CHAPTER 2

LITERATURE REVIEW

The literature review in this study is consisted of four sections. The first section provides a detail of Mild Cognitive Impairment (MCI) definition and diagnosis. The second section covers the concept of gait characteristics in individuals with MCI. In this section, both mean and variability of spatiotemporal gait parameters are reviewed. The third section covers dual-task paradigm and dual-task related gait changes in individuals with cognitive impairment. The last section covers the standardized neuropsychological test often used to evaluate cognitive functions.

2.1 Mild cognitive impairment

At present, the competent way in reducing the number of patients with Alzheimer’s disease (AD) is to identify people with pre-AD symptoms and provide an early intervention. Recent research has identified a transitional state between the cognitive changes of normal aging and AD, known as mild cognitive impairment (7). Storandt et al. (14) reported that the onset of MCI occurs from the age of 50 years and older. Research evidence suggests that individuals with aMCI tend to progress to probable AD at a rate of approximately 10% to 15% per year (7). Data from the Mayo Alzheimer’s Disease Research Center reported a conversion from MCI to AD of up to 80% during approximately 6 years (6). MCI is defined as a transitional state between the cognitive changes of normal aging and pathologic cognitive aging or dementia (7). To date, there is no consensus on the standard criteria for MCI diagnosis. Among several criteria sets for diagnosing MCI, Peterson's criteria (7, 15) have been widely used both in clinical and research settings. Petersen's criteria for diagnosing MCI are: 1) memory complaints preferably corroborated by an informant, 2) objective memory impairment adjusting for age and education, 3) normal general cognitive function as determined by a clinician's judgment based on a structured interview with the patient and an informant interview 4) essentially preserve activities of daily living, 5) Not sufficiently impaired, cognitively and functionally, to meet National Institute of Neurological and Communicative Disorders and Stroke/ Alzheimer's disease and Related Association (NINCDS-ADRDA) criteria for AD, as judged by an experienced AD clinician.

When memory loss is the predominant symptom, it is termed amnestic MCI (aMCI). Persons with aMCI are usually aware of their memory impairment and able to compensate, so that it doesn't affect their daily functioning. The neuropsychological domains that affected first in persons with aMCI are memory, attention, and executive function (4). Other cognitive domains such as language, perceptual skills, constructive abilities, orientation, problem solving and functional abilities are shown to be less detriment or preserved in aMCI.

Non-amnestic MCI (naMCI) is classified as individuals who demonstrate impairment in cognitive domains other than memory. For example, a pronounced language disturbance might progress to primary progressive aphasia, or an alteration in attentional abilities and a dysexecutive syndrome might progress to frontotemporal dementia. aMCI seems to represent an early sign of AD whereas the outcomes of the naMCI subtype appear more heterogeneous including vascular dementia, frontotemporal dementia or dementia with Lewy bodies (7).

2.2 Gait characteristics in individuals with cognitive impairment

2.2.1 Mean spatiotemporal parameters

Age-related changes in gait characteristics are well documented. For decades, researchers dedicated to investigate the characteristics of gait-related changes among elders. Findings showed that elders decrease their walking speed, increase cadence, decrease step length, and spend more times in double limb support phase as compared to adults (16-18). These changes in gait pattern are thought to be a compensatory strategy adopt by elders to overcome their destabilizing gait (17, 18). Recently, there is an increased interest in the study of dementia-related gait changes due to the notion that cognition plays a critical role in gait. Findings showed that dementia-related gait changes include decrease walking speed, decrease stride length, and increase support time (5, 19). Further, some studies found that gait disorders can be identified at an early stage of dementia or even at a pre-dementia stage (11, 20). The presence of gait disorders has been found to precede the onset of dementia by several years (20). However, to date, only few studies investigated gait-related changes in people at a pre-dementia stage or MCI. Verghese et al. (21) investigated gait performance in aMCI compared with healthy older adults. Results revealed that participants with aMCI have significant shorter stride length as compared to healthy older adults. A longitudinal study by Waite et al. (20) found that gait slowing is an independent predictor of dementia incidence. In contrast, a more recent study by Pettersson et al. (22) found that walking speed was not different between MCI and healthy controls.

