assessment, thereby making it possible to test the utility of IIV metrics when it comes to detecting this outcome.

In addition to incorporating measures of DT gait and gait variability, the extent to which key relationships vary according to age will again be examined. As previously mentioned, gait costs associated with dual-tasking and variability in gait both increase with age. There is also evidence that these aspects of gait are more prone to the effects of age than ST gait speed. One recent study reported a significant difference in DT stride time and stride-time variability between adults in their 50s and 70s, but no difference in stride time assessed under ST conditions (LaRoche et al., 2014). Against this background, it is likely that IIV measures would be better predictors of DT gait and gait variability in later old age compared to early and middle old age. This will be tested by examining these associations as a function of age using the same approach as in Study 3. Finally, a mediational approach will again be used to identify potential mechanisms underlying relationships between IIV and gait, and IIV and falls. Given the aforementioned evidence that measures of executive function are more closely linked to DT gait and gait variability than ST gait speed, it is expected that executive measures will mediate associations where IIV is found to predict these outcomes.

To summarise, the present research will build on Study 3 by incorporating a more comprehensive assessment of gait into the methodology. As well as re-examining associations between IIV, gait speed and falls, a number of other aims will be addressed. First, the study will determine whether IIV is significantly associated with measures of dual-task gait (gait speed, DT cost) and gait variability. Second, the study will assess whether relationships between IIV, gait and falls vary according to age. Finally, a mediational approach will be used to investigate mechanisms underlying these relationships. This will involve assessing the extent to which explanatory variables representing physiological and cognitive function are able to attenuate significant associations where they are found.

5.2 Methods

Participants

A total of 61 older adults from the local community took part in the study. A number of these participants also participated in Study 3 (n = 29) and were recruited with follow-up emails or telephone calls. Other volunteers were identified and recruited through visits to local organisations (e.g., community centres). Participants were screened for cognitive impairment using a cut off score of 26 or lower on the Montreal Cognitive Assessment (MOCA; Nasreddine et al., 2005) with one individual excluded on this basis. Another individual was excluded due to severe difficulties with completing the gait assessment. The remaining sample of 59 healthy adults had a mean age of 68.8 years (range 52-90), had spent an average of 13.2 years in full time education and included 42 women (71%). Participants were asked to complete the National Adult

Reading Test (NART) to determine their predicted full-scale IQ. Three of the individuals who took part were from a non-English speaking background and so an alternative formula was used to compute their predicted IQ. The two formulas are based on regression equations that have been calculated previously (Sullivan et al., 2000) and can be seen in Appendix 1A.

Physical Measures

Vision and muscle force tests: The measures used here were identical to those in Study 3. Visual acuity was assessed using a Snellen chart with each participant given an acuity score. Hand grip strength was measured using a handheld dynamometer with the average force (in kilograms) over six trials recorded. Leg resistance strength was measured using a spring gauge attached to the participant's dominant leg with the average force (in kilograms) over three trials recorded. More information about these physical measures can be found in the Methods section of the previous chapter.

Gait assessment: Gait speed was measured using a 4m walkway along which participants were instructed to walk at their usual pace from a standing start. Participants completed a total of 40 trials, 20 of which took place at the beginning of the testing session and 20 at the end. For half of these trials, participants engaged in a serial subtractions task (Kraepelin, 1899) while walking. The Serial 3s version of the task was used which requires the individual to count backwards in multiples of 3 starting from 99 (i.e. 99-96-93-90). Participants were instructed only to count while walking between the start and finish points of the walkway and to start each new trial with the number that followed the last correct answer given. Although participants were instructed to give equal priority to walking and counting, their responses to the Serial 3s task were not recorded and they were not corrected if a mistake was made.

Single-task (ST) and dual-task (DT) trials were counterbalanced according to subject ID. The average time taken to complete the 20 ST trials and 20 DT trials was calculated and used as measures of ST and DT gait speed, respectively. In order to determine the difference in performance between the two conditions, a dual-task cost measure was calculated according to conventions in previous work (e.g., McDowd, 1986). This measure represents the increased average time taken to complete the 4m walk under DT relative to ST conditions. It is expressed as a percentage and was calculated using the following formula:

$$\frac{Average\ DT\ time - Average\ ST\ time}{Average\ ST\ time} \text{ x } 100 \qquad (5)$$

In addition to calculating measures of DT performance, the standard deviation of the time taken to complete the 20 ST trials was calculated and used as a measure of gait variability. This is loosely based on a measure used in previous work that assessed variability in stride velocity between individual steps (Verlinden et al., 2013).

Falls History

The same falls questionnaire (Appendix 1B) that was used in the previous study was administered to participants in order to establish a comprehensive falls history over the two years prior to testing. More information on this questionnaire can be found in the Methods section of the previous chapter.

Cognitive Measures

Cognitive RT tasks: The tasks used here were identical to those in Study 3. Participants completed a short battery of RT tasks that varied in terms of the demands they placed on the individual The battery included two psychomotor tasks: Simple Reaction Time (SRT; 48 trials), 2-Choice Reaction Time (2-CRT; 48 trials) – as well as two response inhibition tasks: Flanker (64 trials) and Stroop (96 trials). More information on these tasks can be found in the Methods section of the previous chapter.

Other cognitive tasks: As in the previous study, participants also completed two paper and pencil tasks: Trailmaking A (TMT-A) and Trailmaking B (TMT-B). The time taken to complete TMT-A (in seconds) was recorded and used as a measure of processing speed. The ΔTMT score (time taken to complete Part B – Part A) was calculated and used as a measure of executive function. More information on the Trailmaking tasks can be found in the Methods section of the previous chapter.

Procedure

The testing session began with the first 10 ST trials and the first 10 DT trials of the gait assessment which were counterbalanced. Following this, basic demographical information was collected from participants and there was a short medical questionnaire that recorded information on a range of past conditions and current medication usage. The NART, MOCA and falls questionnaire were then administered, followed by a short battery of physical measures assessing visual acuity, grip strength and leg resistance strength. Participants then completed the four cognitive RT tasks that were also counterbalanced according to subject ID. The two Trailmaking tasks were administered half way through the battery of RT tasks. Finally, the testing session concluded with the second 10 ST trials and second 10 DT trials of the gait assessment. The entire testing session lasted approximately 60 minutes. Ethical approval for this study was obtained from the School of Psychology Research Ethics Committee and testing began in November 2014.

Data Processing

Calculation of IIV measures: After removing practice trials and incorrect responses, the coefficient of variation (CV) was calculated for the four RT tasks. Computation of the CV measure followed the same procedures that were used in the previous study. Table 5.1 shows the percentage of trials removed from each task during the different stages of data processing.

Missing data: As in Study 3, missing data for variables across the whole dataset were rare and subsequently replaced by imputing new values at the aggregate level. An expectation maximization algorithm was used to do this and the procedure was carried out in SPSS using all of the other available variables. Missing data frequencies ranged from 1.7% to 5.1% with only one variable marginally exceeding the 5% threshold under which it is deemed acceptable to use the EM algorithm (Schafer & Graham, 2002).

Table 5.1: Number of trials removed and replaced at each stage of data processing for the four RT tasks

Task	**Incorrect responses n removed (%)**	**Trials < 150ms n removed (%)**	**Trials > Mean + 3 SD n replaced (%)**
SRT	0	25 (0.85%)	51 (1.74%)
2-CRT	125 (4.27%)	17 (0.58%)	34 (1.16%)
Flanker (congruent)	26 (1.33%)	0	32 (1.64%)
Flanker (incongruent)	108 (5.53%)	1 (0.05%)	26 (1.33%)
Stroop (congruent)	15 (0.51%)	1 (0.03%)	29 (0.99%)
Stroop (incongruent)	131 (4.47%)	0	35 (1.20%)

Notes: 2-CRT = 2-choice reaction time; SD = standard deviation; SRT = simple reaction time

Composite measures: A PPA composite (based on the Physiological Profile Approach to falls risk (Lord et al., 2003)) was computed and consisted of performance on the Snellen, grip strength and leg resistance tests. It represents the functioning of physiological systems with higher scores indicating better physiological function. The PPA composite was computed in SPSS using principal components analysis with varimax rotation. The factor scores from this procedure were then saved.

Statistical Analysis

Analysis of the data proceeded through a number of stages. First, provisional descriptive analyses were carried out identical to those in the previous study. Second, a series of logistic regression analyses examined whether measures of IIV or gait significantly predicted fall status. Third, a series of linear regression analyses explored how strongly measures of IIV were associated with measures of gait (ST gait speed, DT gait speed, DT cost, gait variability). Models of gait variability here additionally controlled for ST gait speed as temporal parameters of gait variability have been shown to be influenced by walking speed (e.g., Kang & Dingwell, 2008). Fourth, Age x IIV and Age x Gait interaction terms were examined in all regression analyses to determine the extent to which relationships between IIV, gait and falls varied as a function of age. In the event that interaction terms were found to be significant after adjusting for the primary effects, the sample was stratified into two subgroups using the median value for age as the cut-off point. The corresponding associations were then retested in both groups to determine if the initial relationships were stronger in early or later old age.

Finally, a series of mediational analyses investigated the mechanisms underlying relationships between IIV, gait and falls where they were observed. In these analyses, explanatory variables representing physiological function and cognitive ability were introduced into significant associations in the younger and older subgroups. These models were examined before and after the explanatory variables were statistically controlled for. In linear regression models, changes in the variance explained (R^2) were examined. In line with the previous study, Salthouse's (1992) formula for calculating mediating effects was used. In logistic regression models, changes in the odds ratio were examined using the same formula. Three explanatory variables were introduced at this stage: 1) a PPA composite representing physiological function, 2) executive function measured with the ΔTMT score, and 3) processing speed assessed with the TMT-A task. As in Study 3, attenuations of less than 20% were interpreted as being small, those between 20% and 40% as interesting, those between 40% and 60% as important, and those above 60% as major.

5.3 Results

Predictors of fall status

Fallers and non-fallers had similar demographic characteristics and did not differ in performance on any of the physical measures, the gait assessment, or the four RT tasks (Table 5.2). Although group differences in Trailmaking A were non-significant, fallers took approximately 20 seconds longer to complete Trailmaking B (p < .05). A series of hierarchical logistic regression models explored the relationship between IIV and falls, and gait and falls, and whether these relationships varied according to age. As none of the demographic variables (e.g., gender, IQ) were significantly correlated with fall status (Table 5.3), these were not included in the models. In line with the

Table 5.2: Demographic, physical and cognitive characteristics of the whole sample, and of fallers and non-fallers

Variable	**Total sample (n=59)**	**Fallers (n = 23)**	**Non-fallers (n = 26)**
Age (years)	68.8 (7.73)	67.6 (8.02)	69.5 (7.55)
Gender – female (n,%)	42 (71%)	25 (69%)	17 (74%)
NART Predicted IQ	122.1 (5.30)	122.0 (5.49)	122.2 (5.25)
Snellen	9.59 (1.29)	9.83 (1.03)	9.44 (1.42)
Grip strength (kg)	20.7 (8.20)	20.3 (6.32)	21.0 (9.28)
Leg resistance (kg)	16.9 (6.60)	16.1 (6.31)	17.4 (6.80)
ST gait (s)	3.86 (0.92)	3.78 (0.80)	3.91 (0.99)
DT gait (s)	4.83 (1.83)	4.96 (1.99)	4.71 (1.75)
DT gait cost (%)	23.0 (26.6)	29.6 (36.1)	18.8 (17.5)
ST gait variability	0.25 (0.11)	0.23 (0.07)	0.25 (0.14)
SRT CV	0.24 (0.10)	0.24 (0.08)	0.25 (0.11)
2-CRT CV	0.20 (0.05)	0.21 (0.05)	0.19 (0.05)
Flanker CV	0.20 (0.10)	0.22 (0.11)	0.18 (0.10)
Stroop CV	0.22 (0.07)	0.22 (0.11)	0.22 (0.07)
Trailmaking A (s)	29.6 (11.4)	32.1 (12.7)	27.9 (10.4)
Trailmaking B (s)	65.6 (32.2)	75.9 (41.7)	59.0 (22.5)*

Notes: * p < .05
Continuous variables are expressed as means (SDs) and differences between fallers and non-fallers were assessed using independent t-tests
Categorical variables are expressed as frequencies (%) and differences between fallers and non-fallers were assessed using chi square tests
2-CRT = 2-choice reaction time; CV = coefficient of variation; DT = dual-task; NART = national adult reading test; SRT = simple reaction time; ST = single-task

Table 5.3: Pearson correlation coefficients for associations between key demographic, cognitive and gait variables

Variable	**Mean (SD)**	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age (years)	68.7 (7.73)	—												
2. Gender – female (n,%)	42 (71%)	-.18	—											
3. NART Predicted IQ	122.1 (5.30)	.07	.11	—										
4. Fallen last 2 years (n,%)	23 (39%)	-.12	.05	-.01	—									
5. ST gait (s)	3.86 (0.92)	.42**	.03	-.08	-.07	—								
6. DT gait (s)	4.83 (1.83)	.47**	-.06	-.03	.07	.79**	—							
7. DT cost (%)	23.0 (26.6)	.31*	-.12	.04	.20	.25	.79**	—						
8. ST gait variability	0.25 (0.11)	.46**	.06	.03	-.09	.70**	.67**	.32*	—					
9. SRT CV	0.24 (0.10)	.12	-.13	.12	-.05	.14	.28*	.32*	.18	—				
10. 2-CRT CV	0.20 (0.05)	.11	-.23	.02	.21	.03	.03	.05	-.03	.02	—			
11. Flanker CV	0.20 (0.10)	.08	-.11	-.10	.17	.05	.22	.34**	.04	.26	.40**	—		
12. Stroop CV	0.22 (0.07)	.30*	-.05	.01	.01	.10	.23	.29*	.09	.20	.36**	.23	—	
13. Trailmaking A (s)	29.6 (11.4)	.27*	-.25	.04	.18	.20	.29*	.30*	.28*	.14	.33**	.31*	.23	—
14. Delta TMT (s)	36.1 (27.2)	.30*	-.33*	-.11	.23	.20	.47**	.55**	.15	.63**	.29*	.13	.30*	.32*

Notes: * p < .05 ** p < .01

Gender is coded as 1 for males and 2 for females; Fall status is coded as 1 for fallers and 0 for non-fallers

2-CRT = two-choice reaction time; CV = coefficient of variation; DT = dual-task; SRT = simple reaction time; ST = single-task; TMT = trail making test

Table 5.4: Logistic regression models for age and IIV measures predicting falls

	SRT CV		**2-CRT CV**		**Flanker CV**		**Stroop CV**	
Model	B	OR	B	OR	B	OR	B	OR
Step 1								
Age	-.26	.77	-.34	.71	-.30	.74	-.30	.74
Predictor	-.08	.92	.50	1.65	.37	1.44	.11	1.12
Step 2								
Age x Predictor	.15	1.16	.57	1.77	.47	1.60	.34	1.40

Notes: Fallers were coded as 1 with non-fallers coded as 0
n fallers = 23 (39%); Step 1, df = 2; Step 2, df = 3
2-CRT = 2-choice reaction time; CV = coefficient of variation; SRT = simple reaction time

Table 5.5: Logistic regression models for age and gait measures predicting falls

	ST gait speed		**DT gait speed**		**DT gait cost**		**Gait variability**	
Model	B	OR	B	OR	B	OR	B	OR
Step 1								
Age	-.25	.78	-.43	.65	-.47	.63	-.22	.80
Predictor	-.05	.95	.33	1.39	.60	1.82	-.11	.90
Step 2								
Age x Predictor	.09	1.10	-.03	.97	-.32	.73	-.16	.86

Notes: Fallers were coded as 1 with non-fallers coded as 0
n fallers = 23 (39%); Step 1, df = 2; Step 2, df = 3
DT = dual-task; ST = single-task

findings from Study 3, variability on each of the four RT tasks did not significantly distinguish between fallers and non-fallers (Table 5.4). Similarly, non-significant primary effects were found for age and all four measures of gait performance (Table 5.5). The Age x IIV and Age x Gait interaction terms were also non-significant after accounting for the primary effects. As a result, none of the predictors of falls were examined further as a function of age.

Predictors of gait performance

A series of hierarchical linear regressions explored the relationships between IIV and gait, and the effect that age had on these relationships. As the demographic variables were not correlated with any of the gait measures (Table 5.3), these were not included in the models. For models predicting ST gait speed, Step 1 significantly added to the

Table 5.6: Linear regression models for age and IIV measures predicting gait performance

	SRT CV		**2-CRT CV**		**Flanker CV**		**Stroop CV**	
Model	β	R^2	β	R^2	β	R^2	β	R^2
ST gait speed								
Step 1								
Age	.40**		.43**		.41**		.42**	
Predictor	.09	.18**	.00	.17**	.02	.17**	-.03	.17**
Step 2								
Age x Predictor	.34**	.10**	-.08	.01	.02	.00	-.07	.00
DT gait speed								
Step 1								
Age	.44**		.47**		.45**		.44**	
Predictor	.22	.27**	-.03	.22*	.18	.25**	.10	.23**
Step 2								
Age x Predictor	.36**	.11**	-.16	.02	.11	.01	-.03	.00
DT gait cost								
Step 1								
Age	.27*		.30*		.28*		.24	
Predictor	.28*	17**	.01	.09	.32*	.19**	.21	.14*
Step 2								
Age x Predictor	.19	.03	-.14	.28	.18	.03	.04	.00
Gait variability								
Step 1								
Gait speed	.70**	.49**	.70**	.49**	.70**	.49**	.70**	.49**
Step 2								
Age	.20^		.21*		.21^		.22*	
Predictor	.08	.04	-.07	.04	.00	.04	-.03	.04
Step 3								
Age x Predictor	.13	.01	-.21*	.04*	-.17	.03	-.08	.01

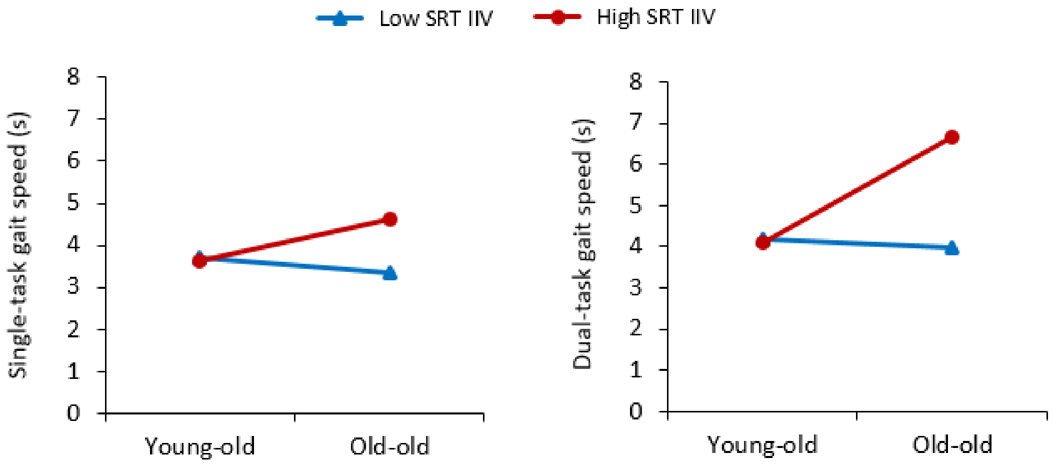
Notes: ^ $p < .06$ * $p < .05$ ** $p < .01$
Step 1, df = 2,56; Step 2, df = 3,55
Models of gait variability additionally controlled for gait speed at Step 1
2-CRT = 2-choice reaction time; CV = coefficient of variation; DT = dual-task; SRT = simple reaction time; ST = single-task

variance explained (Table 5.6). Inspection of the beta weights revealed significant primary effects for age (all ps < .01) but not for any measures of IIV. The addition of an Age x IIV interaction term at Step 2 significantly added to the variance explained in ST gait speed where SRT IIV was the predictor (p < .01). Inspection of the regression lines for this interaction suggested that the effect of variability on ST gait speed increased with age (Figure 5.1). As a result, this association was subjected to further examination (see next section).

Identical results were found for models predicting DT gait speed (Table 5.6). Step 1 significantly added to the variance explained but significant primary effects were only found for age (p < .01 for all models) and not for measures of IIV. At Step 2, the Age x IIV interaction term was significantly associated with DT gait speed where SRT IIV was the predictor (p < .01). Inspection of the regression lines suggests that the effect of variability on DT gait speed increased with age (Figure 5.1). As a result, this association was also re-examined as a function of age (see next section). For models predicting the dual-task cost, Step 1 significantly added to the variance explained for models where SRT IIV, Flanker IIV and Stroop IIV were included as predictors (Table 5.6). Inspection of the beta weights revealed that there was a positive primary effect of age and IIV in the former two models (ps < .05) but neither of these were significant in the model containing Stroop IIV. The addition of an Age x IIV interaction term at Step 2 did not add to the variance explained, indicating that age was not influencing these relationships. As a result, they were not examined further as a function of age.

Finally, for models of gait variability, Step 2 did not significantly add to the variance explained for any of the four models (Table 5.6). Inspection of the beta weights indicated that there was a positive primary effect for age which was statistically significant for models containing 2-CRT IIV and Stroop IIV (ps < .05), and approached significance for the other two models (ps < .06). However, none of the IIV measures were found to be associated with gait variability. The addition of an Age x IIV

Figure 5.1: Plot of the Age x SRT IIV interaction in relation to single-task and dual-task gait speed



interaction term at Step 3 significantly added to the variance in the model where 2-CRT IIV was included as a predictor (p < .05). Subsequently, this association was subjected to further analysis (see next section)

Re-examining significant associations as a function of age

The regression analyses suggested that three relationships between IIV and gait performance varied according to age. In order to better understand how age was influencing these associations, the sample was stratified using median age as the cut-off point. This produced a young-old group (aged 52 to 67 years) and an old-old group (aged 68 to 90 years). The three associations were then tested within these subgroups to determine if they were stronger in later relative to earlier old age. Due to the relatively broad age ranges in the subgroups, chronological age was taken into account in these models. In the first model, SRT IIV did not significantly predict ST gait speed in either subgroup (Table 5.7). In the second model, a significant association was found between SRT IIV and DT gait speed in the old-old group (p < .05) but not the young-old group. In the third model, 2-CRT IIV was not related to gait variability in either age group.

