Early Detection of Dementia of the Alzheimer's Type: Examining the Use of Cognitive Tasks and Neuropsychological Tests for Chinese with Minimal Education

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Abstract

Abstract of thesis entitled: Early Detection of Dementia of the Alzheimer's Type: Examining the Use of Cognitive Tasks and Neuropsychological Tests for Chinese with Minimal Education

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Dementia of the Alzheimer's Type (DAT) has become a critical public health problem with enormous cost to the society and patients' families. Early detection procedure that is sensitive and easily administrated is needed to discriminate DAT from normal aging so as to help to slow down the progress of their disease. In China, early identification of dementia is also of equal paramount importance given its over 100 millions age 60 years and older population and at least 5% of whom (totally 6 to 7 millions) are suffering from dementia.

The present thesis aimed to identify sensitive cognitive tasks and neuropsychological tests that could discriminate very mild DAT from normal aging among Chinese older adults with little formal education. The thesis compromises one major study (Study One) and supplementary studies (Studies Two and Three).

Study One examined whether the adapted attention tasks (face-number switching task, number Stroop switching task) and working memory tasks (counting span task, and digit suppression task) could discriminate people with very mild DAT from normal aging adults. A total of 139 participants (40 very mild DAT adults, 48

normal aging adults, and 51 young adults) were administrated Clinical Dementia Rating scale (CDR; Morris, 1993; Morris, McKeel, Fulling, Torack, & Berg, 1988) to stage the dementia status and employed aforementioned cognitive tasks as measurement of attention abilities. Intraindividual variability analyses and ex-Gaussian distribution analyses were used to capture the characteristics of RT performance for individuals in all three groups. The results showed that the pure trials in face-number switching task and digit suppression task performed as the most discriminating tasks. In comparison, the mixed block in the face-number switch task, the number Stroop switch task and the Counting Span task were comparatively less discriminating. Furthermore, the most discriminating indicators were residualized intraindividual standard devidation of RT performance and the tau value in ex-Gaussian distribution analyses in discriminating very mild DAT from normal aging.

Study Two examined the neuropsychological tests currently used in Hong Kong and tried to identify tests or subtests that would not work or even disadvantage (bias) Chinese illiterates or people with less education. As most traditional tests in screening dementia patients have been constructed in developed countries where 77.4% of older adults finished their high-school education, it is crucial that these tests are carefully scrutinized before their adoption for the Chinese population, where only about 16% and 20% did so in Hong Kong and in mainland China. Other than CDR, various neuropsychological tests were used to assess participants' cognitive functions: the Chinese Mini-Mental State Examination, the Chinese version of ADAS-Cog, the abstract thinking task, digit and visual span tests, and the Verbal Fluency Test. The purpose was to identify instruments that might not be suitable for Chinese with little or no education. Tests and subtests that are suitable for Chinese with little or no

education, for those with more education and for both have been identified respectively.

Study Three tried to tease out potential pathways through which education protect people from dementia. Using the CMMSE subscales as indicators of different dimensions of performance, the study showed that education has a stronger protective effect on memory, orientation and judgment, and possibly through enhancing specific skills such as orientation of time and location and counting or recite downward (i.e., C-MMSE1, C-MMSE2, C-MMSE4).

Clinical implications and limitations of the results in various studies were discussed.

摘要

目前全球有2600萬腦退化症病人，隨著人口老齡化的發展，腦退化症已成為一個重要的社會健康問題。在中國，腦退化症患病率達5% （約600到700萬人）。由於目前尚未發現有效治癒的藥物，通過敏感和適當的篩查工具，有助於儘早發現臨床前期的病人並予以干預，從而努力拖慢病情進展。

鑒於中國長者（較西方國家長者）的受教育水準普遍偏低，一方面，需要設計和發展敏感的、適合低教育水準人群的工具，以便進行早期篩查；另一方面，在使用來自西方國家的篩查量表時，需瞭解其對於中國長者的適用性。本研究旨在探索適合中國長者的篩查工具和敏感的指標。主要包含三個研究，研究一探索了注意和工作記憶任務在區分輕微癡呆病人和正常長者的表現，研究二和研究三分別探索了教育水準對長者在認知功能篩查量表中表現的影響，以及教育對認知功能的保護作用。

共88位長者被試（來自香港一項腦退化症及輕度認知障礙患病率跟進研究，Lam et al., 2008a, 2008b）參與研究一，其中，40位為輕微癡呆病人，48位為正常長者。同時有51位年輕被試作為對比組。除採用臨床癡呆量表（Clinical Dementia Rating, CDR; Morris, 1993; Morris, McKeel, Fulling, Torack, & Berg, 1988），被試還完成了兩個注意力任務和兩個工作記憶任務。

研究一發現最具區分力的任務是面部-數位轉換任務中的兩個單純序列以及數位抑制任務，並且通過將反應時資料進行ex-Gaussian分佈分析以及intraindividual variability的分析，發現tau和residualized ISD為最敏感的指標，能出色的區分輕微癡呆病人與正常長者。

研究二及研究三的資料來自上述跟進研究的788位被試（405位為輕微癡呆病人，383位為正常長者）在一系列認知功能篩查量表的測試資料。在分量表的水準上，研究區分了分別（及同時）適用於較高及較低教育水準的被試的測試題目，特別是，區分了不適用於較低教育水準被試的測試題。

研究三檢查了早期的教育可能令部分認知功能（時間及地點定向能力，注意力）得到提升從而更小機會患癡呆。

西方國家發展的篩查量表是基於較高教育水準的人群而設計，將之引用至教育水準相對較低的中國長者，需非常謹慎，尤其是教育水準對篩查結果的影響。本研究基於西方最近的研究，設計和修改了認知任務，採用面部圖片以及簡單的個位數位作為刺激材料，令即使沒有教育經歷的中國長者也能順利完成測試，並表現出較好的區分力。

找出簡便易行的認知篩查任務（如研究一使用的面部和數位的單純序列，以及數位抑制任務）以及採用更恰當的資料分析和敏感指標（如tau, intraindividual variability），將有助於找到適用于較低教育水準的中國長者的篩查工具。

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Chapter 1 Introduction

1.1 What is DAT and Why early detection?

With an increasing aging population, dementia has become a most critical public health problem with enormous social cost and family burden in taking care of these patients. The main subtype of dementia is Dementia of the Alzheimer's Type (DAT). It is a neurodegenerative disorder that leads to unreversable changes in the brain (e.g., the death of brain cells).