2.2.2 Gait variability

Among gait parameters, gait variability, is proposed to be the robust indicator of gait instability. Gait variability is defined as stride-to-stride inconsistency during walking which shown to be an early indicator of fall risk and predictor of future fall in highly mobile older persons (16, 23, 24). Hausdorff et al. (25) investigated gait variability and association of factors that contribute to gait variability in elders. They found that stride time variability was correlated with many factors such as health status, mental status, muscle strength and balance ability. They concluded that stride time variability can be used as a predictor of future falls. Furthermore, Maki (16) suggested that increased variability of stride length is associated with falls, whereas information from the average gait speed and stride length associated with fear of falling.

Recently, gait dysfunction has been reported to present at the early course in cognitive impairment elders, especially AD patients. However, few studies have measured gait variability in people with AD, despite the high incidence of falls. Webster et al. (12) compared gait variability of ten community-dwelling older adults with AD and found that stride length variability was significantly greater in the AD group compared with the control group. Step width variability was significantly reduced in the AD group compared with the control group at slow speed. In summary, gait dysfunction observed in AD indicated the essential of cognition for efficient gait performance. There is growing evidence that the pre-clinical stage of AD (i.e. MCI) also demonstrates the subtle change of gait dysfunction. For example, a study by Verghese et al. (21) found increased variability in stride length and swing time in aMCI persons as compared to non-cognitive impaired elders.

In summary, during usual walking (single-task walking), certain mean and variability of gait parameters are shown to distinguish aMCI from normal individuals. These gait parameters include mean and variability of stride length, and variability of swing time. Findings on gait speed as an indicator to differentiate aMCI from normal individuals are inconclusive.

2.3 Dual-task paradigm and dual-task related gait changes in individuals with cognitive impairment

Dual-task paradigm is the method used to investigate attention involvement in performing concurrent task. In most studies, the secondary task was used to increase the cognitive demand by divided the participant's attention from the primary task. This method is commonly used to assess cognition involvement in gait performance. The dual-task cost (DTC) calculation is the method widely used to determine the cognition involvement in gait by considering the decrement of gait performance under dual-task conditions compared to single-task. The dual-task cost can be calculated form the following equations: Dual-task cost = (dual condition - single condition)/single condition x 100 or dual-task cost = (single condition - dual condition)/single condition x 100, depending on the dependent variable (whether it generally increases or decreases from single- to dual-task. For example, gait velocity under single-task condition is generally greater than those under dual-task condition. Thus, gait velocity was calculated from equation: (gait velocity under single-task condition - gait velocity under dual-task condition)/ gait velocity under single-task condition x 100. In contrast, swing time under single-task condition is generally smaller than those under dual-task condition. Therefore, swing time was calculated from equation: (swing time under dual-task condition – swing time under single-task condition)/ swing time under single-task condition x 100. Lower DTC represented better performance under dual-task conditions (26).

There are 2 main neuropsychological theories explaining the dual-task paradigm; the capacity-sharing theory and the bottleneck theory. Yogev-Seligmann et al. (3) revealed that “The capacity-sharing theory states that attentional resources are limited in capacity, so the performance of two attention-demanding tasks will cause deterioration of at least one of the tasks. When the time between the presentations of two or more stimuli is reduced, the time of processing will be increased because of the limitations of the shared capacity. This theory assumes that it is possible to voluntarily allocate capacity to a specific task, even when both tasks are over-learned and largely automatic. Thus, the performance of an additional task during walking can alter gait (e.g., stability, speed) or the execution of the second task or both. Another theory, the bottleneck theory proposes that if two tasks are processed by the same neural processor or networks, a bottleneck is created in the processing of information. The processing of the second task will be delayed until the processor is free from processing the first task. This theory explains the delay in the reaction times of the second task as a function of the temporal gap in the presentation of the two stimuli. According to the bottleneck theory, performance of another task during walking might result in a slowed gait or delayed performance of the second cognitive task, but only if the neural networks involved in the two processes overlap” (3).

Since cognitive function is mildly affected and the physical function is preserved in persons with MCI, an assessment of gait performance in unchallenged conditions such as usual walking (walking-single task) may not reveal gait abnormalities. Therefore, dual-task paradigm has been used to interfere walking in individuals with MCI (2). Previous studies often used dual-task paradigm as a method to increase capacity loading without emphasizing on any specific cognitive domains 7). Maquet et al. (27) compared gait characteristics between single- and dual-task condition in individuals with MCI. The results showed that participants with MCI demonstrated slower walking speed and shorter stride length during dual-task condition (walking in concurrent with counting backward) than during single-task condition (usual walking). Montero-Odasso et al. (2) investigated the relationship between cognitive factors and gait performance during dual-tasking in individuals with MCI. Gait velocity was measured while participants performing counting backward aloud from one hundred by ones. The results showed that low executive function and working memory performance were associated with slow gait velocity.

