

CHAPTER 1

RATIONALE OF THE STUDY

The prevalence of dementia has been expected to increase dramatically in future years as the baby boomer generation ages and the average lifespan increases. Approximately 114 million elderly worldwide are expected to have Alzheimer's Disease (AD) by the year 2050 (1). Although dementia cannot be cured, promising evidence reveals that early intervention can delay the disease progression. Individuals with Mild Cognitive Impairment (MCI) are at a transitional stage before converting from normal ageing to dementia (2). They have an increased risk of cognitive and functional decline. The rate of conversion from MCI to AD is 10-15% per year as compared to 1-2% per year in cognitively intact elders (2, 3). Therefore, many research studies presently are dedicated to determining the clinical features and clinical management for individuals with MCI.

The main purpose of this thesis was to investigate motor and cognitive performance in individuals with MCI. This thesis comprises three sub-studies. The first study aimed to develop and evaluate the short-term effect of the cognitive training program that focuses on the core impairment aspects, including episodic memory, attention and executive functions, of individuals with MCI. The second study aimed to investigate gait performance in individuals with MCI during gait initiation and

termination under both single-task and dual-task conditions. The last study aimed to examine the role of MCI in predicting physical decline over 1 year.

At present, there is no consensus on the standard guideline for treatment of individuals with MCI. Pharmacological treatments such as cholinesterase inhibitors are generally considered as the first option to manage MCI symptoms (4, 5); however, their efficacy in delaying progression to AD is not confirmed (6, 7) so it is important to structure non-pharmacological interventions. Recent evidence suggests that a cognitive training program can improve cognitive functions and hinder functional decline of individuals with MCI (8-13). A multifaceted rehabilitation program which is composed of cognitive, motor, and psychosocial training components is proposed to be the most competent method of restoring and promoting cognitive function in persons with cognitive impairment (8, 10, 13). This approach, however, has certain limitations such as the long duration of training and the variations of training protocols among studies. Importantly, it is not known how each training component contributes to the patients' cognitive improvement. Therefore, the aim of our first study was to develop the cognitive training program that focuses specifically on the impairment of memory, attention and executive function. The efficacy of this program was determined at both the behavioral level (determined by cognitive skills) and molecular level (determined by neurochemistry biomarkers).

Traditionally, it is thought that MCI solely affects cognitive function. Thus, cognitive impairment, particularly a memory deficit, is proposed to be a hallmark in identifying individuals with MCI. Recent studies have shown that individuals with MCI

demonstrate cognitive impairment in conjunction with subtle changes in physical functions, especially impaired gait and balance (14, 15). However, this finding is not supported by other studies that have found no differences in gait patterns between individuals with MCI and cognitively intact controls (16, 17). These inconsistencies may be due to the variations in walking tasks and outcome measures used, and it is possible that gait impairment in people with MCI is more pronounced in challenging walking conditions. Gait initiation and termination are complex transition phases due to the increased stability required during a transient period (18, 19). There is evidence that many falls in older adults occur during walks of only short distances in which initiation and termination phases make up a large part (20). In addition, it has been demonstrated that performing a dual-task has an adverse effect on gait performance in people with cognitive impairment (21), and it is possible that such constraints may occur also in people with MCI. Therefore, the aim of the second study was to investigate gait dysfunctions in individuals with MCI during gait initiation and termination, under single-task and dual-task conditions.

According to previous knowledge about a relation between MCI and impaired physical function, the next important question was whether objectively defined MCI could predict physical decline over time. Therefore, the third study emerged to answer this question by following the changes in physical function related to fall incidents over 1 year using Physiological Profile Assessment (PPA). PPA was chosen because it is a valid and reliable method of quantifying physiological fall risk in older people (22). If MCI can

be linked to physical decline over time, it can be used as the clinical marker in predicting future falls.