Currently no effective therapy is available to cure the disease (e.g., Jalbert, Daeillo, & Lapane, 2008). Moreover, it is not easily detected because the pathological abnormality is long existed before clinical symptoms are noticeable (e.g., Bennett et al., 2002, 2006). Considering the high mortality rate of dementia, large population (26 million in the world) suffering from dementia, early detection of the disease is thus imperative for patients to take proper treatment to slow down the progress of the disease (Maurer, Ihl, Dierks, & Frölich, 1997). Meanwhile, with the development of more effective treatments, improved sensitive detection in the earliest possible stages is necessary to ensure the affected individuals are being identified as early and as accurately as possible.

The present research thus aims to examine the performance of a few cognitive tasks and neuropsychological tests in discriminating patients with very early Dementia of the Alzheimer's type (DAT). It focusd especially on adapting and modifying potentially useful tests for use with Chinese participants who were

illiterate or with minimal education. Recent advanced statistical analyses, such as on the response time (RT) distribution and intraindividual variability of RT data, would also be applied.

1.2 Background of Research

Previous studies have suggested that people with fewer than eight years of formal education might be more likely to develop DAT than those with more education (Bruandet et al., 2008; Launer et al., 1999). Unfortunately, the proportion of older adults with no schooling or only pre-primary education is estimated to be at least 35% in Hong Kong (Census and Statistics Department, 2006) and 26% in China (National Bureau of Statistics of China, 2005). China has a population with more than 100 million people at 60 years of age and older (Dong et al., 2007) whose prevalence of dementia is at least 5% (i.e., equivalent to a total of six to seven million people with dementia) (Declaration of Protection and Cure for Geriatric Dementia in China, 2009). Similarly in Hong Kong, the prevalence of dementia among the elderly aged 70 years and over was estimated to be 9.3% in 2006 (i.e., for the total population of about 6 million) (Department of Health, HKSAR, 2006).

Although various traditional psychometric tests have been available for dementia screening, most of them are constructed in developed countries where the educational level of population is much higher than that in developing countries and areas. It is also well demonstrated in various studies that performance in the screening tests is very much influenced by the educational level of these older adults

(Borkowski, Benton, & Spreen, 1967; Koepsell et al., 2008; Schmitt, Ulvestad, Antonucci, & Kinney, 2000). The greatest concern is whether some instruments might erroneously identify people as having dementia just because of their lack of education or schooling. It is imperative, therefore, to examine closely the psychometric properties and characteristics of currently used psychological tests among Chinese population with diversified educational background.

In addition to the psychological screening instruments mentioned above, computer-based cognitive tasks have been used to study the cognitive decline in early stage of DAT. Although memory decline has been well documented as an early clinical marker of DAT, recent studies have suggested that attention tasks (e.g., Stroop task; Spieler, Balota, & Faust, 1996) seem to be more sensitive and accurate measurements than conventional psychological screening tests in early detection in DAT.

There had been few studies in Hong Kong designed specifically to investigate the discriminating power of cognitive indicators in attention tasks. Furthermore, with the improvement and advancements in measures or statistical methods with response time data (e.g., ex-Gaussian distribution analyses and intraindividual variability), new indicators have been found to be more sensitive and accurate than traditional mean-level analyses in capturing the cognitive decline (Balota, Yap, Cortese, & Watson, 2008; Hultsch, Strauss, Hunter, & MacDonald, 2008). In order to improve the sensitivity in discriminating people who are at risk of becoming DAT, it is necessary to test the performance these seemingly more sensitive measures in

Western studies and develop appropriate tasks (e.g., nonverbal task) for Chinese population with much less education.

1.3 General Objectives and Structure of the Thesis

The current research has three main aims. Its primary aim is to examine the discrimination power of two attention tasks and two working tasks in identifying very mild DAT individuals in the Hong Kong Chinese population. In particular, measures of intraindividual variability and the value of tau generated from ex-Gaussian distribution of the attention tasks would be compared with traditional mean-level methods. In addition, the current research is to investigate the interrelationships between the attention task performance and the working memory capacity as measured by the memory tasks.

This research would examine the discriminating power of a number of screening tests that had been widely used in Hong Kong among older adults with diversified educational background. The purpose was to identify tests that might not be appropriate for people with no or limited education. In addition, the relation between education and dementia status was investigated. Specifically, this study aimed to identify the cognitive abilities which might serve as the potential mediators that protect older adults from developing dementia.

The first five chapters of the thesis provide the relevant background information for the three studies. Chapter Two reviews the main types of dementia as well as the prevalence of dementia in the West and in China. The characteristics

of the prevalence across different regions, the risk factors of dementia, and the various assessment methods commonly used have been noted.

Chapter Three reviews the literature on the cognitive impairment in DAT and focuses on memory and attention domains. Chapter Four reviews the neuropsychological tests currently used in Hong Kong and discusses potentially useful strategies and tests for people with minimal education.

Chapter Five reviews the problems in traditional mean-level analyses of response time data. This is followed by a more detailed review on the use of the ex-Gaussian distribution to fit response time data and a discussion on the analyses of intraindividual variability.

Chapter Six to Eight present three studies, each answering the overarching research questions as discussed above. The final chapter presents an overall discussion on the findings and elaborated upon research limitations of the present research.

Chapter 2 Literature Review -- Dementia: Prevalence and Risk Factors

2.1 Types of Dementia and Clinical Symptoms

Dementia is a major health problem of growing public concern around the world in recent years (Berr, Wancata, & Ritchie, 2005; Dong et al., 2007; Liu, Guo, Zhou, & Xia, 2003). It is a progressive fatal disease with prevalence that increases substantially after 60 years of age and will likely double for every five year increase in age for older adults (Evans, 1990; Menzin, Lang, Friedman, Neumann, & Cummings, 1999; for an alternative view, see Gao, Hendrie, Hall & Hui, 1998).

Clinically, dementia is defined by the American Association for Geriatric Psychiatry as *"a clinical syndrome characterized by global cognitive decline with memory and one other area of cognition affected that interfere significantly with the person's ability to perform the tasks of daily life and meet the Diagnostic and Statistical Manual of Mental Disorders, fourth edition text revision (DSM-IV-TR) criteria"* (Lyketsos et al., 2006, p.561).

This chapter will begin with a brief introduction of the main subtypes of dementia, *Dementia of Alzheimer's Type* (DAT) and *vascular dementia* (VaD). Then the prevalence of dementia both in the West and in China is discussed and the characteristics of the prevalence in difference regions are highlighted. Finally, the risk factors of dementia and the implications are outlined.

2.1.1 Dementia of Alzheimer's Type (DAT) and Vascular Dementia (VaD)

The most frequently found dementia subtypes are DAT and VaD (Dubois &

Herbert, 2001; Lobo et al., 2000). DAT refers to the specific type of dementia caused by Alzheimer's disease, accounting for 50 to 70 percent of all cases (Cummings & Cole, 2002). It is often manifested through progressive deterioration in cognition (such as memory and language), a slow onset of neuropsychiatric symptoms, and a gradual losing of the ability in daily activities (APA, 1987; McKhann et al., 1984; Sadik & Wilcock, 2003).

