

THE EFFECT OF SIMPLE AND COMPLEX DUAL-TASKS ON AMBULATION IN
INDIVIDUALS WITH ALZHEIMER'S DISEASE AND HEALTHY OLDER ADULTS: THE
ROLE OF DIVIDED ATTENTION AND OTHER HIGHER BRAIN FUNCTIONS IN GAIT
DUAL-TASK PERFORMANCE

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By
Jocelyn Lee Pook

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OR

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College of Graduate Studies and Research
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107 Administration Place
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Canada

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Abstract

Research using gait-dual task methodology suggests that the ability to divide attention during walking appears to be particularly vulnerable to the effects of Alzheimer's disease (AD), even in the earliest stages of the illness. However, these previous studies are limited by the variability in the types of gait-dual tasks employed, as well as by the inclusion of heterogeneous groups of patients at different stages of disease severity. Study 1 aimed to address these methodological concerns by examining the effects of a simple and complex counting task on gait speed in healthy older adults and individuals with early stage AD. In contrast to previous findings reported in the literature, Study 1 found that when compared to an age appropriate control group individuals with early stage AD were not differentially impaired by a gait dual-task, regardless of the level of task complexity.

Study 2 was designed to be a replication and extension of Study 1. In Study 2, sixteen individuals diagnosed with amnesic Mild Cognitive Impairment (aMCI; Petersen, 1999; 2001), 15 individuals with early-stage AD, 17 individuals with moderate stage AD, and 27 healthy older adults performed a timed walking task and simple and complex verbal counting tasks in single and dual-task combinations. In keeping with the results of Study 1, there were no significant differences among the early stage AD group, aMCI group, and healthy older adults on the gait dual-task, regardless of task complexity. However, significant differences were detected between the moderate AD group and the healthy normal control group on the complex dual-task.

Study 3 examined the relationship between other higher brain functions and gait speed, with and without interference, in the same group of participants as Study 2. Neuropsychological test scores were used to create theoretically derived cognitive composite scores (i.e., Executive Functioning/Attention/Speed; Episodic Memory; Language) that were used as predictors of gait

speed, with and without interference. As expected, The Executive Functioning/Attention/Speed composite was the most potent predictor of gait speed across conditions; however this relationship varied as a function of task complexity and all three factors predicted gait interference in the complex condition, even after controlling for disease severity. In contrast to previous gait dual-task studies, the current research suggests that aMCI and early stage AD are not associated with impaired gait dual-task performance. Rather, these results suggest that when overall degree of dementia severity is controlled for by subdividing patients based on diagnostic criteria, the specific deficit in attention appears later in the progression of AD than previously theorized. Furthermore, these results provide evidence that the relationship between cognition and gait is likely built upon components of cognitive, physical and task prioritization processes that appear to be modulated by task complexity and disease severity.

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General Introduction

While walking has traditionally been considered to be an automated process, there has been increasing recognition in the last decade that higher brain functions have an important influence on gait. Recent evidence from multiple disciplines (i.e., physiology and physical therapy; neuroimaging and brain mapping; and clinical and experimental neuropsychology) has linked cognitive processes such as divided attention and executive functions to gait performance in healthy and pathological aging, such as Alzheimer's disease (AD; Yogev-Seligmann, Hausdorff, & Giladi, 2008). An important methodology leading to these findings has been the use of gait dual-task paradigms to study the effect of concurrent cognitive demand on walking in healthy older adults and individuals with AD. Previous studies have indicated that AD patients perform as well as healthy older adults on some single-task procedures, but show a disproportionate decline in performance when walking and cognitive tasks are performed simultaneously (i.e., dual-task performance; Al-Yahya, Dawes, Smith, Dennis, Howells, & Cockburn, 2011). Therefore, a number of authors have suggested that the early stages of AD are associated with a break-down in the ability to divide attention between tasks and that impairments in divided attention may be an important early hallmark of AD (Fernandez-Duque & Black, 2006; Perry & Hodges, 1999; Saunders & Summers, 2011).

Nonetheless, the information from previous gait dual-task studies has been limited by large methodological variations in the literature. Similarly, the lack of standardization in gait dual-task paradigms has made it difficult to compare results across studies. Therefore, the primary aim of the current research was to clarify whether the observed dual-task related gait changes in AD that have been described previously are related to four main methodological limitations, including: (1) the inclusion of large heterogeneous patient groups at different stages

of disease severity; (2) a failure to manipulate the complexity of the component cognitive task; (3) the types of cognitive tasks employed; and (4) the lack of emphasis on task prioritization processes. A secondary aim was to extend the current gait and cognition literature by utilizing neuropsychological testing to understand how specific cognitive factors (i.e., attention, executive functioning, language, and episodic memory) are related to gait dual-task performance in healthy older adults and individuals with AD.

The following general introduction discusses the role of divided attention and executive functions in gait dual-task performance. The theoretical models and neural basis believed to underlie these relationships are provided, both for healthy older adults and for individuals with AD. Next, the relevant gait dual-task studies in healthy older adults and individuals with AD are presented, and the importance of task prioritization processes and theories of successful aging are discussed. Finally, the limitations of the previous literature are summarized in detail and the overview of the current research demonstrates how the three inter-related studies in this dissertation provide a methodological advantage over previous work by using a simple and complex gait dual task procedure to further investigate the role of divided attention in early-stage AD and in normal aging.

Traditional Models of Dual-Tasking

Dual-task paradigms are used in clinical and experimental research to examine the specific components of attention and executive functioning necessary to divide cognitive resources between two concurrent tasks. With few exceptions, traditional investigations of dual-task performance in normal and pathological aging have used relatively automatized experimental tasks (e.g., finger tapping or visual tracking), with cognitive tasks of articulation (i.e., counting aloud, speeded verbal fluency, seriatum speech tasks) to assess whether there is a

divided-attention deficit in normal and pathological aging – either because of a depletion of processing resources or because of the use of inefficient mental resource allocation (e.g., Baddeley, 1996; Crossley, Hiscock & Foreman, 2004; Grober & Sliwinski, 1991; Parasuraman & Haxby, 1993) .

The Dual-Task Paradigm. The standard dual-task paradigm used in most of these early studies involves measuring performance on each single task condition (Task A, Task B, or baseline conditions) and the simultaneous performance of both tasks (Task A & B) in the dual-task condition in order to determine the degree to which performance on Task A and B decreases under the dual-task condition, relative to their respective baseline conditions (Li et al., 2005; Perry & Hodges, 1999). A classic example would be the combination of box joining and digit span repetition used by Baddeley et al. (1986) or the combination of speeded uni-manual, alternate-key finger tapping and speaking tasks used by Crossley et al. (2004). When performance on one or both tasks is lower when they are done simultaneously, tasks are assumed to interfere with one another, presumably because both tasks compete for a common pool of information processing resources in the brain.

Task Complexity. Research has shown that the level of component task complexity also matters greatly in dual-task procedures. An early study by McDowd and Craik (1988) prompted several important considerations of dual-task paradigms by showing that age-related decrements in divided attention increase as task demands become greater. In their experiment, task difficulty was manipulated and strong evidence for an age-related decrement in dual-task performance was found, especially as task difficulty was increased. Since then, a number of dual-task studies have demonstrated interactions between age or disease (i.e., AD) and task-complexity (e.g., Crossley et al., 2004; Crossley & Hiscock, 1992). That is, while group differences have been minimal

when the component tasks are relatively easy or automatic, older adults and individuals with neurological impairment (i.e., AD) are disproportionately more disadvantaged as one or both tasks increase in difficulty.

For example, Crossley and colleagues (2004) found that dual-task performance in individuals with early stage AD is relatively well maintained when the cognitive tasks (i.e., speech repetition) are highly automatized (i.e., reciting the months of the year), at least when performed in combination with a speeded finger-tapping task. However, the same group of patients compared with normal older adults, had considerably more difficulty dividing attention while performing an “effortful” speech fluency task (i.e., speeded letter word generation) concurrently with speeded finger tapping. The results of Crossley et al. (2004) suggest performance deterioration during dual-task conditions may not be due entirely to the unique nature of the concurrent tasks, but to the increase in level of complexity or difficulty when relatively effortful cognitive tasks are performed in combination with a highly automatized motor task (e.g., speeded finger tapping). Thus, it is clear that manipulating the level of task complexity in the traditional dual-task paradigm described previously is important. This suggests that the standard method of investigation should include both relatively simple and complex cognitive tasks (i.e., simple Task A and complex Task A) in combination with a concurrent task (Task B) to create simple and complex dual-task conditions.

The Dual-Task Decrement. The deterioration in simple or complex dual-task performance relative to the baseline or single task performance is known as the dual-task decrement, or the interference effect (Crossley et al., 2004; Della Sala, Baddeley, Papagno, & Spinnler, 1995; Perry & Hodges, 1999). Although the calculation of the dual-task decrement has varied across dual-task paradigms and studies, the majority of studies (which have not

manipulated the level of task complexity) have shown that older adults and individuals with neurological impairment perform as well as control participants when the two tasks are attempted separately (i.e., in the single-task or baseline conditions), but show a disproportionate decline in performance when tasks are performed concurrently (Verhaeghen, Steitz, Sliwinski, Cerella, 2003). In dual-task research that has manipulated the complexity of the cognitive tasks (e.g., simple repetition vs. complex verbal fluency); participants with neurological impairment (i.e., AD) have been found to perform more poorly than healthy older adults on the single-task and simple dual-task trials, but appear to be differentially more impaired by complex dual-task trials (Crossley et al., 2004; Yogev-Seligmann et al., 2008).

Explaining Dual-Task Costs

Difficulties in the simultaneous performance of two or more tasks, or dual-task costs, led to the development of several early neuropsychological theories on human information processing. Explanations generally fall into one of the three most influential classes of theories, including: (1) processing resource models such as the capacity sharing theory (Somberg & Salthouse, 1982); (2) the bottleneck or multiple resources theory (Anderson, Craik, & Naveh-Benjamin, 1998; DeJong, 1993; Pashler, 1994); and, (3) the cross talk model (Pashler, 1994).

Neuroimaging Studies. These theories have been informed by neuroimaging studies of dual-task performance (i.e., Collette et al., 2005; D'Esposito, 1995; Heath, Klingberg, Yougn, Amunts, & Roland, 2001; Szameitat, Schubert, Muller, & vonCramon, 2002). This technique has been used to help explain the deterioration in performance on dual-task paradigms relative to performance on tasks performed separately. From this perspective, Collette and colleagues (2005) proposed two mechanisms to explain the dual-task decrement: (1) that dual-tasking requires additional cognitive operations and activation of specific brain regions in addition to

those activated by the performance of the single tasks; and (2) that the two tasks will interfere if they activate the same population of neurons at the same time, or if the neural populations inhibit each other when activated simultaneously. Neuroimaging studies have shown that the simultaneous execution of tasks is associated with an increase in cerebral activity in the anterior cingulate cortex (Dreher & Grafman, 2003), the superior parietal cortex (Szmaeitat et al., 2002), the left inferior parietal gyrus (Collette et al., 2005), the inferior and superior prefrontal cortex (Hearth et al., 2001), and the dorsolateral prefrontal cortex (D'Esposito, 1995). Increased activity has also been observed in a larger antero-posterior cerebral network, in combination with the dorsolateral prefrontal cortex (Collette et al., 2005).

These areas have increasingly been associated with the performance of various executive tasks (such as manipulation of information, set- shifting, inhibition and maintaining attention) and suggest that dual-task performance relies on a combination of intact executive functions, and attentional processes, which are subserved by an interconnected network of anterior and posterior cerebral areas (Collette et al., 2005; Szameitat et al., 2002). Although these findings have been used to support the role that higher brain functions play in dual-task performance, such neuroimaging studies have been interpreted to support all three of the theoretical models discussed below. Currently, there is no consensus on the theoretical perspective that best explains dual-task costs (Yogev-Seligmann et al., 2008).

Capacity Sharing Models. Perhaps the most widely accepted model for understanding dual-task interference, the capacity sharing theory assumes that people share “processing capacity” or mental resources among tasks (Salthouse, 1991, 1996, 2010). This model posits that when tasks are performed simultaneously (i.e., dual-tasking), there is less capacity for each individual task, and performance is impaired resulting in the dual-task decrement. This theory

also assumes that it is possible to voluntarily allocate capacity to a specific task, even when both tasks are over-learned and largely automatic. Some capacity theorists have suggested that a single mental resource (i.e., attentional capacity) can account for performance limitations; whereas others have argued for multiple resources (i.e., processing speed, working memory, executive functions; Yogev-Seligmann et al., 2008). In particular, Salthouse (1996, 2010) has been a proponent of this approach, and argues that reductions in general processing speed result in lower dual-task performance because of the added processing stages required to carry out two tasks rather than one.

Bottleneck Models. Although most recent dual-task researchers account for age and disease related deficits using resource reductions models (i.e., general processing resources, speed, attention), an alternative model proposes that the interference or dual-task decrement results from a processing mechanism that is limited to processing only one task at a time (Anderson, Craik, & Naveh-Benjamin, 1998; Pashler, 1994; Ruthuff, Pashler, & Klaassen, 2001; Tombu & Jolicoeur, 2003). According to many authors, such a processing mechanism constitutes a “bottleneck” during the concurrent processing of two tasks, if the tasks are processed by the same neural network (Szameitat et al., 2002). Similarly, if the tasks are processed closely in time, so that they compete for the bottleneck mechanism, interference arises, which some authors suggest needs to be resolved by additional executive functions (Szameitat et al., 2002), either at the time of response selection or through a delay in processing that can occur at any stage (Yogev-Seligmann et al., 2008). However, regardless of the stage, the processing of one task will be interrupted as long as the bottleneck mechanism is processing the other task (Pashler, 1994). Under these circumstances, executive functions are believed to coordinate the interference effects at the stage of the bottleneck by scheduling the order in which the tasks are processed; by

interrupting one of the two tasks; and then switching to and reinstating the interrupted task when the processing in the other task has finished (DeJong, 1995; Szameitat et al., 2002).

Cross-Talk Models. The cross-task theory states that if both tasks are from a similar domain and use the same neuronal populations, they will not disturb each other. Essentially, it posits that it could be easier to perform two tasks concurrently when they involve similar inputs because the same processing mechanisms could be “turned on” and used for both (Pashler, 1994). However, most theorists have usually favored the contrasting multiple resources model, which suggests that if two tasks do not share common resources, dual-task interference will not occur. The multiple resources model is in keeping with research showing that it is more difficult to perform two tasks when they involve similar information (e.g., Beauchet, Dubost, Gonthier, & Kressig, 2005).

Contemporary Dual-Task Paradigms

Gait Dual-Task Methodology.

To this point, the majority of the studies and theories reviewed have largely employed experimental and so called “artificial” tasks to understand dual-task performance (Li et al., 2005). As noted, most prior dual-task studies have combined verbal tasks (e.g., animal naming, counting, seriatum speech tasks) and upper extremity tasks such as finger tapping (Crossley et al., 2004), or speeded box joining (Baddeley, Baddeley, Bucks & Wilcock 2001; Perry, Watson, & Hodges, 2000). These task combinations are easy to perform in the lab, but are described as lacking “ecological validity” and practical clinical applications (Burgess et al., 2006; Li et al. 2005). In contrast, a relatively recent area of dual-task research involves the simultaneous performance of walking and talking tasks, assumed to reflect divided attention and executive functioning in an every-day situation faced by both normal and cognitively impaired older adults.

Since the publication of Lundin-Olsson and colleagues (1997) seminal “stops walking while talking” study, clinicians and experimental researchers have shown an increased interest in the analysis of walking while performing an attention demanding task. Lundin-Olsson et al. (1997) demonstrated that the interruption of walking while talking was related to the occurrence of falls within a 6 month follow up, in healthy older adults. This initial publication of the gait dual-task paradigm or “talking while walking” methodology was the first to highlight the important role of cognition in gait and offered a simple and original approach to assessing fall risk in older adults. Since Lundin-Olsson’s (1997) initial publication, a number of subsequent gait-dual task studies have confirmed that dual-task performance costs, measured as decrements in walking speed, are indeed related to the risk of falls both in healthy normal older adults (Springer, Gialdi, Peretz, Yogev-Seligmann, Simon, & Hausdorff, 2006), and individuals with dementia (Holtzer, Friedman, Lipton, Katz, Xue, & Verghese, 2007; Sheridan & Hausdorff, 2007). Thus, in contrast to standard laboratory cognitive tasks, gait dual-task methodology has been described as a “real-world” dual-task situation that has important clinical implications relevant to everyday functioning for older adults (Li et al., 2005).

The Gait Dual-Task. During a gait dual-task the individual performs an attention demanding cognitive task (Task A), and a walking task (Task B) in single-task conditions (i.e., Task A, Task B), and in dual-task conditions (i.e., Task A concurrently with Task B). As in the previous discussion, the complexity of the cognitive task can also be manipulated to create simple dual-task and complex dual-task conditions. Although there has been a wide range of dual-task methodologies employed, the general picture that emerges from previous research is that gait and balance can deteriorate when a cognitive task needs to be performed simultaneously. This has been shown both when the task was cognitively demanding (i.e.,

subtracting serial 7's) or when it required a motor skill, such as carrying a glass of water or a tray (Bloem, Steijns, & Smits – Englesman, 2003).

The effects of dual-tasking on gait performance have been studied in various populations including healthy young (Dubost, Kressig, & Gonthier, 2006; Ebersbach, Dimitrijevic, & Poewe, 1995; Lajoie, Teasdale, Bard, & Fleury, 1993), middle aged (Lindenberger, Marsiske, & Baltes, 2000) and older adults (Bloem, Valenburg, Slabbekoorn, & Willemsen, 2001; Faulkner, Redfern, & Cauley, 2006; Hollman, Kovash, Kubik, & Linbo, 2006; Schordt, Mercer, Giuliani, & Hartman, 2003), as well as in patients suffering from neurological disease (i.e., post stroke, brain injuries, idiopathic fallers, Parkinson's disease and Alzheimer's disease; see Yogev-Seligmann et al., 2008 or Al-Yahya et al., 2011 for a review). Similarly, dual-task related gait changes have been reported for a wide range of cognitive tasks (i.e., verbal fluency tasks, counting backwards, seriatum speech tasks) and in the various components of gait performance (i.e., gait velocity, stride time, falls, step time, cadence). Collectively, these studies have demonstrated that dual-tasking affects gait in patient populations (i.e., AD and Parkinson's). With respect to healthy older adults, it is well documented that when older adults are asked to walk and simultaneously perform another task, gait speed is reduced (Springer et al., 2006). In impaired patient populations, dual-tasking has also been found to increase the variability of gait, which is a marker that has been associated with increased fall risk (Yogev-Seligmann et al., 2008).

Cognitive Skills Necessary for Successful Gait Dual-Task Performance

Research on the relationship between higher level brain function and gait performance has received considerable attention in the past decade (Al-Yahya et al., 2011; Wollacott & Shumway-Cook, 2002; Yogev-Seligmann et al., 2008). Gait is no longer considered a simple

automatic motor activity that is independent of cognition (Scherder et al., 2007). Rather, the multi-faceted neuropsychological influences on walking and the interactions between the control of mobility and navigating complex environments are becoming increasingly appreciated (Yogev-Seligmann et al., 2008). This is evidenced through the wide breadth of research areas (i.e., physiology and biomechanics, imaging, physical therapy, and neuropsychology) that are now involved in the study of the role of higher brain functions, such as attention and executive functions, in successful locomotion (Sheridan, Solomont, Kowall, & Hausdorff, 2003). For example, empirical evidence from brain imaging studies have demonstrated frontal and parietal activity during actual walking (Miyai et al., 2001; Yogev-Seligmann et al., 2008), imagined walking (Isek, Hanakawa, Shinozaki, Nankaku, & Fukuyama, 2008; Maulbin, Richards, Jackson, Dumas, & Doyon, 2003), and simulated walking (Francis et al., 2009) providing support for the essential role that higher cognitive control systems have in gait control.

Attention. Not all actions can be performed automatically, and attentional control is viewed as a crucial component in the organization, management, and completion of complex cognitive activities including walking, posture control, and balance (Belleville, Chertkow & Gauthier, 2007; Wollacott & Shumway-Cook, 2002). While there is no single and clear-cut definition of attention (Yogev-Seligmann et al., 2008), the term is used generally to refer to an anatomical network whose primary purpose is to influence the operation of other brain networks (Posner & Peterson, 1990). Like other higher brain functions such as memory and executive functioning, attention can be classified into separate, but related functions, including: focused or selective, sustained, divided, and alternating forms of attention (Bellville et al., 2007; Corbetta, Miezen, Dobbmeyer, Shulman, & Petersen, 1991; Perry & Hodges, 1999; Yogev-Seligmann et al, 2008). Often referred to as “concentration”, selective attention enables the filtering of stimulus

information and suppresses distractors (Perry & Hodges, 1999; Yogev-Seligmann et al., 2008). Sustained attention refers to the ability to maintain attention to a task over unbroken periods of time, also known as vigilance (Parasuraman & Haxby, 1995; Perry & Hodges, 1999). The ability to appropriately and rapidly switch back and forth between tasks is known as alternating attention, or “switching.” (Perry & Hodges, 1999; Yogev-Seligmann et al., 2008) In the current research, the focus is primarily on divided attention as it is known to play an important role in gait, and serves as a common variable for examining the attentional demands of various tasks including walking.

Neural Substrates of Attention. In an early and influential review of the anatomical literature, Posner and Petersen (1990) proposed dividing the attentional system into discrete anatomical networks that perform separate, but interrelated functions. This neuroanatomical model provides specific ideas on integration at the levels of neurotransmission, anatomy, and cognition, and proposes that attention can be classified into the separate functions, discussed above (i.e., selective, divided, and sustained). According to Posner and Petersen (1990) these forms of attention are anatomically and functionally distinct, suggesting that attention is carried out by a network of anatomical areas, including the anterior cingulate, the posterior parietal lobes, and the lateral and medial frontal cortex. Their review suggests that the anterior cingulate and the posterior parietal lobe is implicated in selective attention, while sustained attention as well as divided attention may activate regions of the prefrontal cortex, in interaction with subcortical ascending pathways (Posner & Petersen, 1990).

Other, more recent neuroanatomical studies are providing converging evidence for the division of attention into component subsystems. Evidence from diverse techniques such as single-cell activity in monkeys (Bisley & Goldberg, 2003) and cerebral blood flow in normal

humans (Szameitat et al., 2002) point to a major role for the posterior parietal lobe in some forms of attention. Somewhat similar to the pathways suggested by Posner and Petersen (1990), other authors have suggested it is most likely that the posterior parietal lobe acts with the prefrontal cortex and with subcortical regions to form a distributed system of selective attention, while sustained attention and divided attention appear to be more strongly controlled by the prefrontal cortex, and the anterior cingulate (Bellville et al., 2007; Parasaruman & Haxby, 1995). Specific neuroimaging investigations into the anatomy of divided attention have also implicated the prefrontal cortex in processing simultaneous tasks (D'Esposito et al., 1995), and an fMRI study in healthy adults showed activation of the left pre-frontal cortex in a divided attention task (Loose, Kaufmann, Auer, & Lange, 2003). Thus, although many authors have suggested slightly different neural circuitries, most have generally concluded that there is no single "attention center" in the brain and that different attentional processes are mediated by a complex, distributed network of cortical and subcortical systems.

Executive Function. Successful walking and gait-dual task performance also depends on intact executive functioning, which in theoretical terms is often thought to encompass aspects of divided attention (Wollacott & Shumway-Cook, 2002). Although this term is used widely within the gait and cognition literature, there remains little consensus on its exact meaning, or the higher brain functions that it accounts for. Rather, the term executive function is used to refer to a broad range of higher cognitive processes that use and modify information from cortical sensory systems in the anterior and posterior brain regions to modulate and produce behavior (Stuss, 2011).

Research into the neurobiological basis of executive functions supports the notion of executive functions constituting distinct but related constructs, such as energization, monitoring,

task setting, behavioral regulation and metacognition (Stuss, 2011). These integrative functions include both cognitive and behavioral components necessary for effective goal-directed actions, and for the control of attentional resources. Authors such as Stuss (2011) would also suggest that there is a consistent anatomical-functional relationship between cognitive processes and frontal regions. For example, the left dorsolateral cortex for task setting, and right dorsolateral for monitoring (Stuss, 2011). According to Stuss (2011), these two processes (task setting and monitoring) most accurately represent a definition of “executive functions.”

Walking and Higher Brain Functions.

Although walking has long been considered primarily an automatic motor task, an emerging body of evidence has suggested that this notion is far too simplistic (Allali, Kressig, Assal, Herrman, Dubost, & Beauchet, 2007; Sahyoun, Floyer-Lea, Johansen-Berg, & Matthews, 2004). Rather, a number of recent studies have suggested that attentional control and executive functioning may play a key role in routine, well-learned patterns of walking (Fukuyama et al., 1997; Maulbin et al., 2003; Holtzer, Verghese, Xue, & Lipton, 2006). Until recently, analysis of walking in humans has been limited to clinical observations of the mechanics of gait, and peripheral neurophysiological techniques such as EEG (Sheridan & Hausdorff, 2007). However, experiments using new imaging techniques such as functional MRI (fMRI), positron emission tomography (PET) and single photon computed tomography (SPECT) have re-examined various aspects of motor control and have refuted the long-held notion of gait automaticity (e.g., Holtzer, Mahoney, Izzetoglu, Onaral, & Verghese, 2011; Wang, Wai, Kuo, Yeh, & Wang, 2008). For example, in a study using PET and EEG, Maulbin et al. (2003) studied the brain activation of six healthy adults while imagining and physically performing walking tasks. First, they were monitored with EEG while performing actual walking tasks which included both unobstructed

walking, and walking amongst obstacles. Participants then were scanned while lying on their backs imagining the same walking tasks. Surprisingly, a common pattern of activation was found across the imagined and physical tasks; bilateral activation of the dorsal premotor cortices, the left dorsolateral prefrontal cortex (DLPFC), inferior parietal lobule and the right posterior cingulate cortex. According to Maulbin and colleagues (2003) this is among one of the first studies to demonstrate that higher cognitive control is involved in intentional, goal-directed walking.

Several neuropsychological investigations have directly studied the relationships between executive processes and gait function in older adults. For example, in the InChianti study (Ble et al., 2005) 900 healthy older adults walked at a self-paced speed over an obstacle course to assess gait performance, and completed the Trail Making Test to examine executive functioning. Poor performance on the Trail Making Test was associated with decreased gait speed on an obstacle course, suggesting that executive functioning is important in complex gait situations. Similarly Holtzer and colleagues (2006) demonstrated associations between gait speed and performance on measures of speed of processing, attention, and executive functions in healthy older adults. In a subsequent paper, Holtzer et al. (2007) also showed a relationship between lower executive functioning and a higher risk of falls among community dwelling older adults.

Conceptual Framework and Task Prioritization

In addition to the empirical literature demonstrating that there are multi-factorial neuropsychological influences on walking, the current research also adopts the conceptual framework from the model of selection, optimization and compensation (Baltes & Baltes, 1990) as it has been applied to gait dual task methodology by Li and colleagues (2005). This research is also informed by the task prioritization literature which suggests that healthy older adults

prioritize the execution of walking over the execution of cognitive components, often known as the “posture first strategy” (Wollacott & Shumway-Cook, 2002). It has been well demonstrated that the simultaneous performance of two attention-demanding tasks not only causes a competition for attention, but also challenges the brain to prioritize the two tasks (Yogev-Seligmann et al., 2008). Additionally, functional neuroimaging data demonstrate that the prefrontal cortex and the anterior cingulate cortex are both activated in the process of task prioritization, and during dual-tasking (Dreher & Grafman, 2003; MacDonald et al., 2000).

Selection, Optimization and Compensation. Theories of successful aging such as the framework of Selection, Optimization, and Compensation (SOC; Baltes & Baltes, 1990) emphasize the adaptive value of selecting tasks of higher immediate value (i.e., walking) over less critical tasks (Baltes & Baltes, 1990; Freund, Li, & Baltes, 1999; Li et al, 2005; Rapp, Krampe, & Bates, 2006). What these authors have termed the “ecological approach to multitasking”, the SOC model is a lifespan approach which postulates that individuals must continuously adapt to opportunities and constraints in their environment, which change throughout the life course. For the older adult or patient with AD, selection involves goals or outcomes such as prioritizing the maintenance of balance at the cost of cognitive tasks in attentionally demanding or challenging situations. Optimization relates to goal-relevant behaviors, such as practice. Finally, Compensation denotes the use of alternative strategies to maintain performance in the face of declining functions (e.g., using a wheelchair or walking aids to maintain mobility; Li et al., 2005).

According to Li and colleagues (2005), an excellent example of SOC processes at work can be found in the area of gait dual task performance in healthy and pathological aging. In this case, selection involves the maintenance of postural stability at the cost of excelling in cognitive

performance under dual-task conditions. The SOC's model of adaptive resource allocation would predict that when facing potentially threatening challenges (i.e., such as postural sway or the fear of falling), older adults will invest most of their cognitive resources into maintaining their stability. That is, they should prioritize gait at the cost of cognitive performance. In this context, Li and colleagues' (2005) argument for the ecological validity of the gait-dual task stems from the objective risks and subjective fear of falling in older adults, as well as the higher cost in terms of physical impairments.