Table 5.7: Linear regression models for IIV measures predicting gait outcomes in the two age groups

	Young-old group		**Old-old group**	
Model	B	ΔR^2	B	ΔR^2
SRT CV ➜ ST gait speed				
Step 1: Age	.00	.00	.27	.07
Step 2: Predictor	-.15	.02	.29	.07
SRT CV ➜ DT gait speed				
Step 1: Age	-.10	.01	.35	.13
Step 2: Predictor	.13	.02	.45*	.18*
2-CRT CV ➜ Gait variability				
Step 1: Gait speed	.04	.00	.73**	.53**
Age	.20	.04	.22	.05
Step 2: Predictor	.08	.01	-.18	.03

Notes: * p < .05 ** p < .01
Young-old group – Step 1, df =1,26; Step 2, df = 2,25
Old-old group – Step 1, df = 1,29; Step 2, df = 2,28
Models of gait variability additionally controlled for gait speed at Step 1
2-CRT = 2-choice reaction time; CV = coefficient of variation; DT = dual-task; SRT = simple reaction time; ST = single-task

Testing for potential mediators

After establishing that SRT IIV significantly predicted DT gait speed in the old-old group, a mediation analysis was performed on this relationship. The results of his analysis can be seen in Table 5.8. After entering processing speed into the model, the variance in DT gait speed explained by SRT IIV fell by 8.4% with the model remaining statistically significant. Similarly, the variance explained remained unchanged after entering the PPA composite measure. After entering the switching composite measure, however, the effects of SRT IIV were reduced by 53.6%. This represents an important attenuation and subsequently caused the model to become non-significant.

Table 5.8: Explanatory variables entered into linear regression models for IIV measures predicting gait outcomes that were significant in the older age group

Model	Explanatory variable	R^2 change Before	R^2 change After	% attenuation
SRT CV ➜ DT gait speed	PPA	.179*	.191*	0%
	TMT-A	.179*	.083	8.4%
	ΔTMT	.179*	.164	53.6%

Notes: * p < .05
Age was adjusted for at Step 1 (df = 1,29), explanatory variables were entered at Step 2 (df = 2,28) and IIV measures were entered at Step 3 (df = 3,27)
CV = coefficient of variation; DT = dual-task; PPA = physiological profile approach; SRT = simple reaction time; TMT = trail making test

5.4 Discussion

The present experimental work builds on Study 3 by additionally measuring dual-task gait and gait variability. In line with the findings from the previous study, measures of IIV and gait did not predict fall status in the two years prior to testing. Similarly, there were non-significant associations across the whole sample between IIV and measures of ST gait speed, DT gait speed and gait variability. However, variability on the SRT and Flanker tasks was found to predict DT costs across the whole sample, whereas SRT IIV was significantly associated with DT gait speed in an old-old but not a young-old subgroup. In a subsequent mediation analysis, controlling for executive function considerably attenuated the effect of SRT IIV on DT gait speed in the older group.

However, adjusting for physiological function and processing speed had little to no effect.

Predictors of fall status

The lack of a relationship between IIV and falls is in line with the findings from Study 3. However, it contradicts the work reviewed in Studies 1 and 2 which provided evidence that older fallers were more variable than non-fallers on a range of RT tasks. As suggested in the previous study, the relatively low number of falls could have contributed to these findings. Although the rate of single fallers in the present study (39%) was higher than in Study 3 (27%), the rate of recurrent fallers (7%) remained low. This suggests that the majority of falls may have been one-off incidents caused by environmental factors rather than factors specific to the individual (e.g., muscle weakness, chronic disease). Indeed, further examination of the data revealed that 18 of the 31 (58%) total falls were reportedly caused by ice or snow, an object, or an uneven surface. These figures are in line with those in Study 3 and give further support to the notion that age-related cognitive decline is unlikely to be contributing to the falls experienced by older persons here. Additionally, the collection of falls data in this study was done retrospectively using a self-report questionnaire. As mentioned in Study 3, the self-report method has been shown to underestimate the true number of falls experienced compared to other methods such as monthly falls calendars (Garcia et al., 2015). Any discrepancy between the true number of falls and those that were reported could have made it more difficult for IIV measures to distinguish between fallers and non-fallers.

Nonsignificant associations between gait and falls, regardless of the gait measure used, is not consistent with prior expectations. This finding also contradicts previous evidence that gait impairment is a risk factor for future falls (Deandrea et al., 2010), and the positive associated identified in the previous study between ST gait speed and falls. Interestingly, the average time taken to complete the ST trials in the present study (3.86 seconds) was 0.14 seconds quicker than in Study 3, suggesting these individuals were slightly faster. This could be partially attributed to the fact that gait speed was averaged across 20 trials in the present work compared to just three in the previous study. Indeed, the average time taken to complete the first three of these 20 trials was 4.02 seconds which is similar to the time reported in Study 3 (4.00 seconds). Therefore, older persons here may have been walking slower during the first few trials and increased their speed as they became more familiar with the task. This slight reduction in gait speed over the 20 trials may have limited the potential of the gait measure to distinguish between fallers and non-fallers, particularly given the low number of falls that was noted earlier.

Predictors of gait performance

In contrast to Study 3, measures of IIV were not found to be predicting gait performance measured under single-task conditions. However, there was evidence of a relationship with DT gait. First, across the whole sample, higher IIV on the SRT and Flanker tasks was associated with greater DT costs. This was in line with expectations as previous work has demonstrated a link between executive deficits and larger DT costs in older adults (Hausdorff et al., 2008; Sheridan & Hausdorff, 2007). Neuroimaging work has also shown that neural compromise in the pre-frontal areas that mediate executive control is associated with higher gait costs while dual-tasking (e.g., Beurskens et al., 2014) as well as greater IIV levels (e.g., Bunce et al., 2007). Higher costs suggest that an individual is struggling to allocate the necessary attentional resources to the gait task, a process that is thought to be controlled by executive function (Ble et al., 2005). It makes sense then that these costs might be increased in individuals with higher IIV as this is thought to reflect deficits in executive and attentional control mechanisms.

Second, greater SRT IIV was associated with slower DT gait speed in the old-old but not the young-old subgroup. A link between IIV and DT gait speed was expected since variability is closely tied to executive function, measures of which have been shown to predict gait speed in attentionally demanding conditions (Killane et al., 2014; Coppin et al., 2006). It also supports findings from one previous study where IIV on a Flanker task significantly predicted gait speed under DT but not ST conditions (Holtzer et al., 2014). That this association was stronger in later relative to early and middle old age was also in line with expectations. In very old groups there is thought to be an increased reliance on executive abilities to maintain gait performance in complex situations (Yogev-Seligmann et al., 2008). Furthermore, greater IIV is thought to reflect deficits in executive and attentional control. Therefore, in these groups, highly variable individuals who struggle to allocate the necessary attentional resources to their walk when dual-tasking may be particularly prone to reductions in speed. The hypothesis that IIV was influencing DT gait speed through executive function will be discussed in more detail below.

Finally, non-significant associations were reported between measures of cognitive and gait variability. This is surprising since both are thought to be increased in the presence of brain white matter damage (e.g., Srikanth et al., 2009; Bunce et al., 2007) and executive deficits (e.g., Bunce et al., 2008; van Iersel et al., 2008a). However, it does support the findings of one previous study that also found no evidence of a relationship between the two (Sukits et al., 2014). It is possible that the measure used here did not adequately capture the stride-to-stride fluctuations in stride length and step timing that drive this component of gait. This possibility is supported by the finding that ST gait speed and gait variability were highly correlated ($r = .70$) and, after controlling for ST gait speed, the variance explained in gait variability fell considerably (see Table 5.6). This suggests that there was significant overlap between these two measures and that any difference in gait variability were likely to have been driven by differences in walking speed. Though not possible in the current work, researchers elsewhere have used more specialised equipment to measure stride-to-stride fluctuations in a variety of different gait parameters (e.g., Verlinden et al., 2013). Future research would benefit from using such methods to further investigate the links between cognitive and gait variability.

Testing for potential mediators

Potential mechanisms underlying the association between SRT IIV and DT gait speed in the old-old group were explored using a mediational approach. In line with Study 3, controlling for physiological function had little effect on this relationship. The introduction of processing speed only slightly reduced the effects of IIV on DT gait speed, whereas an important attenuation was seen after adjusting for executive function. This is contrary to the findings from the previous study where the same measure of processing speed majorly attenuated the relationship between Flanker IIV and ST gait speed, with executive function not found to be playing a role. These inconsistent findings could be attributed to the fact that explanatory variables here were introduced into models of DT gait speed. However, in the previous study, potential mediators were examined in relation to ST gait speed. It is expected that higher order cognitive processes, and in particular executive abilities, would contribute more to gait performance in attentionally demanding conditions but this is not likely to be the case for processing speed. Indeed, previous work has demonstrated that executive function is a better predictor of DT gait performance (Killane et al., 2014; Coppin et al., 2006), whereas processing speed is more highly associated with measures of ST gait (Lowry et al., 2012; Soumare et al., 2009).

Another explanation for these inconsistent findings concerns the group for whom tests of mediation were performed on. Here, only an older subgroup (aged 68 to 90 years) was subjected to these analyses compared to the whole sample in Study 3. As previously noted, executive abilities are increasingly relied upon in later old age in order to compensate for age-related deterioration in sensory and motor processes, and maintain performance in complex gait situations (Yogev-Seligmann et al., 2008; Shumway-Cook & Woollacott, 1995). It is possible, therefore, that executive function makes a smaller contribution towards gait performance in early and middle old age when these processes are still reasonably intact. Against these considerations, the finding that executive control was accounting for the relationship between IIV and DT gait in the present study is in line with expectations.

Limitations

There are a number of limitations concerning the present study that may have affected the results and, therefore, should be acknowledged. As in Study 3, only cross-sectional data were collected and so it was not possible to infer a causal link between IIV and gait based on the associations that were found. This issue will be explored in more depth in a later chapter. Another limitation common to both studies is the way in which executive function was assessed. According to a well recognise framework, executive function is made up of three distinct components: Task switching, response inhibition, and information updating (Miyake et al., 2000). The ΔTMT score used in Study 3 and Study 4 mainly captures task switching ability but it could be that inhibition and updating are also influencing relationships between IIV and gait. As a result, using the ΔTMT score as an explanatory variable in the present analyses may have led to the role that executive function is playing being underestimated. Future research would benefit from assessing each of these components separately, thereby making it possible to examine the contribution each is making to significant associations between IIV and outcome.

Although including a dual-task condition in the gait assessment was a strength of the present study, the secondary task that was used (Serial 3s) was relatively basic. As a result, it may not have interfered sufficiently with the attentional resources that are required to maintain walking performance in all older adults. Indeed, the average percentage by which gait speed fell in the DT condition (i.e., the DT cost) was 23% and this figure had a large standard deviation of 26.6. This suggests that some older adults struggled with the additional demands of the secondary task whereas others coped reasonably well, in line with previous observations when the same task was used (LaRoche et al., 2014). An important aim of the present research was to investigate factors that may contribute to reduced gait performance in complex walking situations. This aim may be better addressed by incorporating a secondary task that is sufficiently demanding to produce high gait costs in all subjects. Previous research has demonstrated that verbal fluency tasks (e.g., naming as many words as possible that begin with a certain letter) produce greater DT costs in gait speed than backwards counting tasks (Hall et al., 2011). Therefore, a dual-task paradigm where individuals walk while performing a verbal fluency task may more accurately assess the demanding gait scenarios that the present research set out to address.

Finally, IIV metrics in the present study were derived from RT tasks where only the time taken to respond to each trial was recorded. Other investigations of RT performance have broken IIV down into separate components that were then examined separately. For example, a number of studies have looked at variability in the time taken to decide on a correct response (decision time IIV) and the time taken to physically make that response (movement time IIV) in both young and old adults (Gorus et al., 2008; Gorus et al., 2006; Bunce et al., 2004). The findings provided evidence that age-related increases in variability may be attributable to the decision component of the RT task rather than the motor component. Against this background, it is possible that individual components of IIV would be differentially related to falls and gait outcomes. Only one study has investigated this possibility (Reelick et al., 2010), providing some evidence that IIV in decision time and movement time might be associated with different gait variability parameters. However, more research is needed to further examine the relationship between different IIV components and both gait and falls.

Conclusion and future directions

The present study is one of the first to investigate IIV in relation to DT gait performance and has produced some potentially important findings. In line with previous empirical work, IIV was found to be more closely related to DT relative to ST gait outcomes. This was expected since IIV is closely linked to executive function, and walking while performing a secondary task places much greater demands on executive abilities than walking alone. The link between variability and DT gait was also found to be stronger in later old age compared to earlier old age. Again, this was expected as executive function becomes increasingly important for handling complex gait situations with increasing age. The influence of executive function was later confirmed when controlling for the ΔTMT score majorly attenuated the relationship between IIV and DT gait in the older age group. Prior to this study, it was hypothesized that very old adults may have particular difficulty when dealing with the demands of DT walking. Indeed, the average DT cost of the old-old group (29.0%) in the present study was almost twice as high as the young-old group (16.4%; unreported analyses). The identification of older persons with higher DT costs is a potentially important objective as this may signal an inability to perform a number of daily living activities that rely on dual-tasking. The present findings suggest that increased variability may contribute to age-related changes in DT gait performance and, therefore, measures of IIV may have considerable potential with respect to detecting these changes.

The following chapters will address some of the considerations that have been put forward in this Discussion section. First, in the forthcoming study, the gait assessment will incorporate additional dual-task conditions, one of which will involve a secondary motor task and the other a secondary verbal fluency task. This will make it possible to assess how different types of secondary task (i.e., motor versus cognitive) and different task demands (i.e., higher versus lower) influence the relationship between IIV and DT gait. Furthermore, since the verbal fluency condition is expected to produce higher DT costs, this may provide a more valid measure of the challenging walking scenarios that this research is interested in. Second, Study 5 will add a second choice RT task to the cognitive battery. This task will independently measure the time taken to decide on a response (decision time) and the time taken to physically make that response (movement time), and compute IIV measures for both. These different IIV components will then be examined in relation to both gait and falls. Finally, two additional components of executive function, response inhibition and information updating, will be assessed using new RT tasks. This will make it possible to investigate the contributions of each of the three executive abilities (switching, inhibition, updating) to any associations identified between IIV and gait, or IIV and falls.

Chapter 6

Study 5: The relationship between IIV, gait and walking demands

6.1 Introduction

The previous study further investigated the relations between variability, gait and falls, building on Study 3 by examining whether IIV was significantly associated with dual-task (DT) gait and gait variability. In line with observations in Study 3, measures of IIV or gait did not distinguish between fallers and non-fallers. Similarly, non-significant associations were reported between IIV on all five RT tasks and single-task (ST) gait speed. There was evidence that variability was related to dual-task gait, however, with higher IIV on the SRT and Flanker tasks associated with greater DT costs across the whole sample. Furthermore, SRT IIV was found to predict DT gait speed in a younger but not an older subgroup. Tests of mediation were performed on this latter association with the results indicating that executive function, but not processing speed or physiological function, was underlying the effects of IIV on gait performance.

This third experimental study will aim to shed light on a number of issues that have been raised in the previous chapters. First, a key aim of Study 4 was to investigate factors contributing to reduced gait performance in complex walking situations. A dual-task paradigm was administered that involved walking while performing a backwards counting task. However, the relatively low DT costs that were reported in this condition suggest that this task may not have been demanding enough to interfere with the gait of many older adults in the sample. As a result, this may have made it more difficult for IIV measures to detect between-person differences in performance. Previous research has demonstrated that executive abilities are stronger predictors of DT gait outcomes when the secondary task is more demanding (Hall et al., 2011; Srygley et al., 2009; Rochester et al., 2004). This makes sense as executive function is involved in the allocation of attentional resources (Ble et al., 2005) and more demanding DT situations are more likely to draw heavily on these resources.

Given the close theoretical link between IIV and executive function, it is reasonable to expect that associations between variability and DT gait would also strengthen as the dual-task condition becomes more demanding. In addition to backwards counting tasks, tests of verbal fluency have often been used as the secondary task in dual-task paradigms in previous research. Examples of such tests involve naming as many unique words beginning with a certain letter of the alphabet as possible (e.g., Nascimbeni et al., 2015; Hall et al., 2011) or producing as many different animal species as possible (e.g., Montero-Odasso et al., 2009; Reelick et al., 2009). Compared to backwards counting tasks, which are relatively automatic and remain the same difficulty throughout, it is likely that tests of verbal fluency would place a greater demand on individuals and this would increase as the task progresses. Indeed, one previous study reported that gait interference was greater when individuals were required to simultaneously produce words beginning with a certain letter compared to when counting back in threes (Hall et al., 2011). Measures of executive function have also been found to be better predictors of DT gait performance when the secondary task assesses verbal fluency rather than mental arithmetic (van Iersel et al., 2008a). Against this background, there is good reason to expect that IIV measures would be more closely related to gait outcomes when a verbal fluency task is used, rather than the Serial 3s task. This hypothesis will be tested in the present study by incorporating a second DT condition in which participants will be asked to walk while simultaneously enumerating as many words as possible beginning with a certain letter.

To this point there has been a focus on dual-task paradigms with a cognitive secondary task. However, other work has examined walking while performing concurrent motor tasks such as carrying a tray with a glass of water resting on it or buttoning a coat (Beurskens & Bock, 2013; Taylor et al., 2013). These tasks can be thought of as everyday motor activities and, as such, they are unlikely to interfere with the attentional resources needed to maintain gait performance while dual-tasking. Indeed, they have both been found to produce smaller costs in DT paradigms than cognitive tasks that involved backwards counting or visual processing (Beurskens & Bock, 2013; Taylor et al., 2013). Given the relatively small demands that are associated with these tasks, it is unlikely that higher-order executive processes would need to be recruited to ensure sufficient attentional resources are allocated to both the gait task and the secondary task. It is also expected that measures of IIV, which are closely tied to executive function, would be less able to predict DT gait outcomes when such motor tasks are used. This notion will be tested in the current work by incorporating a third DT condition in which individuals will walk while carrying a tray with a glass of water resting on it.

Second, previous research has argued that RT tasks such as the ones used in these studies capture several elements of IIV, some of which are closely tied to and mediated by the speed of the response and others which are not (Dykiert et al., 2012). It is important to understand how these constituent components contribute to the overall variability that is detected, particularly as an important goal of the present work is to identify the unique predictive utility of IIV measures. However, as the RT tasks used so far only captured the individual response times for each trial, it has not been possible to disentangle the relative contributions of different IIV components. Previous empirical work has investigated this issue by administering RT tasks where the different actions that contribute to making a response are measured independently. In their study of reaction time and intelligence, Jensen and Munro (1979) used specialised apparatus to record the time from stimulus onset to the release of a home key (decision time) and the time taken to move from the home key to a response key (movement time) on a choice RT task. After finding only a modest correlation between decision time and movement time (r = 0.37), they concluded that the two contained unique sources of variance and should be treated separately. They also reported that measures of intelligence were positively associated with IIV on the decision component but not the movement component of the tasks.

A number of studies have used similar procedures to look at decision time and movement time on RT tasks but only a handful of these have also measured variability (Gorus et al., 2008; Gorus et al., 2006; Spirduso & Clifford, 1978). One such study examined variability in decision time (decision IIV) and movement time (movement IIV) on several choice RT tasks in old and young adults (Bunce et al., 2004). Here, decision IIV was found to be much higher than movement IIV and significantly greater in the older group, which was not the case for movement IIV. These results suggest that age-related increases in variability may be attributable to the decision component of the task; in other words, the component that draws heavily on cognitive resources and not motor processes. Currently, very little is known about how the cognitive and motor components of variability are related to either gait or falls. The present study will attempt to improve understanding of these relationships by administering a choice RT task that records both the decision and movement times of the response, with variability measures computed for both. These components will then be investigated in relation to falls and gait, with the expectation that decision IIV will be the stronger predictor of these outcomes.

Finally, executive function has been treated as a possible mediator of the effects of IIV in each of the previous experimental studies. The ΔTMT measure that has been used to assess executive function in these works has been widely applied in ageing research and is considered to be a relatively robust indicator of this construct (Sanchez-Cubillo et al., 2009). However, it is limited in that it is thought to largely capture task switching ability. While the extent to which it captures response inhibition and updating, the other two components identified in Miyake's widely recognised model (Miyake et al., 2000), is limited. In healthy ageing, there is evidence that selective deficits occur in different executive abilities as opposed to a more general decline in overall executive function (Lin et al., 2007; Plumet et al., 2005). It is possible that some older adults exhibit signs of decline in one component while the others are reasonably well maintained. If indeed this is the case, it would not have been picked up by the single measure of executive function that was used in Studies 3 and 4. This may have led to the role that executive control was playing in relationships involving IIV being underestimated.

Furthermore, there is evidence to suggest that certain components of executive function may be more closely linked to gait outcomes than others. One study reported that updating was the executive component that best predicted measures of gait variability (Beauchet et al., 2012) whereas another provided evidence that it was task switching (van Iersel et al., 2008a). Other work has shown that DT costs in stride time, stride length and gait speed were associated with performance on a divided attention task, but not working memory or inhibition tasks (de Bruin & Schmidt, 2010). Taken together these findings suggest that components of executive function are differentially related to gait outcomes, although there is mixed evidence as to which component is the strongest predictor. Exploring such associations is beyond the scope of the present work, however, these findings do justify the inclusion of additional measures of executive function for use in tests of mediation. This will provide more insight into the role that higher-order cognitive processes are having on relationships between IIV and gait, and IIV and falls, where they are observed.