From etiology, VaD differs from DAT in that the former is caused by the chronic reduced blood flow in the brain followed by cerebrovascular diseases or stroke (for more details, see UCSF Memory and Aging Center, 2010). On clinical symptoms alone, it is sometimes difficult to distinguish between these two types of dementia. It is because their symptoms are not easily noticeable at the early stage of the disease. Furthermore, they subsequently lead to similar clinical impairments, such as insidious worsening of memory and other cognitive functioning. The possible difference between VaD and DAT, however, is that the deterioration of VaD can sometimes be prevented (intervened) and occasionally even reversed (UCSF Memory and Aging Center, 2010). Between these two types, it is worthy to note that DAT has been the fourth most common cause of death among the elderly population. Life expectancy for them ranges from 4 to 8 years depending on the age and the severity of the disease at the time when the disease is diagnosed (Larson et al., 2004).

2.1.2 Clinical Symptoms

In the early stages of DAT, clinical symptoms of dementia are usually difficult to recognize because the deterioration generally develops slowly (McKhann et al., 1984).

This stage of subtly progressive deterioration can last for 2 to 4 years. During this stage, these people might be less energetic and demonstrate minor cognitive deficits (e.g., slight memory loss; slow reaction; poor planning and judgment), which might be wrongly perceived as normal cognitive decline due to aging (American Health Assistance Foundation, 2011).

As the patients progress to the later stages, from moderate to severe, more salient and noticeable disabilities will emerge (American Health Assistance Foundation, 2011). Thus, for example, patients may have comprehension difficulties in communication, experience more serious memory problems, and may be unable to recognize familiar people, including even significant family members. When patients are aware of their disabilities and incapability in daily function, they may also develop depression and sleeping problems. With the relentless progress of DAT, patients gradually lose daily functioning abilities to take care of themselves and become physically weak and increasingly vulnerable to illness.

2.2 Prevalence of Dementia

Prevalence has been predicted and empirically observed to be increasing at an alarming speed both in the developed and developing regions of the world (Kalaria et al., 2008). In 2000, the worldwide population diagnosed with dementia was estimated to be 25.54 million (e.g., Wimo, Winblad, Aguero Torres, & von Strauss, 2003), with 4.6 million new cases being detected annually (Alzheimer Disease International, 2006; Fuster & Voute, 2005; Wimo et al., 2003).

Among the population with dementia (see Table 1), about 12% live in North America, 30% live in Europe, and almost half (46.5%) live in Asia (about 4.6 million and 1.5 million in China and Japan respectively). It has been estimated that about 52% of the worldwide population with dementia reside in less developed regions, where the prevalence for those 65 years old and above is 5.4% (Wimo et al., 2003). In contrast, among the remaining 48% of the population with dementia in more developed regions, the corresponding prevalence for 65 years of age and older was higher at 7.2% (Wimo et al., 2003, see explanation below for the differences in prevalence between developed and developing countries). Overall, the worldwide prevalence of the population 65 years of age and older was 6.1%. The above surprisingly lower prevalence of dementia in less developed than developed regions could possibly be due to an under-diagnosis or an under-reporting in developing countries (e.g., Rodriguez et al., 2008). This issue will be addressed again later in this chapter when social and cultural factors are also considered.

Table 1

Prevalence (%) of dementia by age groups and Geographic Regions

Geographic regions	Age ≥ 65yr	All age groups
Latin America	5.0	0.2
Northern America	7.9	1.1
Europe	6.9	1.0
Oceania	7.1	0.7
Asia	5.5	0.3
Overall	6.1	0.4

Note. Figures adapted from Wimo et al. (2003).

2.2.1 Prevalence in the West

Prevalence of dementia in the U. S. has been well studied.Ferri et al. (2005) have estimated that the prevalence of North Americans reaches approximately 6.4% out of the 53.1 million elderly aged 60 and older, while Rice et al.'s (2001) estimation is 5.7% among the age 65 and older. Higher prevalence has been obtained in studies for the older population. Thus, for example, in the Aging, Demographics, and Memory Study (ADAMS) Plassman et al. (2007) have reported a high prevalence of 13.9% among age 71 and older in 2002.

The prevalence rates in Europe are comparable to those in the U.S.A. and range from 5.9% to 9.4% for individuals age 65 or over (e.g., Berr et al., 2005). Similarly, based on the review of the European population-based studies in the 1990s, Lobo et al. (2000) estimated that this prevalence was 7.6%.

As prevalence increases with age (see discussion below), logically prevalence will also increase when the older adult population proportionally increases. For U.S.A,

approximately 12% of the population is age 65 or above. By 2020, this population is expected to increase to 16% (3.7% being age 80 or over) (Census Bureau, 2007). Similarly, the Federal Interagency Forum (Aging Related Statistics, 2004) has also estimated that the elderly population (65 years of age and older) in the U.S.A. will likely double from approximately 35 million in 2004 to more than 70 million by 2030.

Looking into the future, as prevalence increases with age, if the current rising trend continues and no preventive treatment is available, the corresponding total DAT population will likely increase by three to four times to about 10 million by 2050 (Brookmeyer, Gray & Kawas, 1998; Evans, 1990; US General Accounting Office, 1998). For the similar period, Herbert et al. (2003) has estimated that there will be around 13.2 million people with DAT in North America, among which more than 8.0 million will be age 85 and older. On a more global perspective for all developing countries, it is estimated that the percentage in population suffering from dementia will increase considerably and account for 64.5% (42.3 million) of all dementia patients in the world by 2020 and 71.2% (81.1 million) by 2040 (Ferri et al., 2005).

2.2.2 Prevalence in China

Overall prevalence. In 2001, China (about 5.0 million people with dementia in 2001), together with European Union (5.0 million) and the U.S.A (2.9 million) are the top three countries/regions with the largest number of patients with dementia (Ferri et al., 2005).

In terms of the older adult population, China has more than 100 million population at 60 years of age and older, which accounts for 10% of the total

population in China (Dong et al., 2007). The prevalence of Chinese older adults is estimated to be at least 5% with a total of six to seven million people suffering from dementia (Declaration of Protection and Cure for Geriatric Dementia in China, 2009). In Hong Kong, a Special Administrative Region of China, the prevalence of dementia among the elderly aged 70 years and over was estimated to be 9.3% in 2006 (Department of Health, 2006).