Gait Dual-Tasking in Normal Aging

With aging, structural changes of the brain occur, especially in the prefrontal regions that have been associated with attention, executive functioning, and gait dual-task performance. (Salthouse, 2010; Seider, Bernard et al., 2010). Among healthy older adults, there is great variability in gait as well as a wide range of cognitive abilities (Hausdorff, Schweiger, Herman, Yogev-Seligmann-Seligmann, & Giladi, 2008; Marco et al., 2008; Watson et al., 2008). Given this variability, it is not surprising that dual-task abilities vary among healthy older adults (Coppin, Shumway-Cook, & Saczynski., 2006; Hausdorff, Yogev-Seligmann, Springer, Simon, & Giladi, 2005; Holtzer, Stern & Rakitin, 2005; Holtzer et al., 2006; Holtzer et al., 2007; Holtzer, Mahoney, Izzetoglu, Onaral, & Verghese, 2011; Springer et al., 2006; Verhagen et al., 2003; Yogev-Seligmann et al., 2008) and are related to both mobility, and cognitive function (Hausdorff et al., 2008; Lundin-Olsson, Nyberg, & Gustafson, 1997a; Lundin-Olsson, Nyberg, & Gustafson, 1997b). For example, the degree to which gait changes during the concurrent performance of another task has been related to the difficulty of the concurrent task and to the nature of the walking task (e.g., obstacle avoidance; Bloem et al., 2001; Persad, Jones, Ashton-Miller, Alexander, & Giordani, 1995), as well as to fall risk and other disabling outcomes

(Lundin-Olsson et al., 1997a; 1997b; Verghese et al., 2002). In other words, age-associated changes may produce variability in dual-task performance that is related to the spectrum of motor and cognitive abilities seen in healthy aging.

Most investigations using gait dual task procedures have shown that when older adults are asked to walk and simultaneously perform another task, gait speed is reduced (Pajala et al., 2005; Springer et al., 2006; Yogev-Seligmann et al., 2008). Indeed, perhaps the most consistent finding is that older adults walk more slowly when asked to perform a cognitive task (Yogev-Seligmann et al., 2008). Although there may be some deterioration in the concurrent cognitive task, gait stability (i.e., variability in gait) is generally not affected by dual-tasking (Li et al., 2001; Sparrow, Bradshaw, Lamoreaux, & Tirosh, 2002; Springer et al., 2006). For example, Hausdorff and colleagues (2008) reported only slight alteration in the gait pattern of healthy older adults in response to dual-tasking. They found that most subjects reduced their gait speed, and increased their stride-to-stride variability, although these changes were generally small. Although there are some exceptions to these findings (e.g., Lindenberger et al., 2000; Dubost et al., 2006), most studies of healthy older adults have observed the “normal” or “posture first” strategy in response to dual-tasking. This is in agreement with the theoretical SOC model discussed previously, which would predict that, to a certain degree, healthy older adults give priority to the stability of gait when walking and performing a cognitive task.

Gait Dual-Tasking in Alzheimer's Disease

As discussed earlier, changes in cognitive and behavioral functioning become increasingly common with age (Rockwood, Bourchard, Camicioli, & Leger, 2007). For the majority of people these changes can be a benign sign of normal aging; however, for others, the perceptible differences that occur with age represent a non-normative decline in previous

cognitive functioning. Since the early 1960's, the disciplines of clinical and experimental neuropsychology have focused on trying to create a clear separation between age-related benign changes and pathological processes, especially Alzheimer's disease (AD) and related dementias (Rockwood et al., 2007; Jacova, Kertesz, Blair, Fisk, & Feldman, 2007). Dual-task paradigms have been used in experimental and clinical settings to characterize the cognitive changes associated with normal and pathological aging, with a particular interest in understanding the role of divided attention and executive functions in the neuropsychological profile of early-stage AD (Della Sala & Logie, 2001).

Diagnostic Subtypes in Dementia.

The dementias are a collection of neurodegenerative disorders (e.g., Alzheimer's disease, Frontotemporal dementia[FTD], dementia with Lewy bodies[DLB], Vascular dementia[VaD]) which are characterized by a progressive loss of cognitive functioning that is sufficiently severe to interfere with social or occupational functioning (Braaten, Parsons, McCue, Sellers, & Burns, 2006; Robillard, 2007; Rockwood et al, 2007). The expert recommendations from the Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD3; Robillard, 2007; Rockwood et al., 2007) provide the most recent guidance on the diagnosis of dementia in Canada. One goal of the CCCDTD3 was to develop evidence based consensus statements by which to guide clinical practice and diagnosis of dementia. These recommendations were based on the existing diagnostic guidelines previously published in the literature, namely the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR; American Psychiatric Association), as well as the criteria used by the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA; McKhann et al.,

1984). Although this expert panel did not specifically provide diagnostic guidelines, a subsequent publication from the CCCDTD3 defines the essential symptoms of dementia as, “an acquired impairment in short and long-term memory, associated with impairment in abstract thinking, impaired judgment, other disturbances or higher cortical function, or personality changes.” (p. 293, Robillard, 2007)

Alzheimer's Disease (AD). Alzheimer's disease is the most common form of dementia, accounting for 63% of all dementias in Canada (Alzheimer Society, 2010). Currently, the diagnosis of AD is based largely on neuropsychological testing (Jacova et al., 2007), clinical judgment, and the standard dementia criteria discussed previously. It is typically associated with an insidious onset and progressive decline in cognitive and adaptive functioning (Braaten et al., 2006; Dubois, Feldman, Jacova, DeKotsky, Barberger-Gateau, Delacourte et al., 2007; Robillard, 2007; Rockwood et al., 2007; Weiner, 2003). In terms of differential diagnosis from other dementia subtypes, the most prominent feature of AD is a disproportionate decline in memory function relative to the other cognitive domains (Rockwood et al., 2007). The neuropathological processes associated with AD involve extensive degeneration of the parieto-temporal regions, including the hippocampus and surrounding cortical structures, thus it is not surprising that deficits in memory and learning are thought to be hallmark features of the disease (Braaten et al., 2006).

The NINCDS-ADRDA criteria published by McKhann and colleagues (1984) for probable AD found support with the CCCDTD3 (Robillard, 2007) and are widely used in clinical practice and research. Since the publication of these criteria in 1984, the understanding of the diagnosis of AD has advanced greatly and these criteria were updated in 2007 by Dubois and colleagues to incorporate neuroimaging findings, as well as other biomarkers that are suggestive

of AD. Nonetheless, the core clinical features of the NINCDS-ADRDA criteria have remained relatively unchanged with time. In addition to progressively worsening memory, the NINCDS-ADRDA guidelines (Dubois et al., 2007; McKhann et al., 1984) suggest that the clinical features of “probable” AD include: onset between the ages of 40 and 90 years; deficits in two or more areas of cognitive functioning on neuropsychological tests; and normal consciousness. Other supportive features for a diagnosis include progressive deterioration of language and praxis, impaired activities of daily living, altered personality and behavior; evidence of medial temporal lobe atrophy on neuroimaging; and a positive familial history (Dubois et al., 2007; Robillard et al., 2007; McKhann et al., 1984). The general consensus based on a number of studies using neuropathologic data as confirming evidence of diagnosis, is that there is acceptable sensitivity of these clinical criteria (average 81%), however, often at the expense of low specificity (average 70%), possibly because there are many common features between different subtypes of dementia (Robillard, 2007). Nonetheless, the NINCDS-ADRDA criteria that are used in the current study to diagnosis AD have demonstrated a high degree of reliability in clinical practice and are supported by the CCCDTD3 recommendations (Robillard, 2007).

Gait in Alzheimer's Disease. Gait disturbances are common in individuals with AD, and the patterns of walking in persons with AD are different from those of age-matched, cognitively intact older adults (Morgan, Funk, Crossley, Basran, Kirk, & Dal Bello-Haas, 2007; Alexander & Hausdorff, 2008). An early, landmark study showed that patients with dementia had shorter step length, slower gait speed and stepping frequency, greater step-to-step variability and larger postural sway (Visser, 1983). Even in the early stages of the disease, patients have been found to typically walk with slow irregular steps, to have slower gait speed, and shorter step length, and find it difficult to negotiate turns or avoid obstacles in their path (Cocchini, Della Sala, Logie,

Pagani, Sacco, & Spinnler, 2004). Obviously, gait impairments can drastically alter mobility in individuals with AD, and result in an increased risk of falling (Beauchet, Annweiler, Allali, Burrut, Herrman, & Dubost, 2008; Bootstma-van der Weil, Gussekloo, de Craen, Van Exe, & Bloem, 2003; Morris, Rubin, Morris, & Mandel, 1987; Shaw, 2002).

Patients who have AD and experience a fall are at an increased risk of sustaining a serious injury (Shaw, 2002). For example, Shaw (2002) placed the annual incidence of fractures at approximately 7% in this patient group, which is 1.5 to 3 times the rate in cognitively normal fallers. In addition to the increased risk for falls and subsequent serious injury (i.e., 50% of the fractures in individuals with AD are hip fractures), patients with AD have a poorer prognosis once a fall has occurred (Shaw, 2002). They are less likely to make a functional recovery after significant injury than are cognitively normal patients who fall, and they are approximately five times more likely to be institutionalized than are patients with dementia who do not fall (Shaw, 2002).

Mild Cognitive Impairment (MCI). It has been acknowledged that the diagnosis of AD is preceded by a relatively long preclinical phase (Bellville et al., 2007). Mild cognitive impairment (MCI) is an evolving construct that is believed to be a transitional cognitive state between normal aging and the early stages of dementia (Griffith, Netson, Harrel, Zamrini, Brockington, & Marson, 2006; Petersen, Smith, Waring, Ivnik, Tangalos, & Kokmen, 1999; Petersen, Stevens, Ganguli, Tangalos, Cummings, & DeKotsky, 2001; Petersen 2004; Petersen & Morris, 2005) for which a number of different criteria have been proposed (Saunders & Summers, 2011). Recently, attempts have been made to redress the problems underlying the heterogeneity in the clinical presentation of MCI by re-conceptualizing MCI as consisting of two distinct subtypes: amnesic MCI (aMCI) and non-amnesic MCI (Petersen & Morris, 2005;

Winblad et al., 2004). Although estimates vary, many studies have shown that those with aMCI are at an increased risk of progression to AD, with 10-15% of aMCI patients developing AD annually (Roach, 2005) compared to 1-2% in the general elderly population (Petersen et al., 1999; 2000).

Recent research suggests that the earliest cognitive changes in the subtype of aMCI is objective and corroborated (i.e., by family member) evidence of memory dysfunction that is detectible on formal testing, and coupled with otherwise normal cognitive functioning (Saunders & Summers, 2011). However, whether aMCI is characterized solely by mild amnesia, or is accompanied by impairments in divided attention and executive functioning is unclear. With the advent of pharmacological therapies, there has been an explosion in research efforts to identify and characterize MCI and its subtypes. However, most of these studies have investigated only the memory impairment in aMCI and the few studies that have used dual-task procedures to examine attentional control typically have used large heterogeneous groups of MCI patients, making it difficult to speak to the specific attentional deficits found in aMCI (e.g., Maquet et al., 2010; Pettersson, Olsson & Wahlund, 2007; Montero-Odasso et al., 2009).

One exception, however, is a recent paper by Lonie and colleagues (2009). These authors used a visuospatial dual-task paradigm to examine divided attention in groups of participants with aMCI, early-stage AD, depression, and healthy older adults. They administered an oral digit span task and a paper and pencil visuospatial tracking task (i.e., connecting empty circles with a meandering line) in single and dual-task conditions to 33 patients with aMCI, 10 patients with early stage AD, 17 controls with depressive symptoms, and 21 healthy older adults, who were all closely matched for age and pre-morbid intellectual ability. After calculating percent decrement scores, the results from Lonie et al. (2009) showed that those participants with aMCI

and early stage AD had comparable performance to healthy older adults and older adults with depressive symptoms. Thus, dual-task performance was not impaired in the stages that they designated as aMCI and early-stage AD. By contrast, the aMCI and early-stage AD group were impaired on tasks of episodic memory and part B of the Trail Making Test, leading the authors to suggest that dual-task performance may not be a sensitive marker of the early cognitive changes associated with AD when participants in the earliest stages are divided by rigorous diagnostic criteria. These results are in keeping with other previous work demonstrating that when participants with AD are divided by severity, only the more severely ill patients are impaired on the dual-task paradigm (i.e., Greene, Hodges, & Baddeley, 1995; Perry, Watson, & Hodges, 2000).

Attention and Alzheimer's Disease

The anatomy of attention, as discussed above, presents a picture of varied and complex attentional networks; however, as mentioned, there are still uncertainties about the elements of the networks, their interconnections, and each system's precise role (Parasuraman & Haxby, 1995). Nonetheless, it is possible to link the brain systems that appear to be relevant for attention, to the relative patterns of neuronal degeneration in AD. In the same way that converging lines of evidence have linked the early loss of episodic memory to medial temporal pathology, it may be possible to predict which attentional processes are likely to be impaired based on our knowledge of the pattern of neuronal degeneration in AD and from what is known about the neural substrates of attention from models introduced by Posner and Petersen (Nestor, Parasuraman, & Haxby, 1991; Perry & Hodges, 1999).

Parasuraman and Haxby (1995) believe that the early involvement of the posterior parietal lobe in AD is one of the keys to understanding the relation between dysfunction of the

AD brain and attentional functioning. They suggest that at the most basic level; early impairments of attention in AD may be due to the loss of connections between neocortical association areas in the frontal and parietal lobes. Other theorists, such as Perry and Hodges (1999), suggest that this explanation is likely a major oversimplification. They point out that the frontal lobes are typically spared early in the course of the illness, making it somewhat surprising that AD produces the marked impairment in attentional functions that have been linked with frontal lobe functions.

In an alternative explanation, Perry and Hodges (1999) suggest that that the pathological process of AD must cause attentional deficits in other ways, most likely through the disruption of the basal forebrain cholinergic system. Damage to the basal forebrain cholinergic system, which provides the major cholinergic innervation to the neocortex, and which is affected by early pathological changes, may be responsible for attentional impairments that can be improved by cholinergic drugs (Perry et al., 2000). However, the role that cholinergic deficiency in AD plays in the impairment of attention, and the introduction of cholinergic therapies for the treatment of AD, still remains relatively controversial and unknown (Perry et al., 2000). As such, it has also been suggested that the attentional deficit in AD be seen as a “disconnect syndrome” in which cognitive deficits can be explained in terms of pathological processes that disrupt the exchange of information between neural circuits linked by cortical tracts (Perry & Hodges, 1999).

The Staging of Attentional Deficits in AD.

It is thought that many of the cognitive deficits of attention in AD can be explained in terms of the pathological processes just discussed. However, when different facets of attention are examined (i.e., sustained, divided, and selective) using neuropsychological tasks, it is clear that not all forms of attention are affected at the same stage of the illness, adding to the

uncertainties about the neural elements and interconnections in the attentional networks (Haxby, Parasuraman, Gillette, & Raffaele, 1991; Perry et al., 2000).

The evidence from numerous studies and reviews clearly indicates that some aspects of attentional functioning are impaired in the early stages of the illness, while others remain relatively spared until later in the progression of the disease. For example, in their review, Perry and Hodges (1999) suggest that each component of attention tends to be differentially affected by the early stages of the illness, with a relative preservation of sustained and focused attention, and more severe impairments in the ability to disengage and shift attention, and to divide attention between two concurrent tasks. Disengagement of attention and attentional switching appear to be the most markedly and consistently impaired in the early stages of the illness (Baddeley et al., 2001), while there remains some uncertainty regarding the consistency of the other impairments of attention, most notably the inability to divide attention in AD.

Divided Attention. Most researchers classify an inability to divide attention as characteristic of the early stages of AD, and ascribe the deficit to a specific dysfunction of the “central executive” system of working memory (LaFleche, & Albert, 1995; Logie, Cocchini, Della Sala, & Baddeley, 2004; Baddeley, Logie, Bressi, Della Sala, Logie, & Spinnler, 1991; Baddeley, 1996; Baddeley et al., 2001; Perry et al., 2000). For example, Baddeley and colleagues (2001) argue that the difficulty in dividing attention in AD results from a breakdown of the central executive component of working memory, and in particular the component of the central executive that coordinates and allocates attentional resources during non-routine tasks. According to this explanation, the capacity of the central executive system is limited and when tasks are complex this capacity is exceeded and performance starts to break down (Perry & Hodges, 1999).

This theoretical interpretation is not wholly accepted. In contrast, other authors have argued that dual-task decrements are attributed to a dementia-related decline in a general-purpose processing resource (Crossley et al., 2004; Salthouse, 1996, 2010). It still remains possible that when two tasks are performed together they compete for processing resources from the same limited pool (Salthouse, 1996). Consequently, performance on the secondary task can alternately be interpreted as reflecting the resources remaining after those needed for the primary task have been expended (Salthouse, 1996). Indeed, like the central executive theory, this assumption has also been confirmed in a number of studies of normal aging which utilized reaction times as the secondary task with either perceptual motor or memory primary tasks (e.g., Somberg & Salthouse, 1982). This pattern of greater impairment of secondary task performance with increased age has been interpreted as indicating that the quantity of processing resources declines with increased age; however, this interpretation is also based on a number of controversial assumptions. As such there currently remains no theoretical winner with respect to the two competing theories, although there remains little doubt that some type of mental resource is needed to divide attention between two or more concurrent tasks.

Current Gait-Dual Task Literature.

A consistent finding in gait dual-task studies is that the ability to divide attention while walking appears to be particularly vulnerable in individuals with AD (see Al-Yahya et al., 2011 for a recent review). For example, in an early study, Camicioli and colleagues (1997) measured walking speed in healthy older volunteers and AD patients while they walked along a straight marked path. Subsequently, individuals in both groups were asked to walk along the same route while performing an oral verbal fluency task (generating male/female names). While both groups

walked more slowly under the dual-task conditions, the AD patients were disproportionately more impaired by the dual-task condition than were the healthy older adults.

A survey of the literature found other gait dual-task studies including procedures that consisted of reciting a forward digit span (Sheridan, Solomont, Kowall, & Hausdorff, 2003), forwards and backwards counting (Allali, Kressig, Assal, Herrman, Dubost, & Beauchet, 2007), and listing words associated with a target word (Cocchini et al., 2004). All the studies described included individuals with probable AD, and all participants were found to have a slower walking speed, and higher gait variability, while concurrently performing the secondary task. For example, Sheridan et al. (2003) found that the inability of AD patients to divide their attention when walking led to an increase in stride time and increased gait unsteadiness. Similarly, AD patients in the study conducted by Cocchini et al. (2004) showed a significantly greater dual-task cost than normal older controls. In general these studies have been interpreted to advance the concept that individuals with AD have significant impairment in the cognitive domain of divided attention, particularly as measured by dual-task performance (Perry, Watson, & Hodges, 2000; Persad, Jones, Ashton-Miller, Alexander & Giordani, 2008).

One aim of the current research is to address some of the methodological limitations of past gait dual-task literature. Recently, there has been a call by authors such as Al-Yahya and colleagues (2011) to standardize dual-task paradigms, as well as improve their ecological validity, to enable a better understanding of neural mechanisms and processes involved in procedures that combine walking with a simultaneous cognitive task. Despite the growing number of studies of divided attention and AD, knowledge from previous work appears to be limited by four large methodological variations: (i) the inclusion of large heterogeneous patient

groups at different stages of AD severity, (ii) a failure to manipulate task complexity, (iii) the types of secondary cognitive tasks employed, (iv) and the unknown emphasis on task priority.

Limitations of Previous Studies

Dementia Severity. Most notably, many gait dual-task studies report divided attention deficits in individuals with AD without referring to the disease severity of the subjects (e.g., Camicioli et al., 1997). Gait dual-task performance has also been compared between relatively small samples of younger healthy adults, and small heterogeneous groups of individuals at different stages of disease severity (Cocchini et al, 2004), as well as in groups of frailer individuals in the later stages of the disease process (Sheridan et al., 2003). For example, Sheridan et al. (2003) examined the influence of divided attention on gait variability in a group of individuals with probable AD. Nearly half of these individuals were institutionalized, and the average MMSE for the group was approximately 13.8, indicating that these participants were in the moderately severe stages of the illness. In that context, dual-task costs are not surprising, but nonetheless were used by the authors to infer that individuals with AD have an inability to divide attention. Many authors cite these studies as evidence that attentional capacities are among the first higher brain functions to deteriorate, despite the broad range of severity (i.e., mild to moderately severe) for participating patients. Consequently, group differences can be attributed to the relatively severely impaired individuals who generally demonstrate deficits on all cognitive measures, not just on measures of divided attention. Furthermore, qualitative descriptions of severity (i.e., inpatients or outpatients; Sheridan et al., 2003) or the use of idiosyncratic scales (i.e., the Milan Overall Dementia Assessment; Cocchini et al., 2004) are not helpful because they do not allow for comparisons across studies.

Therefore, it is of considerable theoretical and practical importance that gait dual-task studies be designed so that different stages of AD severity are compared using reliable and well-validated measures (i.e., Mini Mental State Examination, Modified Mini-Mental State Examination; Tombaugh & McIntyre, 1992) as well as informed by neuropsychological testing. The recent progress in neuropsychology has led to more precise categories of diagnosis (i.e., amnesic mild cognitive impairment, early stage AD) which can allow researchers to better investigate divided attention in AD and aMCI in a more systematic fashion than was previously possible. In particular, the current research aims to limit the sample of AD participants to those with early-stage AD (Study 1) and to further subdivide by severity, examining aMCI, early-stage AD and moderate stage-AD (Study 2) in an effort to speak to the specific dual-task impairments arising at each stage.

Secondary Cognitive Task. The results of previous studies using gait dual task procedures also appear to be dependent on the nature and type of the primary and secondary tasks. For example, in a study of dual-task related gait changes in frail older adults, Beauchet and colleagues (2005) found that different types of cognitive tasks (i.e., verbal fluency vs. counting) produced different dual-task related changes in gait. Although both tasks are declarative cognitive tasks, according to Beauchet et al. (2005) only a concurrent arithmetic task (i.e., counting backwards from 50) significantly interfered with gait stability and stride time. In contrast, the verbal fluency task, although it did appear to decrease gait speed, had little effect on gait stability. According to the reasoning of Beauchet and colleagues (2005) these interference effects could result because verbal fluency relies on semantic memory, and presumably has no direct relation to the executive functions necessary to divide attention (Beauchet et al., 2005). Given that semantic memory also has been found to be impaired in the early stages of AD, it is

difficult to single out the specific deficit in divided attention. On the other hand, counting backwards, which is the strategy employed in the current research, draws on the working memory aspects of the central executive, which is, in part, responsible for the allocation and management of attentional resources (Baddeley, 1996).

Task Complexity. As highlighted at the outset of the introduction, task complexity also matters greatly in dual-task procedures. Crossley and colleagues (2004) found that dual-task performance in individuals with early stage AD is relatively well maintained when the component cognitive tasks are highly automatized (i.e., reciting the months of the year), at least when performed in combination with a speeded finger-tapping task. However, the same group of patients compared with normal older adults, had considerably more difficulty dividing attention while performing an “effortful” speech fluency task concurrently with speeded finger tapping. Thus, deterioration during dual-task conditions may not be due entirely to the unique nature of the concurrent tasks, but to the increase in level of complexity or difficulty when relatively effortful tasks are performed in combination with a highly automatized motor task (i.e., speeded finger tapping). What is less clear is how manipulating task complexity in gait-dual task procedures will affect gait control, which is known to require higher brain functioning.

Task Prioritization. The theoretical models of task prioritization reviewed previously, all refer to situations in which the participants were not given any specific instructions regarding task prioritization. In studies where subjects have been explicitly instructed to direct their attention to either gait or the cognitive task, the overt prioritization resulted in reduced dual-task decrements for the prioritized task (Verghese et al., 2002, 2007). Although this has been studied in healthy older adults (Verghese et al., 2002, 2007), previous gait dual-task methodologies in individuals with AD have not specified task emphasis instructions. Li and colleagues (2005)

consider gait dual-task performance to be “more ecologically valid” when task emphasis instructions are less constrained. To this end, the current study instructs participants to attend equally to both the walking task, as well as the counting task, to understand how the individual is likely to allocate their attention between the two tasks (see Appendix A).

Neuropsychological Testing. A final limitation of previous gait-dual task research is that attention and to a lesser extent, executive functioning, have been studied in isolation without taking into account other possibly concurrent brain functions that contribute to walking. Despite the relation of dual-task performance to neuropsychological measures in healthy older adults (i.e., Holtzer et al., 2006, 2007), this has not been studied in patients with AD. A recent paper by Holtzer and colleagues (2006) examined the relationship between cognitive factors and gait in normal aging. Whereas previous research limited the scope of study of cognition and gait by focusing exclusively on the role of attention in mediating gait, Holtzer and colleagues (2006) demonstrated that both general (Verbal IQ) and specific (speed, executive function, attention and memory) cognitive factors were related to gait performance in normal aging. Given the limited literature concerning the relationship between gait and other neuropsychological measures in individuals with AD, the current research also examines the contribution of other specific (speed, executive functions, memory, attention) cognitive factors to gait interference under simple and complex dual-task conditions in individuals with AD, and in healthy older adults.

In conclusion, given the limitations of previous gait-dual task studies, the current research aims to contribute to the growing body of literature on gait and cognition, by using an arithmetic cognitive task, in simple and complex combinations, to examine the performance of individuals at specified levels of AD severity (i.e., aMCI, early-AD, and moderate-AD) and in healthy older adults. Additionally, this research examines the relationship of simple and complex gait dual-

task performance to theoretically derived neuropsychological composite scores, in an attempt to examine other higher brain functions related to gait performance. From a theoretical point of view, studies of AD patient's performances on paradigms of attention contribute to our understanding of the structure of normal cognition and the organization of cognitive resources in pathological aging. Furthermore, from a functional and clinical perspective, investigating impaired attentional processes in AD may help explain why individuals with AD are more prone to falls under certain circumstances. Similarly, knowledge about individuals gait dual-task performance may be helpful in differentiating AD from normal aging.

Description of Studies.

The aim of Study 1 was to further investigate the effect of divided attention on gait using dual-task methodology with normal older adults compared to individuals in the earliest stages of the AD. In this context, the interest lay in exploring the question of whether or not deficits in divided attention occur in the earliest stages of the illness. To investigate this question, Study 1 identified patients with AD in the earliest stages of disease severity and compared them to a carefully controlled and age appropriate control group, as previous studies have failed to address the range of illness severity of their AD patients. A second aim was to address previous methodological limitations by utilizing a gait dual-task procedure that manipulated the complexity of a concurrent cognitive task that competed directly with the walking task for the resources of the central executive. In this sense, we were interested in investigating the effects on ambulation of easy and difficult arithmetic counting tasks.

Study 2 was designed to be a replication and extension of Study 1. Using a separate sample of patients referred to a memory clinic, Study 2 compared gait dual-task performance in individuals in the earliest stages of cognitive impairment (amnestic mild cognitive impairment;

aMCI), those with early stage AD, and moderate AD to an appropriate, community dwelling group of older adults. This study was intended to include those individual's identified with the earliest stages of cognitive impairment (i.e., aMCI) as they have been identified as persons at risk for eventual conversion to AD (Petersen et al., 1999, 2001). Furthermore, using a categorical approach to designate patients at different stages of disease severity has the most potential for answering the question of whether or not the early neuropsychological profile of AD is accompanied by impairments in divided attention at the earliest stages.

A further limitation of previous gait dual-task research is that attention has been studied in isolation - that is without taking into account other possibly concurrent brain functions that contribute to walking. A recent paper by Holtzer and colleagues (2006) examined the relationship between cognitive factors and gait in normal aging. Whereas previous research limited the scope of study of cognition and gait by focusing exclusively on the role of attention in mediating gait, Holtzer and colleagues (2006) demonstrated that both general (Verbal IQ) and specific (speed, executive function, attention and memory) cognitive factors were related to gait performance in normal aging. Given the limited literature concerning the relationship between gait and other cognitive functions in individuals with AD, Study 3 examines the contribution of other specific (speed, executive functions, memory, and attention) cognitive factors to gait interference under simple and complex dual-task conditions in individuals with AD, and in healthy older adults. Since gait and cognitive impairment are both predictive of falls in AD (Sheridan et al., 2003), characterizing the cognitive mechanisms of gait may in turn provide important information concerning the risk assessment and possible prevention of falls in individuals with AD

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Running Head: GAIT DUAL-TASK IN EARLY AD AND AGING

Study 1: The Effects of a Simple and Complex Gait Dual-Task on Ambulation in Early-Stage
Alzheimer's Disease and Normal Aging

Jocelyn Poock, Margaret Crossley, & Vanina Dal Bello-Haas

University of Saskatchewan

Author Note

Jocelyn Poock, Department of Psychology, University of Saskatchewan; Margaret Crossley, Department of Psychology, University of Saskatchewan; Vanina Dal Bello-Haas, School of Rehabilitation Science, McMaster University

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Correspondence concerning this article should be addressed to Jocelyn Poock, Department of Psychology, Arts 154, University of Saskatchewan, 9 Campus Drive, Saskatoon, Saskatchewan, Canada, S7N 5A5. Email: jocelyn.poock@usask.ca

Abstract

Previous studies with Alzheimer Disease (AD) patients compared to healthy older adults have suggested that walking speed can be differentially affected by a concurrent cognitive task, such as a verbal fluency task or arithmetic counting task (Yogev-Seligmann, Hausdorff, & Giladi, 2008). Study 1 of the current research examined the effects of a verbal cognitive task on gait speed in healthy older adults and probable early AD patients. Fourteen healthy older adults (6 men, 8 women; mean age= 72.9yrs) and 15 participants with early stage AD (i.e., MMSE scores ranging from 21-28) performed a timed walking task and simple and complex verbal counting tasks (i.e., counting forward by 1's or backward by 2's) in single and dual-task combinations. Percent decrement scores were compared using a repeated measures design with between group comparison between the healthy older adults and the probable early AD participants. Contrary to previous findings, the present study found that even though single task walking rates were significantly higher for the healthy older adults compared to the early AD patient's; percent decrement scores indicated that patients with early AD were not differentially impaired by a gait dual-task, regardless of the level of task complexity. Analyses did, however, reveal a predictable main effect for task difficulty. Overall, the present study did not find any differential impairment for participants with early AD compared to healthy older adults using a talking-while-walking dual-task that controlled for single task group differences.