To summarise, this third experimental study will build on investigations carried out in the previous two studies. It will do this by incorporating additional dual-task conditions into the gait assessment and by measuring the constituent components of both IIV and executive function. In addition to re-examining associations involving IIV that were tested in the previous studies, these changes to the methodology will allow several news aims to be addressed. First, the present work will examine the relationship between IIV and gait in DT conditions where the secondary task places low (motor), medium (Serial 3s) and high (verbal fluency) demands on attentional resources. Second, this study will test the hypothesis that IIV on the decision component of a choice RT task is a better predictor of falls and gait performance than IIV on the motor component. Third, as in the previous two studies, the extent to which associations involving IIV vary according to age and the demands of the task used to derive variability measures will be investigated. Fourth, a mediational approach will again be used to identify potential mechanisms underlying relationships between IIV and gait, and IIV and falls, where they are found. However, the present work will build on Studies 3 and 4 by testing the effects that different components of executive function are having on these relationships.

6.2 Methods

Participants

Data were collected for 69 older adults from the local community. All participants had taken part in at least one of the previous two empirical studies and were recruited with follow-up emails or telephone calls. Participants were screened for cognitive impairment using a cut off score of 26 or lower on the Montreal Cognitive Assessment (MOCA) with seven individuals excluded on this basis. This left a total of 62 healthy adults whose data were processed and analysed. This sample had a mean age of 69.6 years (range 55-87), had spent an average of 14.4 years in full time education and was made up of 49 females (79%). They were all asked to complete the National Adult Reading Test (NART) in order to determine their predicted full-scale IQ. Three participants were from a non-English speaking background and their IQ was estimated with an alternative formula (see Appendix 1A).

Physical Measures

Tests of vision, hand grip strength and leg resistance strength were administered to participants that were identical to those used in the previous two studies. More information about these measures can be found in the Methods section of Chapter 4.

Gait Assessment

Gait assessment: Gait speed was assessed using a 4m walkway along which participants were instructed to walk at their usual pace from a standing start. Participants walked from one end of the walkway to the other for a total of 40 trials, ten of which were carried out under single-task conditions. For the other 30 trials, participants walked while completing one of three secondary tasks (10 trials for each).

The first of these was a simple motor task that involved carrying a tray with a full glass of water resting on it. The second task, Serial 3s, was identical to the secondary task used in Study 4 and involved counting backwards in multiples of 3 starting from 99 (i.e. 99-96-93-90). Participants were instructed only to count while walking between the start and finish points of the walkway and to start each new trial with the number that followed the last correct answer that was given. The third task was a test of verbal fluency and involved enumerating as many unique words as possible that started with the letter 'B' (excluding proper nouns). Again, participants were instructed to only name words while walking between the start and finish points of the walkway. For all three DT conditions, participants were instructed to give equal priority to walking and performing the secondary task. For the Serial 3s and verbal fluency conditions, participants made their responses to the secondary task out loud and these were recorded using a Dictaphone.

The average time taken to complete the 10 ST trials and 10 DT trials for each of the three conditions was calculated and used as measures of gait speed. In line with the procedure used in Study 4, a DT cost measure was computed for each of three DT conditions. This measure represents the increased average time taken to complete the 10 trials in each DT condition relative to the 10 ST trials. It is expressed as a percentage and was calculated using the following formula:

$$\frac{Average\ DT\ time - Average\ ST\ time}{Average\ ST\ time} \text{ x } 100 \qquad (6)$$

Falls History

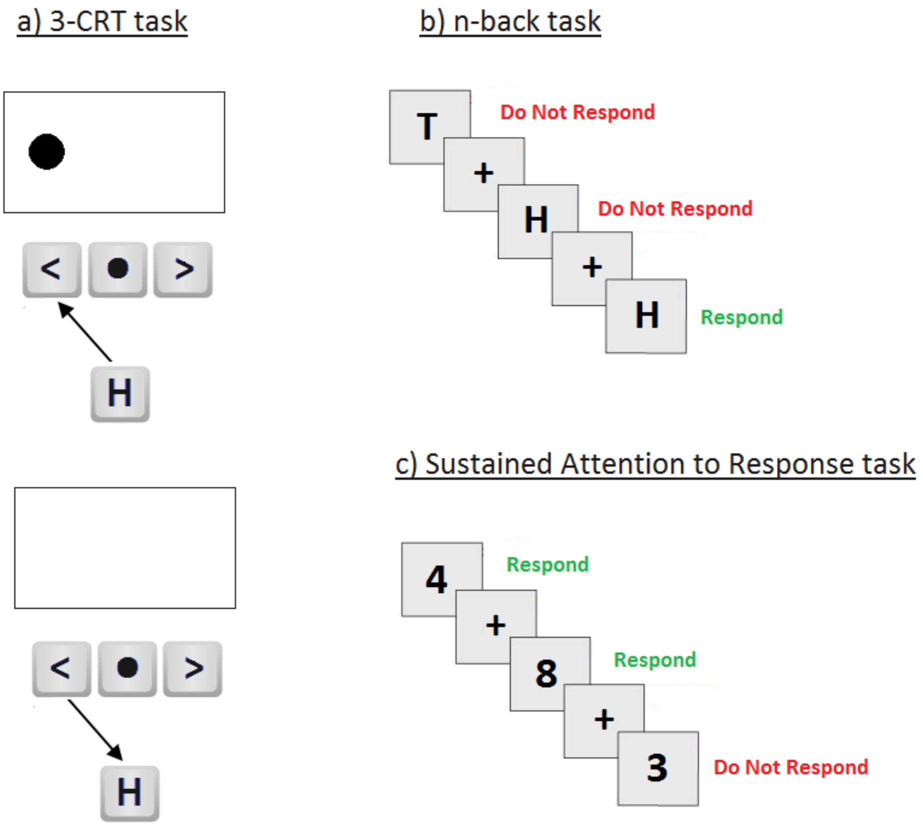
The same falls questionnaire (Appendix 1B) that was used in the previous two studies was administered to participants in order to obtain a comprehensive falls history over the two years prior to testing. More information on this questionnaire can be found in the Methods section of Chapter 4.

Cognitive Measures

Cognitive RT tasks: Participants completed a battery of seven RT tasks. Four of these were identical to those used in the previous two studies: Simple Reaction Time (SRT), 2-Choice Reaction Time (2-CRT), Flanker and Stroop. More information on these tasks can be found in the Methods section of Chapter 4. A further three tasks were introduced in the present investigation. These tasks were also administered on a computer using E-Prime software, with trials presented pseudo randomly and written instructions and practice trials given before each task. Examples of the stimuli used in each of the three new tasks can be seen in Figure 6.1.

Movement and decision RT: A three choice version of the choice RT task (Bunce et al., 2004) was used to separately assess the movement and decision components of response time (see Figure 6.1a). In this task, a black circle with a diameter of 25mm appeared on either the left, middle or right side of the screen. Participants were instructed to respond to the location of the stimulus by pressing the 'Insert', 'Home' or 'Page Up' key on a standard keyboard. These were labelled with a left arrow, a black circle or a right arrow, respectively. Before pressing one of these 3 keys, participants were told to rest their finger on the 'Down Arrow' key which was labelled with an H to indicate “Home”. After pressing one of the 3 keys the black circle disappeared, and

Figure 6.1: Examples of the stimuli used in the three new RT tasks


a) 3-CRT task

b) n-back task

c) Sustained Attention to Response task

participants were instructed to return to the home key and press it which generated a new circle. Participants were told to continually alternate between pressing the home key and one of the three direction keys, always using the same finger from the same hand. There were 72 trials in total. The time taken to move from the home key to one of the directional keys (Decision RT) and the time taken to move back to the home key (Movement RT) was recorded for each trial.

Response inhibition: In the Sustained Attention to Response Task (SART; Robertson et al., 1997), the numbers 1-9 appeared randomly on the screen for 1000 milliseconds at a time (see Figure 6.1c). After each number, a fixation cross appeared on the screen for 500 milliseconds. Participants were instructed to press the spacebar in response to every number that was not a 3, but withhold their response when the 3 appeared. This task consisted of 180 trials, 34 of which were omission trials in which the participant had to inhibit their response to the number 3. Performance was measured with the D-prime, a sensitivity index that was calculated by subtracting the standardised false alarm rate (i.e., the proportion of omission trials where the participant incorrectly responded) from the standardised hit rate (i.e., the proportion of target trials where the participant correctly responded). Greater scores on this metric reflect a greater ability to inhibit natural responses.

Updating: In the n-back test (Braver et al., 1997; Cohen et al., 1994), various consonants from the alphabet (B,C,F,G,H,K,L,M,N,P,R,S,T) appeared randomly on the screen for 500 milliseconds at a time (see Figure 6.1b). After each letter, a fixation cross appeared on the screen for 1000 milliseconds. Participants were instructed to press the spacebar every time the letter currently on the screen matched the letter that previously appeared. If the letters did not match, they were instructed to do nothing. This task consisted of 96 trials – 24 of these were target trials in which the participant was required to make a response. The D-prime was again calculated by subtracting the standardized false alarm rate from the standardized hit rate. Greater scores on this metric reflect a greater ability to update the content of one’s working memory.

Other cognitive tasks: Participants also completed two written tasks: Trailmaking A (TMT-A) and Trailmaking B (TMT-B). The time taken to complete TMT-A (in seconds) was recorded and used as a measure of processing speed. The ΔTMT score (time taken to complete Part B – Part A) was calculated and used to measure the task switching component of executive function. More information on the Trailmaking tasks can be found in the Methods section of Chapter 4.

Procedure

The testing session began with the collection of basic demographical information a short medical questionnaire that recorded information on a range of past conditions and current medication usage. The NART, MOCA and falls questionnaire were then administered, followed by a battery of physical measures that assessed visual acuity, grip strength and leg resistance strength. Participants then completed the 40 trials of the gait assessment with the order in which the four conditions were completed also counterbalanced. Finally, participants completed the seven cognitive RT tasks: SRT, 2-CRT, Flanker, Stroop, 3-CRT, n-back and SART which were also counterbalanced. The two pen and paper cognitive tests, Trailmaking A and B, were administered to participants halfway through the battery of RT tasks. Ethical approval for this study was obtained from the School of Psychology Research Ethics Committee and testing began in June 2015.

Data Processing

Calculation of IIV measures: After removing practice trials and incorrect responses, the coefficient of variation (CV) was calculated for five of the RT tasks (SRT, 2-CRT, Flanker, Stroop, 3-CRT). Computation of the CV measure followed the same procedures that were used in the previous two studies. Table 6.1 shows the percentage of trials removed from each task during each stage of data processing. Separate measures were calculated for the decision and movement components of the 3-CRT task.

Missing data: As in the previous two studies, missing data for variables across the whole dataset were rare, but where appropriate were replaced by imputing new values at the procedure was carried out in SPSS using all of the other available variables. Missing data frequencies ranged from 1.4% to 2.9%, well within the 5% threshold under which it is deemed acceptable to use the EM algorithm (Schafer & Graham, 2002).

Table 6.1: Number of trials removed and replaced at each stage of data processing for the five RT tasks

Task	Incorrect responses n removed (%)	Trials < 150ms n removed (%)	Trials > Mean + 3 SD n replaced (%)
SRT	0	17 (0.57%)	59 (1.98%)
2-CRT	36 (1.21%)	5 (0.17%)	56 (1.88%)
Flanker (congruent)	34 (0.86%)	1 (0.03%)	29 (0.73%)
Flanker (incongruent)	126 (3.18%)	1 (0.03%)	33 (0.83%)
Stroop (congruent)	24 (0.40%)	0	46 (0.77%)
Stroop (incongruent)	106 (1.78%)	5 (0.08%)	53 (0.89%)
3-CRT (decision)	28 (0.63%)	0	87 (1.95%)
3-CRT (movement)	0	0	75 (1.68%)

Notes: 2-CRT = 2-choice reaction time; 3-CRT = 3-choice reaction time; SD = standard deviation; SRT = simple reaction time

Composite measures: A PPA composite (based on the Physiological Profile Approach to falls risk (Lord et al., 2003)) was computed and consisted of performance on the Snellen, grip strength and leg resistance tests. It represents the functioning of physiological systems with higher scores indicating better physiological function. The PPA composite was computed in SPSS using principal components analysis with varimax rotation. The factor scores from this procedure were then saved.

Statistical Analysis

Analysis of the data proceeded through a number of stages. First, provisional descriptive analyses were carried out identical to those in the previous two studies. Second, a series of logistic regression analyses examined whether IIV or gait measures predicted fall status in the two years prior to testing. Third, a series of linear regression analyses explored how strongly each measure of IIV was associated with measures of gait performance (ST gait speed, DT gait speed, DT cost) across the four conditions. Fourth, Age x IIV and Age x Gait interaction terms were additionally examined in all regression models to determine the extent to which relationships between IIV, gait and falls varied as a function of age. Where interaction terms were significantly associated with either gait or falls after taking into account the primary effects, the sample was stratified into two subgroups with the median value for age used as a cut-off point. The corresponding associations were then examined in the two subgroups to determine the strength of these relationships in early and later old age. Due to the increased number of models that were tested in the present study, alpha was set conservatively at $p < .01$ for statistical significance for all regression models to counter the familywise error rate.

Finally, a series of mediator analyses investigated the mechanisms underlying relationships between IIV, gait and falls where they were observed. These analyses followed the same procedure that was used in the previous two studies. In line with these studies, the same measures of physiological function (PPA composite) and processing speed (TMT-A) were included. Three new variables were also introduced that reflected each component of executive function: 1) task switching measured with the ΔTMT score, 2) information updating assessed with the n-back task, and 3) response inhibition assessed with the Sustained Attention to Response Task (SART).

6.3 Results

Predictors of fall status

The fallers in the sample were 5.2 years older on average than non-fallers and performed significantly worse on both the grip strength and leg resistance tests (Table 6.2). Furthermore, all 17 individuals who reported a fall in the two years prior to testing were female. Fallers and non-fallers did not differ in their gait performance across the four conditions. They also had similar IIV levels for each of the five RT tasks and performed equally well on the three tests that assessed executive function. A series of hierarchical logistic regression models examined the association between IIV and falls, and whether these relationships varied according to age. As gender was found to be significantly correlated with fall status (Table 6.3), this was adjusted for in each model. Six IIV measures were computed in total, however, none of these were found to be significant predictors of falls (Table 6.4). Similarly, there were non-significant primary effects for each of the seven measures of gait performance on falls (Table 6.5). After taking into account the primary effects, the Age x IIV or Age x Gait interaction terms were also not associated with falls. This indicated that age was not having an effect on these relationships and, as such, predictors of falls were not examined further as a function of age.

Predictors of gait performance

A series of hierarchical linear regressions explored relationships between IIV and gait performance, and the effect that age had on these relationships. As NART IQ was found to correlate significantly with five of the seven measures of gait (Table 6.3), this was controlled for in the models. Of the six models that were created for ST gait speed, Step 2 only significantly added to the variance explained in one (Table 6.6). Inspection of the beta weights indicated that increased variability on the Stroop task was associated with a slower walking speed under ST conditions. For the six models of DT gait speed assessed in the motor condition, and also the six models of DT costs in the same condition, Step 2 did not significantly add to the variance explained in outcome

Table 6.2: Demographic, physical and cognitive characteristics of the whole sample, and of fallers and non-fallers

Variable	**Total sample (n = 62)**	**Fallers (n = 17)**	**Non-fallers (n=45)**
Age (years)	69.6 (6.72)	73.4 (5.78)	68.2 (6.55)**
Gender – female (n,%)	49 (79%)	17 (100)	32 (71.1)**
NART predicted IQ	114.1 (7.16)	113.7 (7.02)	114.3 (7.29)
Snellen	9.40 (1.27)	9.47 (1.28)	9.38 (1.28)
Grip strength (kg)	21.1 (8.98)	15.9 (4.67)	23.1 (9.46)**
Leg resistance (kg)	16.3 (7.62)	13.4 (5.10)	17.4 (8.17)*
ST gait (s)	3.77 (0.69)	3.84 (0.94)	3.74 (0.58)
DT gait – motor (s)	4.15 (0.89)	4.26 (1.10)	4.11 (0.82)
DT gait – serial 3s (s)	4.67 (1.74)	5.18 (2.84)	4.48 (1.07)
DT gait – verbal fluency (s)	5.38 (2.59)	6.38 (4.56)	5.00 (1.09)
DT cost – motor (%)	10.4 (11.5)	10.9 (10.4)	10.2 (12.0)
DT cost – serial 3s (%)	23.1 (32.1)	31.6 (51.6)	19.8 (20.5)
DT cost – verbal fluency (%)	41.5 (52.0)	61.7 (92.4)	33.9 (20.7)
SRT CV	0.22 (0.10)	0.20 (0.07)	0.23 (0.10)
2-CRT CV	0.19 (0.06)	0.20 (0.05)	0.18 (0.06)
Flanker CV	0.18 (0.09)	0.19 (0.07)	0.17 (0.09)
Stroop CV	0.23 (0.09)	0.26 (0.11)	0.22 (0.08)
3-CRT Movement CV	0.10 (0.07)	0.12 (0.08)	0.09 (0.06)
3-CRT Decision CV	0.11 (0.05)	0.12 (0.05)	0.11 (0.06)
N-back (D-prime)	4.04 (0.50)	3.88 (0.51)	4.10 (0.48)
SART (D-prime)	2.92 (0.70)	3.15 (0.77)	2.83 (0.66)
Trailmaking A (s)	29.7 (8.88)	29.5 (6.67)	29.8 (9.64)
Trailmaking B (s)	61.9 (30.8)	62.8 (29.2)	61.5 (31.7)

Notes: * p < .05 ** p < .01
Continuous variables are expressed as means (SDs) and differences between the two age groups were assessed using independent t-tests
Categorical variables are expressed as frequencies (%) and differences between the two age groups were assessed using chi square tests
2-CRT = 2-choice reaction time; 3-CRT = 3-choice reaction time; CV = coefficient of variation; DT = dual-task; NART = National Adult Reading Test; SART = Sustained Attention to Response Task; SRT = simple reaction time; ST = single-task

and no primary effects of IIV were reported. After controlling for the primary effects of age and IIV measures, no Age x IIV interaction terms were found to be significantly associated with these measures of gait performance.

For models predicting DT gait in the Serial 3s condition, Step 2 did significantly add to the variance explained in all cases (Table 6.6). However, a significant primary effect of variability was only found for IIV on the Flanker task. After controlling for the primary effects, a significant Age x IIV interaction term was also found in the same model suggesting that this relationship did vary as a function of age. As a result, it was subjected to further analysis (see next section). For models predicting DT costs in the Serial 3s condition, there was an identical pattern of results. Variability on the Flanker task was the only IIV measure that was significantly associated with outcome, and this relationship was the only one that was found to vary according to age. Subsequently, it was also subjected to further examination (see next section).

For models of DT gait speed in the verbal fluency condition, Step 2 significantly added to the variance explained in all models. However, Flanker IIV was the only variability measure significantly associated with outcome. After controlling for the primary effects, this relationship was found to vary according to age and was subsequently examined further (see next section). Finally, for the DT cost in the verbal fluency condition, Step 2 significantly added to the variance explained for five of the six models. Once again, a primary effect for variability was only found when IIV was derived from the Flanker task. The corresponding Age x IIV interaction term was also associated with the DT cost and so the initial relationship was subjected to further analysis (see next section).