Prevalence figures in 1990-2009. In order to obtain an unbiased picture and estimation of the prevalence of dementia in China, a systematic digital literature search has been conducted using the online data bases (Psych Info, PsycArticles, Psychology: A SAGE Full-Test Collection, MEDLINE, China Journal Net). The keywords and indexes being used include: (dementia OR Alzheimer's disease) AND (prevalence) AND (China OR Chinese). The selection criteria are: (a) articles in English or Chinese; (b) the study involves a community resident sample rather than hospital-based patient registers or volunteers; (c) the study consists of a two-phase process -- a screening phase and a diagnosis phase, and (d) sufficient information about the prevalence has to be provided in the study. For the period 1990 to 2009, a total of 25 studies on the dementia prevalence in various geographic regions of China have been identified and are now summarized in Table 2.

Table 2

Prevalence of dementia in China, 1990-2009

Source	Geographic Region, Sample Type	Sample Size, Age	Screening tool	Diagnostic criteria and cutoff points	Prevalence by Type			Other findings
					Overall rate	DAT	VaD	
Zhang et al , 1990 (1987)	U Shanghai	N=5055 ⩾55yrs	CMMSE,	DSM-III, NINCDS-ADRDA,	4 6 > = 65yrs			Higher than figures published earlier for China and Japan, few formal education invoked the possibility of increased prevalence in elderly women
Liu et al , 1998, Single-stage community-based (1993)	R Taiwan,	N=1736 ⩾65ys,	CDR,HIS, (CASI),	DSM-III-R	2 5	2 0	0 175	lower prevalence than Western population which was result from genetic and sociocultural factors,
Li, Chen, & Zhang, 1999,	U Beijing	N=1207 ⩾60yrs	CMMSE	DSM-III, HIS	6 13	3 70, F M=4 27 2 69	2 43, F M = 1 68 3 76	
Lai et al , 2000,	U Guangzhou	N=1160 ⩾75yrs,	CMMSE, ADL	DSM-III-R , NINCDS-ADRDA	8 9	7 49	1 16	DAT F M=11 36 2 01
Fan, Yan, & Chen, 2000,	R & U Nanjing	N=3268 ⩾60ys,	CMMSE, HDS	DSM-III-R , NINCDS-ADRDA,	1 47	0 95	0 49	the prevalence was similar to those in previous studies

				HIS					for China
Wang et al , 2000, (1995)	U Beijing, Door-to-door 2-phase	N=5003 ≥60ys N=3728 ≥65ys.	CMMSE. 17 for illiteracy 20 for 3-6yrs schooling 23 for >=yrs education	DSM-III-R, ICD-10. HIS,	2 68 (>=60ys) 3 49 (>=65ys)	1 37 Male 1 23 female 2 32		1 37 1 85 1 0	DAT is most common dementia and prevalence is similar to previous study for China
Tang, Liu, & Zou, 2001 (1995)	R & U Chengdu	N=5353 ≥55yrs	CMMSE	DSM-III, HIS, NINCDS-ADRDA. CDR	2 67, 4 38%>=65yrs	2 06		0 37	DAT was the most popular subtypes
Zhang, Zhao, Xu, & Shi, 2001, (1997-1998)	R & U Beijing	N=5913 ≥55yrs	CMMSE. ADL	DSM-IV, NINCDS-ADRDA,	4 6. 4 2	2 2.	2 0	1 6. 1 5	DAT F M=2 1 1 7, VaD F M=1 3 1 7
Zhang et al . 2001, (1999)	U & R Shanghai	N=1186 ≥55yrs	CMMSE. 17-18 for illiterate level. 21-21 for primary school level, 24-25 for middle school level and above, ADL	ICD-10,HIS	2 61	0 76		0 4	
Qu, Qiao, & Yang, 2001. 1997-1998	U & R Xi'an	N=4850 ≥55yrs	CMMSE	DSM-IV, NINCDS-ADRDA.	3 53	2 06		1 11	
Shen et al , 2002	R Shanghai	N=2038 ≥60yrs	CMMSE	DSM-III-R, HIS	1998 1 13. 1999 1 19. 2000 1 43				prevalence was stable during 1998-2000
Wang et al , 2002	U Guangzhou	N=1524 ≥60yrs	CMMSE, <=17 for illiterate level, 18-20 for primary school level, 21-22 for	HIS	5 25, 7 70 for ≥ 70yrs, 10 29 for >=75yrs				

			middle school level, <=23 for university and college level					
Liang et al., 2003, (2002)	U Nanhai	N=1418 ≥60yrs	CMMSE	DSM-IV, NINCDS-ADRDA,	4 58	3 60	0 99	
Li, Wang, Wei, Shi, & Xu, 2003, (2002)	U Baotou	N=2324 ≥60yrs	CMMSE, 22 for <=6ys schooling, 26 for >=7ys education	CDR-10	2 67	1 33	1 33	Participants were retired workers
Zou, Qi, Zhang, Guan, & He, 2003, (2001)	U Chongqing	N=1519 ≥65yrs	CMMSE	DSM-IV, HIS	5 73	4 8	0 59	
Tang et al., 2003, (1996)	U & R Beijing	N=2788 ≥60yrs	CMMSE, 17 for illiterate level, 20 for primary school level, 22 for middle school level, 23 for university and college level	DSM-IV, NINCDS-ADRDA,	7 4, 5 1 for age-stan, (8 7,7 3 for >=65yrs)	5 0	1 54	
Tang et al., 2005 (1997-1998), 2000-2001)	U Chengdu	N=3908 ≥55yrs	CMMSE	DSM-III, HIS, NINCDS-ADRDA,	2000 2 74	2 00	0 46	Prevalence kept stable during the research period
Ma et al., 2005	R & U Guangzhou	N=3780 ≥65yrs	CMMSE, 19 for illiteracy, 22 for <=6ys schooling, 26 for >=7ys education	DSM-IV, HIS, NINCDS-ADRDA,	4 81 4 54	3 39, 3 17	1 16 1 11	F M=5 98 3 12, 6 03 2 74 (age-standardized)
Yuan et al., 2005, (2002)	U Nanchang	N=2126>=60yrs	CIDI, CRBRS	CIDI, ADL, HIS, ICD-10, CCM-3	4 19	3 19	0 66	