Study 1: The Effects of a Simple and Complex Gait Dual-Task on Ambulation in Early-Stage Alzheimer's Disease and Normal Aging

The nature and progression of the cognitive deficits in individuals with early-stage AD have been studied in increasing detail over the past decade. A generally accepted conclusion is that impairment in the encoding of new episodic memories is most typical of the earliest stage of the disease (Robillard, 2007; Rockwood, Bourchard, Camicioli, & Leger, 2007), which may progress very gradually for several years before impairments in other cognitive domains such as language, semantic memory and spatial function become apparent (Jacova, Kertesz, Blair, Fisk, & Feldman, 2007; Rockwood et al., 2007). Currently, early forgetfulness and episodic memory dysfunction still remain at the diagnostic core of AD, although in recent years evidence has accumulated to support the conclusion that deficits in attention are also a potential early hallmark of the illness (Fernandez-Duque & Black, 2006; Lafleche & Albert, 1995; Perry & Hodges, 1999; Saunders & Summers, 2011).

In an early and influential review of AD and attentional functions, Perry and Hodges (1999) suggested that after the initial amnesic stage in AD, attention is the first non-memory domain to deteriorate, preceding impairment in perceptual and language functioning and impacting the individual's ability to cope with the tasks of daily living. They proposed that disruption to the basal forebrain cholinergic system, including the prefrontal cortex, the thalamus and the parietal lobes, may all play a significant role in the impairment of both memory and attention (Perry & Hodges, 1999). In the same way that that medial temporal pathology has been linked to the early loss of episodic memory in AD, attentional impairments may be among some of the first cognitive indicators of neocortical dysfunction in the early stages of AD (Crossley, Hiscock, & Foreman, 2004; Perry & Hodges, 1999; Saunders & Summers, 2011).

Although the experimental and neuropathological evidence for attentional deficits in individuals with AD appears strong, there is no consensus on how consistently, or how early in the course of the illness attentional dysfunction appears (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Lonie, Tirney, Herrman, Donaghey, Carrol & Ebmeier, 2009; Perry, Watson, & Hodges, 2000). There has been significant progress in neuropsychology in describing attentional processes as separate functions (i.e., orienting, shifting, vigilance, selective attention, divided attention), allowing researchers to investigate attentional dysfunction in AD in an increasingly systematic fashion (Baddeley et al., 2001; Bellville et al., 2007; Perry, Watson, & Hodges, 2000; Perry & Hodges, 1999; Posner & Petersen, 1990). For example, models such as those proposed by Posner and Petersen (1990) have differentiated subcomponents of attention, such as sustained, divided and selective attention.

In their early review, Perry and Hodges (1999) suggest that each component of attention tends to be impacted differentially by the early stages of the disease process, with relative preservation of sustained and focused attention, and more severe impairment in the ability to shift attention and to divide attention between two concurrent tasks. More recent studies from multiple disciplines such as neuroimaging, physiology, and neuropsychology have examined the ways in which different components of attention are disrupted by AD (See Yogev-Seligmann et al., 2008 for a recent review). In particular, in the last two decades, a growing body of research has been devoted to examining the specific components of divided attention necessary to share cognitive resources among two or more concurrent tasks (Beauchet, Dubost, Gonthier, & Kressig, 2005; Camicoli, Howieson, Lehman, & Kaye, 1997; Cocchini, Della Sala, Logie, Pagani, Sacco & Spinnler, 2004; Collette et al., 2005; Coppin et al., 2006; Crossley & Hiscock, 1992; Crossley, Hiscock, & Foreman, 2004; Della Sala, Baddeley, Papagno, & Spinnler, 1995;

Dreher, & Grafman, 2003; Ebersbach, Dimitrijevic, & Poewe, 1995; Grober & Sliwinski, 1991; Hausdorff, Schweiger, Herman, Yogev-Seligmann-Seligman, & Giladi, 2008, Hearth, Klingberg, Young, Amunts, & Roland, 2001; Holtzer, Mahoney, Izzetoglu, Onaral., Verghese, 2011; Holtzer, Friedman, Lipton, Katz, Xue, & Verghese, 2007; Holtzer, Verghese, Xue, & Lipton, 2006; Holtzer, Stern & Rakitin, 2005; Li, Krampe & Bondar, 2005; Lundin-Olsson, Nyberg, & Gustafson, 1997a; Lundin-Olsson, Nyberg, & Gustafson, 1997b; Pashler, 1994; Perry, Watson, & Hodges, 2000; Perry & Hodges, 1999; Salthouse, 1996, 2010, Sheridan & Hausdorff, 2007; Sheridan, Solomont, Kowall, & Hausdorff, 2003; Verhaeghen, Steitz, Sliwinski & Cerella, 2003). To date, most experimental studies of divided attention in AD have used dual-task paradigms, which require participants to perform two tasks, A and B, separately in single-task conditions, and simultaneously, in dual-task conditions (Beauchet et al., 2005; Li, Krampe & Bondar, 2005). It is generally accepted that the decrement in performance in the dual-task conditions relative to performance during the single-task trials is representative of the ability to divide attention, and it is presumed that some type of mental resource is needed to divide attention between two or more concurrent tasks (Li et al., 2005; Logie, Cocchini, Della Sala, & Baddeley, 2004; Verhaeghen, Steitz, Sliwinski, & Cerella, 2003; Yogev-Seligmann et al., 2008).

Traditionally, dual-task studies have combined cognitive tasks and speeded upper extremity tasks such as finger tapping (e.g., Crossley et al., 2004) or box joining (e.g., Baddeley et al., 2001). These dual-tasks are easy to perform in the lab, but lack “ecological validity” and practicality (Al-Yahya et al., 2011; Burgess et al., 2006; Springer, Giladi, Peretz, Yogev-Seligmann, & Simon, 2006; Li et al., 2005). In contrast, a relatively recent area of dual-task research involves the simultaneous performance of walking and talking tasks, which reflects divided attention in an every-day situation faced by both normal older adults and by adults with

cognitive impairment (Li et al., 2005; Wollacott & Shumway-Cook, 2002) “Talking while walking” or gait dual-task methodology focuses on the role of divided attention during functional tasks such as walking while holding a conversation (Lundin-Olsson, Nyberg, & Gustafson, 1997a) or walking while performing simple cognitive tasks such as arithmetic calculations or verbal fluency (Camicoli, Howieson, Lehman, & Kaye, 2007; Cocchini, Della Sala, Logie, Pagani, Sacco & Spinnler, 2004).

To date, the effects of dual-tasking on gait performance have been studied in various populations including the healthy young (Dubost, Kressig, & Gonthier, 2006; Ebersbach, Dimitrijevic, & Poewe, 1995; Lajoie, Teasdale, Bard, & Fleury, 1993), middle aged (Linderberger, Marsiske, & Baltes, 2000) and older adults (Bloem, Valenburg, Slabbekoorn, & Willemsen, 2001; Faulkner, Redfern, & Cauley, 2006; Hollman, Kovash, Kubik, & Linbo, 2006; Schordt, Mercer, Giuliani, & Hartman, 2003), as well as in patients suffering from neurological disease (i.e., post stroke, brain injuries, idiopathic fallers, Parkinson's disease and Alzheimer's disease; see Al-Yahya et al., 2011; Hausdorff, Schweiger, Herman, Yogev-Seligmann-Seligmann, & Giladi, 2008; or Yogev-Seligmann et al., 2008 for a review). Similarly, dual-task related gait changes have been reported for a wide range of cognitive tasks, and in various components of gait performance (i.e., gait velocity, stride time, falls, step time, cadence). This previous research indicates that walking and postural control require attention, and that attentional impairments might underlie gait changes and increased risk for falls among individuals with AD (Lundin-Olsson et al., 1997b; Wollacott & Shumway-Cook, 2002). Thus, for individuals with AD, walking while performing a simultaneous attention-demanding task represents a functional and practical measure of divided attention.

Although gait dual-task methodology is still an emerging area of study, a consistent finding is that the ability to divide attention while walking appears to be particularly vulnerable to the effects of dementia (Yogev-Seligmann et al., 2008). For example, in gait dual-tasks, secondary cognitive tasks such as verbal fluency association tasks (Cocchini et al., 2004), will interfere disproportionately with ambulation in individuals with AD compared to healthy normal older adults. Furthermore, it has been found that dividing attention drastically impairs the ability of individuals with AD to regulate stride-to-stride variations in gait timing, which is a marker of gait unsteadiness and could help to explain why individuals with AD fall under certain circumstances (Sheridan et al., 2003). Falls and injuries related to falls are a major cause of mortality and morbidity in individuals who have cognitive impairment and dementia (Shaw, 2002), and several authors have suggested that the increased risk of falling in individuals with AD may be due, at least in part, to concurrent cognitive demand while walking (Camicioli et al., 1997; Cocchini et al., 2004; Sheridan et al., 2003).

Despite the growing number of studies of divided attention and AD, knowledge concerning the relationship between attention and AD from previous gait dual-task studies has been limited by several factors. First, the progressive nature of the disease raises the issue of who should be tested, and at what stage of disease severity impairments in attention become apparent (Perry et al., 2000). Gait dual-task performance has been compared between relatively small samples of younger healthy adults, and small heterogeneous groups of individuals at different stages of disease severity (Cocchini et al., 2004), as well as in groups of older individuals in the later stages of the disease process (Sheridan et al., 2003). For example, Sheridan et al. (2003) examined the influence of divided attention on gait variability in a group of individuals with probable AD. However, half of these individuals were already in long-term care facilities and the

mean MMSE score for the group (i.e., $M = 13.8$ out of a possible score of 30 points) indicated that these participants were in the moderate to severe stages of AD. In this context, dual-task related costs are not surprising, but nonetheless are used to infer that individuals with dementia have an inability to divide attention, regardless of the staging of the illness. As noted by Perry et al. (2000), it is clear that individuals in the moderate stages of dementia will differ significantly and globally from healthy controls, making it difficult to single out a specific deficit in divided attention.

As noted previously, some authors have suggested that apart from the episodic memory dysfunction that typifies early AD, attentional capacities are among the first higher brain functions to decline (Saunders & Summers, 2011). There appears little doubt that individuals with AD have difficulty dividing attention under dual-task conditions. However, despite the increasing number of studies of divided attention in AD, the stage at which individuals with AD show impairments on tasks of divided attention is still somewhat controversial. It is generally accepted that most individuals in the moderate and severe stages (i.e. MMSE 17 and below) of the illness show impairment in the ability to divide attention (Perry et al., 2000). However, this vulnerability is not consistently found in the earliest stages of the illness. The stage at which individuals with AD show impairment on tests of divided attention varies across studies and type of dual-task methodology. For example, Perry, Watson, and Hodges (2000) found that mildly impaired AD patients were not differentially impaired during tasks combining a verbal digit span task and a speeded box joining task, despite already having significant impairments in episodic memory. Similarly, Greene et al. (1995) found that individuals in the earliest amnesic stages of AD (i.e., "minimal dementia") performed normally on two different dual-task paradigms. Lonie and colleagues (2009) also reached similar conclusions in their study of early AD, amnesic-Mild

Cognitive Impairment (aMCI) and depression, finding that there were no group differences in dual-task performance between healthy older adults, early AD groups and those with MCI.

Therefore, although dual-task deficits in AD may be attributed to an early disease-related decline in attentional processing resources or working memory capacity, these studies suggest that when patients are subdivided using diagnostic criteria and compared to an appropriate control group, individuals in the early stages of dementia can perform normally on tasks of divided attention.

Consequently, the current study was designed to acquire more data on dual-task performance of individuals in the minimal or mild stages of the illness (i.e., aMCI), using a relatively novel combination of ambulation and speaking tasks. This work contributes to our understanding of the early neuropsychological deficits in AD and the theoretical issues that are related to this topic. In addition, this research provides practical information related to differential diagnosis and fall risk among individuals with dementia.

A second methodological limitation in gait dual task research relates to the range of results from previous studies dependent on the nature and type of the primary and secondary tasks. For example, in a study of dual-task related gait changes in frail older adults, Beauchet, Dubost, Gonthier, and Kressig (2005) found that different types of cognitive tasks (i.e., verbal fluency vs. counting) produced different dual-task related changes in gait. Although both tasks are declarative cognitive tasks, according to Beauchet et al. (2005) only a concurrent arithmetic task (i.e., counting backwards from 50) significantly interfered with gait stability and stride time. In contrast, the verbal fluency task, although it did appear to decrease gait speed, had little effect on gait stability. Interestingly, most prior dual-task studies have combined brief walking tasks with secondary verbal fluency tasks. For example, Cocchini et al. (2004) asked participants to produce as many words as possible that were meaningfully associated with a given target

word such as cat, rain or shoe. Similarly, Pettersen et al. (2007) and Camicioli et al. (1997) examined the influence of reciting male or female names on gait performance. These verbal fluency tasks have produced large dual-task effects in individuals with AD, but these interference effects can be interpreted in different ways. According to the reasoning of Beauchet and colleagues (2005) these interference effects could result because verbal fluency relies on semantic memory, and presumably has no direct relation to the executive functions necessary to divide attention (Beauchet et al., 2005). Given that semantic memory also has been found to be impaired in the early stages of AD, it is difficult to single out the specific deficit in divided attention. On the other hand, counting backwards, which is the strategy employed in the current study, draws on the working memory aspects of the central executive, which is, in part, responsible for the allocation and management of attentional resources (Baddeley, 1996). As the study by Beauchet et al. (2005) highlights, two simultaneous tasks will cause significantly greater interference if they compete for the same path of cognitive processing. In the same vein, it is possible that creating a competitive interaction between two executive functions that both require attention, is a more valid and reliable measure of divided attention than previously employed verbal fluency measures.

In addition to the importance of considering the nature of the concurrent cognitive task, the level of task complexity also matters greatly in dual task procedures. Crossley and colleagues (2004) found that dual-task performance in individuals with early stage AD is relatively well maintained when the secondary tasks are highly automatized (i.e., reciting the months of the year), at least when performed in combination with a speeded finger-tapping task. However, the same group of patients compared with normal older adults, had considerably more difficulty dividing attention while performing an “effortful” speech fluency task concurrently with speeded

finger tapping. In contrast to Beauchett et al. (2005), Crossley et al. (2004) suggested performance deterioration during dual-task conditions may not be due entirely to the unique nature of the concurrent tasks, but to the increase in level of complexity or difficulty when relatively effortful tasks (i.e., measures of verbal fluency) are performed in combination with a highly automatized motor task (i.e., speeded finger tapping). Although there is little doubt that task complexity influences upper extremity dual-task paradigms such as speeded finger tapping, what is less clear is how manipulating task complexity will affect gait dual-task procedures.

To our knowledge, no prior study has employed an arithmetic verbal counting task and manipulated task complexity when investigating gait dual-task performance in individuals with early stage AD. Thus, in Study 1 individuals in the earliest stages of probable AD (i.e., MMSE ranges from 21 to 28) and normal age matched control participants engaged in timed walking and arithmetic counting tasks during single and dual-task trials. Arithmetic verbal counting tasks were either relatively simple (i.e., counting forward by 1's) or relatively complex (i.e., counting backwards from 70 by 2's). To control for well-known single task walking speed differences between normal and AD participants, percent decrement scores were calculated as a measure of task interference. The aim of this study was to further investigate the effect of divided attention on gait using dual-task methodology with normal older adults compared to individuals in the earliest stages of the AD. In this context, we were interested in exploring whether or not deficits in divided attention can occur in the earliest stages of the illness. A second aim was to address previous methodological limitations by utilizing a gait dual-task procedure that manipulated the complexity of a concurrent cognitive task that competed directly with the walking task for the resources of the central executive. In this sense, we were interested in investigating the effects on ambulation of easy and difficult arithmetic counting tasks. Based on the previous literature that

has manipulated the level of task complexity (i.e., simple and complex conditions) it was hypothesized that individuals in the early stages of AD would perform as well as the healthy older adults on the simple dual-task measures. However, the early-stage AD group was expected to be differentially more impaired by the complex dual-task procedure, which would be consistent with the findings of previous gait dual-task paradigms.

Methods

Participants

Fifteen individuals (7 males, 8 females; $M = 76.7$ yrs), assessed to be in the early stages of a dementia (as described below) and fourteen healthy older controls (6 males, 8 females; $M = 72.9$ yrs) participated in this study. The AD participants were recruited at the Rural and Remote Memory Clinic in Saskatoon, Saskatchewan, following interprofessional assessment for suspected dementia (Morgan, Crossley, Kirk, D'Arcy, Stewart & Biem, 2009). An initiative of a Canadian Institute of Health Research (CIHR) New Emerging Team on Cognitive Aging, the Rural and Remote Memory Clinic interprofessional team provides a one-day assessment aimed at improving the care of persons with cognitive impairment and dementia who live in rural and northern Saskatchewan (Morgan et al., 2009). Clinical participants met criteria for "possible" or "probable" AD according to the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Associations (NINCDS-ADRDA; McKhann et al., 1984; Dubois et al., 2007) guidelines which were supported by experts of the Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia; CCCDTD3; Robillard, 2007; Rockwood et al., 2007). Further, AD participants were determined to be in the early stages of AD based on their overall neuropsychological profile and research based consensus diagnosis. Last, a Mini-Mental State Examination (MMSE; Folstein,

Folstein & McHugh, 1975) score between 21 and 28 was used to categorize individuals with early stage AD (Feldman & Woodward, 2005). The MMSE is a brief cognitive screening instrument consisting of several short cognitive probes, which are summarized into a score that ranges from 30 (best) to zero (worst). Although not a diagnostic test for the staging of dementia, the MMSE has been used to stage the progression of AD in previous gait dual-task studies and is often used in the literature to communicate information about the severity of dementia (e.g., Sheridan et al., 2004). Further, the MMSE has been found to have good reliability with the Clinical Dementia Rating Scale (CDR; Huges, Berg, Danzinger et al., 1982) which is considered the standard for the staging of dementia (Pernecky, Wagenpfeil, Komossa, Grimmer, Diehl, & Kurtz, 2006). A study by Pernecky and colleagues (2006) found significant agreement (i.e., Cohen's kappa) between the MMSE range of 21-28 and the CDR stage for early or mild AD (i.e., score of 1). Thus, these authors concluded that the MMSE can be used as a reliable measure for the staging of dementia in AD.

The healthy older adults recruited into the study included fourteen family members or other care providers of patients referred to the RRMC. Control participants were required to be "normally healthy" and were excluded if they reported neurological, psychiatric or other medical conditions that could interfere significantly with higher brain functioning or ambulation. The physical therapist on the clinic team (third author) also screened control participants for significant swaying or imbalance due to a neurological condition, dizziness due to vestibular dysfunction, residual effects of stroke or other brain insult, or other conditions that could affect ambulation. Consequently, one participant was removed from the study as a result of severe vertigo and gait instability. All remaining control participants were capable of walking independently, were free of any self-reported major medical illness, and had no cognitive

dysfunction at the time of testing. Informed consent was obtained from all participants, including family member informants, and this study was approved on ethical grounds by the University of Saskatchewan Behavioral Research Ethics Committee.

Measures

To investigate dual-task performance using gait assessment, the following tasks were administered to both clinical and control participants by a licensed physical therapist and the principle researcher in the course of the Rural and Remote Memory Clinic assessment day: The Timed Up and Go (TUG; Podsiadlo & Richardson, 1991), which is a clinical balance screening tool; and a dual-task paradigm combining walking with simple and complex verbal counting tasks.

The Timed Up and Go (TUG). The TUG measures, in seconds, the time taken by an individual to stand up from an arm chair, walk forward 3 meters, turn, walk back to the chair, and sit down again. This task examines basic functional mobility skills of healthy older adults and individuals with dementia (Goodgold, Kiami, Ule, Schoenberg, & Forman, 2001). Although Rockwood, Awalt, Carver and MacKnight (2000) reported that the TUG had poor test-retest reliability, other studies have reported good to excellent reliability. For example, Thomas and Hageman (2003) found that the reliability estimates for the TUG and gait speed were excellent (e.g., ranging from 0.75 to 1.00) in a population of healthy older adults. For the current study, the TUG provided a screen for physical ability to participate in the dual-task paradigm.

Verbal Counting Tasks. The simple and complex counting tasks require participants to start at a given number (1 or 70) and count out loud for 15s trials in both simple (i.e., counting forward by 1's) and complex (i.e., counting backwards by 2's from 70) conditions.

Walking Task. Participants were instructed to walk down a hallway 15 ft, following a line indicated by white tape on the floor, turn and walk back at a “brisk but comfortable pace.” If participants reach the starting line before the 15s trial is complete, they are instructed at the outset of the trial to make a second turn and continue walking until the researcher says “stop.”

Procedure

The lead author and clinic team physical therapist (third author) tested participants individually in a quiet hallway. The TUG and the experimental tasks were conducted along a 15-ft white line, marked in one foot increments, with a line made at each end to indicate where the participant was to turn. Experimenters were positioned at opposite ends of the walkway for safety considerations, and the physical therapist walked along side the participant throughout each single-gait and dual-task trial. As described in detail below, all participants were asked to perform one 15s baseline trial of the walking task, followed by 15s baseline trials of the simple and complex verbal counting tasks. Participants then completed two 15s trials of the simple and complex dual task conditions, followed by a second set of three 15s baseline trials of the single-task experimental measures.

The Timed up and Go (TUG). Clinical participants were seated in a normal armchair with their back against the chair. Participants were instructed to stand-up, walk 3 meters at a “comfortable pace” to a line indicated on the floor, turn around, walk back to the chair, and sit-down. After subjects were familiarized to the test requirements, the total time and number of steps to complete the task was recorded for three trials. Clinical participants who took longer than 30s to complete the TUG, or presented with severe gait disturbances (e.g., spastic, ataxic, dysonic and choreic gaits) were debriefed and excluded from the subsequent dual-task procedures.

Single Task Walking. The single walking task was introduced and demonstrated to the participant with the following instructions (see Appendix A for complete instructions):

“When I tell you to “Go” I would like you to walk at a brisk but comfortable pace until you reach the other line at the end of the hallway. Once you reach the end, turn around and keep walking back towards the starting line. If you make it back to the line before time is up, turn again and continue walking until I tell you to stop.”

Following a few seconds practice on the walking task to confirm understanding, participants were asked to complete a 15s baseline trial. The principle investigator recorded the distance in feet covered by the participant in the 15s trial.

Verbal Counting Tasks. Following the single-task walking trials, the simple single-task counting procedure (i.e., counting forward by 1's) was introduced to the participant using the following instructions:

“Now I would like you to do some counting by 1's. Starting with the number one, please count out loud by 1's as quickly as you can, like this, 1,2,3,4... and so on, until I tell you to stop, but do not count so quickly that I cannot understand what your saying.”

Following several seconds of practice to confirm understanding of the simple verbal counting task, participants completed one 15s baseline trial. The complex verbal counting task was then introduced using the following instructions:

“Now I would like you to do some more counting, but this time I would like you to count backwards by 2's. Starting with the number 70, please count backwards by 2's like this 70, 68, 66, 64 and so on until I ask you to stop.”

Once participants had demonstrated they understood the complex verbal counting task, they completed a 15s baseline trial. For both the complex and simple tasks, the number of valid digits produced and corresponding number of mistakes were recorded.

Dual-Task Condition. After completing the single-task baseline trials, the dual task procedures were introduced and demonstrated to the participant using the following instructions:

“Now we are going to do some more counting and walking, but this time we will do them at the same time. For example, in some trials I will ask you to walk as quickly as you can and count by 1's at the same time. When I ask you to do two things at the same time I want you to remember that both tasks are equally important. That means I want you to walk as quickly as you can, while also counting as accurately as you can.”

Once the participant had an opportunity to practice combining the verbal counting task with the walking task, they completed one 15s, simple dual-task trial (i.e., walking while counting forward by 1's) and one 15s, complex dual-task trial (i.e., walking while counting backwards from 70 by 2's). If participants stopped generating digits or walking during the dual-task trials, they were encouraged to continue by the principle investigator (e.g., “keep going”). The distance in feet covered in 15s was recorded, in addition to the number of digits produced and mistakes made in the counting task. As described earlier, the dual-task trials were followed by a second series of single-task trials for the walking and verbal counting tasks.

Results

Single-Task Walking and Counting

Table 1 shows the average distance covered by the clinical and healthy control groups during single-and dual-task walking trials (i.e., walking while concurrently counting in either simple or complex conditions). The total number of valid digits produced under single and dual-task conditions is also shown. To examine the single-task data for baseline differences between groups, independent samples t-tests were used to compare the single-task walking and counting rates for AD and control participants. As expected, the control group covered significantly more distance in the single task walking trials ($M = 54.03$ ft, $SD = 9.57$) than did the AD group

($M = 40.58$ ft., $SD = 9.09$), $t(27) = 3.88$, $p < .001$. This finding is consistent with previous research indicating that individuals with AD walk significantly slower than cognitively intact older adults (Sheridan & Hausdorff, 2007).

The verbal counting data for the single task conditions were analyzed in a 2 (Group: clinical, control) X 2 (Task Complexity: simple, complex) ANOVA with repeated measures on the second factor. Partial eta squared (η_p^2) is given as a measure of effect size. As predicted, a main effect of task complexity was detected, $F(1,27) = 635.018$, $p < .001$, $\eta_p^2 = .331$ with both groups producing significantly more digits in the simple condition ($M = 33.98$, $SD = 6.17$) than in the complex condition ($M = 13.10$, $SD = 3.77$). A main effect for group was also detected, $F(1,27) = 13.72$, $p = .001$, $\eta_p^2 = .241$ indicating that, for both simple and complex counting tasks, the healthy older adult group, when compared to the early-stage AD group, produced significantly more correct digits. However, there was no significant Group X Complexity interaction $F(1,27) = .855$, $p = .363$, $\eta_p^2 = .018$ suggesting that the group difference was not conditional on the complexity of the counting task.

Dual-Task Walking and Counting

To account for the expected and confirmed single-task differences between the healthy and AD participants, interference in the dual-task conditions was expressed as a percent decrement score. As noted in the introduction, a decrement score allows for an assessment of the proportional change in an individual's performance during dual-task conditions relative to his/her performance during the single-task conditions (Crossley et al., 2004). For the distance covered, percent decrement scores for the simple (i.e., walking and counting by 1's) and the complex (i.e., walking and counting backwards by 2's) trials were calculated and are displayed in Table 1. The dual-task data (i.e., percent decrement scores) were analyzed in a 2 (Group: AD,

control) X 2 (Task Complexity: simple, complex) repeated measures ANOVA. This analysis revealed a significant main effect for task complexity, $F(1,27) = 68.95, p < .001, \eta_p^2 = .395$ indicating that, across groups, the percent decrement score was significantly greater when walking was combined with the complex vs. simple verbal counting task. Unexpectedly, there was no main effect for group $F(1, 27) = .517, p = .478, \eta_p^2 = .019$ or interaction between group and task complexity $F(1,27) = .044, p = .835, \eta_p^2 = .011$. A similar analysis carried out on the percent decrement scores for the counting data revealed no effect of complexity, $F(1,27) = 2.66, p = .115, \eta_p^2 = .025$, group $F(1,27) = .257, \eta_p^2 = .009$ and no significant interactions between group and task complexity $F(1,27) = .075, p = .787, \eta_p^2 = .029$. Even when controlling for single-task group differences, walking rate during dual-task performance was slowed more by complex than by simple counting but this difference in interference effects was similar for individuals with early stage AD and for healthy controls. In contrast to the walking rate data, when single task counting differences were controlled using percent decrement scores, there were no significant main effects or interactions for group or task complexity.

Discussion

Previous gait dual-task studies have found that when compared to healthy older adults, individuals with early stage AD perform more poorly during divided attention tasks (e.g., Camicoli et al., 1997; Cocchini et al., 2004; Sheridan et al., 2003). However, previous gait dual-task studies typically have not used well validated diagnostic criteria (i.e., NINCDS-ADRDA criteria) and reliable cognitive screening tools such as the MMSE to examine divided attention in groups of patients in the very earliest stages of disease severity; nor have they manipulated the level of dual-task complexity. Rather, prior gait dual-task studies have often compared

performance between heterogeneous groups of individuals with AD at differing stages of the illness and healthy younger controls. Presumably, these group compositions and procedures should make it easier to find significant differences on tasks of divided attention, but result in difficulties in interpretation. The gait dual-task paradigm used in the current study combines a simple and complex arithmetic verbal counting task with a walking task in individuals assessed to be in the earliest stages of AD, and compares their performance to an age appropriate, well matched, healthy control group.

In contrast to previous studies, our cohort of early-stage AD patients showed relatively normal performance on measures of simple and complex gait dual-tasks when compared to age-equivalent healthy adults and when single-task differences were controlled. Our analyses did reveal the expected group differences during single-task performance (i.e., AD participants, compared to healthy controls, walked more slowly and produced fewer digits in both simple and complex conditions), and predictable main effects for task difficulty (i.e., both groups produced significantly more digits in the simple condition, than in the complex condition, and both groups walked more slowly when concurrently completing the complex vs. the simple counting task). Nevertheless, once baseline group differences in walking rate were controlled, individuals with early stage AD were not differentially impaired by a concurrent arithmetic counting task, regardless of the level of complexity. That is, although the counting tasks affected walking rates, especially in the complex dual-task condition, when baseline walking rate group differences were controlled for using percent decrement scores, AD patients were not disproportionately slowed compared to healthy older adults under either simple or complex dual-task conditions. Thus, in the stage of AD that we have designated as mild, our AD patients were not impaired by

a gait dual-task paradigm, at least as measured by walking speed. Evidently, divided attention, as measured by the current study, is not always affected in the earliest stages of AD.