Re-examining significant associations as a function of age

The above regression analyses indicated that age relationships between Flanker IIV and four measures of gait performance varied according to age. In order to investigate these further, the sample was stratified using the median value of age as a cut-off point. This produced two subgroups: a young-old group (aged 55 to 68 years) and an old-old group (aged 69 to 87 years). The four associations between Flanker IIV and gait were then examined separately in these subgroups to determine their strength in early and later old age. Due to the relatively broad age ranges in the two subgroups, chronological age was adjusted for in these models. The results of this within-groups analysis showed a similar pattern for all four models (Table 6.7). In the young-old

Table 6.3: Pearson correlation coefficients for associations between the key demographic, IIV and gait variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. Age	—															
2. Gender (n,%)	-.03	—														
3. NART IQ	-.05	.08	—													
4. Fallen last 2 years (n,%)	.35**	.32*	-.04	—												
5. SRT CV	.09	.12	.03	-.15	—											
6. 2-CRT CV	.13	.13	-.15	.15	.41**	—										
7. Flanker CV	.16	-.03	-.01	.07	.41**	.18	—									
8. Stroop CV	.33**	.18	-.09	.23	.16	.10	.33**	—								
9. 3-CRT Movement CV	.09	.04	.01	.16	.29*	.15	.52**	.17	—							
10. 3-CRT Decision CV	.06	.12	-.08	.06	.54**	.20	.41**	.24	.33**	—						
11. ST gait (s)	.26*	.07	-.39**	.07	.07	.07	.09	.42**	.02	.21	—					
12. DT gait - motor (s)	.25	.10	-.30*	.07	.15	.13	.17	.31*	.03	.26*	.85**	—				
13. DT gait - Serial 3s (s)	.43**	-.06	-.39**	.18	.22	.19	.37**	.28*	.16	.20	.61**	.66**	—			
14. DT gait - VF (s)	.39**	.01	-.30*	.24	.27*	.27	.38**	.22	.18	.21	.49**	.55**	.91**	—		
15. DT gait cost - motor (%)	.01	.08	.06	.03	.15	.14	.14	-.06	.02	.12	-.05	.48**	.22	.21	—	
16. DT gait cost - Serial 3s (%)	.39**	-.13	-.27*	.17	.22	.18	.40**	.10	.21	.13	.18	.32*	.89**	.83**	.28*	—
17. DT gait cost - VF (%)	.35**	-.02	-.19	.24	.28	.29*	.39**	.08	.21	.16	.15	.27*	.77**	.93**	.24	.86**

Notes: * *p* < .05 ** *p* < .01

2-CRT = 2-choice reaction time; 3-CRT = 3-choice reaction time; CV = coefficient of variation; DT = dual-task; NART = National Adult Reading Test; SRT = simple reaction time; ST = single-task; VF = verbal fluency

Gender is coded as 1 for males and 2 for females; Fall status is coded as 1 for fallers and 0 for non-fallers

Table 6.4: Logistic regression models for age and IIV measures predicting falls

Model	SRT CV		2-CRT CV		Flanker CV		Stroop CV		3-CRT Movement CV		3-CRT Decision CV	
	B	OR	B	OR	B	OR	B	OR	B	OR	B	OR
Step 1												
Gender	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8
Step 2												
Age	1.04**	2.83**	.84	2.32	.86	2.36	.81	2.25	.85	2.34	.88	2.41
Predictor	-.94	.39	.15	1.17	.03	1.03	.14	1.15	.27	1.31	-.09	.92
Step 3												
Age x Predictor	-.56	.57	.43	1.54	1.14	3.13	.05	1.05	2.01	7.42	.13	1.14

Notes: Fallers were coded as 1 with non-fallers coded as 0
n fallers = 17 (27%); Step 1, df = 1; Step 2, df = 3; Step 3, df = 4
2-CRT = 2-choice reaction time; 3-CRT = 3-choice reaction time; CV = coefficient of variation; SRT = simple reaction time

Table 6.5: Logistic regression models for age and gait measures predicting falls

Model	ST gait speed		DT gait speed (motor)		DT gait speed (Serial 3s)		DT gait speed (verbal fluency)		DT gait cost (motor)		DT gait cost (Serial 3s)		DT gait cost (verbal fluency)	
	B	OR	B	OR	B	OR	B	OR	B	OR	B	OR	B	OR
Step 1														
Gender	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8	20.57	8.6E+8
Step 2														
Age	.92	2.51	.91	2.48	.80	2.23	.76	2.14	.86	2.37	.77	2.16	.75	2.11
Predictor	-.15	.86	-.13	.88	.13	1.14	.24	1.27	.03	.92	.29	1.34	.39	1.48
Step 3														
Age x Predictor	.06	1.06	.00	1.00	-.16	.85	.14	1.15	-.05	.95	-.42	.66	.03	.96

Notes: Fallers were coded as 1 with non-fallers coded as 0
n fallers = 17 (27%); Step 1, df = 1; Step 2, df = 3; Step 3, df = 4
DT = dual-task; ST = single-task

Table 6.6: Linear regression models for age and IIV measures predicting gait performance across the four conditions

Model	**SRT CV**		**TCRT CV**		**Flanker CV**		**Stroop CV**		**3-CRT Movement CV**		**3-CRT Decision CV**	
	β	R^2	β	R^2	β	R^2	β	R^2	β	R^2	β	R^2
ST gait speed												
Step 1: NART IQ	-.39**	.15**	-.39**	.15**	-.39**	.15**	-.39**	.15**	-.39**	.15**	-.39**	.15**
Step 2: Age	.23		.24		.23		.13		.24		.23	
Predictor	.06	.06	-.02	.06	.05	.06	.34**	.16**	.00	.06	.16	.08
Step 3: Age x Predictor	-.02	.00	.30	.06	.10	.01	.24	.05	-.05	.00	.09	.01
DT gait speed (motor)												
Step 1: NART IQ	-.30	.09	-.30	.09	-.30	.09	-.30	.09	-.30	.09	-.30	.09
Step 2: Age	.22		.22		.21		.16		.23		.22	
Predictor	.13	.07	.07	.06	.13	.07	.24	.10	.01	.06	.22	.10
Step 3: Age x Predictor	.09	.01	.40	.10	.13	.02	.27	.07	-.09	.01	.06	.00
DT gait speed (S3s)												
Step 1: NART IQ	-.37**	.15**	-.37**	.15**	-.37**	.15**	-.37**	.15**	-.37**	.15**	-.37**	.15**
Step 2: Age	.40**		.40**		.36**		.37**		.40**		.40**	
Predictor	.19	.21**	.08	.18**	.31**	.26**	.13	.18**	.13	.19**	.15	.19**
Step 3: Age x Predictor	.20	.04	.30	.06	.41**	.16**	.10	.01	.01	.00	.18	.03
DT gait speed (VF)												
Step 1: NART IQ	-.30	.09	-.30	.09	-.30	.09	-.30	.09	-.30	.09	-.30	.09
Step 2: Age	.36**		.35**		.33**		.35**		.36**		.37**	
Predictor	.25	.20**	.19	.18**	.33**	.25**	.08	.15**	.14	.16**	.16	.17**
Step 3: Age x Predictor	.23	.05	.42**	.11**	.50**	.24**	.06	.00	.13	.02	.14	.02

Table 6.6 continued

Model	**SRT CV**		**TCRT CV**		**Flanker CV**		**Stroop CV**		**3-CRT Movement CV**		**3-CRT Decision CV**	
	β	R^2	β	R^2	β	R^2	β	R^2	β	R^2	β	R^2
DT gait cost (motor)												
Step 1: NART IQ	.06	.00	.06	.00	.06	.00	.06	.00	.06	.00	.06	.00
Step 2: Age	.01		.00		.00		.04		.02		.01	
Predictor	.14	.02	.15	.02	.14	.02	-.06	.00	.02	.00	.13	.02
Step 3: Age x Predictor	.19	.03	.27	.05	.06	.00	.13	.02	-.11	.00	-.07	.00
DT gait cost (S3s)												
Step 1: NART IQ	-.25	.07	-.25	.07	-.25	.07	-.25	.07	-.25	.07	-.25	.07
Step 2: Age	.36**		.37**		.33**		.40**		.37**		.38**	
Predictor	.19	.18**	.10	.15**	.34**	.26**	-.05	.15**	.17	.17**	.08	.15**
Step 3: Age x Predictor	.24	.05	.15	.01	.43**	.17**	-.04	.00	.05	.00	.17	.02
DT gait cost (VF)												
Step 1: NART IQ	-.18	.04	-.18	.04	-.18	.04	-.18	.04	-.18	.04	-.18	.04
Step 2: Age	.32		.32		.29		.36**		.33**		.34**	
Predictor	.26	.18**	.23	.17**	.34**	.23**	-.05	.12**	.18	.15**	.12	.13
Step 3: Age x Predictor	.24	.05	.32	.06	.52**	.26**	-.04	.00	.19	.03	.11	.10

Notes: Step 1, df = 1,60; Step 2, df = 3,57; Step 3, df = 4,56
2-CRT = 2-choice reaction time; 3-CRT = 3-choice reaction time; CV = coefficient of variation; DT = dual-task; S3s = Serial 3s; SRT = simple reaction time; ST = single-task; VF = verbal fluency

Table 6.7: Linear regression models for IIV measures predicting gait outcomes in the two age groups

	Young-old group		Old-old group	
Model	B	ΔR^2	B	ΔR^2
Flanker CV ➜ DT gait speed (S3s)				
Step 1: NART IQ	-.53**		-.39	
Age	.42	.25	.32	.29**
Step 2: Predictor	.11	.01	.42**	.17**
Flanker CV ➜ DT gait speed (VF)				
Step 1: NART IQ	-.48		-.28	
Age	.39	.21	.34	.22
Step 2: Predictor	.12	.01	.47**	.21**
Flanker CV ➜ DT cost (S3s)				
Step 1: NART IQ	-.04		-.32	
Age	.22	.04	.27	.20
Step 2: Predictor	.16	.02	.43**	.18**
Flanker CV ➜ DT cost (VF)				
Step 1: NART IQ	-.15		-.08	
Age	.22	.04	.33	.15
Step 2: Predictor	.16	.02	.47**	.21**

Notes: Young-old group – Step 1, df = 2,27; Step 2 = 3,26
Old-old group – Step 1, df = 2,29; Step 2, 3,28
2-CRT = 2-choice reaction time; CV = coefficient of variation; DT = dual-task; S3s = Serial 3s; ST = single-task; VF = verbal fluency

group, non-significant associations were found for Flanker IIV and either gait speed or the DT cost in both the Serial 3s and verbal fluency conditions. By contrast, this measure of IIV significantly predicted all four measures of gait performance in the old-old group. In all cases, higher IIV on the task was associated with slower walking speeds or greater costs in the two DT conditions.

Testing for potential mediators

After establishing that IIV on the Flanker task was associated with all four gait outcomes in the older group, these associations were subjected to tests of mediation. The results of these analyses are presented in Table 6.8. Entering the PPA composite into the four models had mixed results. The effects of Flanker IIV on DT gait speed were attenuated by 20.5% in the Serial 3s condition and 30.3% in the verbal fluency condition, with both models subsequently becoming non-significant. This was compared to smaller attenuations of 0% and 16.4% for the equivalent DT cost

Table 6.8: Explanatory variables entered into linear regression models for IIV measures predicting gait outcomes in the old-old group

Model	Explanatory Variable	R^2 change (sig.) Before	R^2 change (sig.) After	% attenuated
Flanker CV ➜ DT gait speed (S3s)	PPA	.166**	.132	20.5%
	TMT-A	.166**	.113	31.9%
	Switching	.166*	.085	48.8%
	Updating	.166**	.166**	0%
	Inhibition	.166**	.164**	1.20%
Flanker CV ➜ DT gait speed (VF)	PPA	.211**	.147	30.3%
	TMT-A	.211**	.172**	18.5%
	Switching	.211**	.153	27.5%
	Updating	.211**	.211**	0%
	Inhibition	.211**	.210**	0.47%
Flanker CV ➜ DT cost (S3s)	PPA	.179**	.196**	0%
	TMT-A	.179**	.134	25.1%
	Switching	.179**	.135	24.6%
	Updating	.179**	.179**	0%
	Inhibition	.179**	.176**	1.68%
Flanker CV ➜ DT cost (VF)	PPA	.214**	.179	16.4%
	TMT-A	.214**	.189**	11.7%
	Switching	.214**	.201**	6.07%
	Updating	.214**	.214**	0%
	Inhibition	.214**	.213**	0.47%

Notes: Age and predicted IQ were adjusted for at Step 1 (df = 2,29), explanatory variables were entered at Step 2 (df = 3,28) and IIV measures were entered at Step 3 (df = 4,27)
CV = coefficient of variation; DT = dual-task; EF = executive function; PPA = physiological profile approach; S3s = Serial 3s; ST = single-task; TMT = trail making test; VF = verbal fluency

measures. Controlling for processing speed also produced mixed results. The variance explained in gait performance by Flanker IIV fell by between 11.7% and 31.9%. However, processing speed seemed to be having a stronger influence on gait measures in the Serial 3s condition, reducing the effects of IIV by 27.9% on average and subsequently rendering these models non-significant.

A more marked trend emerged after examining the three measures of executive function, with the results indicating that task switching was the most influential component (Table 6.8). Of the four models that were tested, controlling for the ΔTMT score attenuated the effects of IIV on gait by between 11.7% and 48.8%, with three of these models subsequently becoming non-significant. The task switching measure also had the greatest effect on associations where gait was assessed under the Serial 3s condition (28-49% attenuation) compared to the verbal fluency condition (6-25%

attenuation). Controlling for information updating and response inhibition had no effect on associations between Flanker IIV and gait, reducing the variance explained by less than 2% across the four models.

6.4 Discussion

This third experimental study built on the previous two chapters by assessing gait under DT conditions that placed low (motor), medium (Serial 3s) and high (verbal fluency) demands on attentional resources. The current work also measured the individual components of both IIV and executive function. In line with Study 3 and Study 4, measures of variability and gait performance did not predict falls. Across the whole sample, IIV on the Stroop task was significantly associated with ST gait speed, whereas non-significant associations were found between IIV and gait outcomes in the motor condition. Greater IIV on the Flanker task predicted slower walking speed and higher DT costs in both the Serial 3s and verbal fluency conditions. All four of these relationships varied as a function of age, with further analyses revealing significant associations in an old-old but not a young-old subgroup. Tests of mediation were carried out on relationships in the older group, with mixed results. Physiological function and processing speed marginally attenuated the effects of Flanker IIV on some but not all measures of gait. Of the three executive abilities that were measured, switching was found to be the most influential with small to medium attenuations reported for three of the four relationships. Finally, IIV on the decision and movement components of a 3-choice RT task did not significantly predict falls or gait performance.

Predictors of fall status

In accordance with Studies 3 and 4, there was no evidence to suggest that higher IIV was associated with a history of falls. The lack of a relationship between gait performance and falls is also in line with findings from the previous two studies. Varying the demands of the secondary task in the DT conditions did not affect the ability of gait measures to predict falls. This finding supports previous observations that fallers and non-fallers have similar decrements in gait speed in response to a secondary motor task, backwards counting task and verbal fluency task (Nordin et al., 2010). It should be noted that, although gait measures in the most demanding verbal fluency condition did not predict falls, DT costs in this condition were almost twice as high on average in the fallers group (see Table 6.2). However, the standard deviation was over four times higher, suggesting that some fallers coped relatively well with the increased demands of this condition while others struggled considerably. It could be that reduced performance in complex walking scenarios is related to a greater risk of experiencing a certain type of fall (e.g., injurious falls). However, due to the small numbers of falls reported here, it was not possible to explore this possibility further.

Gait performance across the four conditions

In the present study, gait performance was measured under ST conditions and under DT conditions that placed low (motor), medium (Serial 3s) and high (verbal fluency) demands on attentional resources. Compared to ST walking, gait speed was reduced in all three DT conditions. The verbal fluency condition produced the greatest DT cost (42%), followed by the Serial 3s condition (23%), and the motor condition (10%). This result is in line with previous expectations. It also supports capacity sharing theories of dual-tasking which propose that the simultaneous performance of two demanding tasks may exceed the attentional resources that an individual has access to, resulting in reduced performance in one or both tasks (Lajoie et al., 1993; Abernethy, 1988; Kahneman, 1973). The present findings also support previous observations that decrements in gait associated with dual-tasking increase with the demands of the secondary task (Srygley et al., 2009; Rochester et al., 2008). In particular, one study that administered the same Serial 3s and verbal fluency tasks reported similar DT costs (18% and 30%, respectively) to those in the current work (Hall et al., 2011).

Predictors of gait performance

An association between higher IIV on the Stroop task and slower gait under ST conditions is in line with observations from Study 3 but not Study 4. There was also evidence of a relationship between IIV and DT gait performance in the two cognitive conditions, but not the motor condition. This makes sense as the motor task that was used (carrying a tray with a glass of water resting on it) is likely to be a well-practised activity for many of the individuals that were tested. As a result, it may have been performed relatively automatically without interfering with the attentional resources needed for walking. Therefore higher IIV levels, which are thought to reflect deficits in attentional and executive control (Bunce et al., 2004; West et al., 2002; Bunce et al., 1993), may not have manifested as reduced performance in this condition. These findings partially support previous work that examined executive function in relation to DT gait in the same motor condition (Oh-Park et al., 2013). Here, poorer scores on executive measures did not predict higher gait costs regardless of whether the individual was instructed to focus on the walking task or the secondary motor task.

Although an association between IIV and DT gait in the two cognitive conditions was expected, the hypothesis that this association would be stronger in the verbal fluency condition was not supported. This is surprising since DT costs in this condition were almost twice as high compared to when individuals walked while performing the Serial 3s task, suggesting that this condition placed greater demands on attentional and executive resources. Previous work has also demonstrated that measures of executive function are more highly associated with DT gait when the demands of the secondary task are increased (e.g., Hobert et al., 2011; Coppin et al., 2006). It could be that, once a walking situation reaches a certain level of complex, an individual’s ability to maintain attention has a significant impact on their gait performance. However, increasing the demands of the situation further may not necessarily make this impact any more severe. In the present study, it could be that the Serial 3s and verbal fluency conditions were sufficiently demanding enough for IIV measures to detect differences in DT gait performance, but the motor condition was not.

The relationship between IIV and DT gait in the two most demanding conditions was found to vary according to age, with a subsequent within-groups analysis revealing that it was stronger in later relative to early and middle old age. This is line with findings from Study 4 and also previous work demonstrating that executive function, which is closely tied to IIV, plays an increasingly important role in maintaining gait performance during the transition to later old age (Yogev-Seligmann et al., 2008). Furthermore, there is evidence that IIV is substantially greater and DT gait performance is significantly poorer in older persons over the age of 70 compared to those who are younger (e.g., LaRoche et al., 2014; Lovden et al., 2007). Given that the age cut-off for the two subgroups in the present investigation was 69 years, it makes sense that between-person differences in IIV would be a strong predictor of gait differences in the older group here. These results suggest that IIV measures may have considerable utility when it comes to detecting gait impairment in very old individuals during complex walking situations. These same individuals may be struggling to cope with the demands of these situations, potentially making them vulnerable to falls or other adverse outcomes, and limiting their ability to carry out daily living activities that involve dual-tasking.

Components of variability

An important objective of the present work was to fractionate IIV into a decision component and a movement component, thereby isolating the cognitive element of making a correct response. However, the findings here indicated that decision and movement IIV were almost identical, in contrast to prior expectations and previous investigations (e.g., Gorus et al., 2008; Bunce et al., 2004). Furthermore, neither components were found to be significantly associated with either gait performance or falls. One possible explanation of these findings relates to the way the task in the present study was administered. Specifically, participants chose from three response keys located next to each other on a standard keyboard (see Figure 6.1a). In another study, which did find significant differences between decision IIV and movement IIV, older adults chose from eight keys located in a semi-circular arc around a central response key (Bunce et al., 2004).

It could be that some of the older adults here took advantage of the close proximity of the three response keys by moving towards them while still deciding which key was the correct one to choose. Evidence of individuals using such a ‘detection strategy’ in similar paradigms has been provided in the past (Smith & Carew, 1987). If this were the case it would mean that both cognitive and motor processes were influencing the decision portion of the task. Future research investigating different components of variability in relation to falls or gait should aim to restrict the extent to which individuals can decide which response to make after moving their finger away from the home key. One way this could be achieved is with a paradigm that requires individuals to depress the home key in order to show the location of the stimulus. Then, upon releasing the home key, this stimulus would either disappear or all stimuli would be presented. This would ensure that individuals could not continue to sample information on the screen to help make their decision. In support of this notion, previous research employing such paradigms has provided evidence of increased response times for the decision portion of the task (e.g., Stough et al., 1995; Smith & Carew, 1987). This suggests they may aid in reducing the use of detection strategies when assessing different components of variability.

Testing for potential mediators

A mediational approach was used to explore mechanisms underlying the relationships between IIV and DT gait that were found in the older group. These analyses produced mixed results with the switching component of executive function, processing speed and physiological capability all producing small-to-medium attenuations. This contradicts the previous study where controlling for task switching significantly reduced the effects of IIV on DT gait. This suggests that executive function was having a smaller effect on this relationship in the present study, with the other variables subsequently playing a greater role. One possible explanation for these contrasting finding is that the very old adults here had better preserved executive abilities than those in the previous study. A between-studies comparison revealed that they completed the Trailmaking-B task, on average, 7.6 seconds quicker than their counterparts in Study 4 (unreported analysis). Taking these findings into consideration, it is plausible that the effects of IIV on DT gait performance here would be less heavily influenced by between-person differences in executive function. And as a result, other factors such as speed of processing could be expected to make a greater contribution to the unexplained variance that remained.

Another important aim of the present research was to determine the extent to which the three components of executive function were contributing to significant associations involving variability. These components were tested as potential mediators of the relationship between IIV and DT gait found in the older group, with the results indicating that task switching was by far the most influential component. This finding supports previous observations that the ability to switch between tasks or, relatedly, to divide attention is a better predictor of gait performance than response inhibition or information updating (de Bruin & Schmidt, 2010; van Iersel et al., 2008a). However, these findings may also be partly explained by the fact that the tests used to measure inhibition and updating were relatively simple, even for members in the older subgroup. This is particularly likely for the version of the n-back task that was used to assess updating as this had extremely low demands relative to other versions of the task. This possibility is supported by the low proportion of errors that were recorded on both tasks in the present study (unreported analyses). As a result, these measures may have been less able to distinguish between individuals with different levels of gait performance than the switching measure. If this were the case, it is reasonable to expect that they would not significantly attenuate the effects of IIV on DT gait.

Limitations

The present study has several limitations that may have impacted on the results and, therefore, should be acknowledged. A number of these are common to all three experimental studies and will be covered briefly. First, falls data were collected retrospectively using a self-report method. This may have underestimated the total number of falls and subsequently made it difficult for IIV and gait measures to distinguish between fallers and non-fallers. Second, since only cross-sectional data were collected and analysed during this study, no inferences can be made about a causal relationship between IIV and gait based on the associations that were found. This limitation will be addressed in the following study. Finally, the size of the sample was relatively small (n = 62) and a much greater number of regression models were tested here compared to in the previous two studies. This could have potentially increased the chance of making a Type I error. However, in order to reduce this possibility, alpha for statistical significance in the present study was set more conservatively at $p < .01$.

As mentioned in the Methods section, a number of older adults who took part in this study were also tested in Studies 3 and 4 (n = 22). In order to aid comparisons between studies, several measures were included in all three studies and administered under identical circumstances. Due to the relatively small intervals between testing sessions (average time = 349 days), individuals may have become more familiar with these measures and subsequently improved their performance over time. Indeed, further analysis of the 22 individuals that took part in every study revealed some evidence of practice effects on certain cognitive tests, such as reduced IIV on the Flanker and Stroop tasks and faster times on both parts of the Trailmaking test (unreported analysis). This is potentially important as it is expected that older adults would experience greater decline in cognitive abilities. Therefore, these practice effects may partially be masking this age-related decline and, as a result, the relationship between these abilities and other outcomes may have been affected. Although this is a limitation of the present work, the administration of identical tests across all three studies was necessary to provide longitudinal data for the next study.