Zhang et al , 2006, (1997-1998), cross-sectional door-to-door survey	R&U, Beijing, Xian, Shanghai, Chengdu	N=34807 ≥ 55ys, N=8694, N=4850, N=15910, N=5353	CMMSE 19 for illiteracy, 22 for <=6ys schooling, 26 for >=7ys education	NINCDS-ADRDA, RAD, NINDS-AIREN,		2 0, 1 8 2 0, 2 2 2 2		0 8 1 1 1 2 0 6 0 4		
Zhou et al , 2006, (1986-1991)	R Linxian	N=16095	CMMSE 17 for illiterate level, 20 for primary school level, 24 for high school level ADL=18, FOMT.WAIS-RC, WISC-III	DSM-IV, ICD-10	5 26	1 83				
Li et al , 2007, (1997), Community-based	R Beijing	N=1593 ≥60yrs,	CMMSE 17 for <=6ys schooling, 23 for >=7ys education, CRBRS>=2	DSM-IV, ICD-10	2 51	1 38		0 94		prevalence in Beijing was slightly higher than 10 yrs ago DAT was more common
Tang et al , 2007, (2001 9-2002 2)	R & U Guangzhou	N=5276 ≥55	CMMSE, CVFT, HIS	NINCDS-ADRDA, CDR	3 47(183) age-standadised 1 94	2 43	1 28	0 85	0 55	F M=4 35 2 21
Yan et al , 2008, (2004)	U Beijing	N=1562 ≥65yrs	10/66 criteria	ICD-10	4 1					F M=4 1 4 2, Illiterate Educated = 5 6 3 8
Gao, Li, Liu, L , Zhang, & Zhu, (2009), Gao et al (2008)	U Taiyuan	N=435 ≥65yrs	CMMSE, HDS	DSM-III-R	2 33	1 37		0 97		

Note. U = Urban; R = Rural; 10/66 criteria = diagnosis criteria developed by the 10/66 Dementia Research Group; ADL = the Activities of Daily Living Scale; CAMDEX = Cambridge Mental Disorders of the Elderly Examination; CASI = Cognitive Abilities Screening Instrument; CDR = Clinical Dementia Rating Scale; CERAD, the

Consortium to Establish a Registry for Alzheimer's Disease; CIDI = Composite International Diagnostic Interview; CMMSE = Chinese Mini−Mental State Examination; CRBRS = richton Royal Behaviour Rating Scale; CVFT = Category Verbal Fluency Test; DSM = Ⅲ, Diagnostic and Statistical Manual of Mental Disorders, 3rd edition; DSM=Ⅲ-R. the 3rd Edition Diagnostic and Statistical Manual of Mental Disorder, Revised Edition; DSM=Ⅳ, the Diagnostic and Statistical Manual of Mental Disorders, fourth edition; HDS = Hasegawa's Dementia Scale; HIS = the Hachinski Ischemic Score; ICD=10, the 10th Edition of International Classification of Diseases; NINCDS=ADRDA = National Institute of Neurological and Communicative Disorders;

As can be seen in Table 2, CMMSE is the most often used screening tool in these studies and the common diagnostic criteria for dementia include the DSM-III-R, DSM-IV, CDR-10, NINCDS-ADRDA, NINDS-AIREN ADL, CAMDEX, CERAD, and HIS. The 10/66 dementia diagnosis criteria (e.g., Yan et al., 2008), a more recently derived standard that may become more popular, has been used in only one study. Importantly, most studies adopted a multiple screening procedure by combining the results of two or more tools together.

. The 10/66 dementia diagnosis criteria (e.g., Yan et al., 2008), a more recently derived standard that may become more popular, has been used in only one study. Importantly, most studies adopted a multiple screening procedure by combining the results of two or more tools together.

There are possible variations in the prevalence figures found across different studies as well as between the two types of dementia (VaD and DAT). Whereas the differences in the prevalence of the two types of dementia across different geographic regions were found to be similar in Western population-based epidemiological studies (Lobo et al., 2000; Rocca et al., 1991), there are substantial differences in the prevalence between the two types of dementia in Southern and Northern China.

Increasing older populations. The increasing concern on dementia in China, and developing countries in general, is partly due to the changing proportions of the older adult population. WHO (2002) has projected that around 75% of the 1.2 billion age 60 and above will reside in developing countries by 2025. Thus, it is expected that the percentage of dementia population living in developing countries will increase

accordingly.

In mainland China, particularly during the last two decades, life expectancy has increased dramatically, possibly as a consequence of the rapid social and economic development. Thus, it has been observed that the percentage of older adults in mainland China at 65 years of age and older has increased significantly from 5% in 1982 to 7% in 2000 (Ministry of Health China, 2003). Similarly, in Hong Kong, the proportion of older adults (age 65 and older) will increase substantially from 12.4% in 2006 to 26.4% in 2036 (Census and Statistics Department, 2006a; 2006b). The increasing populations among older adults will at least partly explain the rate of increase of people with dementia in China.

Although developing countries such as China tend to have a lower prevalence rate of dementia than developed countries (see explanation below), some recent studies showed that the prevalence figures in China and North America are probably quite comparable now (Ferri et al., 2005; Zhang et al., 2006), because of the increasing prevalence in China. For example, Dong et al. (2007) have systematically estimated the dementia prevalence of adults age 60 and older in China by analyzing 25 studies published in 1980 to 2004, which contained samples ranging from 1000 to 15,000. Using the DSM-III and ICD-10 as the criteria for dementia, they found that the dementia prevalence has been increasing in recent decades. In the four time periods (i.e., 1985-1990, 1991-1995, 1996-2000, 2001-2004), the respective (all types) prevalence figures have been found to be 2.1%, 2.4%, 3.1%, and 4.1%, with the corresponding DAT rates being 0.9%, 1.4%, 2.1%, and 2.7%. Similar trends have

been observed in other studies noting that the prevalence of dementia in Beijing (Li et al., 2007) and Shanghai has increased with the aging of the population during the recent 10 years (an increase of 1.5% per year in Shanghai, Declaration of Protection and Cure for Geriatric Dementia in China, 2009).

2.3 Risk Factors and Bias in Screening

2.3.1 Risk Factors of Dementia

Formost, advanced age has been reported to be the main risk factor for dementia in different studies. Thus, for example, in the U.S.A., the prevalence doubles every five years after 65 years of age (Evans, 1990; Liu et al., 2003; Menzin et al., 1999; Paykel et al., 1997; Weiner, Powe, Weller, Shaffer, & Anderson, 1998). Second, as have been found in both China and the West, a family history of DAT or other dementia (e.g., carrying the apolipoprotein E ε4 allele) has been a well-known genetic factor associated with an increased risk of ultimately developing dementia. For example, the ApoE gene carriers have three times the risk in developing dementia as compared to the non-carriers (e.g., Kalaria et al., 1997).

Thirdly, gender and specifically, being female has been shown to be associated with a higher risk of getting dementia. There has been a consensus that in general, and the prevalence in women is a higher than man within the same age groups (Bachman et al., 1992; Swanwick & Lawlor, 1999). Similar trends have also been found among Chinese population with DAT (see Dong et al., 2007). Studies on Canada population have reported there might be twice as many female suffer DAT

then male (Diamond, 2008). It has been suggested that much of this gender difference might possibly be attributed either to the lower mortality rates in women at various age groups as compared with men (Brookmeyer et al., 1998) or to the decline of estrogen resulting from menopause in women (Jick, Zomberg, Jick, Seshadri, & Drachman, 2000).