These results, however, do provide converging evidence that a significant slowing of gait is present in early AD (Morgan, Funk, Crossley, Basran, Kirk, & Dal Bello-Haas, 2007). Consistent with past research, walking speed during the single- and dual-task trials was significantly slower for AD participants than for normal controls (Al-Yahya et al., 2011; Hausdorff et al., 2005; Montero-Odasso et al., 2009; Yogev-Seligmanne et al., 2008) There is increasing evidence to suggest that a strong relationship exists between dual-task related gait changes and the risk of falling among older adults (Holtzer et al., 2007; Verghese et al., 2002). Therefore, the tendency of the AD group to slow down their rate of walking might represent an adaptive way for individuals with early stage AD to decrease their risk of falling (Li et al., 2005). Numerous researchers have focused on cognitive predictors, such as impaired attention, of early stage or preclinical AD; however, it is possible that declines in gait speed compared to normal older adults might also be typical of the earliest stages of AD and aid in early diagnosis (Morgan et al., 2007). Although evidence suggests that slowing of gait is predictive of falls in healthy older adults (Hausdorff et al., 2005), less is known about the relationship between gait changes and cognition in the earliest stages of AD.

On a broader level, our results are in line with those of Perry et al. (2001) who also showed that individuals in the earliest stages of AD could perform as well as healthy older adults on a well-validated dual-task paradigm. They found that slightly less than 30% of individuals with an MMSE score of 24 or greater performed outside the normal range (i.e., defined as a z-score greater than 2 standard deviations from the control means) on a dual task combining speeded box joining with digit repetition. Similarly, more recent results from Lonie and

colleagues (2009) show that individuals in the “pre-clinical” stages of AD (i.e., Amnesic – Mild Cognitive Impairment; Petersen et al., 1999, 2001) well as those clearly identified with early-stage AD can perform as well as healthy older adults on a dual-task combining oral digit span repetition and a paper and pencil visuospatial tracking task. In keeping with our results, dual-task performance was not impaired in the stages that they designated as aMCI and early-stage AD. By contrast, the aMCI and early-stage AD group were impaired on tasks of episodic memory and part B of the Trail Making Test, leading the authors to suggest that dual-task performance may not be a sensitive marker of the early cognitive changes associated with AD when participants in the earliest stages are divided by rigorous diagnostic criteria.

Taken together with the results of the present study, these findings suggest that when disease severity is limited to the earliest stages, and when performance is compared to an appropriate healthy control group, at least some individuals with AD can perform normally on tasks of divided attention. Nevertheless, as suggested by Perry and colleagues (2001), comparing results across dual-task paradigms (i.e., a gait paradigm vs. an upper extremity dexterity paradigm) can lead to significant challenges in interpretation. Numerous previous dual-task studies, which have utilized upper extremity tasks such as finger tapping, or speeded box joining have consistently provided support for the conclusion reached by Perry and Hodges (1999) that deficits in divided attention consistently occur in the early stages of AD (e.g., Baddeley et al., 2001; Crossley et al., 2004). Although the results of the present study suggest that individuals with early stage AD can efficiently divide attention, caution must be taken when generalizing the results from the present study to other dual-task paradigms, specifically upper extremity motor tasks, and to the neuropsychological profile of early AD in general. Although walking and rhythmic finger tapping share many of the same characteristics and are reported to share similar

neural networks, recent evidence suggests that walking is a much more complex task that utilizes more higher brain functions than does tapping, especially among older adults (Hausdorff et al., 2005). This calls for future research to directly compare gait and upper extremity dual task performance in groups of pre-clinical and early-stage AD patients and in relation to other neuropsychological functions.

Therefore, although relying on dual-task methodology to examine the interplay between attentional functions and early AD is consistent with a large body of literature; recent evidence suggests that separate cognitive processes, in addition to attention, are necessary for successful gait performance (Wollacott & Shumway-Cook, 2002). Thus, in this new context, dual-task methodology is limited by its study of attention in isolation. That is, if walking is indeed multifactorial in terms of its underlying cognitive processes, the cortical correlates of gait would suggest that speeded performance, executive control, and memory functions might also be necessary for successful walking in early AD (Holtzer et al., 2006). Specifically, additional studies are needed to evaluate how other specific and general neuropsychological factors, in addition to divided attention, are related to cognition and gait in individuals with early AD. Performance on a broad range of neuropsychological tests can provide additional useful information relevant to the early diagnosis and treatment of AD symptomatology, and also provide information relevant to the risk assessment of falls in individuals with AD. In light of these limitations, Study 2 and 3 of the current research will incorporate neuropsychological testing to better understand how gait dual-task performance is related to cognitive functioning in healthy older adults and individuals at different stages of AD severity (i.e., aMCI, early-stage AD, and moderate-stage AD). In particular, Study 3 will address how specific theoretically derived cognitive factors (i.e., Attention/Executive Function/Speed, Episodic Memory, and

Language) are related to gait performance under baseline, simple and complex dual-task procedures. Although this strategy has been employed to understand how cognitive factors are related to gait speed in healthy older adults (i.e., Holtzer et al., 2006), this methodology has not been applied to groups of individuals at different stages of disease severity and therefore has a great deal of potential for exploring how cognition relates to gait in individuals with AD.

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AGING, ALZHEIMER'S DISEASE, AND GAIT DUAL-TASK

Table 1. Mean scores (SD) for Alzheimer Disease (AD) participants and healthy age-equivalent controls shown as walking distance in feet and number of digits produced in 15s trials under single and dual-task conditions, and as percent decrements for simple and complex dual-task conditions

	Healthy Control	Alzheimer
N	14	15
Walking Task (Distance in feet)		
Single-task	54.03 (9.57)	40.58 (9.09)
Simple dual-task	51.17 (8.41)	37.85 (9.87)
% decrement	4.87 (7.19)	7.03 (10.51)
Complex dual-task	40.16 (9.71)	29.02 (10.70)
% decrement	26.12 (9.15)	29.39 (18.85)
Counting Task (Digits produced)		
<i>Counting by 1's</i>		
Single-task	36.78 (6.23)	31.37 (4.97)
Simple dual-task	31.14 (7.33)	25.33 (4.82)
% decrement	15.71 (9.90)	18.96 (12.30)
<i>Counting backwards from 70</i>		
Single-task	15.75 (3.60)	10.63 (1.67)
Complex dual-task	13.93 (3.77)	9.33 (2.58)
% decrement	11.15 (14.68)	12.45 (20.36)

Running Head: DUAL-TASK PERFORMANCE AND DISEASE SEVERITY

Study 2: Simple and Complex Gait Dual-Task Performance in Groups of Patients with Preclinical, Mild, and Moderate Alzheimer's Disease Compared to Healthy Older Adults: The Differential Effect of Task Complexity is Evident Only in the Moderately Impaired AD Group

Jocelyn Poock, Margaret Crossley, Vanina Dal Bello-Haas, & Lorin Elias

University of Saskatchewan

Author Note

Jocelyn Poock, Department of Psychology, University of Saskatchewan; Margaret Crossley, Department of Psychology, University of Saskatchewan; Vanina Dal Bello-Haas, School of Rehabilitation Science, McMaster University; Lorin Elias, Department of Psychology, University of Saskatchewan

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Correspondence concerning this article should be addressed to Jocelyn Poock, Department of Psychology, Arts 154, University of Saskatchewan, 9 Campus Drive, Saskatoon, Saskatchewan, Canada, S7N 5A5. Email: jocelyn.poock@usask.ca

Abstract

Past research suggests that the ability to divide attention while walking (i.e., gait dual-task performance) is particularly vulnerable to the effects of Alzheimer's disease (AD; Yogev-Seligmann, Hausdorff, & Giladi, 2008). However, previous studies have been limited by failure to control for the group differences in single-task walking rate, variability in the types of gait dual-tasks employed, and the inclusion of large heterogeneous groups of patients at different stages of disease severity. Previous work in our lab (i.e., Study 1) indicated that when these methodological concerns are addressed, individuals with early stage AD can perform as well as healthy older adults on both a simple and complex a gait dual-task. The current study was designed to replicate and extend our previous work by including patients diagnosed in an interdisciplinary memory clinic with amnesic-Mild Cognitive Impairment (aMCI; Petersen et al., 1999, 2001; $n=16$), early-stage AD ($n=15$), moderate-stage AD ($n=17$), and 27 healthy older adults. Participants performed a timed walking task and simple and complex verbal counting tasks (i.e., counting forward by 1's or backward by 2's) in single and dual-task combinations. Although all groups showed significantly more interference during the complex vs. simple walking and counting dual-task, in keeping with the results of Study 1, there were no significant differences between the early stage AD group, aMCI group, and healthy older adults on the gait dual-task, regardless of task complexity. As predicted, significant differences were detected between the moderate AD group and the healthy normal control group on the complex dual-task. Overall, the moderate AD group showed a unique pattern of interference suggesting that the ability to divide attention during a complex walking and counting dual task is relatively spared until the moderate stages of the illness. Furthermore, our results indicate that the moderate stage

of AD may also be associated with a breakdown in task-prioritization processes, which could be related to an increased risk of falling in this population.

Study 2: Simple and Complex Gait Dual-Task Performance in Groups of Patients with Preclinical, Mild, and Moderate Alzheimer's Disease Compared to Healthy Older Adults: The Differential Effect of Task Complexity is Evident Only in the Moderately Impaired AD Group

Much of the previous gait dual-task research indicates that when compared to healthy older adults, individuals with early stage AD have a specific problem with tasks of divided attention, typically measured by interference in dual-task performance (see Al-Yahya, Dawes, Smith, Dennis, Howells, & Cockburn, 2011 or Yogev-Seligmann-Seligmann, Hausdorff, & Giladi, 2008 for recent reviews). The general interpretation from these experiments, and other laboratory based dual-task paradigms (i.e., pencil and paper tasks, upper extremity motor tasks) has been that in the earliest stages of AD, there is damage to some form of executive coordination function required to divide attention or to allocate resources among concurrent tasks (Fernandez –Duque & Black, 2006; Perry & Hodges, 1999; Salthouse, 2010; Saunders & Summers, 2011). These findings have led some authors to conclude that after an initial amnesic stage in AD, divided attention is among the first non-memory domain to be affected by the illness (Fernandez-Duque & Black, 2006; Perry & Hodges, 1999; Perry, Watson, & Hodges, 2000). Thus, measures of divided attention, such as gait dual-task paradigms, have been described in the literature as possible candidates for differentiating normal older adults from those with AD (Bellville, Chertkow & Gauthier, 2007) as a possible predictor of future development of AD in individuals with amnesic- Mild Cognitive Impairment (aMCI; Petersen et al., 1999, 2001; Saunders & Summers, 2011).

However, variability in the types of tasks used to examine divided attention, and in the disease severity of the AD patients included, has made it difficult to determine if divided attention is consistently impaired in the earliest stages of AD, at least when assessed using a gait

dual-task paradigm. Most notably, gait-dual task performance has typically been compared between relatively small samples of younger healthy adults and small heterogeneous groups of patients at different stages of disease severity (Cocchini et al., 2004), or in groups of frailer individuals in the later stages of the disease process (Sheridan et al., 2003). This raises concerns that group differences can be attributed to the severely impaired participants who generally demonstrate deficits on most cognitive measures, not just measures of divided attention. Furthermore, qualitative descriptions of disease severity (i.e., inpatient vs. outpatient; Sheridan et al., 2003) or the use of idiosyncratic scales for measuring dementia do not allow for comparisons across studies. Presumably, these group compositions and procedures should make it easier to find significant differences on tasks of divided attention; however, they create difficulties in interpretation when these results are generalized to the overall profile of cognitive deficits associated with early-stage AD (Perry, Watson, & Hodges, 2000).

In keeping with this argument, our cohort of early-stage AD participants in Study 1 showed relatively normal performance on measures of simple and complex gait dual-tasks when compared to age equivalent healthy older adults and when single task differences were controlled for using percent decrement scores. Although these analyses revealed the predictable main effects for task complexity (i.e., both groups produced significantly more digits in the simple dual-task condition than in the complex dual-task condition, and both groups walked more slowly when concurrently completing the complex vs. the simple counting task), the early-stage AD group was not differentially impaired by a concurrent arithmetic counting task, regardless of the level of task complexity.

Thus, the gait-dual task paradigm used in this research is believed to present a methodological advantage over previous work, by taking into account the previous limitations in

the literature, which have included a failure to manipulate the level of task complexity, and have included large heterogeneous groups of patients at different stages of disease severity. Although the results obtained in Study 1 contrast prior gait-dual-task studies, previous work typically has not used rigorous diagnostic and research based guidelines to examine patients in the very early stages of disease severity. Nonetheless, the novel results obtained in Study 1 suggest a need to replicate and extend our previous work, to further understand when impairments in divided attention arise in the progression of AD, at least as measured by a gait dual-task paradigm.

To meet this goal, Study 2 was designed to expand upon the results from Study 1 by including a groups of patients diagnosed with amnesic-Mild Cognitive Impairment (aMCI; Petersen et al., 1999, 2001), early-stage AD, and moderate-stage AD, and comparing their performance to an age-matched group of community dwelling healthy older adults. To date, no gait dual-task studies have compared the performance of groups of individuals with AD at different stages of disease severity to a well-controlled group of healthy older adults. Furthermore, very few studies in general have examined divided attention and dual-task performance in individuals in the “pre-clinical” stages of AD, which is conceptualized as aMCI (Lonie et al., 2009; Saunders & Summers, 2011) Although there is little doubt that the moderate stage of AD is associated with impairments in divided attention, considerably less is known about the performance of individuals with aMCI on a dual-task paradigm. Some recent evidence from experimental dual-tasks suggests that those with aMCI can perform normally on a dual-task paradigm. However, these authors have typically used upper-extremity dual-tasks which can make their results difficult to generalize to a gait-dual task paradigm which is believed to require more higher brain functioning (Greene et al., 1995; Lonie et al., 2009; Perry et al., 2000; Yogev-Seligmann et al., 2008).

Given the recent advent of pharmacological therapies aimed at slowing the progression of AD, there has been an increase in interest in understanding the cognitive profile associated with aMCI (Saunders & Summers, 2011). The efforts intensified following the introduction of the Quality Standards Subcommittee practice parameter criteria for MCI in 2001 (Griffith, Netson, Harrell, Zamrini, Brockington, & Marson, 2006; Petersen et al., 2001; Winblad et al., 2004). These criteria, which were proposed by Petersen and colleagues (1999, 2001), define aMCI as a clinical diagnosis that is distinct from the typical cognitive complaints of older adults and define persons displaying subjective complaints of memory loss, psychometric evidence of memory loss, otherwise normal cognitive functioning, generally normal everyday activities of life, and no evidence of dementia (Griffith et al., 2006; Petersen et al., 1999; 2001; Petersen & Morris, 2005; Winblad et al., 2004). Although estimates vary, many studies have shown that those with aMCI are at an increased risk of progression to AD, with 10-15% of aMCI patients developing AD annually (Roach, 2005), compared to 1-2% in the general elderly. In one retrospective epidemiological study that applied aMCI criteria to participants over a 10 year follow-up period, 27% of the participants with aMCI developed dementia within the 10 year-period. Although the diagnosis of aMCI presents a risk factor for future dementia, the existing criteria still display some variability in accurately predicting an individual's risk for developing AD (Saunders & Summers, 2011). Some patients will progress to other forms of dementia, remain stable, or revert to a normal cognitive state on longitudinal follow up (Gauthier & Touchon, 2005).

Recent research suggests that the earliest cognitive changes in the subtype of aMCI is objective and corroborated (i.e., by family member) evidence of memory dysfunction that is detectible on formal testing (Saunders & Summers, 2011). However, whether aMCI is characterized solely by mild amnesia, or is accompanied by impairments in divided attention and

executive functioning is unclear. Most studies of aMCI to date, have investigated only the memory impairment in aMCI and the few studies that have used dual-task procedures to examine attentional control typically have used large heterogeneous groups of MCI patients, making it difficult to speak to the specific attentional deficits found in aMCI (e.g., Maquet et al., 2010; Montero-Odasso et al., 2009; Pettersson et al., 2005). Thus, it is of practical and theoretical significance that individuals with aMCI be included in gait dual-task paradigms to address how divided attention is affected in those individuals who are truly in the very earliest stages of AD.

Therefore, to expand upon the findings in Study 1 that individuals with early-stage AD can perform normally on a simple and complex gait dual-task paradigm, Study 2 included groups of individuals assessed to be in the “pre-clinical” or aMCI stage of AD, and further subdivided participants with probable AD into those at the mild and moderate stages of the disease. The recent progress in neuropsychology and diagnostic guidelines aimed at identifying early AD has led to more precise categories of diagnosis for these groups. This design presents a methodological advantage over previous work, in that it allows the results to speak to the specific impairments, or lack of impairment, arising at each stage of severity. The performance of individuals with aMCI and AD will be compared to a group of community dwelling, healthy older adults who are closely matched to the patient groups in terms of age, education and estimated pre-morbid intelligence. Based on the results of Study 1, it is hypothesized that individuals with aMCI and early-stage AD will not be impaired on the gait-dual-task paradigm, regardless of the level of task complexity. That is, although we would predict the expected effects for task complexity (e.g., all groups will walk more slowly and produce fewer digits in the complex condition), we do not expect individuals with aMCI or early-stage AD to be differentially more impaired by a complex gait-dual task. Rather, it is hypothesized that the

moderate stage of AD will be associated with significantly higher levels of dual-task interference on the complex dual-task trial.

Methods

Participants

In Study 2, groups of patients diagnosed with probable Alzheimer's disease (AD) or amnesic- Mild Cognitive Impairment (aMCI ; Petersen et al., 1999, 2001) were compared to a group of community dwelling, healthy older adults. The patient group consisted of individuals who were referred to the Rural and Remote Memory Clinic (RRMC; Morgan, Crossley, Kirk, D'Arcy, Stewart & Biem, 2009) in Saskatoon, Saskatchewan as part of a one-day interdisciplinary assessment for suspected dementia. Patients were divided into three groups (i.e., MCI-amnesic, early-stage AD, and moderate AD) based on the consensus diagnostic criteria used by the RRMC team (i.e., The Third Canadian Consensus Guidelines on the Diagnosis and Treatment of Dementia; CCCDTD3; Robillard, 2007) which includes the Petersen et al. (1999; 2001) criteria for aMCI, and the diagnostic research criteria for probable AD published by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS – ADRDA; Dubois et al., 2007; McKhann et al., 1984). Decisions about disease severity were made based on the patients overall neuropsychological profile as well as their performance on the Modified Mini-Mental State Examination (3MS; Teng & Chui, 1987). Split-half analysis of 3MS scores revealed a bi-modal distribution which was used to divide patients with Alzheimer's disease into two levels of disease severity: early-stage AD (3MS $M=83.07$; Range 77-91); and moderate stage AD (3MS $M=70.41$, Range 59-76). For the patient group, the diagnostic process also included a thorough history and neuropsychological battery to exclude other conditions that can affect brain function

(i.e., head trauma, psychiatric disorders, alcohol abuse), a medical examination and computed tomography (CT) scan to exclude other forms of focal neurological disease and more diffuse forms of cerebral vascular disease (i.e., vascular dementia), and a physical therapy assessment to screen for peripheral factors that could negatively affect gait performance (i.e., balance impairment, vertigo, dizziness). Patients were excluded from the study if their cognitive deficits could be better attributed to other disorders of the central nervous system that cause progressive deficits in memory and cognition (i.e., cerebrovascular disease, vascular dementia, Parkinson's disease, Huntington's disease, subdural hematoma, normal pressure hydrocephalus, dementia with Lewy-Body, Frontotemporal dementia) or if they have a health condition known to cause dementia or to impair cognitive functioning (i.e., hyperthyroidism, vitamin B12 deficiency, HIV). Based on these exclusionary criteria, five patients were removed from the study due to respective histories of chronic alcohol abuse, meningitis, mild traumatic brain injury, cerebrovascular disease (i.e., mixed dementia), and an adult diagnosis of Attention Deficit Hyperactivity Disorder (ADHD).

Following exclusion based on these criteria, a total of 48 patients from the RRMC were divided into the following three groups: 16 individuals met criteria described by Peterson and colleagues (1999, 2001) for aMCI ($M = 76.1$ yrs; range = 59-87; 2 males, 14 females); 15 individuals met criteria for early-stage AD ($M = 73.9$ yrs; range = 64-82; 2 males, 13 females), and 17 individuals met criteria for moderate stage AD ($M = 73.4$ yrs; range = 54-87; 6 males, 11 females).

Healthy older adults were recruited from the Saskatoon Council on Aging (SCOA) using a mail campaign. Following approval by the University of Saskatchewan Research Ethics Board, SCOA members were invited to participate in a conjoined study of cognition, aging and walking

in individuals with dementia and healthy older adults. The final sample of healthy controls consisted of 27 participants ($M = 74.6$ yrs., range = 57-92 yrs.; 11 males, 16 females). All control participants reported good general health and were screened by a physical therapist for serious physical health conditions and peripheral factors that could negatively affect gait. Volunteers were excluded from the study if they reported poor vision or audition, or serious health conditions that could impair neuropsychological test performance (e.g., medical history of stroke, serious head injury, multiple sclerosis, etc.). Performance on a neuropsychological test battery (described below) ensured that each of the healthy participant's cognitive status was within normal range. Based on these criteria, two control group participants were excluded from the analysis because of a pattern of scores on neuropsychological testing that were suggestive of cognitive impairment (i.e., impairments exceeding 1.5 standard deviations on measures of immediate and delayed memory, attention and verbal fluency).

Demographic information for the four groups is shown in Table 1. There were no statistically significant group differences with respect to age, $F(3, 71) = .360, p = .72, \eta_p^2 = .025$ or education, $F(3, 71) = .570, p = .636, \eta_p^2 = .019$. However, there were small but statistically significant differences among groups on the reading subtest of the Wide Range Achievement Test-Third Edition (WRAT-III; Wilkinson, 1993), $F(3, 67) = 5.21, p < .05, \eta_p^2 = .035$. Post-hoc analyses revealed that the Moderate AD group's performance ($M = 41.1, SD = 6.22$) was significantly lower than the normal healthy control group ($M = 47.7, SD = 5.94$). No significant differences in WRAT-III reading scores were detected among the healthy controls, the MCI-amnesic group ($M = 45.1, SD = 4.50$), or the early-stage AD group ($M = 47.3, SD = 5.60$) suggesting that the difference between healthy older adults and those with moderate AD was due to disease severity rather than pre-existing differences in intellectual functioning. In fact,

estimates of reading ability that are commonly used as indicators of premorbid intellectual functioning have been shown to be sensitive to the effects of dementia, especially in the moderate to late stages of the illness, suggesting that other indicators of premorbid ability (e.g., education, occupation, etc.) are more reliable in moderate to late stage AD (McCarthy, Burns, & Sellers, 2005).

Measures

Neuropsychological Test Battery. All participants completed a comprehensive battery of neuropsychological tests which form part of the standardized battery at the Rural and Remote Memory Clinic (Morgan et al., 2009). These included a cognitive screening instrument (The Modified Mini-Mental State Examination; Teng & Chui, 1987) and measures of attention and executive functions, including the Stroop Neuropsychological Screening Test (Stroop Test; Trennery, Crosson, DeBoe, & Leber, 1989), the Trail Making Tests, Part A & B (Reitan, 1992), and the Digit Span Forward and Backward subtests of the WAIS-III (Wechsler, 1997). Also included were measures of episodic, semantic, and prospective memory (Grasshoppers & Geese Test; Lanting and Crossley, 2007), as well as measures of phonemic fluency (Controlled Oral Word Association Test; FAS, Spreen & Benton, 1977), semantic fluency (Animal Naming; Goodglass & Kaplan, 1983), confrontational naming (Grasshoppers & Geese Test; Lanting & Crossley, 2007) and processing speed (Symbol Search subtest of the WAIS-III, Wechsler, 1997). All participants also completed the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998), which was designed to screen for dementia in older adults. The RBANS consists of 12 subtests assessing the cognitive domains of immediate and delayed memory, attention, visuospatial/constructional abilities, and language (Randolph, 1998).

Verbal Counting Tasks. The simple and complex counting tasks require participants to start at a given number, either 1 or 70, and count out loud in both simple (i.e., counting forward by 1's) and complex (i.e., counting backwards by 2's from 70) conditions.

Walking Task. Participants were instructed to walk, at a "brisk but comfortable pace", back-and-forth along a 15 foot GaitRite mat during 15s trials. At the outset of each walking trial, participants were reminded to continue walking until the researcher says "stop." (See Appendix A for full and detailed instructions)

Procedure

General Procedure. This research was approved by the Behavioral Research Ethics Board at the University of Saskatchewan. All participants were informed prior to consent that the procedure will require them to walk as quickly and as comfortably as they can, while also simultaneously counting out loud. Consent forms were completed by all participants prior to the experimental trials (See Appendix B for a copy of the consent forms used in this study). Once consent was obtained, all participants were tested by the writer or a trained research assistant, together with a registered physical therapist, in a gymnasium in the Department of Physical Therapy at Royal University Hospital (RUH). The presentation order of the simple and complex dual-task trials was counterbalanced across participants.

Single Task Walking. The single task walking trial was introduced and demonstrated to each participant using the instructions shown in Appendix A. Participants then completed one 15s baseline trial. The dependent variable – the distance (in feet) covered in 15s was then recorded by the experimenter (See Appendix C for recording form).

Single Task Counting. Following the single-task walking trials, participants completed one 15s single-task trial of the simple counting task (i.e., counting forward by 1's) and another

of the complex counting task (i.e., counting backwards from 70 by 2's). The number of correct digits produced and number of errors were recorded.

Dual-Task Conditions. After completing the single-task walking and counting trials, participants were asked to combine the walking task and counting task, in one 15s simple dual-task trial (i.e., walking and counting forward by 1's) and one 15s complex dual-task trial (i.e., walking and counting backwards from 70 by 2's). The distance covered, as well as digits produced and errors were recorded by the experimenter for each trial.

Single Task Walking and Counting. Last, participants were asked to complete each task (i.e., walking, and simple and complex counting) once again in 15s single task conditions.

Results

Neuropsychological Testing

One-way ANOVA's were used to examine neuropsychological test scores for between-group differences. The required post-hoc analyses were carried out using Gabriel's pairwise test procedure which has been shown to have tight Type I error control when sample sizes differ across groups (Field, 2009). Average scores and standard deviations are shown in Table 2. There were significant differences among all four groups on the Modified Mini Mental State Examination (3MS), $F(3, 71) = 129.5, p < .001$. As expected, the normal healthy control group (3MS $M = 96.3, SD = 2.61$) performed significantly better than the aMCI ($M = 87.3, SD = 5.92$), early-stage AD ($M = 83.1, SD = 3.92$), and moderate AD ($M = 70.4, SD = 4.91$) groups. Group differences were also detected on a number of attentional and executive measures including the Trail Making Test A, $F(3, 70) = 8.27, p < .001$ and B, $F(3, 51) = 9.56, p < .001$, the Stroop color $F(3, 63) = 4.613, p < .05$, and word-color tests $F(3, 59) = 12.64, p < .001$. All groups performed equivalently on the forward version of the digit span subtest, $F(3, 71) = 2.03, p = .117$; however, as

expected, significant group differences were detected on the backwards version, $F(3,70) = 4.47$, $p < .05$, with the moderate AD group performing significantly lower than both the healthy control group and the MCI-amnesic group. Similar significant group differences were detected on the Grasshoppers and Geese tests of semantic, $F(3,66) = 21.19$, $p < .001$, episodic, $F(3,69) = 26.7$, $p < .001$, and prospective, $F(3,70) = 84.1$, $p < .001$, memory. With respect to measures of language, groups differed significantly on test of confrontational naming, $F(3,69) = 5.22$, $p < .05$, phonemic verbal fluency (i.e., FAS), $F(3,71) = 3.19$, $p < .05$, and semantic fluency (i.e., Animal Naming), $F(3,71) = 20.37$, $p < .001$. A test of processing speed (i.e., WAIS-III symbol search), also revealed similar significant group differences, $F(3,55) = 14.2$, $p < .001$. Please refer to Table 2 for a detailed description of the expected and observed between group differences across the neuropsychological test measures.

On the subtests of the RBANS, there were significant group differences for nearly all comparisons, including: list learning, $F(3,71) = 34.8$, $p < .001$; story memory, $F(3,71) = 36.1$, $p < .001$; figure copy, $F(3,70) = 11.1$, $p < .001$; line orientation, $F(3,66) = 4.01$, $p < .001$; picture naming, $F(3,71) = 9.57$, $p < .001$; semantic fluency $F(3,71) = 22.8$, $p < .001$; coding, $F(3,70) =$ $p < .001$; list recall, $F(3,71) = 32.8$, $p < .001$; list recognition, $F(3,70) = 24.0$, $p < .001$; story recall, $F(3,71) = 26.8$, $p < .001$; and figure recall, $F(3,70) = 29.3$, $p < .001$. In keeping with the results of the general neuropsychological battery described above, no significant group differences were detected on a measure of digit span, $F(3,71) = 2.5$, $p = .65$. All index scores on the RBANS also differed significantly, including the total scale score, $F(3,66) = 59.2$, $p < .001$, and scale score measures of immediate memory, $F(3,71) = 58.2$, $p < .001$, visuospatial/constructional skills, $F(3,66) = 10.7$, $p < .001$, language, $F(3,71) = 25.7$, $p < .001$, attention, $F(3,70) = 11.4$, $p < .001$, and

delayed memory, $F(3,69) = 70.5, p < .001$. These between group differences are also summarized in Table 2.