Finally, tests of response inhibition were used in the present study to derive IIV measures and also to create explanatory variables for use in tests of mediation. This is potentially important given that a number of associations involving Flanker IIV were subjected to these analyses. It is reasonable to expect that there would be a large overlap in the abilities required to complete the Flanker and SART tasks. As a result, controlling for performance on the SART may attenuate the effects of Flanker IIV more than IIV measures that are not derived from tests of response inhibition. Inspection of the findings suggest this was unlikely, however, as the rates of attenuation were less than 2% across all four associations that were tested. Nevertheless, tests of executive function have been used throughout the experimental work reported here to produce IIV metrics and potential mediators of associations involving these metrics. This may have led to inaccurate estimations about the role that executive function was playing in relationships between IIV and outcome and, as a result, should be avoided in empirical work going forward.

Future directions

In the final experimental study, longitudinal data will be used to examine how the relationships between IIV, gait and falls change over time. This is an important development of the cross-sectional work described so far for two key reasons. First, although a number of studies have previously looked at variability in relation to falls, only three have done so by collecting prospective falls data (Bunce et al., 2016b; Mirelman et al., 2012; Allcock et al., 2009). Prospective data are needed to establish whether cognitive measures such as IIV are able to detect future falls, and therefore may be a useful addition to screening tools for identifying at-risk older populations. Second, to date no empirical work has examined the longitudinal relationship between IIV and gait performance. This is an important omission as there is considerable debate in the literature over the temporal direction of the relationship between cognitive function and gait. While some work has shown that baseline levels of cognition predict later changes in gait performance (e.g., Buchman et al., 2011; Atkinson et al., 2010; Watson et al., 2010), other studies have provided evidence for this relationship in the opposite direction (e.g., Mielke et al., 2013; Inzitari et al., 2007b; Abbott et al., 2004). Due to this inconsistency in previous findings, there remains a need for longitudinal work to better elucidate how relationships between cognition and gait, and particularly IIV and gait, change over time. Furthermore, such work is needed to establish the predictive utility of IIV metrics when it comes to detecting future gait impairment, one of the main objectives of the present research.

Chapter 7

Study 6: The longitudinal relationship between variability, gait speed and falls

7.1 Introduction

The previous three chapters examined cross-sectional associations between variability, gait and falls in groups of cognitively intact older adults. In Study 3, IIV measures were considered as predictors of fall status or single-task (ST) gait speed, with dual-task (DT) gait measures added in the subsequent investigations. This work provided no evidence that IIV was related to falls, possibly due to the low rate of falls and the types of falls (e.g., slipping on ice) that were reported. IIV on the more demanding Flanker and Stroop tasks predicted ST gait speed in Study 3 but these findings were not replicated in the work that followed. Studies 4 and 5 produced significant associations between IIV and DT gait outcomes when the gait condition involved a secondary cognitive task, but not a secondary motor task. The extent to which these associations varied according to age was also examined, with the findings revealing that IIV was a better predictor of DT gait in older groups (i.e., those over 67 years old). Finally, a mediational procedure was used to investigate potential mechanisms underlying the relationship between IIV and gait. Here, processing speed played an explanatory role when gait was measured under ST conditions, whereas executive control underpinned the effects of IIV on DT gait. Furthermore, there was evidence that the task switching component of executive function provided greater explanatory power than either the inhibition or updating components.

Although this work comprehensively examined the relationship between IIV, gait and falls, all three studies were limited in that they only analysed data cross-sectionally. Consequently, it was not possible to infer causality between any of the variables that were studied. This is an important limitation since one of the main motivations for the present work is the early identification of populations at risk of future falls or gait impairment. The detection of older adults without a current history of falls is particularly important as the experience of a first fall has been found to predict subsequent falls in the following years (e.g., Deandrea et al., 2010). However, this is only possible in longitudinal designs that administer baseline performance measures and then collect falls data over a follow-up period. Given the pressing need to reduce falls in older persons, it is not surprising that a large body of research has examined cognitive predictors of future falls. In particular, measures of executive function have been found to be particularly useful in distinguishing fallers from non-fallers in longitudinal work (Kearney et al., 2013). Furthermore, in one study that assessed a group of individuals with no history of falls, executive deficits at baseline predicted falls outcomes over the following two years (Herman et al., 2010).

While there is compelling evidence that cognitive markers, and particularly measures of executive function, may be useful in the prediction of falls, the longitudinal relationship between cognition and gait is less clear. Indeed, there is some debate in the literature regarding the temporal direction of this relationship. This issue has been examined in depth with a number of studies demonstrating that global cognitive measures such as the Mini Mental State Examination (MMSE) predict the development of mobility problems or reductions in walking speed up to six years later (Atkinson et al., 2010; Rivera et al., 2008; Atkinson et al., 2007). Furthermore, deficits in specific cognitive domains such as executive function, processing speed and working memory have been shown to predict gait decline up to five years later (Buchman et al., 2011; Watson et al., 2010; Soumare et al., 2009). By contrast, other empirical work has provided evidence that baseline gait performance is linked to future changes in cognition. Three such studies found individuals who walked more slowly were more likely to be diagnosed with cognitive impairment up to nine years later (Wang et al., 2006; Abbott et al., 2004; Marquis et al., 2002). Similarly, baseline gait speed has been shown to predict longitudinal changes in a number of cognitive domains including processing speed and executive function (Mielke et al., 2013; Inzitari et al., 2007b).

These contrasting findings suggest that the relationship between cognition and gait is not operating in the same temporal direction at all times. While cognitive deficits may be occurring prior to gait decline on some occasions, there is evidence that on other occasions the opposite is true. Several hypotheses have been proposed to explain how age-associated changes in gait may contribute to cognitive decline. For example, a reduction in physical activity may lead to a depletion in cognitive resources (e.g., Kramer & Erickson, 2007). Common cause hypotheses have also been advanced suggesting that declines in cognition and gait may both be driven by neurobiological changes such as compromised white matter integrity (e.g., Rosano et al., 2012; Christensen et al., 2001) or reduced functioning of the central nervous system (e.g., Rosso et al., 2013; Rosano et al., 2007). Against this background, there is a need for more longitudinal research to examine associations between cognitive and gait performance, and how they vary over time. Such research is particularly important for establishing the potential utility of cognitive measures as predictors of future gait impairment and falls, a major motivation for the work described here.

Across the broader cognitive ageing literature, there has been an increase in longitudinal work examining IIV in relation to different age-related outcomes (Haynes et al., 2017). For example, higher baseline IIV on simple and choice RT tasks has been linked to an increased risk of developing Mild Cognitive Impairment (e.g., Cherbuin et al., 2010) and dementia (e.g., Kochan et al., 2016), as well as a shorter time to death (e.g., Kochan et al., 2017; Batterham et al., 2014). Prospective work has also demonstrated that IIV measures are useful in the prediction of future cognitive decline. In one such investigation, higher IIV on a perceptual speed task was associated with a greater reduction in perceptual speed and verbal fluency 13 years later (Lovden et al., 2007). Another study found that a composite IIV measure, comprising performance on a 1-back choice RT task and a switching task, predicted three year change in perceptual speed, verbal fluency and memory (Bielak et al., 2010a). Of most relevance to the present work, higher IIV on the same composite measure was later found to predict performance decrements on the Trailmaking B test of executive function (Yao et al., 2016). Taken together, these findings provide evidence that IIV measures predict various cognitive outcomes associated with old age. Furthermore, sudden increases in variability may signal impending decline in cognitive function that may not be detected by more commonly used neuropsychological measures (Haynes et al., 2017).

As discussed in the earlier review chapters, previous cross-sectional work has provided evidence that IIV is associated with both falls (e.g., O'Halloran et al., 2011; Reelick et al., 2011) and gait performance (e.g., Bauermeister et al., 2017; Holtzer et al., 2014a). Given the aforementioned link between variability and other long-term outcomes, there is good reason to expect that IIV measures would predict future falls and changes in gait. This argument is strengthened by evidence that baseline IIV levels are associated with later changes in executive function (Yao et al., 2016), deficits in which have previously been identified as a reliable risk factor for falls and gait impairment (Kearney et al., 2013). It is possible that age-related increases in IIV accompany a decline in executive control which contributes to mobility problems. These problems, in turn, may make individuals more vulnerable to falls. If this is the case, it would provide strong justification for incorporating IIV measures into existing early screening batteries for falls and gait impairment.

In line with this possibility, a handful of longitudinal studies have examined baseline levels of variability in relation to future falls (Graveson et al., 2016). In one study, higher IIV on a Go-NoGo task was associated with greater fall frequency during a 66 month follow-up period (Mirelman et al., 2012). Furthermore, a composite IIV measure derived from three RT tasks was found to predict frequency of falls over the following year (Allcock et al., 2009). By contrast, another investigation found that baseline IIV on simple and choice RT tasks was not associated with falls outcomes in healthy older adults over the following 12 months (Bunce et al., 2016a). However, variability on a choice stepping task did predict falls in a cognitively impaired subsample. These contrasting findings highlight the need for more prospective research to examine the longitudinal relationship between IIV and falls. No empirical work to this point has investigated IIV measures in relation to future changes in gait performance. Such prospective work is needed to establish whether baseline measures of IIV are associated with longitudinal gait decline, thereby providing justification for the use of such measures in early screening assessments.

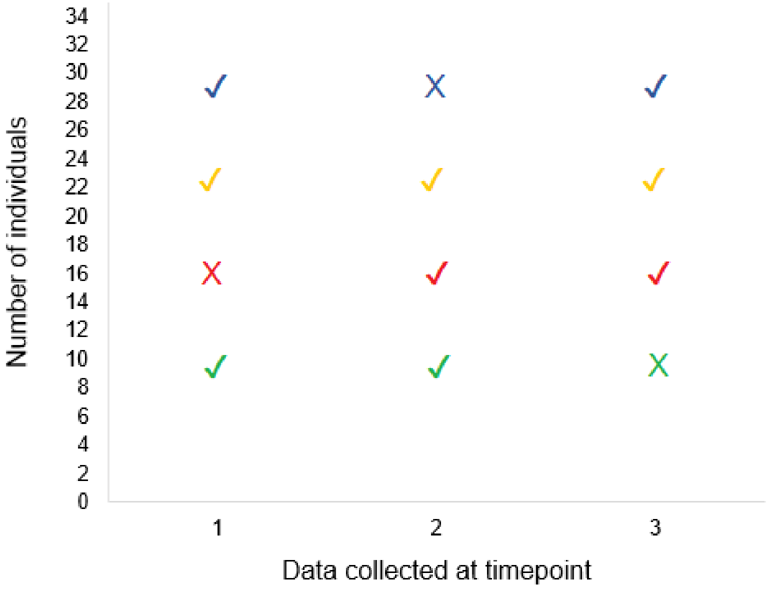
Therefore, in the present study, prospective data will be used to investigate longitudinal associations between IIV, gait speed and falls in cognitively intact older adults. In order to do this, data from the previous empirical work (collected over a period of approximately two years) will be combined. As is common with longitudinal designs, participants were tested at different times with unequal intervals between testing sessions. In accordance with previous longitudinal work (e.g., Bunce et al., 2014), mixed effects modelling will be used to assess the longitudinal relationship between IIV and gait. This statistical procedure has the advantage of dealing with missing data, and can account for unequal intervals between time points. With regard to falls, the effect of baseline IIV levels on time to first fall during follow-up will be examined using Cox proportional hazard models. Using these statistical techniques, the current longitudinal study will fulfil a number of aims. First, this work will determine the extent to which baseline measures of variability, or gait speed, are predictive of time to first fall over a period of up to two years. Second, this study will determine whether baseline IIV measures are significantly associated with baseline gait speed and changes in gait speed over time. Third, the extent to which longitudinal relationships between IIV and falls, gait and falls, and IIV and gait, vary according to age will also be examined.

7.2 Methods

Participants

A total of 76 cognitively intact older adults took part in at least two of three cross-sectional studies that were described in the previous chapters. Figure 1 shows the number of individuals for which data was collected at each of the three timepoints. The follow-up period (i.e., the time between the first and last testing session for each individual) ranged from 156 to 645 days. All participants were screened for cognitive impairment during baseline testing with either the MMSE (baseline only) or the Montreal Cognitive Assessment (MOCA; Time 2 and Time 3 only). A cut-off score of less than 26 was used to identify possible impairment on both measures, however, no individuals were excluded on this basis. At baseline, the sample had a mean age of 68.5 years (range 53-86), contained 60 women (79%), and had an average predicted IQ of 123 (range 106-134). IQ was estimated using the National Adult Reading Test (NART), more information on which can be found in the Methods sections of the previous experimental studies.

Figure 7.1: Number of individuals with data collected at each timepoint. The three columns represent the three cross-sectional studies whereas the ticks and crosses indicate which studies each group of individuals took part in.



Physical Measures

Vision and muscle force tests: Visual acuity was assessed using a Snellen chart with each participant given an acuity score that ranged from 1 to 11. Hand grip strength was measured over six trials using a handheld dynamometer, with the average force (in kilograms) recorded. Leg resistance strength was measured over three trials using a spring gauge attached to the participant's dominant leg, with the average force (in kilograms) recorded. More information about these measures can be found in the Methods section of Chapter 4

*Gait: G*ait speed was measured using a 4m walkway along which participants were instructed to walk at their usual pace from a standing start. Although the procedure under which gait was assessed varied over the three studies, each study recorded the time taken to complete at least three trials under single-task conditions. Therefore, to ensure comparability of measures, the average gait speed (in cm/s) over the first three single-task trials was used in the present study. This was calculated by dividing the length of the walk (in metres) by the average time taken to complete the three trials (in seconds).

Falls History

An identical falls questionnaire (see Appendix 1B) was administered to participants in each of the three testing sessions to obtain a comprehensive falls history for the two years prior to each session. More information about this questionnaire can be found in the Methods section of Chapter 4. The exact date of each fall was not recorded so the midpoint between six monthly intervals was used as an estimate, in line with previous longitudinal work (Kochan et al., 2016). This date was then subtracted from the date of the individual’s first session to estimate how many days after baseline that fall had occurred. For example, an individual may report a fall that occurred 6-12 months before their final testing session. This session may have taken place 500 days after their initial visit. This fall would be estimated as taking place 274 days before the date of the final session (the midpoint between 183 days and 365 days) and, therefore, 226 days after baseline testing.

Cognitive Measures

Cognitive RT tasks: Participants completed the same four RT tasks under identical conditions in each of the three studies. Two of these were psychomotor tasks: Simple Reaction Time (SRT; 48 trials), 2-Choice Reaction Time (2-CRT; 48 trials). The other two were response inhibition tasks: Flanker (64 trials) and Stroop (96 trials). More information on these tasks can be found in the Methods section of Chapter 4.

Pen and paper tasks: Participants also completed two written tasks: Trailmaking A (TMT-A) and Trailmaking B (TMT-B). The time taken to complete TMT-A (in seconds) was recorded and used as a measure of processing speed. The ΔTMT score (time taken to complete Part B – Part A) was calculated and used as a measure of executive function. More information on the Trailmaking tasks can be found in the Methods section of Chapter 4.

Procedure

Information on the procedures for each of the three studies can be found in the Methods section of the appropriate chapters. Only measures relevant to the longitudinal analyses used in this study have been described here. Ethical approval for the three studies was obtained from the School of Psychology Research Ethics Committee and testing took place between October 2013 and June 2015.

Data Processing

The coefficient of variation (CV) was used as a measure of IIV for each of the four RT tasks. More information on the procedure used to calculate this measure can be found in the Methods sections of the previous chapters. Missing data across the three cross-sectional studies were rare and subsequently replaced by imputing new values at the aggregate sample level using an expectation maximization algorithm (Schafer & Graham, 2002). Missing data frequencies for each of the three studies can be found in the Methods section of the appropriate chapters.

Statistical Analysis

Analysis of the data proceeded through a number of stages. First, predictors of future fall status were examined. This involved dividing the sample into those who had fallen during then follow-up period and those who had not. Independent t-tests or chi square tests then identified significant differences in demographic, physical or cognitive characteristics between these groups. Following this, a series of Cox regression analyses were run in SPSS version 21 (IBM, 2012) to examine whether baseline measures of IIV or gait speed predicted time to first fall during the follow-up period. In the event that demographic variables (e.g., gender, predicted IQ) significantly differed between the two groups, these were taken into account in the regression models. Age x IIV and Age x Gait interaction terms were also examined in these models to determine whether any of the initial relationships varied according to age. Where interaction terms were found to be significantly associated with time to first fall, the sample was stratified into younger and older subgroups using the median value for age as the cut-off point. The corresponding associations were then retested in these subgroups to determine whether they were stronger in early or later old age.

Second, relationships between baseline IIV and future changes in gait speed after taking age into account were examined. A series of mixed-effects models were built using the MIXED procedure in SPSS version 21 (IBM, 2012). A forward selection procedure was used with changes in gait speed initially assessed using only an intercept term. A fixed effect for time was entered in the second model, with a random effect for time added in the third model. Here, fixed effects refer to those that remain constant across individuals, whereas random effects are those that vary at the individual level. The number of days between baseline testing and the final follow-up session served as the time variable. In Model 4, fixed effects of age and the Age x Time interaction term were introduced to determine whether baseline age was associated with baseline gait speed, or with changes in gait speed over time. Fixed effects of IIV and the IIV x Time interaction were entered into the fifth model. In Model 6, fixed effects of the interaction between Age x IIV and a three-way interaction between Age x IIV x Time were added to the model. As age and variability were measured continuously, where interactions were found to be significant, further analysis was carried out in a seventh model. Here, age was re-entered as a categorical variable with the median value for age used to create young and old subgroups. Then, associations between baseline IIV and baseline gait speed, or changes in gait speed, were tested again in these groups. All regression models used an unstructured covariance matrix structure and a maximum likelihood method of estimating missing data.

7.3 Results

Predictors of time to first fall

Of the 76 older adults who took part in at least two testing sessions, 22 of these (28.9%) fell at least once during the follow-up period. As shown in Table 7.1, fallers were, on average, 2.9 years older than non-fallers and more likely to be female (both ps < .05). Fallers also performed significantly worse on the leg resistance strength test and were found to be more variable on the Stroop task (both ps < .05). However, there was no evidence that fallers and non-fallers differed in terms of their predicted IQ and performance on all other physical and cognitive measures. A series of Cox proportional-hazard models examined the relationships between baseline IIV or gait speed and time to first fall, and whether these relationships varied according to age. As the gender composition of the faller and non-faller groups was found to be significantly different (Table 7.1), gender was adjusted for in each model.

Table 7.1: Baseline demographic, physical and cognitive characteristics of those who fell at least once during the follow up period and those that did not

Variable	**Total sample (n = 76)**	**Fallers (n = 22)**	**Non-fallers (n = 54)**
Age (years)	68.5 (6.68)	70.5 (5.82)	67.6 (6.88)*
Gender – n female (%)	60 (78.9)	21 (95.5)	39 (72.2)*
NART predicted IQ	123.0 (5.13)	122.7 (4.59)	123.1 (5.37)
Snellen	9.61 (1.17)	9.73 (0.88)	9.56 (1.27)
Grip strength (kg)	23.1 (9.14)	20.6 (4.92)	24.2 (10.2)
Leg strength (kg)	17.8 (6.59)	15.25 (6.91)	18.7 (6.91)*
Gait (s)	3.85 (0.64)	4.00 (0.60)	3.79 (0.65)
SRT CV	0.25 (0.10)	0.27 (0.12)	0.24 (0.10)
2-CRT CV	0.20 (0.05)	0.20 (0.05)	0.20 (0.05)
Flanker CV	0.19 (0.08)	0.21 (0.08)	0.19 (0.09)
Stroop CV	0.22 (0.08)	0.25 (0.10)	0.21 (0.06)*
Trailmaking A (s)	30.2 (9.18)	31.8 (9.98)	29.5 (8.86)
Trailmaking B (s)	61.1 (22.0)	66.6 (22.1)	58.8 (21.8)

Notes: * p <. 05
Continuous variables are expressed as means (SDs) and differences between fallers and non-fallers were assessed using independent t-tests
Categorical variables are expressed as frequencies (%) and differences between fallers and non-fallers were assessed using chi square tests

Table 7.2: Cox proportional-hazard models for IIV measures and gait speed predicting time to first fall

Model	**SRT CV**			**TCRT CV**			**Flanker CV**			**Stroop CV**			**Gait speed**		
	B	Wald	HR	B	Wald	HR	B	Wald	HR	B	Wald	HR	B	Wald	HR
Step 1															
Gender	1.85	3.27	6.37	1.85	3.27	6.37	1.85	3.27	6.37	1.85	3.27	6.37	1.85	3.27	6.37
Step 2															
Age	.18	.79	1.20	.21	1.32	1.23	.29	.90	1.20	.18	.87	1.19	.19	.87	1.21
Predictor	.09	.17	1.10	.04	.03	1.04	1.00	.18	1.10	.17	.74	1.19	.04	.04	1.04
Step 3															
Age x Predictor	-.13	.47	.88	-.19	.76	.83	-.24	1.78	.78	.00	.00	1.00	-.60*	4.90*	.54*

Notes: * p < .05
n fallers = 22; Step 1, df = 1; Step 2, df = 3; Step 3, df = 4; Fallers were coded as 1 and non-fallers were coded as 0
2-CRT = 2-choice reaction time; CV = coefficient of variation; HR = hazard ratio; SRT = simple reaction time

Table 7.3: Cox proportional-hazard models for gait speed predicting time to first fall in the two age groups

Model	**Young-old group**			**Old-old group**		
	B	Wald	HR	B	Wald	HR
Step 1: Age	.84*	4.09*	2.31*	-.01	.09	.99
Step 2: Gait speed	.83*	3.88*	2.28*	-.07	.07	.93

Notes: * p < .05
Young-old group – n fallers = 6; Step 1, df = 1; Step 2, df = 2
Old-old group – n fallers = 16; Step 1, df = 1; Step 2, df = 2

The analyses revealed no primary effects of either age, IIV or gait speed on time to first fall (Table 7.2). After taking into account the primary effects, none of the Age x IIV interaction terms were found to be significant. However, there was a significant Age x Gait Speed interaction with respect to falls ($p < .05$). This suggests that age was influencing the relationship between gait speed and falls and, consequently, further analysis was carried out. Here, the sample was stratified using the median value of age as the cut-off point. This produced young-old (aged 53 to 66, $n = 35$) and old-old group subgroups (aged 67 to 85, $n = 41$). The association between gait speed and time to first fall was then retested in both groups. Due to the low number of male fallers in the young-old group ($n = 1$), gender was not adjusted for in these models in order to prevent non-convergence of the models. The results of this within-groups analysis are presented in Table 7.3, and show that both age and gait speed were significant predictors of time to first fall in the younger group (both ps < .05). Inspection of the hazard ratios revealed that a 1 SD increase in time taken to complete the 4m walk increased the risk of falling by 128%. By contrast, in the older group, gait speed was not associated with time to first fall.