Lastly, but not necessarily least important, a lack of formal education has been consistently observed to be another risk factor for DAT in the U.S.A, China, or other countries (Schmitt et al., 2000; Zhou et al., 2006; in Korea, Lee et al., 2008). It has been suggested that people who have less than eight years of formal education might be more likely to develop DAT than those who have more education (Bruandet et al., 2008; Launer et al., 1999). Specifically, the less number of years of education the older adults received in early life, the higher the prevalence of DAT they will likely have when they become older. Importantly, education in early life has been found to be a protective factor for DAT in different countries (e.g., Katzman, 1993; Lee et al., 2008; Stern et al., 1994; Valenzuela & Sachdev, 2006; see also meta-analysis by Caamaño-Isorna, Corral, Montes-Martinz, & Takkouche, 2006).

Different hypotheses have been proposed to explain why education can serve as a protective factor for dementia (McDowell, Xi, Lindsay, & Tierney, 2007). Some researchers have proposed that individuals with a higher level of education tend to have a higher socioeconomic status and lead a healthier life-style and enjoy better health care than those with less education (e.g., Hall, Gao, Unverzagt, & Hendrie, 2000). Others suggest that a sustained high level of complex brain activities helps as a

cognitive reserve in increasing efficiency of processing and hence delaying (though not necessarily preventing) the onset of dementia symptoms (e.g., Bennett et al., 2003; Valenzuela & Sachdev, 2006). Education may also change the brain structure in early life by developing more neurons and synapses, or by making more efficient use of the brain's networks for compensation, and subsequently enable the shifting of the brain activity to alternative networks in later life when necessary (e.g., Garibotto et al., 2008; Kempermann, Kuhn, & Gage, 1997; Scarmeas & Stern, 2003). Also worthy of note is a recent debate challenging whether education is a genuinely beneficial factor or whether it just delays the onset of the DAT syndrome and therefore leads to a faster and earlier death after diagnosis (e.g., Bruandet et al., 2008; Perneczky et al., 2009, but see Paradise, Cooper, & Livingston, 2009). More empirical and focused investigations will be needed to tease out the validity of different hypotheses and speculations.

2.3.3 Bias for Different Educational Groups

It is possible that in some screening items that involve numeracy or literacy, older adult illiterates or people with little education would be misclassified as having very mild cognitive impairment (e.g., 0.5 in Clinical Dementia Rating, CDR) even though they are cognitively healthy (e.g., 0 in CDR) (Anderson, Sachdev, Brodaty, Trollor, & Andrews, 2007; Ganguli et al., 1995; Lim et al., 2007; Parker & Philp, 2004; Prince, Acosta, Chiu, Scazufca, & Varghese, 2003). This misclassification may happen even when popular screening tasks like Mini-Mental State Examination (MMSE) are used. The higher scores in MMSE can be attributed to better test-taking skills or cognitive reserve, while the patients should already be classified or progressing into early stages

of DAT (e.g., Anthony, LeResche, Niaz, Von Korff, & Folstein, 1982; Jones & Gallo, 2002; Snitz et al., 2009). Hence, it is important to test whether the tasks/items are equally efficient in differentiating people with and without dementia irrespective of their educational background.

To tackle the problem that scores in dementia screening tasks are artificially inflated or deflated by education, various adjustment strategies can be adopted, including (a) mathematical adjustment of raw scores based on educational level (e.g., Anthony et al., 1982), (b) development of different norms (e.g., with different cutoffs) in accordance with educational level (e.g., Dufouil, Clayton, & Brayne, 2000; Schmand et al., 1995; Uhlmann & Larson, 1991), and (c) combing the screening test scores (e.g., MMSE) with other information (e.g., from informants using Questionnaire of Cognitive Decline in the Elderly, e.g., Bottino et al., 2009) in making the assessment judgment.

Most screening tasks have been designed in the developed countries where the majority of older adults have received some education and are generally non-illiterates. In contrast, there are a greater number of older adults in the developing countries, who are either illiterates or have much less education. For example, almost 77.4% of older adults finished their high-school education in the United States (U.S. Census Bureau, 2008), whereas only about 16% and 20% did so in Hong Kong (Hong Kong Council of Social Service, 2002) and in mainland China (National Bureau of Statistics of China, 2005), respectively. The proportion of older adults with no schooling or only pre-primary education is estimated to be at least 35% in Hong Kong (Census and Statistics Department, 2006) and 26% in China (National Bureau of Statistics of China, 2005). Thus, tasks may not be suitable for older adults with limited education if they rely heavily on their reading and writing abilities (e.g.,

copying the overlapping pentagon figure). Reading aloud and remembering words may not be suitable for illiterates. Similarly, tasks that are related to school curricula but out of context for the patient's daily-life activities (e.g., identifying the differences between elevator and escalator) may be inappropriate. A more careful scrutiny of bias in various assessment instruments, and a greater reliance on tasks suitable for people with minimal education are definitely much needed.

Chapter 3 Literature Review -- Cognitive Impairment of Alzheimer's Disease

There have been accumulating studies indicating that cognitive impairments occur preceding the further diagnosis of DAT (Bäckman, Jones, Berger, Laukka, & Small, 2005; Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991; Elias et al., 2000). And these preclinical cognitive deterioration is not generally observed across all cognitive domains, with the most typically affected being memory and attention (Bäckman & Small, 1998; Perry & Hodges, 1999).

This chapter attempted to review the cognitive impairments of memory and attention in individuals with DAT, which are recognized to be the most vulnerable cognitive domains in the gradual deterioration of the cognitive impairment and occur early in the disease (Bäckman et al., 2005). Impairment in subcomponents of memory, such as episodic memory, semantic memory, and working memory, would be reviewed. Then impairment in selective attention, divided attention, executive function would be discussed.

3.1 Memory Impairment in DAT

The memory impairment in DAT is manifested mainly as a disorder in the acquiring, and encoding of information in cognitive activities (Crober & Dawas, 1997). Memory impairment is included in both the two most widely used diagnostic criteria of dementia as defined by the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease

and Related Disorders Association) and DSM-IV (the Diagnostic and Statistical Manual of Mental Disorders, fourth edition) .

Before the review of semantic memory impairment in DAT, the relationship between two forms of declarative memory, semantic memory and episodic memory, will be discussed.

The relation of semantic memory and episodic memory has been a contentious theoretical issue. Some assumed that these two types of memory belong to functionally independent neural systems that process different types of information (Tulving, 1987). Supporting evidence from neuropsychological studies showed that different brain regions are activated in these two types of retrieval processing (e.g., Cabeza & Nyberg, 2000; Gabrieli, 1998; also see Burianova, McIntosh & Grady, 2010; for review, see Rajah & McIntosh, 2005). For example, for patients with temporal lobe damage, their autobiographical memory (i.e., the memory system consisting of episodic information collected from personal experiences) would be impaired, but not that of their semantic memory (Gadian et al., 2000).