Experimental Results

Single-Task Walking and Counting Rates. The average walking and counting rates during the two 15s single-task baseline trials for the four groups are shown in Table 3.

Single-task walking. To examine the single-task walking data for baseline differences among groups, a one-way ANOVA was used to analyze the average single-task walking rates for the four groups (healthy controls, aMCI, early-stage AD, moderate AD). Partial η_p^2 is reported as a measure of effect size. Analyses revealed significant group differences in baseline walking rates, $F(3,71) = 3.19, p < .05, \eta_p^2 = .261$. Post-hoc analyses were conducted using Gabriel's pairwise test procedure to control for type I error given the differences in sample size among the groups. Contrasts revealed that the healthy control group ($M = 52.8$ feet, $SD = 8.9$) walked significantly further during the 15s baseline trials than the moderate AD group ($M = 44.8, SD = 9.6$) $F(3, 71) = 7.34, p < .001, \eta_p^2 = .201$. There were no significant differences in walking rates among the healthy control group, the MCI-amnesic group ($M = 45.7, SD = 9.7$) or the early AD group ($M = 47.3, SD = 10.8$).

Single-task counting. The verbal counting data for the single-task conditions were analyzed in a repeated measures 4 (Group) X 2 (Complexity: simple, complex) ANOVA with group as the between-participants factor and task complexity (i.e., simple or complex) as the within-participants repeated measure. A main effect of task difficulty was detected, $F(1,71) = 103.4, p < .001, \eta_p^2 = .359$ with all four groups producing significantly more digits in the simple ($M = 36.0$ digits) condition when compared to the complex condition (overall $M = 12.3$ digits). A main effect for group was also detected, $F(3,71) = 7.36, p < .05, \eta_p^2 = .203$ indicating

that, across conditions, counting rates differed significantly across the four groups. A significant Group X Task Complexity interaction was also detected, $F(3,71) = 3.06, p < .05, \eta_p^2 = .191$ suggesting that the main effect for group was conditional on the complexity of the counting task. Contrasts revealed that while groups did not differ on simple counting, patients in the moderate group produced significantly fewer digits, $F(3,71) = 13.25, p < .001, \eta_p^2 = .235$ in the complex condition ($M = 8.6, SD = 2.8$) than the healthy control group ($M=15.6, SD=3.8$), the MCI-Amnesic group ($M=12.3, SD=3.7$), or the early-stage AD group ($M=.12.5, SD=3.8$)

Dual-Task Walking and Counting

To account for the expected and confirmed single-task differences between the healthy and cognitively impaired participants, interference in the dual-task condition was expressed as a percent decrement score. A decrement score allows for an assessment of the proportional change in an individual's performance during dual-task conditions relative to his/her performance during the single-task conditions. For distance covered and for digits produced, the percent decrement scores for the simple (i.e, walking and counting by 1's) and the complex (i.e., walking and counting backwards by 2's) trials were calculated and are displayed in Table 3. For the walking and counting dual-task data, two separate 4(Group) X 2 (Complexity) repeated measures ANOVA's, with group as the between participants factor and task complexity (i.e., simple, complex) as the within participants repeated measure, were carried out on the walking and counting percent decrement scores. Partial η_p^2 is reported as a measure of effect size.

Walking Decrement Scores. The average distance in feet covered during the dual-task trials and the corresponding percent decrement scores are presented in Table 3. The analysis on the walking percent decrement scores revealed a significant main effect for task difficulty, $F(1,71) = 116.8, p < .001, \eta_p^2 = .336$ indicating that, regardless of group, the percent decrement

score was significantly greater when walking was combined with the complex versus the simple verbal counting task. Across groups, walking rates decreased by 4.5% in the simple dual-task condition and by 21.8% in the difficulty dual-task condition, relative to the single-task walking rate. Unexpectedly, there was no main effect for group, $F(3,71) = 1.59, p=.200, \eta_p^2 = .044$ however, a significant Complexity by Group interaction was detected, $F(3,71) = 6.384 p<.001, \eta_p^2 = .212$ indicating that significant group differences were evident, but only during the complex dual task. Post-hoc comparisons on the walking decrement data revealed that the moderate AD group ($M=31.5\%, SD=12.9$) was disproportionately more impaired than the healthy control group ($M=16.1\%, SD=12.9$) by the concurrent performance of a complex counting task $F(3,71) = 5.52, p<.01, \eta_p^2 = .189$. As hypothesized based on Study 1 results, contrasts revealed that there were no significant differences between the healthy control participants, the aMCI patients ($M=20.6\%, SD=14.2$), or the early-stage AD patients ($M= 22.5\%, SD=14.9$) on the complex walking dual-task decrement data .

Counting Decrement Scores. The analysis on the counting percent decrement scores revealed no main effect for complexity, $F(1,71) = .799, p=.374, \eta_p^2 = .011$ or group, $F(1,71) = .515, p=.674, \eta_p^2 = .009$. However, a significant group by complexity interaction was detected, $F(1,71) = 3.11, p<.05, \eta_p^2 = .125$. As can be seen from Figure 1, this interaction appears to be due to the fact that the moderately impaired AD group members performed differently than the other groups on the simple and complex counting tasks. Although pairwise comparisons only approached significance, the moderate AD group had the least amount of interference in the complex counting conditions ($M=5.52\% SD = 25.3$) whereas they had the highest amount of interference in the simple counting condition ($M= 17.0\%, SD=16.7$). In contrast to the other groups, the moderate AD participants showed relatively small interference

effects when walking was combined with a complex counting task. This is an unusual pattern of results, which is most informative when reported in relation to the gait dual-task decrement scores. As shown in Figure 1, although all groups performed equivalently during the simple baseline counting task (i.e., forward by 1's), there was a significant and expected difference between the healthy older adults and moderate AD groups during baseline walking. When simple counting was combined with speeded walking, the walking rate was relatively well preserved for all four groups, but presumably at some cost to the speeded counting rate for the mild and moderate AD groups. In contrast, during the baseline complex dual-task, the Moderate AD group produced significantly fewer digits compared to the other groups. When combined with speeded walking, the complex counting rate was relatively well maintained by the Moderate AD group (5.5% decrement) compared to the other groups (13.9%, 17.2%, and 16.5% interference, respectively), but at a greater cost to the speeded walking rate which dropped over 30% in this group. In summary then, although the healthy participants, the aMCI participants, and the early stage AD groups tended to perform equivalently across the single and dual-task conditions, in Study 2, the Moderate AD group demonstrated unique and contrasting patterns of interference during the simple and complex dual-task trials. Specifically, moderately impaired AD participants were able to maintain their speeded walking rate in simple dual-task conditions when compared to single task performance, but at some cost to speeded cognitive task performance. However, during complex dual-tasks, speeded walking rates showed significantly higher levels of interference for the moderately impaired group, while the counting rate was relatively well maintained when compared to their single task performance.

Discussion

This study further investigated conclusions derived from previous research that after an initial amnesic stage in AD, divided attention, as measured by a gait-dual task, is among the first non-memory domain to be affected by the illness. To account for the limitations of previous studies, which have failed to specify the severity of their AD patients, the current study examined the concurrent performance of a simple and complex arithmetic verbal counting task on a walking task in three diagnostic groups with aMCI (3MS scores from 90-100), early stage AD (3MS scores from 77-91), and moderate AD (3MS scores from 59-76) and compared their performance to a group of healthy older adults.

In keeping with previous dual-task literature that has manipulated the level of task complexity (i.e., Crossley et al., 2004) analysis of the gait dual-task percent decrement scores revealed a significant and expected effect for task difficulty, indicating that regardless of group the percent decrement score was significantly greater when walking was combined with the complex versus the simple counting task. Specifically, across groups, walking rates decreased by 4.5% in the simple dual-task condition and by 21.8% in the difficult task condition, relative to the single-task walking rate. However, in contrast to previous gait dual-task studies, but consistent with Study 1 from our lab, when percent decrement scores were examined for between group differences, analyses showed that those with aMCI and early-stage AD had comparable performance to the group of community dwelling, healthy older adults, on both a simple and a complex dual-task. That is, although the counting tasks affected AD patients walking rate, when baseline slowing rates were accounted for using percent decrement scores, individuals with aMCI and early stage AD were no slower than the community dwelling healthy older adults under simple and complex dual-task conditions. As hypothesized, there were no significant

differences between the healthy control participants (16.1%), the aMCI patients (20.6%) or the participants with early-stage AD (22.5%) on the complex dual-task. Therefore, in keeping with the results of Study 1, the current study lends further support to the notion that aMCI and early stage AD are not associated with impaired gait dual-task performance. In comparison, significant differences were detected between the moderate AD group (31.5%) and the normal healthy control group (16.1%) on the complex dual-task condition. This suggests that when overall degree of dementia severity is controlled for by subdividing patients according to diagnostic and staging criteria, the specific deficit in divided attention is apparent much later in the progression of AD than has been previously theorized, at least as measured by gait dual task performance.

By contrast, and in keeping with diagnostic criteria, impairments in episodic memory, attention and executive functioning were present in the early-stage AD, moderate-stage AD groups, and to a lesser extent in the group with aMCI on formal neuropsychological testing, when compared to the healthy older adults. Specifically, individuals with early-AD, moderate AD, and aMCI performed more poorly than the healthy older adults on part B of the Trail Making Test, which is also known to require divided attention and executive functioning. Not surprisingly, the Moderate AD group was also found to perform more poorly than the aMCI and early-stage AD group on this measure as well. Similarly, and by definition, the aMCI group, early-AD group and moderate AD group also performed significantly lower than the healthy older adults on a task of episodic memory (i.e., Grasshoppers and Geese test). Also, although there were no difference between the aMCI group and the early-stage AD group, the patients with AD and aMCI performed significantly worse than the normal controls on the RBANS measures of immediate and delayed memory. These findings help to shed light on previous lines of research which have suggested that gait-dual-task performance is sensitive to the influence of

deficits in executive functioning and divided attention, even early in the progression of AD (Yogev-Seligmann et al., 2008).

Few previous dual-task studies have used well-established clinical and research criteria to define patient groups for the purposes of investigating divided attention in early and pre-clinical AD. However, when taken together with the current results, what these studies suggest is that when participants with probable and “pre-clinical” AD are divided by severity using a rigorous methodology, only the more advanced patients (who generally demonstrate impairments on most cognitive measures) are impaired on the dual-task paradigm (i.e., Greene et al., 1995; Perry et al., 2000; Lonie et al., 2009). In keeping with this argument, Perry and colleagues (2000) have reported intact dual-task performance in “mildly impaired” AD patients during tasks combining speeded box joining and a verbal digit span task, despite already having impairments in episodic memory. Similarly, Greene et al. (1995) found that individuals in the earliest amnesic stages of AD (i.e., minimal dementia) performed normally on two different dual-task paradigms. Lonie and colleagues (2009) also examined the potential use of the dual task paradigm as a sensitive measure of AD, early in the disease process. They administered a modified dual task paradigm (a digit span and visuospatial tracking task) to groups of individuals with aMCI, early AD, and depressive symptomatology and compared their performance to a group of healthy older adults. As in the current study, all groups were closely matched for age and pre-morbid intellectual ability. In keeping with our results, Lonie and colleagues found there were no group differences in dual-task performance, despite the fact that the aMCI and early AD group were impaired on tasks of episodic memory. Therefore, it appears that the interpretation of cognitive performance in groups of patients designated with probable AD, largely depends on subdividing patients

according to dementia severity in order to understand and isolate when specific impairments in divided attention become apparent.

However, one of the limitations of the current study is the extent to which comparisons between previous laboratory based upper extremity dual-tasks and functional gait dual-task procedures can be drawn. Although the dual-task paradigm in general is well regarded as a valid measure of divided attention, caution must be taken when generalizing the results of the current study to previous dual-task work, particularly upper-extremity dual-tasks such as finger tapping. Indeed, the majority of previous experimental dual-task studies have utilized less ecologically valid measures, such as finger tapping or speeded box joining, and have provided support for the conclusion that deficits in divided attention consistently occur in the earliest stages of the illness (i.e., Crossley et al., 2004, Perry & Hodges, 1999). Although speeded walking and finger tapping share similar characteristics and are both believed to be relatively automatized motor tasks, recent evidence suggests that walking is a much more complex and attentionally demanding task that may require other specific cognitive processes, especially in individuals with AD (Rapp, Krampe, & Baltes, 2006; Hausdorff, Yogev-Seligmann, Springer, Simon & Giladi, 2005).

Empirical evidence shows that postural control and gait, which are often viewed as highly automatized skills, become increasingly difficult in both normal and pathological aging and that this deficit is apparent in dual-task situations when individuals are given an attentional load while walking (Li, Krampe, & Bodnar, 2005). Not surprisingly then, there is also increasing evidence that a relationship exists between dual-task related gait changes and falls among older adults, especially those with AD. Although these changes certainly relate to higher brain functions such as attention and pathological processes in brain structures that modulate gait, other authors have suggested that dual-task performance in AD also involves a breakdown in a

cognitive “priority process” by which healthy subjects favor the execution of motor components over the execution of cognitive strategies (Bloem et al., 2006; Rapp et al., 2006; Yogev-Seligmann et al., 2008). Termed by some authors as the “posture first” strategy, it has been suggested that young and neurologically healthy individuals are able to cope with complex dual-task situations by adopting “safe strategies” (i.e., prioritizing balance over other concurrent tasks), and that such behavior is less often seen in older persons, and in particular, persons with AD. Rather, authors such as Yogev-Seligmann and colleagues (2008) suggest that patient populations (i.e., AD and Parkinson’s disease) inappropriately use a “posture second” strategy which decreases their performance under dual-task conditions and exacerbates their risk of falling.

Similar theories of successful aging such as the framework of Selection, Optimization and Compensation (SOC; Baltes & Baltes, 1990) also emphasize the adaptive value of selecting tasks of higher immediate value (i.e., walking) over less critical tasks (Baltes & Baltes, 1990; Freund, Li & Baltes, 1999; Li et al, 2005; Rapp et al., 2006). In what authors have termed the “ecological approach to multitasking”, the SOC model is a lifespan approach which postulates that individuals must continuously adapt to opportunities and constraints in their environment, which change throughout the life course. For the older adult or patient with AD, selection involves goals or outcomes such as prioritizing the maintenance of balance at the cost of cognitive tasks in attentionally demanding or challenging situations. Optimization relates to goal-relevant means, such as practice. Finally, Compensation denotes the use of alternative means to maintain performance in the face of loss of means (i.e., using walking aids to maintain mobility; Li et al., 2005).

According to Li and colleagues (2005) an excellent example of SOC processes at work can be found in the area of gait dual task performance in healthy and pathological aging. In this case, selection involves the maintenance of postural stability at the cost of excelling in cognitive performance under dual-task conditions. The SOC's model of adaptive resource allocation would predict that when facing potentially threatening challenges (e.g., such as postural sway or the fear of falling), older adults and those with AD will invest most of their cognitive resources into maintaining their stability. That is, they should prioritize gait at the cost of cognitive performance.

Interestingly, the moderately impaired AD group in the current study showed a unique and contrasting pattern of interference in the simple and complex dual-task trials which is consistent with the predictions of the SOC model and suggests that the later stages of AD may be associated with a breakdown in the posture first strategy. It is important to note at the outset that individuals in the current study were not given any specific instructions regarding task prioritization, rather they were told to direct their attention equally to both the walking and the cognitive task. In the simple dual task trial, individuals with moderate AD were able to protect their walking rate (2.2%) over their counting rate (17.0%), which would suggest a relative prioritization of balance over the cognitive task under relatively simple conditions. However, when percent decrement scores are examined in the complex dual-task condition, individuals with Moderate AD, show a relative preservation in their counting rate (5.5%) at a large expense to their walking rate (31.5%). In fact, when single task differences are controlled for, individuals with Moderate AD counted faster and made fewer errors in the complex condition than did the normal healthy controls (13.9%); the group with aMCI (17.2%), or early stage AD (16.5%), when compared to baseline performance. This is an unusual pattern of interference when

compared to the other diagnostic groups which all showed higher interference in dual-task counting rates during complex dual-task trials. Thus, these results suggest that under increasing cognitive demand (i.e., a complex dual-task) individuals with moderate AD may have a breakdown in those cognitive prioritization processes that allow them to prioritize gait over the competing cognitive task. It is possible that individuals with Moderate stage AD use a “posture second” strategy which may be a contributing factor to their slowed gait performance (Bloem et al., 2003) and well-documented increased risk of falling (Shaw, 2002).

The added element of task prioritization and selection and optimization while walking may help explain some of the discrepancies between the findings of upper-extremity dual-tasks, and the current gait-dual task procedure. As noted previously, most upper extremity gait dual tasks (i.e., finger tapping, box joining) show that individuals in the earliest stages of AD are impaired on tasks of divided attention. However, given that there is likely little perceived threat to poor finger tapping or box joining performance, experimental upper extremity tasks may be considered a “purer” measure of divided attention as they likely do not trigger task prioritization cognitive processes. In contrast, previous research has shown that balance and gait is considered a task with high adaptive value in normal and pathological aging: falls, and accidents related to falls are a major cause of morbidity and mortality in older individuals with and without AD, and the rate of falls increases with progressive dementia (Li et al., 2005). Given the increased fall risk, maintaining postural control has higher immediate functional value than a cognitive task. Therefore, from the perspective of SOC, gait dual-task procedures would add the additional cognitive load of successful task prioritization.

In summary, it is possible that a clear interpretation of impairments in divided attention from gait dual-task studies is confounded by the additional cognitive process of goal setting,

selection, optimization and compensation that are unique to walking based experimental measures. In a sense, poor gait dual-task performance may be accounted for by a decline in divided attention, as well as by inappropriate prioritization of limited cognitive resources. Other theorists have also suggested that individuals with progressive AD may make poor decisions about task priority due to behavioral problems, such as a lack of insight due to co-existent cognitive deficits (Alexander & Hausdorff, 2008). Decreased attention and judgment in individuals with AD may cause them not to recognize obstacles or hazards, an issue which is yet to be addressed in the gait-dual task literature.

Regardless of the important functional implications of task prioritization models, few studies have specifically investigated dual-task performance in older adults and patients with AD to explore patterns of task prioritization between a cognitive and a motor task. The issue of task prioritization was addressed by Rapp, Krampe, and Baltes (2006), however, who combined a working memory with a postural control task under easy and difficult conditions in patients with mild AD, older adults, and young adults. Consistent with previous studies of divided attention in aging and AD, the authors found a large dual-task performance decrement with age and more so in AD. Importantly, when the authors manipulated the difficulty of the balance task to be of higher functional significance (i.e., increase fall risk), a reversal in the pattern of dual-task performance was observed in the older adults and more so in the patients with AD. That is, in the more difficult balance task, older adults' and AD patients' relative level of performance increased rather than decreased. At the same time, performance levels on the cognitive task decreased when balance was made more difficult. Therefore, Rapp and colleagues (2006) concluded that the maintenance of postural control occurred at the expense of working memory performance in older adults and patients with AD. They suggest that these results indicate that

the selective allocation of resources (i.e, goal selection) may be functionally different from divided attention performance and that goal selection is preserved in mild AD, despite large performance deficits in divided attention. According to Yogev-Seligmann et al. (2008) this conclusion makes intuitive sense, as the simultaneous performance of two attention demanding tasks not only causes a competition for attention, but challenges the brain to prioritize one task over another. This conclusion is also supported by neuroanatomical studies which show that the prefrontal cortex and the anterior cingulate cortex are activated both under dual-task conditions and during the process of prioritization.

In conclusion, the current study used a gait-dual task procedure to further investigate divided attention performance in normal aging, aMCI, early stage AD, and moderate stage AD. In contrast to previous gait dual-task studies which generally involve one group of patients varying in severity from minimal to severe, our results suggest that when participants with AD are divided into distinct diagnostic categories using a reliable method, only those individuals with Moderate AD are impaired on the complex dual-task condition. By contrast, the individuals with aMCI, early-stage AD, and moderate stage AD were impaired on formal neuropsychological measures assessing episodic memory, attention and executive functioning (i.e., Trails B, Grasshoppers and Geese episodic memory trial, RBANS Immediate and Delayed Memory Index scores). Thus, it is possible that individuals in the earliest stages of AD are not impaired on gait dual-tasks as previously widely theorized or that the gait dual-task paradigm is relatively insensitive for use as an adjunct cognitive tool in the early identification of AD. Therefore, the strengths of this study include using a clinical and research based methodology to examine participants at different stages of AD severity, an approach which has not been widely used in the gait dual-task literature. The gait dual-task paradigm used in the current study also

differs from previous studies by manipulating the level of task complexity, and utilizing an arithmetic counting task which is known to be a more reliable secondary task than verbal fluency procedures (Beauchet et al., 2005). Last, the current study compared the performance of groups of individuals with AD to an age and education equivalent healthy control group, which allowed for good control for the effects of age and education.

An examination of the literature on task prioritization suggests that the interpretation of these results is limited in breadth by current models of attention, dual-task performance and executive control. The unexpected pattern of interference observed on the counting complex dual-task condition in the moderately impaired AD group suggests that the progression of AD, while almost certainly associated with deficits in divided attention, may also be associated with a breakdown in the cognitive prioritization processes necessary for successful maintenance of balance and gait. Thus, how cognition affects gait in individuals with AD likely involves factors not assessed by the current gait dual-task paradigm, and this system is likely built by components of cognitive, physical, and task prioritization capacities, and modulated by disease severity, task complexity and the environment (Yogev-Seligmann et al., 2008).

Therefore, a fruitful avenue for future research could aim at identifying the neural and cognitive processes underlying adaptive resource allocation in healthy and pathological aging. In particular, the nature of the relationships among dual-task methodology, divided attention performance, and the mechanisms of task prioritization remain unclear. Also, the possibility of improving gait stability and brain functioning using methods of cognitive rehabilitation and dual-task training has not been well studied. According to some authors, the re-training of dual tasking abilities should be possible for individuals affected by dementia and this has been examined in some neuropsychological studies (Brauer et al., 2011; Beherer et al., 2006; Li et al.,

2010; Pellecchia, 2005; Schwenk, Zieschang, Oster, & Hauer, 2010; Toulotte, Thevenon, & Fabre, 2006; Verghese & Holtzer, 2010; Yang, Wang, Chen, & Kao, 2007). For example, a pilot study in 2006 by Toulotte, Thevenon, and Fabre found that individuals could be trained using single and dual task exercises aimed at improving balance, and that significant improvements in balance and gait speed were observed under single and dual-task conditions. Although these findings suggests that interventions can be designed to help patients improve their functioning, many questions remain about best practice interventions to improve dual-tasking during walking in clinical and normal older adult groups. Given that the majority of the neuropsychological literature to date has focused on describing the deficits associated with AD, developing strategies that hold promise for intervention is an emerging area of study that certainly warrants increased research efforts.

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Table 1.

Age, Education and Estimated Premorbid IQ Scores for Healthy Controls and for Clinical Groups with aMCI, Early-stage AD, and Moderate AD.

	Healthy Controls	aMCI	Early AD	Moderate AD	F	<i>p</i>
	Mean (<i>SD</i>)	Mean(<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)		
<i>N</i>	27	16	15	17		
Age (yrs.)	74.8 (8.88)	76.1(7.19)	73.9(5.59)	73.4(8.67)	.360	.728
Range	57-92	64-82	64-82	54-87		
Education(yrs.)	12.1(2.26)	11.4(3.76)	11.9(2.89)	11.0(2.55)	.570	.636
Range	8-16	8-22	8-17	8-16		
WRAT-III(raw)	47.7(5.94)	45.1(4.50)	47.3(5.60)	41.1(6.39)	5.21	.003*
Range	37-57	36-52	39-56	30-50		

*indicates significance at $p < .05$

Wide Range Achievement Test (3rd Edition; WRAT-III) Reading subtest is scored out of a total of 57

Table 2.

Average (SD) Neuropsychological Test Scores for Healthy Controls, aMCI, Early-Stage AD, and Moderate-Stage AD groups.

	Healthy Controls	aMCI	Early Stage AD	Moderate AD	<i>p</i> -values
Instrument					
N	27	16	15	17	
<i>Screening Instrument</i>					
3MS ¹	96.3(2.61) ^a	87.3(5.93) ^b	83.07(3.92) ^c	70.41(4.91) ^d	<i>p</i> <.001
<i>Pre-morbid IQ</i>					
WRAT-III reading ²	47.7(5.94) ^a	45.1(4.50) ^a	47.3(5.60) ^a	41.1(6.39) ^b	<i>p</i> <.001
<i>Attention & Executive Functions</i>					
Digit Span ³					
Forwards	6.37(1.04) ^a	6.25(.86) ^a	5.80(1.21) ^a	5.71(.92) ^a	NS
Backwards	4.70(1.33) ^a	4.63(1.31) ^a	3.80(1.27) ^{ab}	3.44(1.10) ^b	<i>p</i> <.05
Trail Making Test ⁴					
Trails A	37.8(9.83) ^a	42.5(14.9) ^a	57.8(23.4) ^a	89.1(67.0) ^b	<i>p</i> <.001
Trails B	93.9(40.7) ^a	134.5(41.7) ^{ab}	148.8(63.6) ^b	198.5(60.5) ^{bc}	<i>p</i> <.001
Stroop Test ⁵					
Color	112.0(.56) ^a	111.8(.60) ^{ab}	111.7(.62) ^{ab}	111.0(1.67) ^b	<i>p</i> <.05
Color-word	86.7(18.7) ^a	65.9(18.5) ^b	56.8(22.9) ^b	46.3(21.2) ^b	<i>p</i> <.001
<i>Memory</i>					
Grasshoppers & Geese ⁶					
Semantic Pairs	51.2(1.42) ^a	48.4(3.27) ^b	45.8(3.62) ^{bc}	44.1(4.17) ^c	<i>p</i> <.001
Episodic	27.0(2.18) ^a	25.1(2.10) ^a	20.4(3.11) ^b	21.7(3.07) ^b	<i>p</i> <.001
Memory					
Prospective	.42(.76) ^a	3.38(1.09) ^b	3.53(1.06) ^b	3.94(.24) ^b	<i>p</i> <.001
<i>Language</i>					
COWA ⁷	37.1(13.4) ^a	34.6(12.4) ^{ab}	35.5(9.84) ^{ab}	26.1(10.6) ^b	<i>p</i> <.05
Animal Naming ⁸	19.1(5.04) ^a	12.8(4.92) ^b	11.5(4.76) ^b	8.5(3.64) ^b	<i>p</i> <.001
Confrontational Naming ⁹	32.7(2.73) ^a	31.8(3.32) ^a	30.2(5.58) ^{ab}	27.9(4.28) ^b	<i>p</i> <.05
<i>Processing Speed</i>					
WAIS-III Symbol Search ¹⁰	25.3(5.0) ^a	21.7(7.31) ^{ab}	17.9(6.69) ^{bc}	11.7(6.46) ^c	<i>p</i> <.001
<i>RBANS Index</i> ¹¹					
Immediate Memory	103.3(12.6) ^a	77.4(10.5) ^b	70.2(11.4) ^b	58.6(11.5) ^c	<i>p</i> <.001
Visuospatial	101.0(15.3) ^a	94.2(14.1) ^a	83.1(18.4) ^b	75.1(13.1) ^b	<i>p</i> <.001
Language	105.5(10.4) ^a	95.1(10.4) ^b	86.0(12.6) ^b	78.4(9.1) ^b	<i>p</i> <.001
Attention	101.6(16.5) ^a	90.33(10.3)	82.5(18.4) ^{ab}	75.1(14.7) ^b	<i>p</i> <.001

AGING, ALZHEIMER'S DISEASE, AND GAIT DUAL-TASK

Delayed Memory	95.5(12.1) ^a	59.7(14.6) ^b	54.3(8.7) ^{bc}	48.6(10.0) ^b	$p < .001$
Total Scale Index	101.4(13.9) ^a	77.8(6.7) ^b	67.4(10.4) ^{bc}	59.1(6.9) ^b	$p < .001$
<i>RBANS Subscales</i>					
List learning ¹²	26.1(4.5) ^a	17.8(3.9) ^b	14.5(3.9) ^b	14.4(3.2) ^b	$p < .001$
Story memory ¹³	17.3(3.2) ^a	13.2(2.8) ^b	10.1(3.5) ^b	7.2(3.7) ^c	$p < .001$
Figure copy ¹⁴	17.6(1.8) ^a	17.0(2.0) ^{ab}	15.5(2.6) ^b	13.8(2.5) ^b	$p < .001$
Line orientation ¹⁵	16.3(3.4) ^a	15.9(2.6) ^a	13.6(4.2) ^b	12.7(4.8) ^b	$p < .001$
Picture naming ¹⁶	9.9(.36) ^a	9.3(.62) ^a	9.2(1.0) ^{ab}	8.7(.85) ^b	$p < .001$
Fluency ¹⁷	21.2(4.3) ^a	17.6(3.9) ^b	15.5(4.8) ^b	11.0(2.8) ^{bc}	$p < .001$
Digit Span ¹⁸	10.1(2.2) ^a	9.5(1.7) ^a	8.7(2.3) ^a	8.7(1.8) ^a	NS
Coding ¹⁹	39.4(7.2) ^a	33.3(5.0) ^a	27.7(10.9) ^{ab}	19.5(12.5) ^b	$p < .001$
List recall ²⁰	4.4(2.5) ^a	.94(1.9) ^b	.07(.26) ^b	.30(.99) ^{bc}	$p < .001$
List recognition ²¹	18.9(1.4) ^a	15.8(2.3) ^b	15.7(1.8) ^b	13.7(2.7) ^{bc}	$p < .001$
Story recall ²²	8.7(2.2) ^a	3.8(1.9) ^b	1.5(1.7) ^{bc}	.65(1.1) ^d	$p < .001$
Figure recall ²³	9.7(4.7) ^a	3.1(4.4) ^b	1.2(1.4) ^b	.82(1.8) ^c	$p < .001$

Note: Groups with differing subscript are significantly different from one another at $p < .05$. Pairwise comparisons were conducted using Gabriel's pairwise procedure which has been shown to have tight control over Type I error.