Predictors of baseline gait speed and gait speed change

Estimates of the fixed and random effects for each model, and information about model fit (represented as changes in the chi-square statistic) are detailed in Table 7.4. In Model 1, inspection of the intercept indicated an average gait speed during baseline testing of approximately 106 cm/s ($df = 3$, $X^2 = 1380.9$). The addition of a fixed effect for time in Model 2 did not significantly improve model fit ($\Delta df = 1$, $\Delta X^2 = 0.46$), although it was improved after introducing a random effect for time in the third model ($\Delta df = 2$, $\Delta X^2 = 11.2$, $p < .01$). In Model 4, there were significant effects for both age and the Age x Time interaction, and this significantly improved the model fit ($\Delta df = 2$, $\Delta X^2 = 15.2$, $p < .01$). Inspection of the estimates revealed that an additional year of life was associated with a gait speed that was 0.99 cm/s slower at baseline ($p < .01$). Contrary to prior expectations, an additional year of life at baseline was also associated with an improvement in gait performance over time. This improvement equated to a 0.04cm/s per month increase in speed which was significant at the $p < .05$ level.

Model 5 examined baseline IIV in relation to baseline gait speed, and changes in gait speed over time. A significant effect of variability was found only for the Flanker task, with a one SD increase in IIV levels associated with a gait speed that was 3.75 cm/s

Table 7.4: Parameter estimates from mixed effects models examining change in gait speed as a function of age and IIV

Model	**SRT CV**	**2-CRT CV**	**Flanker CV**	**Stroop CV**
	Gait speed	Gait speed	Gait speed	Gait speed
	Estimate (SE)	Estimate (SE)	Estimate (SE)	Estimate (SE)
Model 1				
Fixed effect: intercept	105.21 (1.56)**			
Random effect				
Residual	68.19 (9.58)**			
Intercept	154.63 (30.01)**			
Model fit, df = 3	$X^2 = 1380.87$			
Model 2				
Fixed effects				
Intercept	105.75 (1.69)**			
Time in study (months)	-0.054 (0.081)			
Random effects				
Residual	67.93 (9.55)**			
Intercept	154.54 (29.98)**			
Model fit, df = 4	$\Delta X^2 = 0.46$			
Model 3				
Fixed effects				
Intercept	105.72 (1.78)**			
Time in study (months)	-0.062 (0.091)			
Random effects				
Residual	30.64 (8.05)**			
Intercept	212.64 (39.91)**			
Time in study (months)	0.356 (0.115)**			
Model fit, df = 6	$\Delta X^2 = 11.24$**			
Model 4				
Fixed effects				
Intercept	173.72 (16.73)**			
Time	-1.95 (0.923)*			
Intercept x Age	-0.993 (0.243)**			
Age x Time	0.037 (0.013)*			
Random effects				
Residual	30.06 (7.90)**			
Intercept	170.01 (32.93)**			
Time	0.332 (0.109)**			
Model fit, df = 8	$\Delta X^2 = 15.17$**			
Model 5				
Fixed effects				
Intercept	171.86 (17.46)**	173.26 (16.79)**	164.63 (16.64)**	171.19 (16.98)**
Time	-2.03 (0.979)*	-1.84 (0.919)	-1.53 (0.939)	-2.17 (0.938)*
Intercept x Age	-0.966 (0.254)**	-0.987 (0.244)**	-0.861 (0.242)**	-0.957 (0.247)**
Age x Time	0.029 (0.014)*	0.026 (0.013)	0.021 (0.014)	0.031 (0.014)
Intercept x IIV	-0.632 (1.70)	-0.475 (1.63)	-3.75 (1.62)*	-1.36 (1.65)
IIV x Time	-0.023 (0.099)	0.103 (0.087)	0.180 (0.093)	-0.093 (0.092)
Random effects				
Residual	30.15 (7.94)**	30.09 (7.88)**	28.04 (7.27)**	31.43 (8.31)
Intercept	169.60 (32.89)**	169.76 (32.90)**	158.79 (30.64)**	167.00 (32.71)**
Time	0.331 (0.109)**	0.321 (0.107)**	0.332 (0.103)**	0.306 (0.108)**
Model fit, df = 10	$\Delta X^2 = -3.63$	$\Delta X^2 = -3.59$	$\Delta X^2 = 3.77$	$\Delta X^2 = -0.57$

Notes: * $p < .05$ ** $p < .01$

2-CRT = 2-choice reaction time; CV = coefficient of variation; IIV = intraindividual variability; SRT = simple reaction time

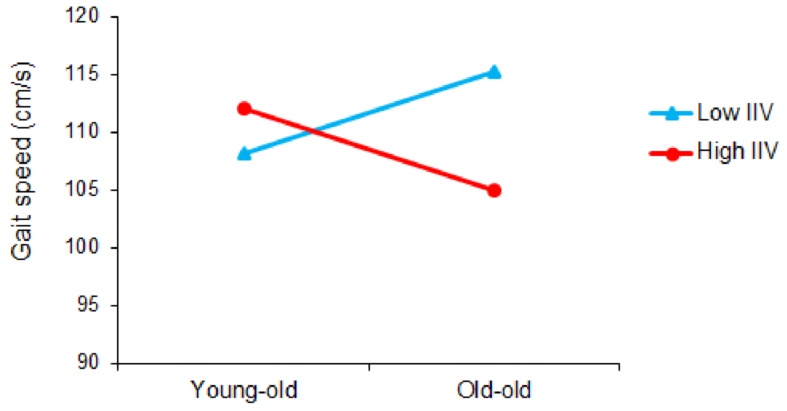
Table 7.4 continued

Model	**SRT CV** Gait speed Estimate (SE)	**2-CRT CV** Gait speed Estimate (SE)	**Flanker CV** Gait speed Estimate (SE)	**Stroop CV** Gait speed Estimate (SE)
Model 6				
Fixed effects				
Intercept	169.50 (17.76)**	172.44 (16.69)**	158.09 (16.73)**	168.93 (16.50)**
Time	-1.99 (0.984)*	-1.91 (0.839)*	-1.56 (0.956)	-2.26 (0.937)*
Intercept x Age	-0.928 (0.260)**	-0.972 (0.243)**	-0.756 (0.245)**	-0.913 (0.240)**
Age x Time	0.028 (0.014)	0.027 (0.012)*	0.022 (0.014)	0.032 (0.014)*
Intercept x IIV	8.33 (13.83)	20.15 (15.68)	22.81 (15.41)	37.75 (18.37)*
IIV x Time	-0.115 (0.783)	-2.72 (0.842)**	0.395 (0.901)	0.762 (1.08)
Age x IIV	-0.129 (0.198)	-0.300 (0.227)	-0.391 (0.226)	-0.564 (0.264)*
Age x IIV x Time	0.001 (0.011)	0.041 (0.012)**	-0.003 (0.013)	-0.012 (0.015)
Random effects				
Residual	30.18 (7.96)**	34.14 (9.19)**	27.97 (7.26)**	31.36 (8.24)**
Intercept	168.40 (32.72)**	162.35 (32.62)**	151.71 (29.53)**	155.28 (30.85)**
Time	0.330 (0.110)**	0.202 (0.102)*	0.332 (0.103)**	0.300 (0.107)**
Model fit, df = 12	$\Delta X^2 = 1.48$	$\Delta X^2 = 1.22$	$\Delta X^2 = 6.86$*	$\Delta X^2 = 3.76$
Model 7				
Fixed effects				
Intercept		102.49 (2.37)**		103.28 (2.32)**
Time		0.030 (0.114)		0.057 (0.119)
Intercept x Age group		7.20 (3.49)*		6.79 (3.43)^
Age group x Time		-0.236 (0.179)		-0.283 (0.186)
Intercept x IIV (by Age)				
Young-old		0.167 (2.63)		1.91 (2.55)
Old-old		-1.41 (2.35)		-5.18 (2.33)*
IIV x Time (by Age)				
Young-old		-0.051 (0.134)		-0.122 (0.148)
Old-old		0.219 (0.114)		-0.039 (0.120)
Random effects				
Residual		30.96 (8.13)**		31.65 (8.38)**
Intercept		198.63 (37.76)**		183.1 (35.42)**
Time		0.312 (0.108)**		0.322 (0.111)**
Model fit, df = 12		$\Delta X^2 = 0.78$		$\Delta X^2 = -5.56$

Notes: * p < .05 ** p < .01
2-CRT = 2-choice reaction time; CV = coefficient of variation; IIV = intraindividual variability; SRT = simple reaction time
The young-old group (n = 35) was coded as 0 and served as the reference category in Model 7

slower at baseline (p < .05). IIV x Time interaction terms were not found to be significant, indicating that baseline variability levels were not associated with future changes in gait performance. Furthermore, the addition of IIV measures did not significantly improve the model fit for any of the four models at this stage. Model 6 examined whether the relationships between IIV and baseline gait speed, and IIV and changes in gait speed, varied as a function of age. The Age x Stroop IIV interaction term was found to be a significant predictor here (p < .05) whereas the Age x 2-CRT IIV x Time interaction was also significantly associated with gait speed (p < .05). This suggests that the relationships between Stroop IIV and baseline gait speed, and 2-CRT

Figure 7.2: Plot of the Age x IIV interaction in relation to baseline gait speed



IIV and changes in gait over time, were being affected by age. As a result, they were examined further in the final model. Despite these significant effects, the addition of Age x IIV and Age x IIV x Time interaction terms did not significantly improve the model fit for any models at this stage.

Finally, in Model 7, age was entered as a categorical variable with the median value (66 years) used as the cut-off point. Then, the two associations that were found to vary as a function as age were re-examined in the young-old and old-old subgroups. First, for the model that included 2-CRT IIV as a predictor, no significant effects of IIV or IIV x Time were found in either group. Second, for the model that included Stroop IIV as a predictor, there were no significant effects for the IIV x Time interaction. However, as demonstrated in Figure 7.2, there was an interaction between age and IIV. Here, higher variability levels were found to predict baseline gait speed in the older subgroup ($p < .05$) but not the younger group. Inspection of the estimates revealed that a one SD increase in baseline IIV was equivalent to a gait speed that was 5.18 cm/s slower. Re-examining these two models with age as a categorical variable did not significantly improve the model fit relative to Model 5.

7.4 Discussion

The present study examined the longitudinal relationships between variability, gait and falls in older adults aged 53 to 85 years at baseline over a period of approximately two years. The main aim was to establish whether baseline measures of IIV were associated with the future occurrence of a fall or changes in gait speed. Twenty-two of the 76 individuals (29%) reported a fall during the follow-up period. Although Cox's proportional hazard models found that baseline IIV on four RT tasks did not predict time to first fall, a significant interaction was identified between age and gait speed. Further examination revealed that slower gait speed was associated with less time to first fall in the old-old but not the young-old subgroup. A series of mixed effect models then investigated baseline IIV in relation to baseline gait speed and gait changes during follow-up, and whether these relationships varied according to age. The results indicated that younger individuals were faster at baseline, but were also more likely to show a greater decline in gait speed over time. Individuals with higher IIV on the Flanker task walked more slowly at baseline, and a significant Age x IIV interaction was found for the Stroop task. Here, further analysis revealed that higher IIV was also associated with slower gait at baseline but only in an older subgroup. Finally, there was no evidence that baseline IIV measures were predicting future changes in gait performance. Although a significant Age x IIV x Time interaction was identified for the 2-CRT task, further analysis did not reveal a significant association in either the young-old or old-old subgroups.

Predictors of time to first fall

The absence of a relationship between variability and future falls is contrary to previous work which has demonstrated that baseline IIV levels predict the number of falls experienced over subsequent years (Mirelman et al., 2012; Allcock et al., 2009). However, these non-significant findings are in line with observations from the cross-sectional work described in previous chapters. There are several possible explanations for the lack of association here. First, the rates of single (29%) and multiple (4%) falls observed during the follow-up period were much lower than in the two investigations that did report a positive association. In the current study, falls data were gathered retrospectively using a self-report questionnaire whereas the aforementioned studies used monthly falls diaries to collect information prospectively. As discussed in previous chapters, self-report methods have been shown to underestimate the true number of falls compared to monthly diaries or calendars (e.g., Garcia et al., 2015). It is possible, therefore, that several individuals in this sample may have been wrongly classified as non-fallers, thereby making it less likely that IIV measures would distinguish group differences prospectively. Second, the relatively short follow-up period (mean = 470 days) may also have contributed to the low rate of falls, and the utility of IIV measures to detect these falls over that time period. Many of the studies that have demonstrated an association between executive function and future falls followed participants for at least two years (e.g., Mirelman et al., 2012; Herman et al., 2010), whereas studies with follow-up periods of less than 12 months tended not to find evidence for this association (e.g., Nordin et al., 2010; Kudo et al., 2009). Future research, therefore, should examine IIV and falls outcomes over a number of years in order to increase the chances of detecting a significant association, and to improve understanding of the factors contributing to this relationship.

The present study provided evidence that slower gait speed at baseline was associated with less time to first fall during follow-up. This is line with other longitudinal work that has identified slow gait as a risk factor for future falls outcomes up to three years later (e.g., Callisaya et al., 2011; Bootsma-van der Wiel et al., 2003). However, here, the association between gait and falls was only significant in a subgroup representing early and middle old age. This is surprising given that the sensorimotor processes that control postural responses decline with increasing age (Li et al., 2001; Shumway-Cook & Woollacott, 1995). It was expected that very old individuals with gait impairments would be less able to respond to alterations in balance, thereby making them more prone to falling. Further investigation of the six fallers in the young-old group revealed that they performed significantly worse on tests of grip strength and leg resistance than non-fallers, and also fallers in the old-old group (unreported analysis). This suggests that these individuals had suffered greater declines in physical function than other adults of similar age, which may explain their increased vulnerability to falling. Additionally, it is possible that some individuals in the older group consciously reduced their walking speed in an effort to prevent falls. Evidence that a slower gait may act as a protective mechanism against falls has been demonstrated previously (Quach et al., 2011; Kelsey et al., 2005). It follows that very old adults may choose to employ such a strategy if they have a history of falls and are less confident of their physical abilities. If some individuals in the old-old group were consciously slowing down, it would have made it more difficult for gait measures to distinguish between fallers and non-fallers in this group.

Predictors of baseline gait speed

Individuals who were more variable on the Flanker and Stroop tasks also walked more slowly at baseline. This is line with findings from Study 3 and the wider literature where IIV has been shown to better predict gait performance when derived from tasks that place a higher demand on executive abilities (Graveson et al., 2016). The current work, therefore, gives further weight to the notion that IIV is a more sensitive predictor of outcomes when measured under cognitively demanding conditions. This work also provided evidence that the association between IIV and baseline gait strengthened with increasing age. This is consistent with expectations since IIV is closely tied to attention and executive function, both of which become increasingly important for maintaining walking performance in later old age (Yogev-Seligmann et al., 2008). Consequently, one would expect variability to be a stronger predictor of gait speed in an older subgroup relative to a younger subgroup. This finding, however, does not concur with the previous cross-sectional work where the relationship between IIV and ST gait did not vary as a function of age. This inconsistency is likely due to methodological differences, with the present study possessing increased power due to the mixed effects statistical procedures employed.

Predictors of gait speed change

Contrary to prior expectations, higher IIV at baseline was not associated with changes in gait performance over time. This is surprising given the substantial evidence that deficits in global cognitive function, and specific cognitive processes such as executive function, have previously been linked to deleterious changes in gait (e.g., Atkinson et al., 2010; Watson et al., 2010; Soumare et al., 2009). Furthermore, individuals with higher IIV levels at baseline are more likely to experience greater decline in cognitive domains such as verbal fluency and executive function over the following years (e.g., Yao et al., 2016; Bielak et al., 2010b). The lack of an association between IIV and gait could partly be due to the fact that individuals were followed for a relatively short time (range of follow-up: 156 to 645 days). Short follow-up periods may reduce the likelihood of observing a meaningful decline in gait for most subjects, particularly as the sample here was relatively young, high functioning and more highly educated (average predicted IQ = 123) compared to other investigations that have examined longitudinal gait change (Clouston et al., 2013). Further analysis revealed that the average reduction in gait speed between each individual’s baseline and final testing session was only 1.02 cm/s, providing support for this possibility.

However, rather than a small reduction in gait speed common across the whole sample, many individuals (49%) walked more quickly in their final testing session relative to baseline (unreported analysis). Although contrary to expectations, other longitudinal work has also provided evidence of older adults exhibiting improved gait performance when followed over short durations (e.g., Hardy et al., 2007). Practice effects may underlie this finding. For example, it is possible that some older adults in the present study performed better because they felt more comfortable with the gait assessment and the testing procedure during the follow-up sessions. Other explanations for short-term improvements in gait that have been proposed include recovery from illness, changes in medication and increases in physical activity (e.g., Chou et al., 2012; Lopopolo et al., 2006). If such factors were underlying changes in gait performance observed here, they could have important clinical implications. For example, an increase in normal walking speed over one year has been linked to positive long-term outcomes such as improved health status, fewer disabilities and longer life (Studenski et al., 2011; Purser et al., 2005).

Irrespective of the underlying mechanisms, the observation that individuals exhibited both positive and negative changes in gait performance over time may have made it less likely that IIV measures would capture effects. Particularly as these changes may have been associated with methodological factors (e.g., practice effects), as opposed to age-related deterioration in cognitive or physical function. As previously mentioned, investigations of the longitudinal relationship between cognition and gait have produced mixed findings in the wider literature. Many studies have demonstrated that baseline cognitive measures predict future gait decline whereas other investigations have failed to find evidence for this (Clouston et al., 2013). It is possible that, as with the present work, short-term improvements in gait performance made it more difficult for cognitive predictors to distinguish between individuals in some of these studies. Future research, therefore, should pay close attention to short-term fluctuations in gait parameters, especially as they may have significant clinical implications for older individuals.

Limitations

The current longitudinal work has several limitations that may have impacted on the findings and, therefore, should be acknowledged. Some of these have been mentioned previously such as the way in which falls data were collected and the relatively short length of the follow-up period. Another limitation concerns the relatively small number of individuals in the sample (n = 76) and, particularly, those who took part in all three studies (n = 22). Other longitudinal investigations of cognition and gait have typically been based on samples containing 400 to 2000+ older adults (e.g., Clouston et al., 2013). Although sophisticated statistical procedures were used to analyse the data in the current study to deal with attrition and missing data, the relatively low sample size may have reduced the power of the models. Particularly for associations that were examined in relation to age, as the young-old and old-old subgroups used were approximately half the size of the original sample. This, consequently, could have resulted in Type II errors and potentially significant effects being overlooked. One possible example of where this may have affected the findings is in the seventh mixed-effects model where age was treated as a categorical variable. Despite the previous model providing evidence that the relationship between IIV on the 2-CRT task and future changes in gait speed varied according to age, a significant association was not found in either the younger or older subgroup. As a result, it was concluded that baseline IIV measures were not predictive of future gait outcomes. This example highlights the potential impact that small sample size may have had in the present study, and the importance of using large samples in longitudinal investigations going forward.

Finally, as only a small number of individuals (n = 38) took part in Studies 4 and 5 where gait was assessed under dual-task conditions, it was not possible to examine baseline IIV in relation to future changes in DT gait performance. This is unfortunate since executive function is thought to be heavily implicated in dual-task walking (e.g., Killane et al., 2014), particularly in later old age when executive abilities is needed to ensure attentional resources are appropriately allocated to both the walking and secondary tasks. Studies 4 and 5, as well as empirical work elsewhere (e.g., Holtzer et al., 2014b), provided evidence that IIV measures are more strongly associated with DT relative to ST gait outcomes. Against this background, it is possible that the longitudinal relationship between IIV and gait would have been stronger had gait been assessed under dual-task conditions. Future research should aim to investigate this possibility further. It could be that variability metrics are particularly good at detecting individuals whose gait performance deteriorates in demanding situations, a finding that would also have significant clinical applications.