Other researchers believe that episodic memory and semantic memory are interrelated and interact very closely especially during the process of encoding and retrieval (Squire & Zola, 1998). While episodic encoding may elicit semantic retrieval and is dependent on semantic knowledge, semantic knowledge is built up on episodic memory (Dalla Barba & Goldblum, 1996; Tulving, 2001). This is in line with the other argument that access of semantic memory may help recall or recognition of prior episode, while repetition and rehearsal of the episode will prompt to create

relations with semantic knowledge (Squire & Zola, 1998).

The above relations between episodic and semantic memory have to be interpreted in the context of variations in task paradigms, experimental designs, and methods of data extraction (e.g., using a neutral condition as the baseline vs. subtracting the control response performance from the experimental one). Some researchers considered the activation differences between episodic and semantic retrieval as points along the continuum in a memory task processing (e.g., Rajah & McIntosh, 2005). For example, it has been noted that the left lateral temporal lobe is involved in both semantic memory and accurate episodic retrieval (Menon, Boyett-Anderson, Schatzberg, & Reiss, 2002). More recent supportive evidence suggested that hippocampal formation was involved in both episodic and semantic retrieval (Burianova & Grady, 2007; Prince, Tsukiura, & Cabeza, 2007; Ryan, Cox, Hayes, & Nadel, 2008). These findings implied that the two forms of declarative memory were closely interrelated and performed in distinct yet interdependent ways (e.g., Burianova et al., 2010; Rajah & McIntosh, 2005).

3.1.1 Episodic Memory in DAT

Episodic memory, according to Tulving (1972, 2002), refers to the part of memory which enables people to recall specific past events in terms of place and time (e.g., I went to dine at an Italian restaurant last Friday). It contains detailed and vivid information about personal experiences. The loss of episodic memories is often characterized by impaired encoding and/or retrieval of the information related to a certain contextual background. This impairment has long been recognized as

one of the most easily observable symptoms in identifying people with DAT (Balota, Dolan & Duchek, 2000; Fox, Warrington, Seiffer, Agnew, & Rossor, 1998; Kopelman, 1985b). This is an important symptom because it reflects the DAT patient's poor performance in encoding new materials and hence has been considered a sensitive marker of initial stages of DAT (Petersen & Morris, 2003, 2005).

Free recall task has been suggested to be more effective than recognition tasks as an episodic memory measure in delineating the progression and characteristics of dementia (see Bäckman & Small, 1998; Howieson et al., 1997). A meta-analysis on 47 studies on cognitive impairment of early stage DAT patients (Bäckman et al., 2005) consolidates this claim. In this meta-analysis, the discrimination power of the episodic memory tasks were compared along three types of conditions: (i) the retention time interval (immediate recall vs. delayed recall), (ii) the retrieval type (recognition vs. free recall) and (iii) type of the learning stimuli (verbal vs. nonverbal). The results of the meta-analysis showed that the discrimination power of episodic tasks were larger in conditions with delayed test, free recall retrieval and verbal stimuli.

Despite the fact that free recall tasks have been considered more sensitive in the early detection of dementia as discussed earlier (e.g., Bäckman & Small, 1998), there are limitations to its generalizations. For example, when participants are asked to recall newly acquired items, their performance could be affected and confounded by irrelevant factors, such as their educational background (e.g., Borrini, Dall'Ora, Della Sala, Marinelli, & Spinnler, 1989) or age (Springer, McIntosh, Winocur &

Grandy, 2005). Thus, one may erroneously take illiterate normal aging adults as having impairment and very mild DAT individuals with high level of education as normal functioning. This is because low level of education together with advanced age might result in poor strategies in encoding and retrieval, suggesting that episodic memory tasks generally measure and reflect more than episodic memory. In other words, poor performance in the free recall test might be a result of the patients' low level of education and/or their age-related memory loss, and therefore may not be a good definitive and specific symptom marker for DAT.

Recently researchers have used a cued recall paradigm to disentangle the above effect (e.g., between education and episodic memory) in the measurement of the "pure" episodic memory impairment for people with DAT. In this approach, semantic cues are provided to help encoding and retrieval, and thus provide a better detection of the encoding deficit in episodic memory (Buschke, 1984; Ivanoiu et al., 2005). Specifically in the study (Ivanoiu et al., 2005), participants' performance in cued recall, free recall and visual recognition memory were compared and the result showed that participants with DAT had more difficulties in making use of the rich cues at the encoding and retrieval stages. The results suggested that the cued recall test was a more sensitive diagnostic tool in discriminating participants with and without DAT. As summarized by Belleville, Bherer, Lepage, Chertkow, and Gauthier (2008; p.367), individuals with mild cognitive impairment benefited little from the semantic orientation cues and failed to make use of them to facilitate their coding or retrieval. In contrast, their healthy counterparts made use of and

performed better when semantic cues were provided.

3.1.2 Semantic Memory in DAT

Episodic memory deficit is by no means the only clinical manifestation of DAT. Semantic memory impairment in DAT has also been well investigated in a number of studies (Chertkow & Bub, 1990; Hodges & Patterson, 1995; Hodges, Salmon, & Butters, 1990).

Semantic memory refers to the memory of not only lexical information (e.g., concepts and meanings) but also facts and knowledge of the world (e.g., rules and facts) that make up and serve as the basis of our knowledge independent of specific context and personal experiences.

As to the semantic impairment in DAT, studies have shown that the impairment in semantic dementia is related to severe disruption of the functioning of the language-dominant temporal lobe (see Mummery et al., 1999, 2000). Semantic deficits in DAT have been investigated using a variety of neuropsychological tests, such as the category fluency test (Lam, Ho, Lui, & Tam, 2006), visual-verbal semantic matching (Hodges & Patterson, 1995), the recall items in the Mini-Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975) and the Alzheimer's disease Assessment Scale cognitive subscale (ADAS-Cog, Rosen, Mohs, & Davis, 1984). DAT patients had difficulties in performing the semantic related tasks in these tests. Specifically, the impairment in the category fluency has been consistently considered as a sign of early semantic degradation (Adlam, Bozeat,

Arnold, Watson, & Hodges, 2006; Albert, Moss, Tanzi, & Jones, 2001; Perry, Watson, & Hodges, 2000).

The above research findings have to be interpreted with caution, because semantic memory includes not only semantic knowledge (e.g., names, features and events) but also the semantic information processing (Koening, Smith, & Grossman, 2010; Koenig, Smith, Grossman, Glosser, & Moore, 2007). Poor performance of DAT patients in semantic memory tasks, therefore, might reflect either a breakdown of the patients' semantic knowledge (i.e., loss of knowledge content), the disability in using knowledge (i.e., loss of access to semantic knowledge), or both (see Hodges, Patterson, Oxbury, & Funnell, 1992).