¹ The Modified Mini-Mental State Examination(3MS) is a cognitive screening instrument with a maximum score of 100 and a clinical cut-off score of 77/78. ² Wide Range Achievement Test (3rd Edition) Reading subtest is scored out of a total of 57. ³ Digits forward and digits backward are part of the Digit Span subtest of the WAIS-III. The reported scores are the number of digits repeated in the forward and backward order. ⁴ Scores for the Trail Making Test Part A are the number of seconds taken to sequentially join numbers in a random array; scores for Part B are the number of seconds taken to alternatively join number and letter sequences; the higher the score the poorer the performance. ⁵ Stroop neuropsychological screening test are the number of colors and color-words correctly labeled in 120 seconds. ⁶ The Grasshoppers and Geese semantic pairs total is the number of correctly identified items out of 53; episodic memory is the total correctly recalled out of 30; prospective memory requires the participant to recall previous instructions spontaneously, higher scores are indicative of poorer recall. ⁷ The Controlled Oral Word Association Test score is the total number of words beginning with the letters 'F', 'A', and 'S' reported in three 1-min trials. ⁸ The Animal Naming score is the total number of animals named during a 1-min trial. ⁹ The Confrontational naming score is a subtest of the Grasshoppers and Geese; the total score is the number of correctly identified objects out of 35. ¹⁰ The WAIS-III symbol search subtest score is the number of correctly identified symbols in 120s. ¹¹ The RBANS provides an overall total score and index scores for immediate memory, visuospatial/constructional, language, attention and delayed memory; these scores have a mean of 100 and a standard deviation of 15. ¹² The list learning score is the number of correctly recalled words out of 40. ¹³ The story memory score is the number of correctly recalled story details out of 24. ¹⁴ Figure copy tests the examinees ability to copy a complex figure; scores are out of 20. ¹⁵ Line orientation tests the examinees ability to visually identify matching lines; scores are out of 20. ¹⁶ The picture naming score is the number of correctly identified objects out of 10. ¹⁷ The semantic fluency score is the number of correctly names fruits and vegetables in 60s. ¹⁸ The digit span score is the number of digits repeated in the forward condition. ¹⁹ The coding score is the number of boxes correctly coded in 90s. ²⁰ The list recall subtest tests the examinees ability to recall the list of words presented in the list learning subtest; scores are out of 10. ²¹ The list recognition score is the number of correctly identified words from the list learning subtest; scores are out of 20. ²² The story recall subtest requires the examinee to retell the story from the story memory subtest; scores are out of 12. ²³ The figure recall subtest requires the examinee to draw the figure from the figure copy subtest from memory; scores are out of 20.

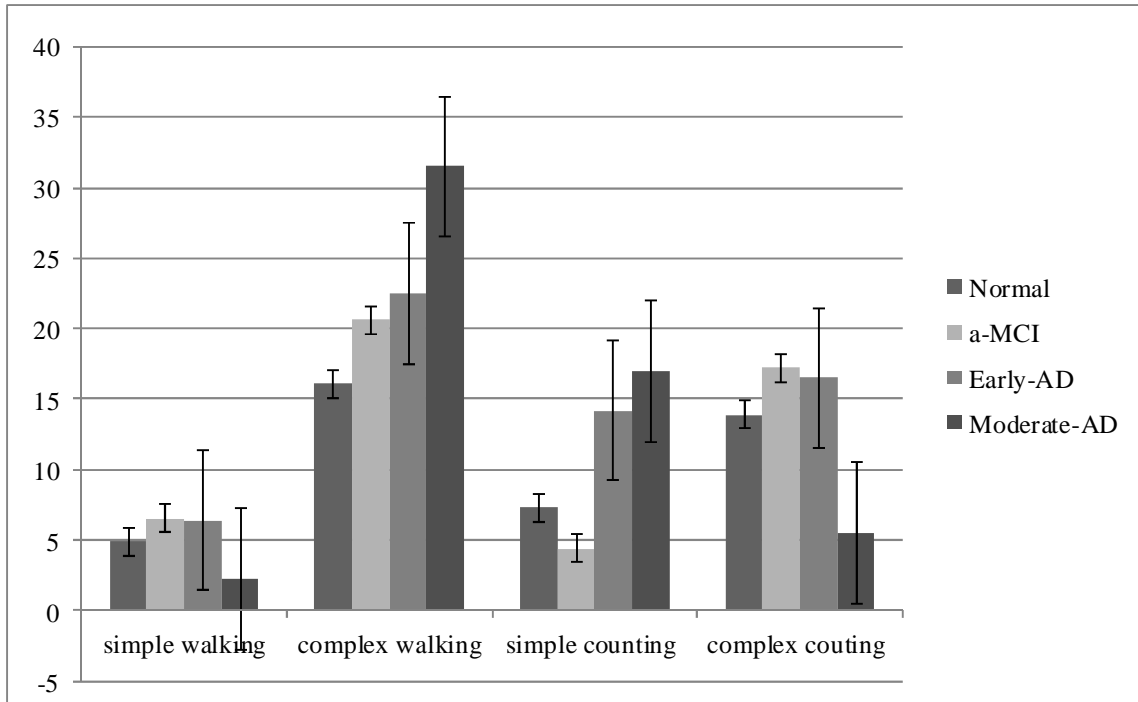
Table 3.

Mean scores (SD) for Healthy Controls and aMCI, Early-Stage AD, and Moderate-Stage AD Patient Groups, Shown as Walking Distance in Feet and Number of Digits Produced Under Single and Dual-Task Conditions, and as Percent Decrements Under Single and Dual Task Conditions.

	Healthy Controls	aMCI	Early-Stage AD	Moderate AD
N	27	16	15	17
Walking Task (Distance in feet)				
Average single-task rate	52.8(8.9)	45.7(9.7)	47.3(10.8)	44.7(9.6)
Average simple dual-task rate	50.3(9.3)	42.9(10.5)	43.9(9.5)	43.9(13.6)
% decrement	4.9%(6.1)	6.5%(6.9)	6.4%(12.1)	2.2%(18.6)
Complex dual-task rate	44.3(8.9)	36.6(11.0)	36.1(8.4)	30.7(9.2)
%decrement	16.1%(8.6)	20.6%(14.2)	22.5%(14.9)	31.5%(12.9)
Counting-Task (Digits produced)				
<i>Simple Condition</i>				
Average single-task rate	37.8(5.0)	34.7(4.3)	35.3(4.9)	36.2(6.2)
Simple dual-task rate	34.9(5.9)	33.2(5.7)	30.3(6.4)	29.6(5.5)
% decrement	7.3%(11.3)	4.4%(12.3)	14.2%(14.2)	17.0%(16.7)
<i>Complex Condition</i>				
Average single-task rate	15.6(3.7)	12.3(3.7)	12.5(3.8)	8.6(2.8)
Complex dual-task rate	13.3(3.7)	10.1(3.6)	10.6(4.2)	7.8(2.4)
% decrement	13.9%(15.6)	17.2%(27.2)	16.5%(15.7)	5.5%(25.3)

Figure 1.

Walking and Counting Percent Decrement Scores with error bars representing standard deviations for the Simple and Complex Dual-Task Conditions for the Healthy Older Adults, and aMCI, Early-Stage AD, and Moderate-Stage AD Clinical Groups.



Running Head: GAIT AND HIGHER BRAIN FUNCTIONS

Study 3: The Role of Higher Brain Functions in Gait Dual-Task Performance

Jocelyn Poock, Margaret Crossley & Vanina Dal Bello-Haas

University of Saskatchewan

Author Note

Jocelyn Poock, Department of Psychology, University of Saskatchewan; Margaret Crossley, Department of Psychology, University of Saskatchewan; Vanina Dal Bello-Haas, School of Rehabilitation Science, McMaster University

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Correspondence concerning this article should be addressed to Jocelyn Poock, Department of Psychology, Arts 154, University of Saskatchewan, 9 Campus Drive, Saskatoon, Saskatchewan, Canada, S7N 5A5. Email: jocelyn.poock@usask.ca

Abstract

The current study examined the relationship between higher brain functions and gait dual-task performance, in simple and complex conditions, and in healthy older adults and individuals at different stages of AD severity (i.e., aMCI, early AD, moderate AD). Neuropsychological test scores were used to create three theoretically based cognitive composite scores (i.e., executive function/attention/speed; episodic memory; language). Multiple regression analyses revealed that the Executive function/Attention/Speed composite was the most potent predictor of gait dual-task performance; however this relationship varied as a function of task complexity. All three composite scores predicted gait performance in the complex dual-task condition, even after controlling for disease severity. These findings suggest that a number of higher brain functions play an important role in mediating gait performance under simple and complex walking conditions.

The Role of Higher Brain Functions in Gait Dual-Task Performance

The significant amount of emerging literature that has investigated dual-task effects on gait performance reflects the importance of this research area and its potential clinical applications. Dual-task paradigms, or “talking while walking” methodology is now the standard way to assess the interaction between gait and cognition (For recent reviews see Al-Yahya, Dawes, Smith, Dennis, Howells, & Cokburn, 2011; Scherder et al., 2008; Yogev-Seligmann, Hausdorff, & Giladi, 2008). In particular, many studies during the past decade have used dual-task procedures to investigate whether gait requires executive functioning and attention, specifically, the ability to divide attention (Al-Yahya et al., 2011; Yogev-Seligmann et al., 2008). Divided attention has been identified as playing an important role in walking in multi-tasking situations, serves as a common dependent variable for examining the attentional demands of various tasks including walking, and has clinical implications for fall risk (Holtzer, Friedman, Lipton, Katz, Xue & Verghese, 2007).

The interference, or dual-task costs, between a cognitive task and walking in dual-task conditions, has been reported for different populations (i.e., healthy older adults, patients with neurological disease), for a wide range of cognitive tasks (i.e., verbal fluency, working memory tasks, reaction time), and in the various components of gait performance (for a recent review see Al-Yahya, 2011; Verhaeghen, Steitz, Sliwinski, & Cerella, 2003). The general interpretation from these experiments is that in the normal aging, and to a larger extent in pathological aging, there is a progressive loss of the executive coordination required to divide attention or to allocate specialized resources among concurrent tasks (Logie, Della Sala, Cocchini, & Baddeley, 2004). Similarly, others have theorized that the progression of AD is associated with a breakdown of task prioritization processes, whereby individuals are no longer able to prioritize posture and

balance over cognitive demands (Rapp, Krampe, & Baltes, 2006). Therefore, the assessment of gait dual-task abilities is increasingly important in the clinical assessment of gait disturbances and the risk of falls.

Despite its clinical importance, the depth of knowledge concerning the relationship between gait and cognition in normal and pathological aging has been limited in previous gait dual-task studies. A large body of recent research shows that gait is multifactorial in terms of its underlying cortical control mechanisms (Al-Yahya, 2011; Holtzer, Mahoney, Izzetoglu, Onaral, & Verghese, 2011; Holtzer, Verghese, Xue, & Lipton, 2006; Holtzer, Stern, & Rakitin, 2005; Persad, Jones, Ashton-Miller, Alexander & Giordani, 2008; Scherder et al., 2007; Wang, Wai, Kuo, Yeh, & Wang, 2008; Watson et al., 2010). Gait is no longer considered a simple automatic motor activity that is independent of cognition; rather it is treated as a higher level of cognitive functioning that involves the integration of attention, planning, memory and other motor and cognitive processes. This gives rise to the possibility that other cognitive processes, rather than solely divided attention are related to gait performance. However, with the exception of a few limited studies, the relation of dual-task performance to other neuropsychological measures in general has not been extensively studied (e.g., Holtzer et al., 2006; Holtzer, Stern, & Rakitin, 2005). This is surprising given the interest in the role of executive functions in gait and the possibility that an informative relationship may exist between standardized neuropsychological measures and gait dual-task performance (Yogev-Seligmann et al., 2008; Holtzer et al., 2005). Neuropsychological assessment has been absent from most previous gait dual-task studies, despite the fact that identifying associations between specific higher brain functions and gait performance has significant clinical and theoretical implications. For example, these associations can provide detailed information relevant to fall risk, demonstrate how specific

cognitive functions may be etiologically related to falls, and identify shared neural substrates that can be implicated in cognitive performance and specific motor outcomes such as gait (Holtzer et al., 2007).

As indicated above, walking is likely multifactorial in terms of its underlying cortical control mechanisms, which in turn gives rise to the notion that separate cognitive processes, like separate neural mechanisms, are also differentially related to walking performance (Holtzer et al., 2006). Specifically, the involvement of the dorsolateral prefrontal cortex (DLPFC), the cingulate gyrus, parietal association areas and the hippocampus would suggest that executive functions, speed of functioning, attention and memory may be cognitive functions that play a role in successful walking (Scherder et al., 2007). If this is indeed the case, cognitive impairment, such as in Alzheimer's disease (AD) should have a negative effect on walking performance, which numerous studies have indicated it does (Al-Yahya et al., 2011). Cognitive impairment has been noted to associate with disorders of balance and gait, and resulting falls in particular (Alexander & Hausdorff, 2008; Sheridan & Hausdorff, 2007; Morgan, Funk, Crossley, Basran, Kirk, & Dal-Bello-Haas, 2007). Individuals with AD have slower gait speed, greater step-to-step variability, larger postural sway (Alexander, Mollo, Giordani et al., 1995; Morgan et al., 2007), and poorer performance on timed balance tasks (Franssen et al., 1999). Compared with age-matched controls, individuals with AD are more likely to land closer to an obstacle after crossing it and are more likely to contact an obstacle in their path (Alexander et al., 1995). Most importantly however, patients with AD are at an increased risk of falls (Herman, Mirelman, Schweiger, & Hausdorff, 2010). A large scale prospective study found that AD patients, when compared to cognitively intact older adults had a three-fold increase in falls causing fracture or hospitalization and that these falls were associated with institutionalization (Shaw, 2002). Falls

in older adults are a significant source of morbidity and mortality and have typically been linked to multiple physical risk factors including muscle strength, motor function, impaired cognitive abilities, and postural control (Herman et al., 2010).

According to Alexander and Hausdorff (2008) research is also now suggesting that declines in cognitive functions such as attention, psychomotor processing, problem solving, and awareness of self and surroundings have a larger impact than physical conditioning on postural control gait and falls than previously recognized. In particular, they suggest that executive function measures are thought to be particularly good predictors of falls (Holtzer et al., 2007; Sheridan & Hausdorff, 2007). Disease related deficits in attention and executive functioning are thought to impair an older adult's ability to compensate for age-associated changes in gait and balance by compromising safe negotiation in complex everyday environment and studies using the dual-task paradigm have been used to study this dependence (for a review see Al-Yahya et al., 2011).

In AD, the progressive decline in cognition is believed to cause disorganization of the network that controls walking, which leads to impaired gait and an increased risk of falls (Sheridan & Hausdorff, 2007). However, to date, no study has been able to fully establish the relationship between gait performance in AD and distinct cognitive processes that deteriorate in AD (e.g., executive and attentional skills). A limitation of previous gait dual-task methodology is the study of divided attention in isolation (Holtzer et al., 2006). That is, without taking into account other brain functions that might contribute to walking. Furthermore, many studies refer to the importance of "executive functions" in general without specifying the constituent processes that it accounts for. Given the literature reviewed here, gait disturbances and fall risk in AD might also reflect the loss of memory functions or a decline in speed of information

processing that are associated with the parietal regions, the DLPFC, the cingulate gyrus and the hippocampus. To date, no studies have examined the relationship between multiple cognitive functions and walking in individuals with AD, using neuropsychological predictors.

In a recent paper, Holtzer and colleagues (2006) attempted to characterize the relationship between higher brain functions and gait in healthy older adults. Whereas previous literature on gait and aging has also been limited by its almost exclusive study of the role of attention in mediating gait, Holtzer and colleagues demonstrated that both general (i.e., verbal IQ) and specific (i.e., executive function, speed of processing, memory) functions were also related to gait in normal aging. They submitted various neuropsychological test scores to factor analysis and revealed four common factors: Verbal IQ, Speed/Executive functions, Attention, and Memory. Subsequent regression analyses revealed that these factors were significant predictors of gait velocity in normal adults, suggesting that the cognitive correlates of successful gait are indeed multifaceted, and that gait is a complex task requiring the involvement of higher order brain functions.

The study described above by Holtzer and colleagues (2006) is the first to characterize the relationship between statistically independent cognitive factors and gait in healthy older adults. However, as Holtzer and colleagues (2006) suggest, it is critically important to replicate these findings, as well as demonstrate them in larger samples with a wider range of cognitive performance. Whereas previous studies have relied on a gait dual-task paradigm to study divided attention in isolation, the current study adapted a two-pronged approach similar to Holtzer and colleagues to evaluate whether specific cognitive factors are related to gait performance under simple and complex dual-task conditions in healthy older adults and individuals at different stages of AD severity. Based on the findings of Holtzer et al. (2006) it was hypothesized that

specific empirically derived cognitive factors (i.e., episodic memory, language, executive functioning/speed/attention) that are related to cognitive decline in AD would predict interference under dual-task conditions. It was further hypothesized that the relationship would vary and executive functioning would be a more significant predictor under complex dual-task conditions.

Methods

Participants

Study 2 and Study 3 report data from the same participant groups. Thirty-two patients referred to a Rural and Remote (RRMC) interdisciplinary memory clinic (Morgan et al., 2009) met the diagnostic standard for probable AD based on the consensus diagnostic criteria used by the RRMC team (i.e., the Third Canadian Consensus Conference on the diagnosis and treatment of dementia, CCCDTD3; Robillard, 2007) and the research criteria published by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS – ADRDA; McKhann et al., 1984). The remaining 16 clinical participants met criteria for amnesic – Mild Cognitive Impairment based on the guidelines of Petersen and colleagues (aMCI; Petersen et al., 1999, 2001). Twenty-seven healthy older adults were recruited from the Saskatoon Council on Aging (SCOA) using a mail campaign. In comparison to Study 2, this study focused on the pooled sample of 75 participants (M age = 74.6) for regression purposes.

The exclusionary criteria for this study have been outlined in detail in Study 2. Briefly, this process included a clinical history, neuropsychological test battery and examination by a physical therapist for all participants. Patients referred to the RRMC also received a medical examination and computed tomography scan (CT) to exclude other forms of neurological disease

as part of their assessment for suspected dementia. All participants reported good general health; however, two healthy volunteers were excluded from the analysis because of a pattern of scores on neuropsychological testing that were suggestive of cognitive impairment. Similarly, five patients were removed from the study due to respective histories of chronic alcohol abuse, meningitis, mild traumatic brain injury, cerebrovascular disease (i.e., mixed dementia), and an adult diagnosis of Attention Deficit Hyperactivity Disorder (ADHD).

Measures

Neuropsychological Test Battery. All participants completed neuropsychological tests which form part of the standardized battery at the RRMC (Morgan et al., 2009) and were selected to encompass a broad range of cognitive functions. The protocol included both standardized neuropsychological measures as well as research tests, previously developed to assess specific cognitive abilities (i.e., Grasshoppers & Geese Test; Lanting & Crossley, 2007). The tests included a cognitive screening instrument (The Modified Mini-Mental State Examination; Teng & Chui, 1987), measures of attention and executive functions, including: the Stroop Neuropsychological Screening test, (Trennery, Crosson, DeBoe & Leber, 1989); Trail Making Tests, Part A & B, (Reitan, 1992), and the Digit Span Forward and Backward subtest of the WAIS-III (Wechsler, 1997). Also included were measures of episodic, semantic, and prospective memory (Grasshoppers & Geese Test; Lanting & Crossley 2007), as well as measures of phonemic fluency (Controlled Oral Word Association test or FAS; Spreen & Benton, 1977), semantic fluency (Animal Naming, Goodglass & Kaplan, 1983), confrontational naming (Grasshoppers & Geese Test; Lanting & Crossley, 2007) and processing speed (Symbol Search subtest of the WAIS-III, Weschler, 1997). All participants also completed the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998), which was

designed to screen for dementia in older adults. The RBANS consists of 12 subtests assessing the cognitive domains of immediate and delayed memory, attention, visuospatial/constructional abilities, and language.

Cognitive Composite Scores. To reduce the number of variables for analysis and to provide more stable measures of underlying cognitive abilities, three theoretically determined composite scores were formed from standardized Z-scores of the constituent neuropsychological tests for each cognitive domain described above. A composite score is a sum or average of other variables, and is used frequently in neuropsychological research (Bentler, 2007). In this case, each composite is an average of the constituent age corrected Z-scores, whereby each variable is equally weighted. This process is described in detail below.

A number of advantages to using theory driven Z-score composites over more data driven approaches (i.e., factor analysis) have been noted, particularly when working with constructs that are multifactorial in nature, such as executive functioning. As noted by Strauss, Sherman & Spreen (2006) factor analysis often does not provide adequate insight into the measurement of complex abilities such as attention and executive functioning. These tasks in particular tend to load on multiple, abstract factors, such as “cognitive set-shifting,” “visuospatial sequencing,” “rapid visual search,” “focused mental processing speed,” and “ability to divide attention” (Strauss et al., 2006). Miyake et al. (2000) also noted that the intercorrelations among different executive tasks are often low and tend to yield multiple separate factors (rather than a single unitary factor) on batteries of executive tasks. Miyake et al. (2000) used these findings to argue that factor analysis is not appropriate for categorizing higher brain functions that are multifactorial in nature, and to suggest that a theoretically driven composite score can have a higher degree of internal consistency if properly developed (Miyake et al., 2000). Furthermore,

from a statistical perspective, Z-scores composites are an effective way to reduce the number of variables for analysis while helping to control for multicollinearity when working with measures, such as neuropsychological tests, that tend to be highly correlated with one another.

The present study aimed to use a balanced composite development approach based on the recommendations of Bentler (2007) who suggested that composite development be guided by the following: (1) the use of measures with a high degree of construct validity; (2) the intercorrelations between measures; (3) the purported use of the measure in the literature and the theoretical constructs it is assumed to capture; and, to a lesser extent, (4) previous data-driven factor analytic approaches. Decisions about including neuropsychological tests in the three composite scores are described in detail below. Although five composite scores (i.e., Immediate Memory, Delayed Memory, Visuospatial/Constructional Skills, Language, Attention/Executive Functions, and Processing Speed) were originally proposed, the number of composites was reduced to three to ensure adequate power to detect both the overall regression model and the contribution of each individual predictor.

Executive Functioning/Attention/Speed Composite. The following tests represented the Executive Functioning/Attention/Speed Composite domain and included both verbal and nonverbal materials: Trail Making Test - Form A (time); Stroop color form (time), and word color form (number correct); Digit Span Backwards subtest of the WAIS-III; Symbol Search subtest of the WAIS-III; Attention Index score of the RBANS (comprised of Digit Span Forward and Coding subtests; and, COWA test including letters F, A and S. Table 2 shows the raw correlation matrix among these constituent neuropsychological measures. It can be seen that the correlations between measures generally supports the idea that they are measuring similar constructs as each set of tests had moderately high and significant internal correlations.

In addition to being intercorrelated, neuropsychological tests were included in this composite to reflect the multicomponent model of executive functioning, which is often associated with working memory and attentional control (e.g., Baddeley, 1986; Burgess & Shallice, 1997) as well as frontal lobe functioning. Therefore, this composite incorporated speech based phonological information (i.e., Digit Span), visuospatial information (i.e., Trail Making Test), and information processed by the central executive system which is thought to more generally reflect executive functioning, such as cognitive shifting, inhibition and planning. Numerous factor analytic studies have shown that these processes of shifting and problem solving also load highly on tests of attention, which has been described as a kind of supervisory control system for other higher brain functions (Spreeen & Strauss, 2006). In this model, attention is conceptualized as sharing several overlapping functions with executive functions. The inclusion of tasks of processing speed in this composite is also an important one. Most tests of attention and executive functioning are timed measures, requiring motor speed and information processing speed. As noted by Holtzer and colleagues in their study of neuropsychological predictors of gait velocity, any interpretation of the relationship between this predictor and the outcome variable, must be made in the context of the relationship between executive functioning, attention, and speed of processing. Thus, this composite domain was constructed to be comprehensive and to reflect these multicomponent processes.

Episodic Memory Composite. The following tests represented the episodic memory domain: Episodic Recognition of the Grasshoppers and Geese Test; and, Delayed Recall Index score of the RBANS (comprised of List Recall and List Recognition, Story Recall and Figure Recall subtests). The Episodic Recognition memory measure was significantly related to the

overall RBANS Memory Index, $r=.64$, p (one-tailed) $<.001$, suggesting a high degree of internal consistency for this domain.

Tests were included in this domain to reflect episodic memory functioning for both verbal and non-verbal material, as well as different retrieval conditions, including free recall, cued recall and recognition. Memory is not a unitary construct, however, this domain was constructed to focus on the early episodic memory deficits in individuals with AD, which is often considered the hallmark of the illness and is typically associated with neural substrates located in the temporal lobes. Episodic memory deficits in persons with diagnosed AD, and those who are at high risk to develop AD (i.e., MCI-amnesic) are evidence of some of the earliest brain changes, and therefore this memory domain is most relevant to the current study.

Language Composite Score. The Language domain was comprised of measures of semantic fluency, phonemic fluency, confrontational naming, and general language functioning. These tests included: Animal Naming; The Grasshoppers and Geese Confrontational Naming subtest and Semantic Pairs subtest; and, the Language Index Score of the RBANS which is comprised of Picture Naming and Semantic Fluency subtests. The correlation matrix for these measures, presented in Table 3, also shows moderate, significant correlations among these constituent tests.

Statistical Analyses

Transformation to Z-Scores. The use of different variables within one dimension that inherently measure that dimension differently, requires a common metric. To make metrics from different tests comparable, one must consider how much above or below the average of the sample the participant performed on each respective test. A common statistical approach which relates an individual's performance to the average performance in the sample is a standardized

score, or Z-score (Bentler, 2007). A Z-score is the number of standard deviation units a patient's score is below or above the average score (Field, 2009). Given that the underlying measurements are continuous, a Z-score can be created for each participant that yields a "unitless" score that is no longer related to the original units of analysis (i.e., seconds or percent correct). According to Bentler (2007), it is a common statistical approach to combine Z-scores into composite scores because they measure the number of standard deviation units and therefore can be readily used for comparisons.

To make the metrics from the neuropsychological test scores comparable, first, age-corrected standard scores were calculated for each test based on published test norms or a set of norms selected for use in the Rural and Remote Memory Clinic. In other words, the age corrected standard score for each subject represents the extent to which that subject deviates from the norms for their age. The average raw scores for the neuropsychological measures for the entire sample are presented in Table 1.

Secondly, standard scores were transformed, where necessary, to Z-scores. Thus, for all participants, neuropsychological test scores were expressed as age-corrected Z-scores. Third, Z-scores were reflected so that a lower score reflected poorer performance. Only the Trail Making Test measured deterioration in function as an increase in score (i.e., time), while for the remainder of the battery a decrease in score reflected a deterioration in function. In this case, Bentler (2007) recommends that the direction of the Z-score for different neuropsychological measures be adjusted so that in all cases higher Z-scores respond to a better outcome. As such, the Z-score for the Trail Making Test was multiplied by -1 to make the direction of the Z-score the same as the rest of the battery where a lower score is indicative of poorer performance. Fourth, the data was inspected for missing values, assumptions of normality, and outliers using

SPSS Explore procedures. In the calculation of Z-scores for use in composite scales, special consideration must be given to the computation of missing data to ensure equal weighting. Scores for Form B of the Trail Making Test were not found to be missing at random, but rather reflected the patient's inability to complete the measure. Of the 48 clinical participants, 20 were unable to complete Trails B (41.6%). Although some authors suggest assigning a maximum Z-score to missing values, this strategy is not recommended when the amount of missing data exceeds 20% (Field, 2009). As such, Trails B was excluded from the composite scores. Less than 5% of the remaining data set was found to be missing at random, and all other missing data was addressed using the mean substitution technique (Field, 2009). Alternative strategies for dealing with missing data have been suggested by other authors, however, there has been shown to be little difference between strategies when the amount of missing data is less than 5% (Field, 2009). All neuropsychological test scores were found to have relatively normal distributions (i.e., skewness values $<2.5SD$), with the exception of the Stroop color form, which demonstrated a ceiling effect. However, the distribution of scores on this measure did not influence the distribution of the overall Executive/Attention/Speed composite and so it was entered into the composite untransformed. A small number of outliers (i.e., Z-scores exceeding 3.29 SD: Field, 2009) were detected (i.e. less than 1% of all cases) and were addressed by assigning these cases the average Z-score for that variable plus 2 standard deviations (Field, 2009).

Finally, composite scores were formed by averaging the age-corrected Z-scores for each theoretically determined cognitive domain as described above. Each composite score was found to be normally distributed and no outliers were detected. The correlation matrix for the three composite scores is presented in Table 4. There are relatively high and significant intercorrelations between composites, which might be expected given the multifactorial nature of

many cognitive processes. Although high intercorrelations raise concerns about multicollinearity, none of the collinearity diagnostics from any of the regression models indicated that this assumption had been violated. Using the criteria from Field (2009), none of the intercorrelations between composite scales exceeded $r=.8$. Furthermore, none of the tolerances from the regression models approached zero, and the average Variance Inflation Factor (VIF) for each model did not exceed 1.00. As such, these diagnostics help to resolve concerns about multicollinearity among the predictor variables.