Conclusion

The present study is the first empirical work to date to investigate the longitudinal relationships between IIV, gait speed and falls in old age. In line with observations from the three cross-sectional studies, baseline measures of IIV did not predict falls during a follow-up period of up to two years. There was, however, evidence that those who walked more slowly at baseline were at greater risk of falling in a subgroup of individuals representing earlier old age. Consistent with the cross-sectional work, a significant association was found between IIV on the Flanker task and baseline gait speed across the whole sample, whereas IIV on the Stroop task was a significant predictor of this outcome in an older subgroup. These findings strengthen the existing evidence that IIV is a stronger predictor of gait outcomes when derived from tasks with higher executive demands, and that the relationship between IIV and gait strengthens with increasing age. Contrary to expectations, higher variability at baseline was not associated with a greater decline in gait speed during follow-up. This may have been due to a significant portion of the sample actually improving their gait performance over time, as well as methodological limitations with the present work such as the short interval between testing sessions and the small sample size. Given the paucity of longitudinal work that has been carried out to date, there is a need to further examine how variability is related to future falls and gait outcomes. Such work should aim to build on limitations in the present work by, for example, prospectively collecting falls data and measuring gait under both single- and dual-task conditions.

Chapter 8

General Discussion

Main objectives of the research

As noted throughout the preceding chapters, a major thrust behind the research in this thesis was the early detection of gait impairment and falls in the older population. Previous research has provided evidence that age-related cognitive decline, and particularly deficits in executive function, contribute to these outcomes. The current work aimed to explore associations between executive function, gait and falls with particular reference to measures of intraindividual variability (IIV). Here, IIV, or simply variability, refers to an individual's trial-to-trial fluctuations in response time across a particular cognitive task. It was hypothesised that higher levels of variability would be associated with a greater risk of falling and gait impairment (e.g., reduced walking speed) in predominately healthy and cognitively intact older adults. A major objective of the research was to test this hypothesis and to evaluate the utility of IIV measures as a predictor of gait and falls in old age.

Another objective of the current set of studies was to investigate the extent to which relationships between IIV and falls, and IIV and gait, varied according to how these key constructs were assessed. For example, variability measures can be derived from various RT tasks that place higher or lower demands on executive processes. The current work tested the notion that IIV measures would better predict both falls and gait performance when derived from tasks with higher executive demands relative to tasks with lower demands. Additionally, gait performance can be measured under various conditions, the simplest of which is single-task (ST) walking where the individual walks without distraction. By contrast, dual-task (DT) gait assessment involves simultaneously performing a secondary task that may also vary according to the demands that it places on the individual. The present research tested the hypothesis that more attentionally-demanding walking conditions would produce stronger associations between IIV and gait.

A further objective of the present work was to examine whether associations between IIV, gait and falls varied as a function of age. With increasing age, there is evidence of increased reliance on higher-order executive processes in order to maintain safe and steady walking (Yogev-Seligmann et al., 2008). Against this background, it was suggested that IIV measures placing higher demands on executive control would better predict falls and gait outcomes in later old age relative to earlier old age. Finally, this research aimed to identify potential mechanisms that may underlie significant relationships between IIV and falls, and IIV and gait. More specifically, the extent to which these relationships were attenuated after controlling for cognitive (e.g., psychomotor speed, executive function) and physiological factors (e.g., grip strength, visual acuity) was examined. The objective here was to elucidate the pathways through which variability was having its effect on age-related falls and gait outcomes.

Findings from the six studies

The first two studies reviewed published empirical work that had previously examined IIV measures in relation to either falls or gait performance in older adults. To be included in these reviews, potential studies had to report at least one cross-sectional or longitudinal association between IIV and outcome. Additionally, only investigations of healthy and cognitively intact adults with a mean age of over 65 years were considered. Eleven studies were identified that met these inclusion criteria. Six of these studies investigated IIV in relation to falls, four in relation to gait, and one in relation to both. Building on a recent review from our group (Graveson et al., 2016), Study 1 qualitatively reviewed these investigations. Here, six of the seven studies that examined falls reported that variability measures were a significant predictor of outcome. Of the five studies that investigated gait, three reported at least one significant association between higher IIV and poorer gait performance. Associations between mean RT and either gait or falls were also considered in this review. It was found that six studies reported instances where, when mean RT and IIV were measured on the same task, a significant association was only found for IIV. However, there were no examples of mean RT predicting either gait or falls outcomes when the equivalent IIV measure was not a significant predictor. Finally, this review examined how relationships involving IIV varied according to the demands of the task used to derive these measures. A total of ten associations were tested where IIV was assessed using psychomotor tasks (e.g., simple and choice RT tasks), and only two of these were found to be significant. By contrast, all 11 associations involving IIV measures derived from tasks that placed higher demands on executive function (e.g., Flanker, Stroop) were significant.

Study 2 developed the qualitative review by examining the same 11 investigations using meta-analytic procedures. Additional data were obtained from study authors where necessary to enable analyses of associations between IIV and falls for seven studies, and IIV and gait speed for eight studies. Associations involving equivalent measures of mean RT were also included. Initially, these analyses were carried out on effect sizes that had been averaged across all RT tasks. Here, higher IIV and slower mean RT were both associated with a greater risk of falls and a slower walking speed. Separate analyses were then carried out on effect sizes averaged across tasks placing either lower (psychomotor tasks) or higher (executive tasks) demands on executive abilities. For psychomotor tasks, IIV significantly predicted falls but mean RT did not, whereas neither measure did so for gait speed. For executive tasks, however, both IIV and mean RT were significantly associated with falls and gait speed. Taken together, the findings from these reviews provided strong evidence for an association between IIV and falls, and slightly less compelling evidence for a link between IIV and gait. Importantly, the results suggested that variability measures were more sensitive in detecting falls and gait outcomes than measures of mean RT. There was also evidence that the demands of the task used to produce IIV measures was influencing the extent to which these measures predicted outcome. Specifically, tasks placing higher demands on executive control produced the strongest associations with falls and gait than lower demand psychomotor tasks.

In Study 3, the first of four experimental investigations, cross-sectional associations between IIV, gait and falls were examined in a group of cognitively intact older adults. Here, a history of falls over the previous two years was obtained for each individual, gait speed was recorded under ST conditions and five neurocognitive RT tasks were administered that varied according to the demands they placed on the individual. For each task, the coefficient of variation was computed using a procedure that controlled for mean response time on the same task, and used as a measure of variability. The results indicated that IIV did not significantly predict fall status, and neither did gait speed. However, higher IIV on the two RT tasks placing the greatest demands on executive control (Flanker, Stroop) was associated with slower walking speed. This was evident both when gait was measured continuously and when using a clinically significant cut-off of <1.0 m/s that has previously been linked to adverse outcomes such as hospitalisation and disability (e.g., Rosano et al., 2008; Cesari et al., 2005). However, the three tasks with lower executive demands (SRT, 2-CRT, Visual Search) produced non-significant associations here. The extent to which relationships between IIV, gait speed and falls varied according to age was also investigated. This was done by examining Age x IIV or Age x Gait interaction terms in relation to outcome after the primary effects had been accounted for in the regression models. However, none of these interaction terms were found to be significant. Finally, in accordance with widely recognised guidelines (Preacher & Hayes, 2004; Baron & Kenny, 1986), tests of mediation were carried out on significant associations between IIV and gait in order to identify underlying mechanisms. Here, explanatory variables were introduced into regression models and the variance explained by the respective models before and after controlling for these variables was compared. The results suggested that processing speed, as measured with the Trailmaking A task, was explaining some of the shared variance when IIV was derived from the Flanker task but not from the Stroop task.

Study 4 extended the investigation of IIV, gait and falls by adding a dual-task condition to the gait assessment. It was expected that DT gait performance, which places greater demands on attentional and executive resources, would be more readily detected by variability measures than performance in less demanding conditions. Here, the DT condition involved walking while simultaneously performing a backwards counting task. Gait variability was additionally assessed by calculating the standard deviation of the time taken to complete all 20 trials in the ST condition. In line with the findings from Study 3, measures of IIV and gait performance did not distinguish between fallers and non-fallers. However, higher IIV on the SRT and Flanker tasks was associated with greater DT gait costs (i.e., the difference in speed between the ST and DT conditions) across the entire sample, whereas no significant effects were found for ST gait performance. The extent to which relationships varied according to age was again tested and three instances were found where Age x IIV interaction terms were significantly associated with gait performance. Further investigation revealed that IIV on the SRT task predicted DT gait speed in a subgroup of older aged persons (aged 68 to 90 years), but not in a subgroup representing middle and early old age (aged 52 to 67 years). Finally, tests of mediation were performed on this significant association between SRT IIV and DT gait speed in the older group. Controlling for executive function, measured using the ΔTMT score (i.e., the difference in time taken to complete Parts A and B of the Trailmaking test), substantially attenuated this association. This suggested that executive function was playing an important role in the initial relationship.

In Study 5, additional DT conditions were added to the gait assessment, requiring individuals to walk while performing a simple motor task or a verbal fluency task. This was done to examine whether increasing or decreasing the demands of the walking situation had any effect on the relationship between IIV and DT gait. An additional choice RT task was also administered which enabled the calculation of IIV measures for the decision and motor components of the task. It was hypothesised that IIV on the decision component would be higher than on the motor component, and would also be a better predictor of falls and gait outcomes. In line with the previous two studies, measures of variability and gait were not associated with falls. IIV on the Stroop task, but not the other RT tasks, significantly predicted gait speed under ST conditions. In line with attentional resources theories (Tombu & Jolicoeur, 2003; Abernethy, 1988; Kahneman, 1973), dual-task decrements in gait performance were greatest for the more demanding verbal fluency condition and lowest for the less demanding motor condition. Higher IIV on the Flanker task was associated with poorer gait performance (slower speed and higher DT costs) in the more demanding verbal fluency and backwards counting conditions, but not the motor condition. However, no other significant associations between IIV and DT gait were found. All relationships involving Flanker IIV varied according to age with further analysis revealing significant associations in the older (aged 69 to 87 years) but not the younger subgroup (aged 59 to 68 years). Finally, tests of mediation revealed that processing speed, physiological function and the task switching component of executive function (measured with the ΔTMT score) were all contributing to the relationship between IIV and DT gait. Controlling for the response inhibition (measured with the Sustained Attention to Response Task) and information updating (measured with the n-back task) components of executive function (Miyake et al., 2000) did not attenuate this relationship. However, it was suggested that the relatively low demands of the tasks used to measure these constructs may have been contributing to these non-significant findings.

Taken together, the findings from the three cross-sectional studies suggested that higher IIV was not associated with a history of falls. This is contrary to the findings from the qualitative and quantitative reviews, and other work that has identified deficits in executive function as a risk factor for falls (Kearney et al., 2013). The three studies produced conflicting evidence in favour of a relationship between IIV and ST gait performance. Similar inconsistent findings have also been reported elsewhere in the literature (Bauermeister et al., 2017; Holtzer et al., 2014b; de Frias et al., 2007) suggesting that this relationship may be subject to considerable fluctuation. The current work provided evidence that associations between IIV and gait strengthen as the demands of the gait task increase. This is in line with previous findings that executive function is more strongly associated with gait performance when assessed under dual-task conditions (e.g., Killane et al., 2014; Coppin et al., 2006). Additionally, variability measures derived from tasks with higher executive demands were found to be better predictors of DT gait outcomes than those derived from lower demand tasks. This is consistent with findings from the two review chapters. The relationship between IIV and DT gait was also found to vary as a function of age, with stronger associations consistently reported in subgroups representing later old age. This finding was in line with prior expectations since there is thought to be an increased reliance on higher-order executive processes to maintain safe and steady walking with increasing age (e.g., Yogev-Seligmann et al., 2008). Finally, tests of mediation provided evidence of a dichotomy where processing speed measures explained effects of IIV on single-task walking, whereas higher-order executive function measures played a more important role when gait was assessed under more demanding DT conditions.

Finally, Study 6 described a longitudinal investigation of relations between IIV, gait speed and falls. Here, a total of 76 older adults were followed for a period of up to two years. ST gait speed was measured on at least two occasions for each individual and falls history for the previous two years was recorded at each assessment point, making it possible to estimate time to first fall after initial baseline testing. A series of Cox regression analyses revealed that baseline IIV on four tasks (SRT, 2-CRT, Flanker, Stroop) was not associated with time to first fall, and these associations did not vary as a function of age. A series of mixed models examined baseline IIV in relation to future changes in gait speed, and whether this relationship varied according to age. The results indicated that higher Flanker IIV at baseline was associated with a slower walking speed at baseline, whereas Stroop IIV was found to predict baseline gait performance in an older group (aged 53 to 66) but not a younger group of adults (aged 67 to 85). Contrary to prior expectations, baseline IIV levels did not predict future changes in gait speed, and the longitudinal relationship between IIV and gait did not vary with age. These results suggest that variability metrics may have limited predictive utility when it comes to detecting future gait impairment. However, the non-significant findings reported here may partially be attributed to the fact that many older adults improved their gait performance between the first and last testing sessions. This suggests that the effects of age-related gait decline may have been masked by other factors such as practice effects, the sensitivity of the gait measure and the atypically high IQ of the sample.

How do the findings inform theory?

In the first chapter of this thesis, four prominent theories of cognitive ageing were outlined. Each theory proposed that age-related change in cognitive function was attributed to a particular cognitive or biological mechanism. First, in the speed of processing account of cognitive ageing, Salthouse suggested that generalised slowing of information processing was a major factor underlying cognitive decline in old age (Salthouse, 1996, 1985). He also provided evidence that age-related variance on many cognitive tasks can be explained by performance on a variety of perceptual speed tasks. A second perspective, the inhibitory deficits hypothesis advanced by Hasher and Zacks (1988), suggested that age-related variation in cognitive performance can largely be explained by differences in the ability to inhibit irrelevant information interfering with working memory during ongoing cognitive processing. Taking a more neurobiological approach, in the frontal lobe hypothesis, West proposed that age-associated cognitive decline was related to atrophy in the frontal areas of the brain brought on by advancing age (West, 2000; West, 1996). He also provided evidence that consequent deficits in executive function account for many of the observed age differences in broader cognitive performance. In a final account, the neural noise hypothesis suggested that increasing age is associated with an increase in neural fluctuations that interfere with transmissions in the central nervous system (Welford, 1981, 1965). The resulting decreases in the ratio of signal to noise causes the processing of information to become slower and more variable, leading to performance decrements on a range of cognitive tasks.

The findings from the studies described in this thesis speak to several of these theoretical perspectives. Particularly, the findings regarding associations between IIV and gait are of note here. This research provided evidence that the speed of processing account more readily explained the relationship between IIV and gait when measured under conditions that placed lower demands on the individual. By contrast, the frontal lobe perspective, placing emphasis on the important role of executive control, provides the most parsimonious explanation when these constructs are assessed under more attentionally-demanding conditions. For example, throughout the experimental work conducted in this thesis, there were weak and largely non-significant associations reported between IIV on tasks with lower cognitive demands (e.g., SRT, 2-CRT) and gait performance. Previous work has demonstrated that mean RT and IIV measures derived from simple and choice RT tasks are often highly correlated (e.g., Deary & Der, 2005). Therefore, it is possible that these weak associations between IIV and gait stemmed from IIV on less demanding tasks mainly capturing individual differences in response speed. This notion supports the speed of processing account that general age-related slowing underlies between-person variation in variability on these lower demand tasks.

In comparison to simple and choice RT tasks, IIV on tasks with higher executive demands (Flanker, Stroop) was more closely related to gait performance across both the cross-sectional and longitudinal investigations. This suggests that frontally mediated executive processes were making an important contribution to the relationship between variability and gait. Given the strong linkage between executive function and gait (e.g., Watson et al., 2010; Soumare et al., 2009; Atkinson et al., 2007), it is possible that deficits in executive processes are only reflected as higher IIV when the task used to measure IIV draws highly on these processes. This is consistent with the frontal lobe perspective where executive deficits are thought to mediate much of the age-related variation in cognitive performance. The inhibitory deficits hypothesis of cognitive ageing is also relevant here since the ability to inhibit responses has been posited as a component of executive function in widely-recognised conceptual frameworks (e.g., Miyake et al., 2000). Furthermore, the Flanker and Stroop tasks used in the present work are both thought to primarily capture inhibition. Therefore, the extent to which older adults were able to inhibit irrelevant information would have significantly contributed to performance (i.e., IIV levels) on these tasks, and consequently, the utility of these measures to detect differences in gait performance.

Another key finding was that the relationship between IIV and gait strengthened as the conditions under which gait was assessed became more demanding. Specifically, there was weak and inconsistent evidence linking higher IIV to poorer gait performance when gait was assessed under ST conditions, or a lower demand DT motor condition where individuals walked while carrying a tray with a glass of water on it. Previous work has demonstrated that processing speed measures are better predictors of gait outcomes assessed under ST relative to DT conditions (e.g., Lowry et al., 2012; Soumare et al., 2009). As previously mentioned, response speed was controlled for in the computation of IIV measures, and the general slowing perspective of cognitive ageing suggest that differences in information processing underlie differences in wider cognitive abilities. The lack of a relationship between IIV and gait when measured under conditions with lower demands is, therefore, in line with this perspective.

By contrast, variability measures were found to predict DT gait outcomes when individuals walked while performing a more demanding backwards counting or verbal fluency task. This finding is in line with capacity sharing theories of attention which suggest that individuals have access to a finite amount of attentional resources (Tombu & Jolicoeur, 2003; Abernethy, 1988; Kahneman, 1973). The successful performance of multiple tasks is possible as long as the resource limit is not exceeded. Beyond this threshold, however, there will be performance deficits in at least one of the tasks. In the context of the present findings, it is reasonable to assume that when gait was assessed under dual-task conditions involving a demanding secondary task, many older adults may have exceeded their resource limit resulting in poorer gait performance. These reductions in performance would have created larger between-person variation that, subsequently, may have been more readily detected by IIV measures. This finding is consistent with the frontal lobe account of cognitive ageing since higher-level executive processes are important in the appropriate allocation of attentional resources in complex situations (Ble et al., 2005). It was expected that older adults with executive deficits in the present work may have been more prone to decrements in gait performance when the attentional demands of the gait task were increased. Therefore, the extent of these deficits would have determined the extent to which variability measures were able to predict differences in gait performance in this group.

Finally, where associations between IIV and gait were found to be significant, tests of mediation were conducted to investigate the mechanisms that underpin these relationships. These analyses provided evidence that processing speed, measured with the Trailmaking A task, had explanatory power in the relationship between IIV and gait in less demanding situations (e.g., single-task conditions). This finding supports earlier research which found that controlling for processing speed significantly attenuated the association between prefrontal brain white matter volume and walking speed (Rosano et al., 2012). By contrast, the role of processing speed in the relationship between IIV and gait in more demanding DT conditions was considerably weaker. This is consistent with expectations given that walking under ST conditions is less likely to have drawn on higher-level cognitive resources, in contrast to walking while performing an additional cognitive task. Therefore, it is reasonable to expect that between-person differences in gait speed under less demanding conditions was more readily explained by differences in response speed. Again, this finding supports the speed of processing perspective that general slowing may underlie the effects of variability on gait performance in situations where demands are low.

Tests of mediation also examined executive function as a potential mechanism underlying the relationship between variability and gait. In Study 3, controlling for executive function did not attenuate the effects of IIV on ST gait speed. This finding was not unexpected since, as noted previously, walking under ST conditions is unlikely to have placed high demands on frontally mediated executive processes. In Study 4, executive function was found to be playing a key role in the relationship between IIV and gait when individuals had to walk while simultaneously performing a backwards counting task. This observation was in line with prior expectations since executive measures have been previously been shown to predict dual-task gait outcomes (e.g., Hausdorff et al., 2008; Sheridan & Hausdorff, 2007). It also suggests that differences in executive function were accounting for the age-related variation in IIV levels that was observed here, consistent with the frontal lobe account of cognitive ageing. In Study 5, however, the extent to which executive function was attenuating the effects of variability on DT gait performance was found to be considerably lower. This suggests that the underlying role of executive deficits in relation to age-related cognitive decline, as represented here by higher IIV, may differ according to the characteristics of the group being studied. In partial support of this notion, there was evidence that the reduced influence of executive function in Study 5 may have been due to better preserved executive abilities in the individuals that were sampled.

To summarise, findings regarding the association between variability and gait in the present work are of most relevance to the theoretical accounts of cognitive ageing that were outlined in the introductory chapter. These findings provide evidence for a dichotomy where the extent to which this relationship can be explained by certain perspectives depends on the demands placed on the individual when both IIV and gait performance were measured. More specifically, the general slowing account provided the best explanation when IIV measures were derived from tasks with lower executive demands, and when gait was assessed under less demanding conditions. By contrast, the frontal lobe perspective had greater explanatory power when the demands of both the tasks used to produce IIV measures and the conditions under which gait was assessed were higher. Support for this dichotomy comes from different findings within specific studies, while there also appears to be consistent evidence across studies. This suggests it is a stable and robust phenomenon and, as such, it represents a major theoretical contribution of this current research.

Methodological considerations

In each of the experimental studies described here, it was noted that the rate of single and recurrent fallers was relatively low compared to previous investigations of variability and falls. This is likely to have contributed to the unexpected finding that IIV measures did not significantly predict falls. Several explanations were put forward to account for this low number of falls. For example, the self-report method used to collect falls data here has previously been shown to underestimate the total number of falls compared to prospective methods such as monthly fall diaries (Garcia et al., 2015). Therefore, it is possible that older adults sampled here experienced more falls than the results suggested, and this “floor” effect may have made it more difficult for IIV measures to distinguish between fallers and non-fallers. It was also noted that the individuals who took part in this experimental work were relatively young, highly functioning, had above average IQs and were less likely to display signs of cognitive impairment compared to participants in previous investigations. Therefore, it is reasonable to assume that the types of falls experienced by these individuals were less likely to have been associated with age-related cognitive decline (represented here by increased IIV levels). Indeed, examination of the falls data in Studies 3 to 5 revealed that between 54% and 70% of the total falls reported were caused by ice and snow, objects, or uneven surfaces. These figures suggest that a large proportion of the falls experienced by the current sample are likely to have been one-off incidents caused by environmental factors (e.g., weather conditions) rather than factors specific to the individual (e.g., age-related cognitive deficits). This possibility is supported by the particularly low rates of recurrent fallers that were reported in each of the studies.