In summary, since persons with MCI are functionally independence, an assessment of gait performance in unchallenged conditions such as usual walking may not reveal gait abnormalities. Dual-task paradigm is proposed to be a challenging task by divided the participant's attention from the primary task. Exploring gait characteristics in challenging condition as adding secondary task may reveal gait dysfunctions in individuals with MCI. The evidences showed that MCI demonstrate slower gait velocity and shorter stride length under dual-task condition compared to those under single-task condition. This findings may be due to individuals with MCI have limit capacity to divide attention between walking and performing the secondary task.

2.4 Neuropsychological test for specific cognitive domains

At present, studies on cognitive function and gait have been expanded to include multidisciplinary areas of research such as physiology, biomechanics, neuroimaging, and neuropsychology. This review covers two specific cognitive domains proven to play important role in gait performance. These two cognitive domains are executive function and attention (3, 28).

2.4.1 Executive function domain

Executive function refers to a diversity of higher cognitive processes that use and modify information from many cortical sensory systems to plan, monitor and execute a sequence of goal-directed complex actions. These include initiation, planning, problem solving, working memory, and attention (28). The areas of frontal lobe especially the dorsolateral prefrontal cortex and related brain networks have been suggested to be responsible for executive function (3).

Standardized neuropsychological tests that are widely used to evaluate individuals executive function ability include serial 3 subtractions test, Stroop Color test, Wisconsin Card Sorting test (WCST), Digit symbols test (29, 30). In this study, the Serial 3 Subtractions test was used to assess the executive function in persons with aMCI. The serial 3 subtractions is widely accepted as a practical method in examining executive function ability during walking. To administer the Serial 3 Subtractions, a participant is asked to subtract three from random digit numbers, and then keep subtracting three from the prior answer.

2.4.2 Attention domain

There is no single, clear definition of attention. The term "attention" can be defined as a dynamic function driven by sensory perception and ability to select a preferred stimulus for a particular action while ignoring the unnecessary stimuli (31). Woollacott and colleagues (32) defined attention as the information processing capacity of an individual. Attention can be classified into 3 types; selective, sustained (or focused) and divided attention. Selective attention refers to the ability to focus on a single stimulus while disregarding extraneous stimuli. Sustained or focused attention refers to the ability to maintain attention to a task over a period of time. Lastly, divided attention refers to the ability to carry out more than one task at the same time (33).

There are several standardized neuropsychological tests that used to evaluate attention, for example, digit span test and trail making test (3, 33, 34). In this study, the Digit Span test was used to test participant's attention ability when performing two tasks simultaneously. This test is proposed to be a suitable method in assessing the ability to divide attention when walking and performing cognitive task.

Digit span is a subtest of the Wechsler batteries, one of the most widely used tests in neuropsychological research and clinical evaluation (34). The digit span test contains two subtests including digits forward and digits backward. To administer the digit span test, series of digits strings are read to participants and the subjects are required to repeat vocally in the correct sequence (either forward or backward). The number of digits in each string increases from 3 to 9 forward and 2 to 8 backward.

2.5 Verbal fluency

The verbal fluency is included in the testing condition to ascertain that the alteration in gait performance during dual-task is resulted from the impairment on executive and attention domains not by an influence of the articulo-motor component (i.e. speaking). Previous work reported that verbal fluency is preserved in individuals with aMCI (15). Verbal fluency is defined as the ability to create the right words in correct meaning and use it at the right time. The performance in verbal fluency can reflect the capability of speech and language in generating the words, which related to semantic knowledge (35). To administer the verbal fluency, participants are required to say as many words as possible from a category in a given time (usually 60 seconds). This category can be semantic such as animals, fruits or phonemic such as words that begin with letter p. The number of correct words in the given time are measured in verbal fluency (35).

In summary, the aim of the present study was to investigate the effects of specific cognitive domains, mainly attention and executive function on gait performance in individuals with aMCI. The serial 3 subtractions test was used to assess executive function and the digit span test was used to assess attention. Finally, verbal fluency was used to control for an influence of the articulo-motor component (i.e. speaking) during walking.