Experimental Measures

As Study 2 and 3 report data from the same participant group, the experimental procedure and materials have been outlined in detail in Study 2. Briefly, all participants were required to complete single-task walking and counting trials (simple and complex), as well as combine the walking task and counting task in one 15s simple dual-task trial (i.e., walking and counting forward by 1's) and one 15s complex dual-task trial (i.e., walking and counting backwards from 70 by 2's).

Statistical Analyses

Prediction of Interference Effects. Hierarchical multiple linear regression analyses using SPSS examined whether individual differences on the cognitive composites predicted interference effects in the baseline walking condition (i.e., no interference), the simple dual task condition (i.e., simple interference) and the complex dual-task condition (i.e., complex interference). The distance covered (i.e., ft) in 15 seconds was used as the dependent measure in the baseline walking condition for the first regression model. Percent decrement scores in the simple and complex dual-task conditions served as dependent measures in two subsequent regression analyses. Last, to examine whether the specific cognitive factors would remain

significant after controlling for disease severity, the 3MS scores were entered in the first block, followed by the neuropsychological composite scores in the second block in three subsequent hierarchical regression analyses.

To account for the expected single-task differences between the healthy and clinical participants, interference in the simple and complex dual-task conditions was expressed as a percent decrement score. A decrement score allows for an assessment of the proportional change in an individual's performance during dual-task conditions relative to his/her performance during the single-task conditions. The neuropsychological composite scores served as predictors in all three models, and were entered using a hierarchical approach. According to Field (2009) it is critical that predictors be added to regression models based on previous research and theoretical importance, rather than on relying on a purely mathematical approach. He suggests that known predictors should be entered into the model first in order of their importance in predicting the outcome, instead of employing a stepwise approach which can often contrast dramatically with the theoretical importance of a predictor in a model. Therefore, the Executive Functions/Attention/Speed composite score was entered in the first block. The potency of the Executive Functions/Attention/Speed factor in predicting gait velocity in baseline and interference conditions was noted by Holtzer and colleagues (2006) in their study of healthy older adults. This finding is also consistent with recent research (e.g., Hausdorff et al., 2005; Herman et al., 2010) which suggests that walking requires the involvement of attention and other executive control processes. The Episodic Memory Composite and Language Composite were then entered simultaneously into the second block. Although the composite scores were controlled for age by using age-corrected Z-scores, initially demographic variables (i.e., age and education) were included in a third block. However, because these two variables were not

significant predictors in any of the regression models, they were excluded from the final analyses. A summary of the results of these analyses are presented in Table 5.

Results

Multiple Linear Regression Analyses – Prediction of Gait Interference

Baseline Walking Condition. Hierarchical multiple regression analyses were examined to investigate the relationship between the baseline walking condition and the neuropsychological predictors. Tables 5 and 6 summarize the descriptive statistics and analysis results for this model and the subsequent analyses described below. An examination of the correlations between the criterion and predictors, showed positive and significant correlations between the Executive/Attention/Speed Composite $r = .247$ and the Language Composite $r = .220$ scores, indicating that those with higher neuropsychological scores on these measures tended to cover more distance walking. The first model, including only the Executive Functioning/Attention/Speed composite, produced $R^2 = .075$, $F(1,74) = 5.93$, $p < .05$, accounting for 7.5% of the overall variance in walking rate. The second model, which included the Episodic Memory Composite and Language Composite produced $R^2 = .085$, $F(1,74) = 2.02$, $p = .095$, which accounted for only about 1% additional variance to the overall model after controlling for the Executive Function/Attention/Speed factor.

Table 6 shows the standardized coefficients for each of the predictors. The standardized beta coefficients were used to provide information about the magnitude of the relationship between each of the neuropsychological composite scores and the dependent measure. As judged by the coefficient size, the Executive/Attention/Speed factor had the largest contribution to the prediction of gait speed among the neuropsychological factors, and as can be seen from the table, is the only significant predictor. The Episodic Memory composite contributed slightly less, and

the Language composite made only a marginal contribution to the overall prediction of the model. The Executive Function/Attention/Speed composite was a significant predictor of gait speed when entered in Step 1 of the Model, however it did not remain significant after the addition of the remainder of the composite scores. Apparently, the relationship between the Executive Functions Attention Speed composite and baseline walking condition is mediated by the relationship between the remaining two composites and gait speed.

Simple Interference Condition. An examination of the correlations between the predictors (i.e., cognitive composite scores) and the criterion (i.e., interference in gait speed during simple counting as measured by percent decrement scores) showed the expected relationships with all three composites scores (i.e., those with higher percent decrement scores had lower neuropsychological test performance), however as in the baseline walking task, only the relationships between the percent decrement scores and the Executive Functioning/Attention/Speed composite, $r = .268, p < .01$ as well as the Language composite, $r = .221, p < .05$ were statistically significant. As can be seen from Table 5, the Executive Function/Attention/Speed Composite was a significant predictor of simple interference, $R^2 = .072, F(1,74) = 5.64, p < .05$ accounting for 7.2% of the variance. The addition of the Episodic Memory Composite and the Language Composite in step two, accounted for less than 1% of additional variance in the model $R^2 = .077, F(1,74) = 1.98, p = .125$

As can be seen from the standardized beta coefficients in Table 6, the Executive Function/Attention/Speed composite had the largest contribution to the prediction of the simple interference effects. The Language composite has the next largest coefficient size, and the Episodic Memory Composite was negatively weighted and contributed least to the overall model. In keeping with the results of the baseline walking condition, the Executive

Function/Attention/Speed composite was a significant predictor of simple interference effects in Step 1 of the model, however, it did not remain significant after the addition of the other two composite scores to the model.

Complex Interference Condition. An examination of the correlations between the predictors and criterion in the complex interference condition revealed significant negative relationships between the Executive Function/Attention/Speed composite, $r = -.260$, $p < .01$ the Episodic Memory Composite, $r = -.348$, $p < .001$, and the Language Composite, $r = -.314$, $p < .01$. The size and direction of the relationships suggest that those with lower neuropsychological scores, tend to have higher percent decrement scores in the complex condition, and therefore higher interference effects. In the first model, the Executive Functioning/Attention/Speed composite produced $R^2 = .067$, $F(1,74) = 5.27$, $p < .05$, accounting for 6.7% of the variance. The addition of the Episodic Memory composite and Language composite, significantly improved the model, and produced $R^2 = .136$, $F(1,74)$, $p < .05$, accounting for an additional 6.9% of the variance. Although the first model, improved the ability to predict the outcome variable, the second model was significantly better; altogether 13.6% of the variance in the complex interference condition was predicted by the test scores on these three neuropsychological composite scores.

As can be seen in Table 6, The Executive Functioning/Attention/Speed composite was again a significant predictor of complex interference effects in the first model. However, the size of the relationships differed in the second model, following the addition of the other two composite scores. The weight of the standardized beta values show that the Executive Function/Attention/Speed composite contributed significantly less to the overall prediction of the second model, than did either the Episodic Memory composite or the language composite, which

were weighted fairly evenly. This strongly suggests that the relationship between the complex interference effects and the Executive Functioning/Attention/Speed factor is mediated by performance on the other two neuropsychological composites.

Additional Multiple Linear Regression Analyses – Controlling for Disease Severity

Although the relationship of a clinical diagnosis to gait interference was intuitively assumed, three additional hierarchical regression analyses were carried out to control for disease severity. Including disease severity as an additional covariate, 3MS scores were added to the model to provide the most stringent test for the relationship between the neuropsychological composite scores and gait interference. Again, a hierarchical method was used with the 3MS scores entered in the first block, and the neuropsychological composite scores entered simultaneously in the second block. Hence, the regression coefficients of the neuropsychological predictors were adjusted for disease severity in the second block. Gait speed served as the dependent variable in the baseline walking condition, and gait interference as measured by the percent decrement scores served as the criteria in the simple and complex dual-task conditions. Tables 7 and 8 summarize the descriptive statistics and analysis results for this model and the subsequent analyses described below.

Baseline Walking Condition. Not surprisingly, an examination of the correlations between gait speed and the 3MS scores, $r = .248, p < .05$, the Executive Functioning/Attention/Speed composite, $r = .274, p < .05$, the Episodic Memory Composite, $r = .232, p < .05$, and the Language Composite, $r = .220, p < .05$ all showed significant positive relationships between the criterion and predictors. As can be seen from Table 6, the 3MS scores were a significant predictor of gait speed in the baseline walking condition, $R^2 = .061, F(1, 74) = 4.78, p < .05$, accounting for 6.1% of the variance. However, the addition of the neuropsychological composite scores in the second block did not significantly improve the

overall model, $R^2 = .089$, $F(1,74) = 1.71$, $p < .095$ only accounting for 2.8% of additional variance.

As can be seen from the table of standardized beta coefficients presented in Table 8, the 3MS scores were a significant predictor of gait speed when entered alone in the first model. However, this predictor did not remain significant after the addition of the neuropsychological composites in the second model. Executive Function/Attention/Speed composite had the largest contribution to the prediction of overall gait speed in step two, with the 3MS scores and the Episodic Memory composite weighted relatively evenly. The Language Composite was negatively weighted and contributed least to the model. These results suggest that performance in the baseline walking condition is mediated by a relationship between 3MS scores and the neuropsychological predictors.

Simple Interference Condition. An examination of the correlations between the predictors and criterion in the simple interference condition did not show a significant relationship between the 3MS scores and the percent decrement scores, $r = .165$, $p = .091$, or the Episodic Memory Composite, $r = .115$, $p = .163$. However, a significant positive relationship was detected between the percent decrement scores and the Language Composite, $r = .221$, $p < .05$ as well as the Executive Functioning/Attention/Speed Composite, $r = .268$, $p < .05$. In the first model, the 3MS scores were not a significant predictor, $R^2 = .024$, $F(1,74) = 1.81$, $p = .182$, only accounting for 2.4% of the variance in gait interference. Similarly, the addition of the neuropsychological composite scores produced $R^2 = .079$, $F(1,74) = 1.50$, $p = .212$, accounting for approximately 5% of additional variance in the overall model. The weight of the standardized beta coefficients in Table 8 show that the Executive Functioning/Attention/Speed Composite contributed the most to the overall model, followed by the language composite and

the 3MS scores. However, no individual predictor was significant at either Step 1 or Step 2 of the model.

Complex Interference Condition. The correlations between the predictors and criterion in the complex interference condition revealed strong negative relationships between the percent decrement scores and the 3MS scores, $r = -.403$, $p < .001$, the Executive Function/Attention/Speed Composite, $r = -.260$, $p < .001$, the Episodic Memory Composite, $r = -.348$, $p < .001$, and the Language Composite, $r = -.314$, $p < .001$. The size and direction of these relationships show that those with lower neuropsychological scores tend to have higher levels of interference effects in the complex walking condition. In the first model, the 3MS scores produced a significant $R^2 = .163$, $F(1,74) = 14.18$, $p < .001$ accounting for 16.3% of the variance in the percent decrement scores. Although the first model improved the ability to predict the outcome, the second model was significantly better, $R^2 = .173$, $F(1,74) = 3.67$, $p < .001$ accounting for a total of 17.3% of the variance. This suggests about 1% of the overall variance in the percent decrement scores in the complex walking condition can be accounted for solely by the neuropsychological composite scores, after controlling for disease severity.

Looking at the standardized beta coefficients, the 3MS scores were again a significant predictor of gait interference in the complex condition in Step 1 of the model. It remained the strongest predictor at Step 2 of the model, although it only approached significance. The size of the relationships differed somewhat between the neuropsychological composite scores and the percent decrement scores in the complex interference condition. Whereas the Executive Functioning composite contributed the most to the prediction in the baseline walking and simple interference conditions, it contributed the least to the model in the complex condition. Rather, the Episodic Memory Composite was weighted heaviest followed by the Language Composite score.

Overall, this model strongly suggests that the relationship between the percent decrement scores in the complex condition and the 3MS scores are mediated by performance on the remaining neuropsychological composite scores, largely the Episodic Memory composite.

Discussion

This study forms part of an important emerging literature that aims to characterize the relationship between theoretically derived cognitive factors and gait interference using a dual-task paradigm in individuals with AD and healthy older adults. Whereas previous dual-task studies have focused on studying divided attention in isolation, the current study is the first to use cognitive composite scores measuring Episodic Memory; Executive Functioning/Speed/Attention; and Language to predict interference effects under baseline, simple and complex dual-task conditions, after controlling for disease severity and other demographic variables.

First, consistent with the literature on healthy aging and AD, performances on neuropsychological measures of cognitive function were related to walking speed in the baseline condition and interference effects in the dual task conditions in the expected direction; lower cognitive performance was related to slower walking speed and higher rates of dual-task interference. This result is consistent with a large body of literature indicating that when healthy older adults and individuals with AD are asked to walk and simultaneously perform another task, gait speed is reduced (Hausdorff et al., 2008; Sheridan & Hausdorff, 2007; Yogev-Seligmann et al., 2008)

Secondly, in the first set of multiple regression analyses, the current results show that separate cognitive functions predicted gait speed and interference effects in healthy older adults and individuals with AD, even after adjusting for the effects of demographic variables. As

hypothesized, and in keeping with previous results, this study shows that the Executive Functioning/Attention/Speed composite was the most potent predictor of gait slowing and interference effects in both the baseline and the simple and complex interference conditions. Specifically the Executive functioning/Attention/Speed composite was a significant predictor of gait speed in the baseline condition, explaining 7.5% of the variance. This composite was also a significant predictor of interference effects in the simple and complex dual-task conditions accounting for 7.2% and 6.7% of the explained variance, respectively.

The finding that the Executive Function/Speed/Attention composite was a reliable predictor of gait performance in the baseline and simple and complex conditions is consistent with the findings of Holtzer et al. (2006) and other research examining the role of executive functions in gait (Hausdorff et al., 2007). Further it adds additional evidence to the important role that executive control processes play in walking in both normal and pathological aging.

However, in evaluating the importance of the Executive Function/Attention/Speed composite, it should be emphasized that the contribution of this factor was clearly mediated by performance on the other neuropsychological measures, most notably the Episodic Memory composite. The current findings also suggest that while speed, attention and executive control processes are important, they are not exclusive predictors of interference effects. The relationship between the cognitive composites and gait interference effects varied as a function of dual-task complexity, which supported the second hypothesis of this study. While the Executive Function/Attention/Speed composite was most strongly related to gait interference in the simple condition, in the complex dual-task condition, the addition of the Episodic Memory and Language Composites further improved the model and accounted for 13.6% of the explained variance. That is while, the Executive function/Attention/Speed composite accounted for 6.7% of

the variance when entered into the model alone, the addition of the Episodic Memory and Language composites explained an additional 6.9% of the variance. In the baseline and simple interference condition, the addition of the Episodic Memory and Language Composites were not significant predictors of gait interference. Therefore, when cognitive demands increase during the gait dual-task conditions the predictive value of the separate cognitive composites change, suggesting that additional higher order brain functions are required for walking under more complex situations, such as navigating obstacles or in a busy environment.

These results suggest that the reliance on higher brain functions to mediate gait increases as the walking and the counting tasks become more difficult and challenging. Although executive control was an important predictor, it was not an exclusive predictor of gait performance under complex conditions. Specifically, the Episodic Memory Composite was also a potent predictor of dual-task performance under complex conditions. The relationship between dysfunction in the temporal lobe and decline in episodic memory has been well established in AD, however we believe this is the first study to use neuropsychological measures to directly link episodic memory functioning, AD, and gait performance. This suggests that in addition to its prominent role in cognition, medial temporal lobe structures also appear to be strongly involved in the control of gait under complex conditions. This is further supported by a PET study showing an association between the hippocampal regions and increasing complexity of walking (i.e, walking and avoiding obstacles; Maloubin et al., 2003).

A strength of the current study is the additional analyses carried out to control for disease severity of the participants. Although the relationship of a clinical diagnosis to gait performance assumed based on the results of Study 2, 3MS scores were added to the analyses to provide the most stringent test for the relationship between the neuropsychological composite scores and gait

performance. Not surprisingly, 3MS scores were found to be positively correlated with gait speed in the baseline conditions, accounting for about 6.1% of the variance, and negatively correlated with gait interference in the simple and complex dual-task conditions. Most interestingly however, in the complex dual-task condition, 3MS scores accounted for 16.3% of the explained variance in the interference effects. After the addition of the neuropsychological composite scores, this improved to 17.3% of the observed variance, which indicates that about 1% of the overall variance in the complex interference effects can be accounted for solely by the cognitive composite measures, after controlling for disease severity.

Based on the current literature, this is the first study to show the relationship between cognitive composite scores and gait performance in healthy individuals and individuals with a range of AD severity, after controlling for the effects of demographic variables, and disease severity. These results show that specific cognitive factors (i.e., Executive Functions, Attention, Speed of Processing, Language and Episodic Memory) are reliable predictors of gait performance under simple and complex dual-task conditions. However, it is also important to note that although the cognitive factors used in the current study were formed based on theoretical rationale and statistical analysis, establishing construct validity for the cognitive composite scores is difficult. Within the gait and cognition literature generally, a methodological concern relates to generally referring to “executive functions” as underlying gait control, without demonstrating its constituent components (i.e., planning, volition, judgement). For example, Yogev-Seligmann et al. (2008) demonstrated in a theoretical review, how different components of executive function can possibly negatively affect gait. That is, impairment in inhibition may impact an individual's ability to walk safely. Similarly, poor insight or impaired planning ability could result in getting lost or an increased risk of falling. Thus, there is a need for future research

that directly examines how specific executive functioning properties (i.e., Stuss, 2011) affect specific parameters of walking. A similar limitation is the shared relationship between the Executive Functions/Attention/Speed factor and overall processing speed. The neuropsychological measures that comprise this factor all rely on speed of processing. As the current study also used gait speed as a dependent variable, it is likely that shared demands on speed of processing strongly contributed to the relationship between gait performance and the Executive Function/Attention/Speed factor.

In conclusion, whereas previous gait-dual task studies have compared dual-task performance in older adults and individuals with AD, this study used a moderate sized sample of individuals who ranged from normal to moderately impaired, to infer a relationship between theoretically derived composite scores of higher brain functions and gait performance under simple and complex dual task conditions. This presents a methodological advantage over previous studies, by using simple and complex procedures, as well controlling for demographic and individual confounds such as the effects of aging and disease severity. These findings suggest that individual differences in executive functioning, speed of processing, attention, language and episodic memory are important for understanding the variance in gait performance in aging and in individuals with AD. An important avenue of future research should focus on how these factors are related to falls in individuals with AD. Abnormal gait patterns are known to predict future risk of AD (Verghese et al., 2002) and are a sensitive proxy for falls in cognitively normal older adults (Holtzer et al., 2007). Adding performance on neuropsychological tests, especially those accessing executive functions, attention, speed of processing and episodic memory, and contrasting those with dual-task procedures, may provide

important diagnostic information relevant to the risk of falls in individuals in both healthy older adults and those with AD.

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Table 1.

Descriptive Statistics of Demographic Variables, Neuropsychological Tests (Raw scores), and Percent Decrement scores in the Simple and Complex Conditions

Variable	M (SD)
N = 75	
Age (years)	74.6 (7.83)
Education (years)	11.6 (2.80)
Gender (%)	
Male	28
Female	72
WRAT-III reading ¹	100.8 (10.0)
<i>Executive Functions/Attention Speed</i>	
Digit Span ²	
Forwards	6.1 (1.04)
Backwards	4.2 (1.34)
Trail Making Test ³	
Trails A	54.6 (39.4)
Trails B*	123.9 (57.6)
Stroop Test ⁴	
Color	111.7 (.92)
Color-word	70.12 (22.8)
COWA ⁵	33.7 (12.5)
Symbol Search ⁶	19.1 (7.9)
<i>Episodic Memory</i>	
Grasshoppers & Geese ⁷	
Semantic Pairs Total	48.0 (4.01)
Episodic Memory	24.1 (3.67)
<i>Language</i>	
Animal Naming ⁸	13.8 (6.25)
Confrontational Naming ⁹	30.9 (4.20)
<i>RBANS¹⁰</i>	
Immediate Memory Index	81.0 (21.3)
Visuospatial Index	90.5 (18.3)
Language Index	93.2 (15.0)
Attention Index	89.3 (18.4)
Delayed Memory Index	69.0 (22.7)
Total Scale Index	81.1 (20.3)
Baseline walking (feet)	48.4 (10.1)

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Percent decrement simple	4.95 (11.3)
Percent decrement complex	21.8 (13.4)

¹ Wide Range Achievement Test (3rd Edition) Reading subtest is scored out of a total of 57.² Digits forward and digits backward are part of the Digit Span subtest of the WAIS-III. The reported scores are the number of digits repeated in the forward and backward order. ³ Scores for the Trail Making Test Part A are the number of seconds taken to sequentially join numbers in a random array; scores for Part B are the number of seconds taken to alternatively join number and letter sequences; the higher the score the poorer the performance. ⁴ Stroop neuropsychological screening test are the number of colors and color-words correctly labeled in 120 seconds. ⁵ The Controlled One Word Association Test score is the total number of words beginning with the letters 'F', 'A', and 'S' reported in three 1-min trials. ⁶ The WAIS-III symbol search subtest score is the number of correctly identified symbols in 120s. ⁷ The Grasshoppers and Geese semantic pairs total is the number of correctly identified items out of 53; episodic memory is the total correctly recalled out of 30⁸ The Animal Naming score is the total number of animals named during a 1-min trial. ⁹ The Confrontational naming score is the number of correctly identified objects out of 35. ¹⁰ The RBANS provides an overall total score and index scores for immediate memory, visuospatial/constructional, language, attention and delayed memory; these scores have a mean of 100 and a standard deviation of 15.

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Table 2:

Correlation Matrix of Age –Corrected Standardized Neuropsychological Test Scores for Executive Functions/Attention/Speed Composite

Neuropsychological Test	1	2	3	4	5	6	7
1. Trails A	-						
2. Stroop Test color	.302**						
3. Stroop Test Word-color	.487**	.309**					
4 RBANS Attention Index	.506**	.307**	.613**				
5. Digit Span Backward	.289**	.205*	.494**	.618**			
6. WAIS III SS	.407**	.245*	.546**	.604**	.362**		
7. COWA	.208*	.143	.539**	.454**	.521**	.448**	-

** . Correlation is significant at the 0.01 level (1-tailed).

* . Correlation is significant at the 0.05 level (1-tailed).

Table 3:

Correlation Matrix of Age –Corrected Standardized Neuropsychological Test Scores for Language Composite

Neuropsychological Test	1	2	3	4	5
1. Animal naming	-				
2. RBANS Language Index	.660**				
3. G&G Confrontational naming	.437**	.563**			
4. G&G Semantic Pairs Total	.512**	.645**	.654**		
5. WRAT-III Reading	.402**	.405**	0.142	.232*	-

** . Correlation is significant at the 0.01 level (1-tailed).

* . Correlation is significant at the 0.05 level (1-tailed).

Table 4:

Correlation Matrix of Neuropsychological Composite Scores, Dependent Variables and Demographic Variables

	1	2	3	4	5	6	7	8
1. Executive/Attn/Speed	-							
2. Episodic Memory	.538**							
3. Language	.710**	.639**						
4. % Decrement complex	-.260*	-.348**	-.314**					
5. % Decrement Simple	.268*	.115	.221*	.254*				
6. Single walk distance	.274**	.232*	.220*	-0.09	0			
7. Age (years)	0.178	0.136	-0.02	-0.01	-0.02	-0.1		
8. Education (years)	0.16	-0.05	.258*	-0.11	0.008	0.043	-.233*	-

** . Correlation is significant at the 0.01 level (1-tailed).

* . Correlation is significant at the 0.05 level (1-tailed).

Table 5:

Summary of Regression Analyses Predicting Gait Performance in the Baseline and Simple and Complex Interference Conditions

Condition	R	R ²	F
<i>Baseline walking- No Interference</i>			
Model 1	.274	.075	5.93*
Model 2	.292	.085	2.02
<i>Simple % Decrement- Simple Interference</i>			
Model 1	.268	.072	5.64*
Model 2	.278	.077	1.98
<i>Complex % Decrement – Complex Interference</i>			
Model 1	.260	.067	5.27*
Model 2	.369	.136	3.73*

Note. Model 1 = Executive Functioning/Attention/Speed Composite. Model 2 = Executive Functioning/Attention/Speed Composite, Episodic Memory Composite, Language Composite.

* $p < .05$

Table 6:

Standardized Regression Coefficients and Standard Error of the Neuropsychological Composite Scores for the Baseline Walking, Simple and Complex Interference Conditions

Condition	B	SE B	Standardized Beta
<i>Baseline Walking</i>			
Model 1			
Constant	49.15	1.17	
Executive/Attention/Speed	4.61	1.89	.27*
Model 2			
Constant	48.9	1.22	
Executive/Attention/Speed	3.65	2.74	.22
Episodic Memory	1.39	1.69	.12
Language	-.174	2.30	-.01
<i>Simple Interference Condition</i>			
Model 1			
Constant	5.80	1.32	
Executive/Attention/Speed	5.07	2.14	.27*
Model 2			
Constant	6.03	1.38	
Executive/Attention/Speed	4.49	3.10	.24
Episodic Memory	-.997	1.91	-.08
Language	1.496	2.61	.10
<i>Complex Interference Condition</i>			
Model 1			
Constant	20.85	1.57	
Executive/Attention/Speed	-5.818	2.53	-.26*
Model 2			
Constant	21.20	1.58	
Executive/Attention/Speed	-.724	3.55	-.03
Episodic Memory	-3.69	2.19	-.25
Language	-2.314	2.99	-.13

Note. Model 1 = Executive Functioning/Attention/Speed Composite. Model 2 = Executive Functioning/Attention/Speed Composite, Episodic Memory Composite, Language Composite.

* $p < .05$

Table 7:

Summary of Regression Analyses Predicting Gait Performance in the Baseline and Simple and Complex Interference Conditions Controlling for Disease Severity

Condition	R	R ²	F
<i>Baseline walking- No Interference</i>			
Model 1	.248	.061	4.78*
Model 2	.298	.089	1.71
<i>Simple % Decrement- Simple Interference</i>			
Model 1	.156	.024	1.81
Model 2	.281	.079	1.50
<i>Complex % Decrement – Complex Interference</i>			
Model 1	.403	.163	14.18**
Model 2	.416	.173	3.67**

Note. Model 1 = 3MS scores . Model 2 = 3MS Scores, Executive Functioning/Attention/Speed Composite, Episodic Memory Composite, Language Composite.

* $p < .05$

** $p < .001$

Table 8:

Standardized Regression Coefficients and Standard Error of the Neuropsychological Composite Scores for the Baseline Walking, Simple and Complex Interference Conditions Controlling for Disease Severity

Condition	B	SE B	Standardized Beta
<i>Baseline Walking</i>			
Model 1			
Constant	28.35	9.23	
3MS Scores	.233	.107	.248*
Model 2			
Constant	39.85	16.68	
3MS Scores	.104	.190	.110
Executive/Attention/Speed	3.44	2.78	.205
Episodic Memory	1.03	1.82	.091
Language	-.908	2.68	-.070
<i>Simple Interference Condition</i>			
Model 1			
Constant	-9.23	10.61	
3Ms Scores	.165	.123	.156
Model 2			
Constant	12.60	18.90	
3MS Scores	-.075	.215	-.071
Executive/Attention/Speed	4.64	3.15	.245
Episodic Memory	-.733	2.07	-.058
Language	2.02	3.04	.139
<i>Complex Interference Condition</i>			
Model 1			
Constant	65.28	11.63	
3MS Scores	-.506	.134	-.403**
Model 2			
Constant	58.68	21.20	
3MS Scores	-.427	.241	-.340
Executive/Attention/Speed	.146	3.54	.007
Episodic Memory	-2.18	2.32	-.145
Language	.708	3.41	.041

Note. Model 1 =3MS Scores . Model 2 = 3MS Scores, Executive Functioning/Attention/Speed Composite, Episodic Memory Composite, Language Composite.

* $p < .05$ ** $p < .001$

General Discussion

Dual-task paradigms have been used frequently in experimental and clinical settings to characterize the cognitive changes associated with normal and pathological aging, with a particular interest in understanding the role of divided attention and executive functions in the neuropsychological profile of early-stage AD. Typically, the early stages of AD are characterized by deficits in episodic memory caused by medial-temporal lobe atrophy (Robillard, 2007; Rockwood et al., 2007) and neuronal loss in the basal forebrain cholinergic system (Fernandez-Duque & Black, 2006; Crossley, Hiscock & Foreman, 2004). Although memory impairments will always remain at the diagnostic core of AD, over the past decade, evidence has accumulated for early deficits in attention, even before impairments in language and semantic memory become apparent (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Bellville, Chertkow, & Gauthier, 2007; Fernandez-Duque & Black, 2006; Logie, Cocchini, Della Sala, & Baddeley, 2004; Parasuraman & Haxby, 1993; Perry & Hodges, 1999).

Attention refers to many different cognitive abilities such as orienting to sensory stimuli, maintaining the alert state, and planning tasks that cannot be performed automatically (Bellville et al., 2006; Fernandez-Duque & Black, 2006; Saunders & Summers, 2011). In an early, yet very influential review of attention and executive processes in AD, Perry and Hodges (1999) suggest that each component or sub-component of attention (i.e., sustained attention, selective attention, and divided attention) tends to be impacted differentially by the early stages of the AD disease process, with relative preservation of sustained and focused attention, and more severe impairments in the ability to shift attention and divide attention between two concurrent tasks.