In the wider literature on ageing and falls, a distinction has previously been made between “clinically relevant” fallers who fall often and incur falls-related injuries and those who suffer occasional slips or trips. Furthermore, a number of studies have demonstrated that cognitive deficits, and particularly decrements in executive processes, are significantly associated with both injurious falls and recurrent falls (Delbaere et al., 2010; Pijnappels et al., 2010; van Schoor et al., 2002; Nevitt et al., 1991). Against this background, it seems likely that the variability measures used here would have been better predictors of these more serious types of fall as opposed to the non-injurious single falls reported here. Unfortunately, the low number of total falls prevented an examination of IIV in relation to different types of falls (e.g., single, multiple, injurious) or falls with different causes (e.g., those caused by environmental factors versus those caused by person-specific factors). However, it is likely that a lack of clinically relevant falls was driving the nonsignificant associations with variability that were reported here.

A second consideration concerns sample size. Across the three cross-sectional investigations, the number of participants sampled ranged from 59 to 67. This increased to 76 in the final longitudinal study. These samples are relatively small compared to those in previous work looking at variability in relation to either falls or gait (e.g., O'Halloran et al., 2014; O'Halloran et al., 2011). Due to the resulting low statistical power, the use of such small samples may have made it more difficult for IIV measures to predict outcome. This possibility is particularly likely where associations between IIV and gait were examined as a function of age, as these tests were performed on groups that were approximately half the size of the original sample. In addition to small sample sizes, another factor that may have affected the results was age. It has already been noted that the older adults sampled here were, on average, relatively young and that this may have contributed to the lack of a relationship between IIV and falls. It is also worth noting that, in addition to the relatively low average age, there was a high concentration of individuals clustered just a few years either side of the average age. As a result, when associations were tested in young-old and old-old subgroups, the difference in age between many individuals in these groups would have been very low. This, combined with the small sizes of these subgroups, may have made it more difficult to capture effects associated with age.

In all three cross-sectional studies described here, identical measures of IIV, ST gait speed and falls were administered. However, in a number of cases, relationships between these constructs were not found to be consistent over time. For example, in Studies 4 and 5, different measures of IIV were associated with DT gait performance. Variability on the Flanker and Stroop tasks predicted ST gait speed in Study 3, however, this was not replicated in Study 4 and was only replicated for Stroop IIV in Study 5. These contrasting findings regarding IIV and ST gait are in line with the broader literature. The inconsistency in this particular relationship could be attributed to a number of factors. First, higher-order cognitive abilities linked to variability, such as executive function and attention, might not have made significant contributions to gait when the walking demands were low. Therefore, it is reasonable to expect that age-related decline in these abilities would not consistently manifest as a reduction in gait performance. This is particularly the case for the relatively young and highly functioning adults sampled here, who were likely to have had relatively well maintained sensorimotor processes and attentional resources compared to older groups in other investigations.

Second, the 4-metre speed test used to measure ST gait in the present work may have been particularly sensitive to changes in performance over time. These changes may have prevented cognitive measures from consistently making accurate predictions about gait performance. Partial support for this notion was provided in the longitudinal study where approximately half of the older adults completed the gait test more quickly in the final testing session relative to baseline, whereas the other half did so more slowly. It is possible that these short-term improvements may have been due to the relatively short interval between testing sessions. Alternatively, these improvements may have been associated with health and lifestyle changes such as recovery from illness, changes in medication and increases in physical activity (e.g., Chou et al., 2012; Lopopolo et al., 2006). Irrespective of the underlying cause, the present work provides evidence that associations between variability and ST gait performance are susceptible to change even if the conditions under which these associations are tested remain constant. As a result, it would be wise to exercise caution when interpreting findings that correspond to this relationship here and in the wider literature.

Finally, in order to facilitate a longitudinal analysis of the relationship between IIV, gait and falls in the final study, several older adults participated in more than one of the cross-sectional investigations. This involved repeat testing on many of the cognitive (e.g., RT tasks, Trailmaking A and B) and physical (e.g., tests of grip strength, leg resistance strength and ST gait speed) measures. As previously noted, the interval between studies was relatively short, with participants waiting an average 349 days between testing sessions. These short intervals may have helped some individuals to improve their performance on certain measures over time. It has already been suggested that this was the case for gait after finding that approximately half of the older adults completed the ST gait trails faster in the final testing session relative to baseline. This issue was investigated in more depth in Study 5 where additional analyses were carried out on the 22 individuals that took part in all three studies. This analysis provided some evidence of improved performance on certain cognitive measures including the Flanker and Stroop tasks (reduced IIV) and both parts of the Trailmaking test (faster completion times). Given that there is general decline in cognitive and physical function associated with increasing age, these improvements can most easily be attributed to practice effects. As a result, these effects may have masked age-related differences in performance that the measures in the current work were trying to detect.

Clinical and applied implications

As mentioned at the outset of this chapter, an important objective of the present research was to assess the potential of variability measures as early screening tools for falls and gait impairment in applied settings. In relation to falls, the two review chapters provided evidence that higher IIV was associated with a history of falls, and was also a risk factor for future falls. This was not replicated in the experimental studies that followed as both cross-sectional and longitudinal associations between variability and falls were found to be non-significant. However, it was suggested that methodological limitations associated with the present research (e.g., size and characteristics of the sample, methods used to collect data) may have largely accounted for the lack of a relationship here. Therefore, the work described in this thesis provides mixed evidence that higher IIV levels may be a risk factor for future falls, and that IIV measures would be a useful supplement to existing falls risk assessment batteries.

In relation to gait impairment, there was some evidence provided by the review chapters that IIV was detecting this outcome. This link was strengthened considerably by the experimental work where greater IIV on tasks with higher demands was associated with poorer gait performance. This was particularly the case for more demanding DT conditions where individuals had to walk while performing a cognitive task. Furthermore, the present work provided evidence that the relationship between IIV and DT gait varied according to age, with stronger associations found in groups representing later old age. These findings suggest that increased variability in very old groups may be a marker for those at risk of reduced gait performance in demanding walking situations. Given that everyday walking often draws on dual-tasking (e.g., crossing a busy street), these individuals may also struggle to cope with certain daily living activities. This, in turn, could pose a threat to their capacity to live independently and safely, and to their overall health and wellbeing. As previously mentioned, Study 6 was the first longitudinal investigation of the relationship between IIV and gait, and did not produce evidence that variability was identifying persons at risk of future impairment. However, it was suggested that methodological issues (e.g., practice effects, small sample size) may have been underlying the lack of an association found here. Despite these non-significant results, on balance, the findings reported in the other studies point to the potential of IIV measures as an early screening tool for identifying older adults at risk of developing mobility problems. Furthermore, variability metrics would serve as a particularly good screening tool in clinical settings given that the measures are quick to administer with little training required, and they contain minimal linguistic content making them suitable for use with a variety of patient groups.

Another key objective of the research described here was to determine whether IIV measures were capturing unique information about falls and gait outcomes not picked up by average performance indicators (e.g., mean RT). The two review chapters provided strong evidence that variability was a better predictor of falls than mean RT obtained from the same task, but slightly weaker evidence that this was the case for gait. The present experimental work used IIV metrics that controlled for average response time in their calculation, enabling a direct examination of the unique predictive utility of these measures. The nonsignificant associations between variability and fall status found here suggested that IIV was not capturing information about falls beyond that being picked up mean RT. By contrast, the same IIV metrics were significantly associated with several measures of gait, suggesting they were making unique predictions about gait performance. These findings provide evidence for the inclusion of variability metrics that control for same-task mean RT in assessments of gait impairment given that the may detect at risk individuals earlier then existing neuropsychological measures. For use in applied settings, the coefficient of variation measure of IIV that the present work employed would be an appropriate choice since it can be calculated quickly and easily using basic computer software.

As mentioned previously, IIV on tasks with higher executive demands (Flanker, Stroop) was a greater predictor of gait outcomes than IIV on tasks with lower executive demands (e.g., simple and choice RT tasks). These findings have relevance in applied contexts as they suggest that IIV may only be useful for detecting age-related outcomes when the tasks are sufficiently demanding to capture effects. To the same end, when using IIV in applied settings, great care should be taken not to administer tasks with excessively high demands. This may cause a high proportion of older individuals to record very poor scores (i.e., a floor effect) which would limit the extent to which measures are able to detect effects. Finally, throughout the experimental work described here, IIV on the Flanker task emerged as a reliable predictor of gait outcomes, particularly when gait was assessed under DT conditions. This is in contrast to other RT tasks (SRT, 2-CRT, Stroop, Visual Search) that, in total, produced only a few significant associations between IIV and gait. Previous research has also demonstrated that performance measures derived from the Flanker task, including IIV, are a good predictor of mobility outcomes in old age (Gothe et al., 2014; Holtzer et al., 2014b). When taken together with the present findings, there is considerable evidence in favour of incorporating the Flanker task into existing screening tools for gait impairment. This is underlined by its wide usage elsewhere in the cognitive ageing literature, and the volume of empirical research that has been carried out using this task.

Future directions

The present research provided an in-depth examination of the relationship between IIV, gait and falls in old age. The experimental work described here developed previous investigations of this topic in a number of ways. In particular, Study 6 is the only longitudinal work to date to look at IIV in relation to both future falls and future gait impairment. Therefore, there is a pressing need for similar prospective investigations to establish the predictive utility of IIV metrics when it comes to detecting populations at risk of these outcomes. Regarding falls, the nonsignificant findings reported here suggests further evidence is needed so strengthen the link with variability, and identify the conditions and demographic groups in which the strongest associations exist. For example, previous research suggests executive function measures predict multiple and injurious falls (e.g., Delbaere et al., 2010; Pijnappels et al., 2010) and, given the link between IIV and executive control, this may also be the case for measures of variability. Regarding gait, baseline IIV levels were not found to be predictive of future changes in ST gait speed. This suggests that more prospective research is needed to determine the strength of the longitudinal relationship between IIV and gait and to establish under which conditions variability measures may be useful in the detection of future gait impairment. As noted in previous chapters, there is some debate in the literature regarding the temporal direction of the relationship between cognitive decline and gait impairment. While many studies have provided evidence that baseline cognitive measures predict future gait outcomes (e.g., Atkinson et al., 2010; Watson et al., 2010; Rivera et al., 2008), a number of investigations have found the opposite to be true (e.g., Mielke et al., 2013; Inzitari et al., 2007b; Wang et al., 2006). Although beyond the scope of the current work, future research would benefit from looking at gait performance in relation to future changes in IIV, thereby providing insights into these contrasting findings.

Studies 4 and 5 provided evidence that IIV measures are good predictors of gait performance in attentionally demanding situations, particularly in very old groups. Of particular note, in Study 5, participants were asked to walk while performing either a backwards counting task, a verbal fluency task or a simple motor task. In line with prior expectations, the verbal fluency task produced the greatest gait costs but IIV measures were equally strong predictors of gait outcomes in this and the backwards counting condition. This is surprising given that the verbal fluency condition was thought to place higher demands on attentional resources, the allocation of which is controlled by higher-order executive processes (Ble et al., 2005). It is possible that once the attentional demands of the gait task exceed a certain threshold, differences in performance are readily detected by cognitive measures. However, increasing the demands further may not increase the predictive utility of these measures. Future research should attempt to examine associations between IIV and DT gait in a variety of conditions that place increasing demands on attentional resources. Such work will shed more light on the conditions under which IIV metrics can best be utilised to make predictions about gait performance.

Study 4 examined how the extent to which measures of cognitive and gait variability were associated with one another. No evidence was found that higher IIV was associated with more variable gait performance, although it was suggested that the relatively basic measure of gait variability may have contributed to these null findings. Indeed, there is good theoretical reason to expect a link here. For example, more variable gait patterns have been observed in older adults with executive deficits (e.g., van Iersel et al., 2008a; Hausdorff et al., 2005) and compromised frontal white matter integrity (e.g., Srikanth et al., 2009; Rosano et al., 2007). The same groups have also been found to be more cognitively variable (e.g., Bunce et al., 2008; West et al., 2002). Investigating the factors that contribute to age-related increases in gait variability is important given that it has been linked to a number of adverse outcomes such as incident mobility disability (Brach et al., 2007) and dementia (Verghese et al., 2007). Furthermore, measures of gait variability have been found to distinguish between fallers and non-fallers better than other measures of gait (e.g., Taylor et al., 2013; Callisaya et al., 2011). Two studies have previously examined associations between cognitive and gait variability, however, these investigations produced contrasting findings (Sukits et al., 2014; Reelick et al., 2010). As a result, further empirical work is needed to determine how useful IIV measures are at detecting individuals at risk of developing an unsteady gait. Such work may also contribute to the prevention of other outcomes associated with increases in gait variability such as falls.

Finally, an important objective of the present research was to investigate the mechanisms through which IIV was having its effects on gait and falls. Unfortunately, it was not possible to examine the relationship between IIV and falls here as no significant associations were identified. However, an earlier study from our laboratory provided evidence that motor function, but not executive function, was attenuating associations between variability and falls (Bauermeister et al., 2017). This is surprising given that IIV is thought to reflect fluctuations in executive control processes, deficits in which have been identified as a reliable risk factor for falls (Kearney et al., 2013). In regard to gait, there was evidence that processing speed was underlying the relationship between IIV and ST gait speed, whereas executive function was playing an important role in the relationship between IIV and DT gait. However, these findings were not consistent across all studies. Such inconsistencies provide evidence against the possibility that one single mechanism is underlying these relationships in any given situation, and suggest that any mediation effects are potentially sensitive to change over time. Given that no other studies have investigated this issue in relation to gait performance, there is a need for future research to build on the present results. Such work will shed light on the considerations raised above and provide a clearer understanding of the pathways through which variability contributes to both falls risk and gait impairment in old age.

Conclusion

The set of studies described in this thesis examined intraindividual variability in relation to gait and falls in the healthy older population. Reviews of previous empirical work provided evidence that higher IIV was associated with falls outcomes and, to a slightly lesser extent, gait impairment. Contrary to this earlier work, the experimental research described here did not find IIV measures to be associated with falls, though it was suggested that these non-significant methods may have been attributed to methodological issues. By contrast, variability measures did predict gait performance across the three cross-sectional studies. This relationship was strongest when IIV was derived from tasks placing higher demands on executive function, and when gait was assessed under more demanding DT conditions. Furthermore, the relationship between IIV and DT gait performance varied as a function of age, with stronger associations found in groups representing later old age. Finally, tests of mediation suggested that processing speed was accounting for associations between IIV and ST gait performance, whereas executive function played a greater explanatory role when gait was measured under higher demand DT conditions.

Given the caveats outlined above, the overall findings of the present work suggest that variability measures may have considerable potential as an early screening tool for older persons at risk of gait impairment and, to a lesser extent, falls. There was evidence that the extent to which IIV predicted age-related outcomes varied according to several factors, most notably the way in which variability and gait were measured. These factors should, therefore, be taken into consideration when moving from the laboratory to applied settings to ensure maximum clinical utility. For example, based on the present findings, a strong argument could be made for only using IIV metrics derived from tasks placing higher demands on cognitive resources. The Flanker task, in particular, was shown to be a consistent predictor of gait outcomes, making it appropriate for use in clinical settings. Furthermore, the use of IIV measures that control for mean RT from the same task is recommended as this adjustment takes into account the influence of general slowing on more variable responding. The coefficient of variation metric employed in the current work is attractive in this respect and also has the advantage of being quick and easy to calculate without the need for any specialist software or training.

Finally, the present research provided evidence that the cognitive mechanisms underlying relations between IIV and gait varied according to the demands placed on the individual when measuring these constructs. When assessments of IIV (e.g., simple and choice RT tasks) and gait (e.g., single-task conditions) placed lower demands on the individual, general slowing accounts gave the best explanation of the findings. By contrast, executive function became increasingly important as task demands increased, consistent with frontal lobe accounts of cognitive ageing. This finding is a potentially important contribution of this thesis and should be explored in more depth by future research. For example, it is not clear if the relationship between IIV and DT gait performance strengthens as the demands of the gait condition increases, or if these associations are equally strong after a particular threshold for task demands is reached. Furthermore, given the paucity of previous work and the inconsistent findings reported here, examining cognitive and physiological variables as potential mediators of relationships involving IIV remains an important direction for future research.

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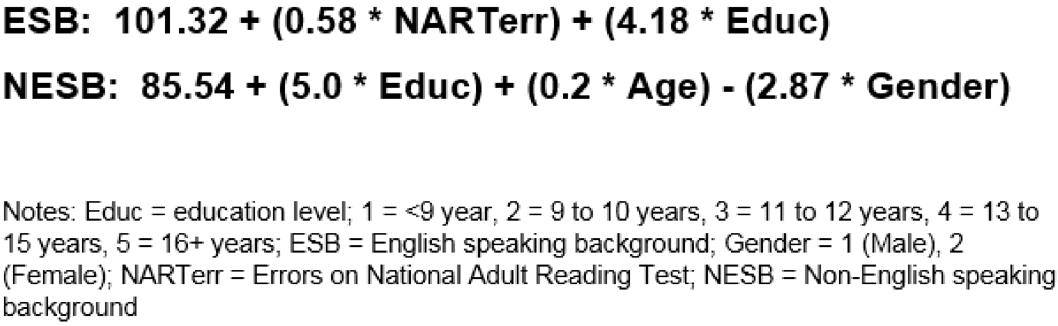
Appendices

Appendix 1A: Formulas used to calculate predicted IQ

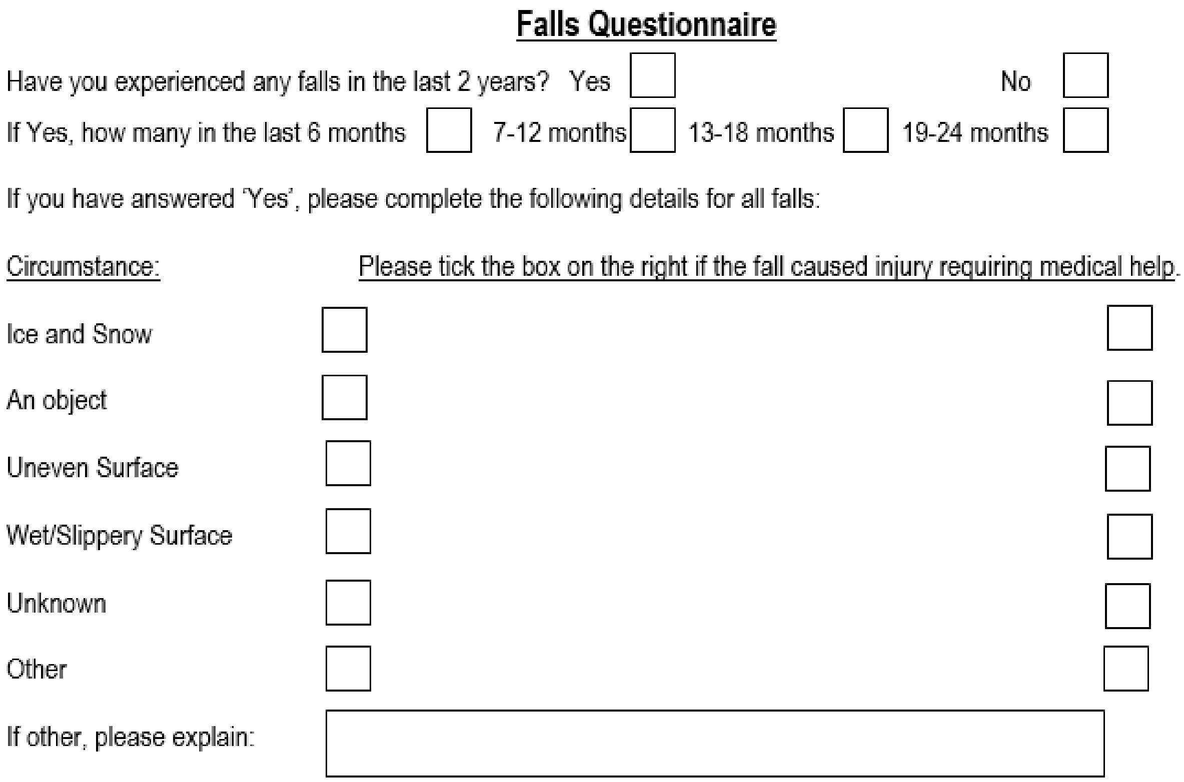


ESB: $101.32 + (0.58 * \text{NARTerr}) + (4.18 * \text{Educ})$

NESB: $85.54 + (5.0 * \text{Educ}) + (0.2 * \text{Age}) - (2.87 * \text{Gender})$

Notes: Educ = education level; 1 = <9 year, 2 = 9 to 10 years, 3 = 11 to 12 years, 4 = 13 to 15 years, 5 = 16+ years; ESB = English speaking background; Gender = 1 (Male), 2 (Female); NARTerr = Errors on National Adult Reading Test; NESB = Non-English speaking background

Appendix 1B: Falls questionnaire



Falls Questionnaire

Have you experienced any falls in the last 2 years? Yes ☐ No ☐

If Yes, how many in the last 6 months ☐ 7-12 months ☐ 13-18 months ☐ 19-24 months ☐

If you have answered 'Yes', please complete the following details for all falls:

Circumstance:		Please tick the box on the right if the fall caused injury requiring medical help.
Ice and Snow	☐	☐
An object	☐	☐
Uneven Surface	☐	☐
Wet/Slippery Surface	☐	☐
Unknown	☐	☐
Other	☐	☐

If other, please explain: ☐

Outputs from the research

Bauermeister, S., & Bunce, D. (2015). Cognitive variability and physical predictors of falls in older adults. British Psychological Society conference, Birmingham (UK), November 2015.

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