Perry and Hodges (1999), as well as more recent authors, suggest that the ability to divide attention appears to be particularly vulnerable to the effects of AD, and that an inability to divide

attention may, like memory dysfunction, be an early hallmark of the illness (Bellville et al., 2006; Logie et al., 2004). Thus, attentional control mechanisms, such as divided attention and executive functions, have been described in the literature as excellent indicators that can be used to differentiate normal older adults from those with AD (Bellville et al., 2006) and as early predictors of future development of AD in individuals with amnesic-Mild Cognitive Impairment (aMCI; Petersen et al., 1999; 2001; Saunders & Summers, 2011).

A key methodology leading to these conclusions has been the use of dual-task paradigms to study the effect of concurrent cognitive demand in individuals with AD (Della Sala & Logie, 2001). Classic upper extremity dual-tasks (i.e., finger tapping) and functional gait dual-task paradigms (i.e. “talking while walking”) have been used to investigate resource based theories of normal aging (Crossley & Hiscock, 1992; Verhaeghen, Steitz, Sliwinski, & Cerella, 2003) and dementia related changes in higher brain functions (Crossley et al., 2004; Fernandez-Duque & Black, 2006; Logie et al., 2004). A substantial body of literature indicates that although AD patients can sometimes perform as well as controls on single – task conditions, they show a disproportionate decline in performance when two tasks are performed concurrently (Crossley et al., 2004; Perry & Hodges, 1999; Perry, Watson, & Hodges, 2000). Thus, it is generally proposed that individuals with AD have difficulty performing tasks of divided attention when compared with normal older adults.

Nonetheless, the stage at which individuals with AD show impairment on tasks of divided attention currently remains controversial. Although it has been well established that most individuals in the moderate to severe stages of the illness show impairment in the ability to divide attention (Perry et al., 2000), this vulnerability is not consistently found in the earliest stages of the illness. (Bellville et al., 2007; Greene et al., 1995; Lonie et al., 2009; Perry et al.,

2000). In particular, previous studies that have investigated gait dual-task performance in AD have been limited by a number of methodological limitations (Al-Yahya et al., 2011). Although the application of dual-tasking to evaluate the role of attention during walking is well accepted, there are a number of specific procedural issues that are not yet standardized and make it difficult to compare results across studies (Yogev-Seligmann et al., 2008). Similarly, it is unclear if the previously observed gait dual-task changes in individuals with AD are systematically related to methodological limitations. For example, many dual-task studies report divided attention deficits in individuals with early-stage AD without reporting the measure of disease severity of the participants (e.g., Camicoli et al., 1997). It is obvious that if even some moderately impaired individuals are included in these samples, they are likely to be in a stage of general global cognitive decline, and thus will be poor at all tasks, not just tasks of attention. This leads to serious problems in interpretation because different cognitive impairments appear at different stages of AD (Perry & Hodges, 1999). Furthermore, reporting average results on dual-tasks for patients with severity ranging from mild to severe does not inform our understanding of divided attention deficits in the earliest stages of the illness; any group differences between clinical and normal older adults can be attributable to the severely impaired patients in the group who generally demonstrate deficits on all measures. Furthermore, the choice of the cognitive task used to evaluate the effects of interference on gait in dual-tasks also varies widely and there is no agreement on which task creates optimal attentional loading (Beauchet, Dubost, Gonthier, & Kressig, 2005). However, studies by Beauchet and colleagues (2005) have shown that only a concurrent arithmetic task (i.e., counting backwards from 50) significantly interferes with gait variability and stride. In contrast, verbal fluency tasks, which have been widely employed in the gait dual-task literature, have been shown to have little effect on gait, presumably because they

are not effortful enough to disrupt gait performance or do not draw on the same types of executive functions required for gait dual-task performance. In another example of methodological variability, some dual-task studies explicitly prioritize one task over another, while others do not instruct the subject at all with regard to task emphasis (Yogev-Seligmann et al., 2008).

The primary aim of the current research was to address methodological variations in the gait dual-task literature and the following four related limitations: (1) the inclusion of large heterogeneous patient groups at different stages of disease severity; (2) a failure to manipulate the complexity of the component cognitive task; (3) the types of cognitive tasks employed (i.e., verbal fluency vs. arithmetic counting); and (4) the lack of previous emphasis on task prioritization processes. A second aim of the current research was to examine the relationship between specific higher brain functions (i.e., episodic memory, language, executive functions) and gait dual-task performance. Whereas previous dual-task research has been limited by the almost exclusive focus on divided attention and executive functioning in mediating gait-dual task performance, the current research also utilizes neuropsychological data to understand how specific, theoretically derived cognitive factors (i.e., Executive Function/Attention/Speed; Episodic Memory; Language) are related to gait performance in a sample that includes healthy older adults and individuals diagnosed with either amnesic - Mild Cognitive Impairment (aMCI) or Alzheimer's Disease.

To accomplish this goal, the current research examined gait dual-task performance in healthy older adults recruited from the community and individuals referred to an interdisciplinary memory clinic who were diagnosed with AD, at different stages of severity (i.e., aMCI, early stage-AD, moderate stage AD) using well established clinical and research based criteria (i.e.,

CCCDTD3, Robillard, 2007; NINCDS-ADRDA, McKhann et al., 1984; aMCI, Petersen et al., 1999, 2000). In all studies, the healthy older control group was matched as closely as possible to the clinical groups in terms of age, education, and estimated pre-morbid intelligence. The dual-task paradigm used across studies manipulated the complexity of the cognitive task in that it combined simple (i.e., counting forward by 1's) and complex (i.e., counting backwards from 70 by 2's) verbal counting tasks with a speeded walking task in baseline and dual-task conditions. The choice of the cognitive secondary tasks was guided by empirical literature demonstrating that concurrent arithmetic, such as counting backwards, draws on the working memory aspects of the central executive, which is believed to be responsible in part for the allocation of attentional resources (Beauchet et al., 2005). The expected differences between healthy older adults and the clinical groups in single task performance were controlled through the use of a percent decrement score that expressed interference during dual-task performance as a function of change from each participant's baseline performance. Last, we controlled for individual differences in the allocation of resources between the two concurrently performed tasks by emphasizing that both tasks were equally important. This provided an "ecologically valid" approach to the dual-task procedure and allowed interpretation to be guided by a theoretical framework which accounts for task prioritization processes in dual-task procedures (see Li, Krampe, & Bondar, 2005 for a discussion of this issue).

In Study 1, the sample of AD participants was limited to a group of individuals referred to a Rural and Remote Memory Clinic and diagnosed with early-stage AD (i.e., MMSE 21-28). The healthy older adults recruited into Study 1 included family members or other care providers of the referred patients. In contrast to previous gait dual-task studies, both groups were closely equated in terms of age, education and estimated pre-morbid intelligence. These analyses

revealed the expected group differences during single task performance. For example, individuals with AD were found to walk more slowly, which is consistent with a large body of literature (Yogev-Seligmann et al., 2008). There was also a predictable main effect for task complexity, in that all individuals walked more slowly when completing the complex vs. the simple gait dual task. However, in contrast to previous findings, the analyses revealed that when compared to an age-appropriate and well controlled group of healthy older adults, individuals in the earliest stages of AD did not differentially show more interference during either simple or complex gait dual-task performance.

Given these novel results, Study 2 was designed to be a replication and extension of Study 1. Using a separate sample of patients referred to the Rural and Remote Memory Clinic, Study 2 compared gait dual-task performance in individuals in three diagnostic groups (aMCI, 3MS scores from 100-90; early stage AD, 3MS scores from 91-77; and moderate AD, 3 MS scores from 76-59) to the performance of a group of healthy, community dwelling older adults. This study was specifically designed to assess individuals across the dementia spectrum, from the earliest or “pre-clinical” stages (i.e., aMCI; Petersen et al., 1999, 2001) to moderate stage AD. Based on the results of Study 1, it was hypothesized that individuals with aMCI and early-stage AD would not be differentially more impaired by a complex dual-task. Rather, it was believed that the impairment in gait dual-task performance would occur in the moderate stage AD group, which is further in the progression of the illness than previously theorized. In keeping with the results of Study 1, Study 2 lends further support to the notion that aMCI and early stage AD is not associated with impaired gait dual-task performance. As expected, there were no significant differences between the normal healthy control group, the aMCI group, or the participants with early-stage AD. In contrast, significant differences were detected between the

moderate AD group and the healthy older adults, suggesting that the specific deficit in divided attention as assessed by a gait-dual task is apparent later in the progression of AD.

Study 3 was designed to further extend previous gait dual-task literature by examining the contribution of other specific cognitive factors (i.e., executive function, language, episodic memory, speed of processing) to gait interference under baseline, simple and complex dual-task procedures in a heterogeneous group containing all the clinical participants and healthy older adults included in Study 2. Neuropsychological test scores were used to create three theoretically driven cognitive composite scores (i.e., Executive Function/Attention/Speed; Episodic Memory; and Language). In keeping with previous research that has examined the cognitive predictors of gait performance in healthy older adults (Holtzer et al., 2006) multiple regression analyses revealed that the Executive Function/Attention/Speed composite was the most potent predictor of gait dual task performance. However, this relationship varied as a function of task complexity and all three composite scores predicted gait performance in the complex dual-task condition, even after controlling for disease severity. These findings suggest that the interpretation of previous dual-task studies have been limited by solely studying divided attention in isolation and indicate that a number of higher brain functions, including episodic memory, have an important relationship to gait performance.

However, it is important to highlight that although the cognitive factors used in Study 3 were constructed based on a theoretical rationale derived from the current literature, the neuropsychological measures used demonstrate high intercorrelations with one another and establishing construct validity for the cognitive composite scores is difficult. A similar limitation is the shared relationship between the Executive Functions/Attention/Speed factor and overall processing speed. The neuropsychological measures that comprised this factor all rely on speed

of processing. As Study 3 also used gait speed as a dependent variable, it is possible that the shared demands of processing speed strongly contributed to the relationship between gait performance and the Executive functions/Attention/Speed factor. Given that this appears to be a limitation that applies to the gait and cognition literature in general, future research should examine how specific executive functioning properties (for a review see Stuss, 2011) affect specific parameters of walking. For example, gait variability has been shown to be a potent predictor in fall risk for healthy older adults and individuals with AD (Holtzer et al. 2007), and it would be a most beneficial avenue to research how different components of executive functioning are related to gait variability and the risk of falls in individuals with AD. A recent theoretical review by Yogev-Seligmann and colleagues (2008) provides some direction in this regard by demonstrating how separate executive functions such as inhibition, poor insight, or impaired planning ability may all differentially impact an individual's ability to walk safely.

Based on the current literature, this is the first body of research which has investigated the effects of a simple and complex gait-dual task in individuals in well described stages of AD severity and compared their performance to an age appropriate and adequately controlled group of healthy older adults. Furthermore, Study 3 is the first to characterize the relationship between theoretically derived neuropsychological composite scores and gait interference effects in baseline, simple and complex dual-task conditions using a heterogenous group of healthy individuals and clinical participants at different stages of AD. The current research presents a methodological advantage over previous gait-dual task studies, by using simple and complex dual-task procedures, as well as controlling for demographic (i.e., age, education, premorbid IQ) factors and confounds such as disease severity. Taken together, the current research suggests that higher brain functions such as attention, executive functioning; episodic memory and speed of

processing are closely linked to walking, both in healthy older adults and those with AD. This close relationship is also supported by epidemiological studies demonstrating links between physical activity and the risk for dementia (Verghese et al., 2003); clinical studies with healthy older adults that have examined a relationship between gait and specific cognitive processes (Holtzer et al., 2006) and neuroimaging studies which have examined a neural basis for such a relationship (Malouin et al., 2003).

In contrast to the previous gait dual-task literature, the results of Studies 1 and 2 suggest that decline of attention control and executive functions as measured by a gait-dual task are not among the earliest higher brain functions affected in “preclinical” and early-stage AD. Studies 1 and 2 did reveal predictable and expected effects for task difficulty. Across studies, the percent decrement scores were greater when walking was combined with the complex versus the simple counting task, regardless of diagnostic group. That is, both studies revealed that dual-task performance is associated with a slowing of gait under conditions with higher attentional demands. However, in contrast to previous gait dual-task findings, Studies 1 and 2 show that when baseline walking rates are controlled for using percent decrement scores, individuals in the “pre-clinical” (i.e., aMCI) and early stages of AD are not disproportionately more impaired by a gait dual-task procedure. This strongly suggests that when overall degree of dementia severity is controlled for by subdividing patients based on rigorous diagnostic criteria individuals determined to be in the early stages of AD have comparable performance to healthy older adults on both simple and complex dual-task procedures.

Therefore, divided attention, as measured by the current dual-task paradigm, is evidently not always affected in the early stages of the illness. In contrast, these results suggest that dual-task performance, as measured by the current paradigm, appears to be affected in the moderate

stages of AD. This suggests that the interpretation of cognitive performance in groups of patients designated with probable AD largely depends on subdividing patients according to dementia severity in order to understand and isolate when specific impairments in divided attention become apparent. This belief is further reinforced by a recent study by Lonie and colleagues (2009) who administered a paper and pencil dual-task (i.e., digit span and visuospatial tracking task) to individuals with aMCI, early-stage AD and healthy older adults. As in the current research, AD patients were diagnosed according to strict research and clinical guidelines and efforts were made to equate the groups on age, and levels of pre-morbid functioning. In keeping with the results of Studies 1 and 2, there were no group differences in dual-task performance. Those with aMCI and early stage AD had comparable performance to healthy older adults. Taken together with the current research, these results suggest that when participants with “pre-clinical” and “probable” AD are carefully subdivided using diagnostic guideline, only those patients in the later stages of AD are impaired on the dual-task paradigm.

Accordingly, future dual-task studies are needed to compare the performance of individuals at well-known stages of AD severity to the performance of age appropriate and well controlled groups of healthy older adults on gait dual-task paradigms to provide further evidence for the utility of this methodology and to re-evaluate when deficits in divided attention become apparent in AD. It is of theoretical and practical importance that future gait dual-task studies be designed so that different stages of AD severity are compared using reliable and well validated measures. This would be a significant step towards the standardization of gait dual-task procedures and allow researchers to investigate divided attention in the early stages of AD in a more systematic fashion.

A number of previous gait dual-task studies have failed to address theories of task prioritization in the interpretation of their results. Theories of successful aging such as the framework of Selection, Optimization and Compensation (SOC; Baltes and Baltes, 1990; Li et al., 2005) emphasize task prioritization processes whereby individuals emphasise the adaptive advantage of selecting tasks of higher immediate value (i.e., walking) over less critical cognitive tasks (Li et al., 2005). Termed the “ecologically valid approach to multitasking” or the “posture first strategy”, Li and colleagues (2005) suggested that young and neurologically intact individuals are able to cope with complex dual-task situations by adopting “safe strategies” (i.e., prioritizing balance over other concurrent tasks), and that such behavior is seen less often in elderly persons and individuals with AD (Li et al., 2005). In Study 2, the moderately impaired AD groups showed a unique and contrasting pattern of interference on the simple and complex dual-task trials which suggests that individuals in the later stages of AD may use an ineffectual “posture second” strategy under dual-task conditions. In keeping with the predictions of the SOC model, individuals with moderate AD, showed a relative preservation and unusual increase in their counting rate, at a larger expense to their walking rate on the complex dual-task. Thus, these results suggest that the progression of AD while almost certainly associated with deficits in divided attention may also be associated with a breakdown in those cognitive priority processes which allow an individual to prioritize gait over a competing cognitive task. This may help explain in part, why individuals with AD are at a higher risk of falls. However, this is an area of research which is yet to be addressed in the current gait-dual-task literature and only a few studies have explored how patterns of task prioritization between a cognitive and a motor task affect mobility and balance in healthy older adults (Rapp, Krampe, & Baltes, 2006).

It would also be a fruitful avenue of future research to understand how the severity of AD and the patient's awareness of their limitations affect gait dual-task performance. Decreased judgement, poor insight, lack of inhibition, and even wandering behavior in individuals with dementia may cause a lack of recognition of obstacles or hazards in the environment, which may in turn be casually linked to the increased risk of falling (Alexander & Hausdorff, 2008). Ultimately, how cognition affects mobility, dual-task performance, and fall risk in healthy older adults and those with AD likely involves a number of factors that are beyond dual-task paradigms. These interrelationships are likely built upon components of cognitive, physical and task prioritization processes, and modulated by disease severity, task complexity as well as the demands of the environment. Therefore, future research should rely on a comprehensive model that incorporates cognitive, physical, as well as task prioritization processes in understanding how higher brain functions influence gait dual-task performance.

A limitation of the current research is the extent to which comparisons can be drawn between previous laboratory based upper extremity dual-tasks, such as the one used by Lonie and colleagues (2009), and the current gait-dual task paradigm. Although speeded walking and upper extremity tasks are both coordinated motor movements, a large body of evidence suggests that walking is a much more complex and attentionally demanding task that requires input from other higher brain functions. This belief is further supported by the findings of Study 3 which showed that separate cognitive functions predicted gait speed and interference effects in healthy older adults and individuals with AD, even after adjusting for demographic variables and disease severity. As hypothesized, and consistent with previous studies, Study 3 showed that the Executive Functions/Attention/Speed factor was the most potent predictor of gait slowing and interference effects in the simple and complex dual-task. However, the contribution of this factor

was clearly mediated by performance on the other neuropsychological measures, most notably the episodic memory composite. Thus, it appears that although gait dual-tasks and upper extremity dual-tasks may share similar characteristics, walking is a much more complex task that utilizes higher cognitive processes. Therefore, caution should be taken when generalizing the results of the current study to other dual-task paradigms. Although it has not yet been addressed in the literature, it would be an interesting avenue of research to compare the same groups of participants on both a classic upper extremity dual-task (i.e., finger tapping) and a gait dual-task to assess the qualitative and quantitative differences in performance across these paradigms. Indeed, future research from our lab at the RRMC is aimed at comparing dual-task performance in individuals with AD and healthy older adults on both a gait dual-task paradigm and a finger-tapping dual-task paradigm.

Finally, to date, the majority of the neuropsychological dual-task literature has focused on describing the deficits that are associated with AD as well as normal aging. Recently, some authors have suggested that developing strategies for intervention, rather than continuing to describe patterns of decline, is an area of research that warrants increased attention (Al-Yahya et al., 2011). In particular, the treatment of an impaired ability to walk safely while performing another task (e.g., talking) has important everyday implications and could reduce the risk of falls in individuals with AD and those with reduced mobility. The potential of “dual-task training” as a means to improve gait and balance in individuals with an inability to divide attention between tasks has inspired a number of recent studies, suggesting that the training of task coordination processes is beneficial in healthy older adults (Li et al., 2010; Pellecchia, 2005; Toulotte, Thevenon, & Fabre, 2006), and in individuals with dementia (Schwenk, Zieschang, Oster, &

Hauer, 2010; Verghese & Holtzer, 2010) and other neurological populations, such as stroke and Parkinson's disease (Brauer et al., 2011; Yang, Wang, Chen, & Kao, 2007).

For example, Li and colleagues (2010) found that cognitive dual-task training in healthy older adults was an effective means of improving body sway in a task assessing dual-task standing, balance and mobility. Pellecchia (2005) measured balancing in healthy young and middle aged adults assigned to single-task, dual-task, or no-training groups. Following training, it was reported that only the dual-task training group was able to reduce their body sway to single-task levels (Pellecchia, 2005). A pilot study in 2006 by Toulotte, Thevenon, and Fabre found that healthy elderly fallers and non-fallers could be trained using single and dual-task exercises aimed at improving balance, and that significant improvements in dual-task performance were observed in both groups. Dual-task training has also been shown to improve motor functions in neurological conditions such as Parkinson's disease (Brauer et al., 2011) and stroke (Yang et al., 2007). However, dual-task training has not routinely been applied to older adults with AD, a population with high fall risk, or even with individuals at high-risk of developing AD (i.e., individuals diagnosed with aMCI). The exception is a recent study by Schwent and colleagues (2010) who evaluated the effectiveness of a 12 week dual-task training program in 60 individuals with dementia (the subtype was not specified), who were randomized into intervention and control groups. The intervention group received simple and complex dual-task training, such as doing mental arithmetic and walking. The main finding of this study was that dual-task training improved performance on complex dual-task conditions (i.e., walking and doing serial 3 subtractions) in the intervention group compared to the control group, and that training reduced the dual-task costs by half. Furthermore, these results showed that participants must be adequately challenged by the complexity of the cognitive task, as there was no effect of

training with tasks of lesser complexity (i.e., walking while doing serial 2 additions). This study demonstrates that cognitive remediation approaches are feasible in individuals with cognitive impairment, and it could provide a future avenue by which clinicians and researchers can help address the management of dementia, especially the risk of falls. Although it will be critically important to determine whether dual-task training will translate to “ecologically valid” gains in everyday functioning such as increased mobility and reduced fall rates, future research aimed at developing effective dual-task training interventions specifically developed for individuals with moderate AD holds great potential in helping to develop strategies for cognitive rehabilitation in individuals affected by this disease.

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APPENDIX A: INSTRUCTIONS FOR GAIT DUAL-TASK

Instructions for walking and number reciting

In this task, we are going to do some walking and some counting.

1.) Timed Up and Go Risk Assessment

I'd like you to take a seat here. In just a minute I am going to ask you to rise from this chair and follow the white tape on the floor until you reach the end (*demonstrate*). Once you reach the end, turn around, and return back to the seated position (*demonstrate*). Remember to walk at your regular and comfortable pace. If at any point you feel unsteady, tell me immediately and I'll be there to assist you. (If they have any assisted walking devices, please remind them at this point that they are allowed to use them throughout this procedure).

Now it's your turn. Rise from the chair and follow the white tape on the floor until you return to the seated position. Remember to walk at a brisk but comfortable pace, and keep going until your back to the starting position. *If at any point it is clear that the participant does not understand the tasks, say Stop! And correct any mistakes until they clearly understand the task.*

Good work....Let's try it again, and this time I am going to measure the time and number of steps that you make. Ready?...Go! *Watch participant carefully for any sign of unsteadiness, while recording the time, number of steps and any other gait abnormalities. Repeat for Trials 2 and 3.*

2.) Single-Task Trials

- **Walking**

Now we are going to do some more walking, but this time I am going to take the chair away and I would like you to stand at this line (*point out starting line*). When I tell you to "Go" I would like you to walk at a brisk but comfortable pace until you reach the other line at the end of the mat, like this (*demonstrate, pointing out line*). Once you reach the end, turn like this (*demonstrate*) and keep walking back towards the starting line. If you make it back to the starting line before time is up, turn again and continue walking until I tell you to stop, like this (Demonstrate making the second turn).

Now I would like you to try, When I say go I want you to start walking at a brisk but comfortable pace and continue walking until I tell you to stop. Ready? Go! *If at any point it is clear the participant does not understand the task, say Stop! Correct any mistakes until the participant understands the task. Time for 15 seconds. At the end of 15 seconds record the distance covered and any gait abnormalities.*

- *Counting by 1's*

Now I'd like you to do some counting by ones. Starting with the number 1, please count aloud by ones for me, as fast as you can. Like 1, 2, 3, 4...and so on. Ready? Go. *If the participant clearly does not understand the task, say Stop! Correct any mistakes and continue practice until the task is clearly understood.*

Time for 15 seconds. At the end of 15 seconds say Stop! Record the number reached and the number of mistakes.

- *Counting backwards by 2's from 70*

Now I'd like you do some more counting, but this time I would like you to count backwards by 2's. Starting with the number 70, please count backwards by 2's like this 70, 68, 66, 64 and so on...Ready? ...Go. *If the participant clearly does not understand the task, say Stop! If not, correct any mistakes and continue practice until the task is clearly understood.*

Time for 15 seconds. At the end of 15 seconds say Stop! Record the number reached and the number of mistakes.

3.) Dual Task Trials

Now we are going to do some more counting and walking, but this time we'll do them at the same time. For example, in some trials I will ask you to walk as quickly as you can and count by 1's at the same time. When I ask you to do two things at the same time I want you to remember that both tasks are equally important. That means I want you to walk as quickly as you can, while counting as accurately as you can. Do you understand? *Make sure participant understands the task emphasis and the dual task design.*

- *Walking and Counting by 1's*

First, I'd like you to count by ones as fast as you can while also repeating the walking task. Like this (demonstrate 1, 2, 3 etc while walking). Now you give it a try. Walk at a brisk but comfortable pace and remember that both tasks are equally important. Starting with the number 1, count by ones as fast as you can, like 1,2,3... while also walking at a comfortable pace. Remember to stop if you feel unsteady, and don't stop counting or walking until I tell you to stop. Again, start with the number 1. Ready? Go, *If the participant clearly does not understand the task, say Stop! If not, correct any mistakes and continue practice until the task is clearly understood.*

Time for 15 seconds. At the end of 15 seconds say stop! Record the distance covered, number of digits produced, mistakes made and any other gait abnormalities.

- *Walking and Counting backwards from 70 by 2's*

Now I'd like you walk the same path again while counting backwards from 70 by 2 like we practiced before, like this (*demonstrate, 70, 68, 66, 64 while walking*). Now you give it a try and remember that both tasks are equally important. Starting with the number 2, walk at a brisk but comfortable pace counting backwards from 70 by 2's . Again, start with the number 70. Go ahead. *If the participant clearly does not understand the task, say Stop! If not, correct any mistakes and continue practice until the task is clearly understood.*

Time for 15 seconds. At the end of 15 seconds say stop! Record the distance covered, number of digits produced, mistakes made and any other gait abnormalities.

4.) Single-task trials

- *Walking*

Now we are going to do each of the tasks individually one more time. First, I would like you to complete the walking task again. You don't have to count this time, just remember to walk at a brisk but comfortable pace until I tell you to stop. Ready? Go. *Time for 15 seconds. At the end of 15 seconds say stop and record the distance covered.*

- *Counting by ones*

Now I'd like you to count by ones again. Start with the number 1 and count as fast as you can by ones, like this (*demonstrate 1, 2, 3. etc...*), until I say stop. Remember to count quickly, but not so quickly that I can't understand what you're saying. Ready? Go! *Time for 15 seconds. At the end of 15 seconds say Stop, record the digits produced and number of mistakes.*

- *Counting backwards from 70 by 2's*

Great job! Now for the last task I would like you to count backwards from 70 by 2's one more time, like this (*demonstrate 70, 68, 66, 64 etc...*). Count as quickly as you can. Ready? Go! *Time for 15 seconds at the end of 15 seconds say Stop, record the digits produced and the number of mistakes.*

APPENDIX B: CONSENT FORM



CONSENT FORM

Rural and Remote Memory Clinic

*You are invited to participate in a study entitled: **Measuring Dual-Task Performance Using Gait Assessment in Dementia and Normal Aging.** Please read this form carefully, and feel free to ask any questions you may have about the study.*

Student-Researcher: Jocelyn L. Pooch, Department of Psychology, University of Saskatchewan TEL: (306) 664-6658.

Supervisor: Dr. Margaret Crossley, Department of Psychology, University of Saskatchewan TEL: (306) 966-5923.

Purpose and Procedure: Our purpose is to investigate your ability to divide your attention between two tasks at the same time, specifically, your ability to talk while walking. This project will require you to walk a short distance while carrying out an easy and difficult counting task. We will also ask you to complete two brief cognitive evaluation measures, the Modified Mini-Mental State Examination and a Wide Range Achievement Test. This should take approximately 30 minutes of your time.

Potential Risks: Walking is a common daily activity which underlies the increased risk of falling for older adults. Although we will take every precaution to prevent falls, there will always be some risk that a fall may occur during this study.

Confidentiality: Any information gained from your participation in the project is confidential and will only be shared with members of the project team. All data collected in this project will contain no identifying information, and the data and consent forms will be stored separately by the supervisor at the University of Saskatchewan. The findings will be presented at conferences, and the project team will travel to participating communities to present our findings to residents and health care professionals.

Participation is Voluntary: You may withdraw from the project for any reason, at any time, without penalty of any sort and without losing access to the services available through the Memory Clinic. If you choose to withdraw from the project, any information that you have contributed will not be used and will be destroyed.

Questions: If you have any questions concerning the project, please feel free to ask at any point; you are also free to contact the researchers at the numbers given above. This project has been approved on ethical grounds by the University of Saskatchewan Behavioral Research Ethics Board. Any questions regarding your rights as a participant may be addressed to that committee through the Office of Research Services at 966-2084.

CONSENT TO PARTICIPATE:

I, _____, have been informed of the nature of the ***Measuring Dual-Task Performance Using Gait Assessment in Dementia and Normal Aging project***, I have received a copy of this consent form for my records. I freely consent to participate in this project.

Participant Signature: _____ Phone # _____

Caregiver Signature: _____

Investigator Signature: _____

Date: _____

APPENDIX C: RECORD FORM FOR GAIT DUAL-TASK

Counting and Walking
Recording Form

1.) **Timed Up and Go**

Number of Steps _____

Total Time _____

2.) **Single Task Trials**

Walking

Distance Walked _____

Counting by 1's

Trial

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35
36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66
67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97
98 99 100

Numbers recited: _____ Errors: _____

Counting backwards by 2's from 70

Trial

70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10

Numbers Recited: _____ Errors: _____

3.) **Dual Task Trials**

Walking and Counting by 1s.

Counting by 1s

5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37
38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68
69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99
100

Numbers Recited: _____ Errors: _____

Distance Walked _____

Walking and Counting Backwards by 2's from 70

Counting backwards from 70

70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10

Numbers Recited: _____ Errors: _____

Distance Walked _____

4.) Single Task Trials

Walking

Distance Walked _____

Counting by 1's

Trial

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35
36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66
67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97
98 99 100

Numbers recited: _____ Errors: _____

Counting backwards by 2's from 70

Trial

70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10

Numbers Recited: _____ Errors: _____