Studies investigating the loss of knowledge and loss of access were summarized as follows. Research showed that the knowledge part of the semantic category might be unaffected among DAT patients, whereas other specific attributes such as functions and properties of concepts are affected (Chertkow, Bub, & Seidenberg, 1989; Martin & Fedio, 1983; but see Nebes & Brady, 1988). For example, in naming tasks, DAT patients might inappropriately name a "*banana*" for an "*apple*" (i.e., name of other objects that come from the same category as "banana") or "*fruit*" (the superordinate category of "*apple*"), suggesting that they might have difficulties in differentiating the names of objects from the same category and failed in the word-finding process (e.g., Martin & Feido, 1983; for a review, see Giffard, Desgranges & Eustache, 2005). In a multiple-choice task, DAT patients would experience difficulties in recognizing the names of pictured objects (e.g., an "*apple*") if the distractor (e.g., a "*banana*") and the

objects are within the same category, but not so if the distractor is from different categories (e.g., a *"dog"*) (Chertkow et al., 1989).

The semantic breakdown in DAT patients shows that their superordinate knowledge (e.g., naming/categorizing a table as "*furniture*") is more vulnerable to be impaired than subordinate knowledge (e.g., naming a table as "*dining table*"; Hodges et al., 1992). It has also been found recently among amnesic mild cognitive impairment individuals that their semantic knowledge about entities such as famous people, buildings and public events is more significantly affected than their general knowledge about common objects (Ahmed, Arnold, Thompson, Graham, & Hodges, 2008; Thompson, Graham, Patterson, Sahakian, & Hodges, 2002; Vogel, Gade, Stokholm, & Waldemar, 2005).

Other researchers have argued that DAT patients can keep their knowledge about the attributes of concepts and therefore will be able to perform as well as their normal aging counterparts in tasks requiring the knowledge about relationships between objects and respective attributes (Grober et al., 1985; Nebes & Brady, 1988). One possible explanation for the discrepant findings is that patients with DAT might fail in tasks that require them to specify the attributes of a certain concept. This is because the cognitive demands required by such tasks might be much greater than those to judge the relationship between a concept and one of its attributes (e.g., Nebes, 1992; for a review, see Becker & Overman, 2002). It is predicted that abstract thinking test might be useful in discriminating very mild DAT from normal aging, in tasks such as pointing out the similarity and difference between two objects.

To answer the question on whether the breakdown in semantic memory of DAT patients is a result of their loss of knowledge or their loss of semantic knowledge access, researchers proposed a semantic priming paradigm in which semantic knowledge and its relative processing could be investigated implicitly (e.g., Nebes Martin, & Horn, 1984). According to Shalice (1988), if semantic knowledge is impaired in DAT, a reduced or no semantic priming effect will be observed. Studies have shown that people with DAT performed similarly as healthy elder adults in semantic priming. This suggests that DAT patients have intact semantic content but are impaired in accessing their semantic knowledge (Multhaup et al., 2003; Ober, 2002; Perri et al., 2003).

3.1.3 Working Memory Impairment in DAT

One of the theoretical frameworks that used to investigate DAT-related impairment of working memory is the working memory model proposed by Baddeley and Hitch (1974; Baddeley, 2000). This model proposes that (Baddeley & Hitch, 1974; Baddeley, 2000) the term *working memory* refers to "the whole set of cognitive processes that comprise the model, which includes higher-level attentional and executive processes, as well as storage systems specialized for particular information domains" (Roediger III & Byrne, 2008, p. 34). There are three components in this model, the phonological loop, the visuo-spatial scratchpad, and the central executive component. The first two components serve as the "slave" (storage) for storing and rehearsing the information in the temporary verbal and visuospatial memory respectively, whilethe third component, the central executive

component, is an attentional controller at a higher level that is responsible for "cognitive control processes, strategy selection and the coordination of a variety of processes required for the temporary storage and processing of information" (Amieva, Phillips, Della Sala, & Henry, 2004, p.951).

Empirical studies suggested that the phonological loop remains relatively intact in the early stage of DAT, but becomes deteriorated with the progress of the disease (Baddeley, 1986). For patients with DAT impaired in visuospatial sketchpad, it is critical to point out that such impairment involves a potential impairment of both the visuospatial sketchpad and central executive component (Huntley & Howard, 2010; Macpherson, Della Sala, Logie, & Wilcock, 2007; Money, Kirk, & Mcnaughton, 1992). The central executive component, however, has been consistently reported to be impaired in DAT, which accounts for the deficit in the working memory in the early stage of DAT (Collette, van der Linden, Bechet, & Salmon, 1999b; Peters et al., 2007; for review, see Huntley & Howard, 2010). In particular, the more complex a task is, the greateris the load on the central executive system (Lonie et al., 2008).

Patients with DAT can also be impaired in both visuo-spatial pad and central executive system. This has been supported by functional neuroimaging and PET studies which demonstrated activation in the prefrontal cortex and anterior cingulated gyrus in dual-task but not in single task (D'Esposito et al., 1995; Jonides et al., 1993).

Due to the close connection between the central executive component and attentional control, working memory has often been studied as an attention-related

concept (Baddeley & Hitch, 1994). Some researchers have considered executive function as a set of diverse functions and working memory as one subcomponent involved in executive functions (Blair, Zelazo, & Greenberg, 2005; Fletcher, 1996; Pennington, Bennetto, McAleer, & Roberts, 1996; Zillmer & Spiers, 2001; for good summary, see McCabe et al., 2010), such as inhibition, switching, and divided attention (Baddeley, 1996). Practically, attention control in some attentional models (e.g., Norman & Shallice, 1986) might be closely related to the executive control component in working memory model (Baddeley, 1996). For example, the poor performance in divided attention task (e.g., dual task paradigm) has often been explained as a deficit in the central executive component of working memory (e.g., Baddeley, Baddeley, Bucks, & Wilcock, 2001; Rosen, Bergeson, Putnam, Harwell, & Sunderland, 2002).

As such, more detailed discussion about the relationship between working memory and attention and the related findings will to be turned in the section of attention impairment in DAT.

3.2 Attention Impairment in DAT

As reviewed by Twamley, Ropacki, and Bondi (2006), among 91 studies on preclinical DAT by 2005, only 10% of them investigated attention. Importantly their extremely consistent findings suggested that attention deficit could discriminate DAT individuals from the control group. With the recent development of a variety of attention theory, more and more studies show that attention deficit is a sensitive

marker in the earliest stage of DAT (see Faust & Balota, 2007).

3.2.1 Attention Impairment vs. Memory Impairment

The presence of memory deficit has been well documented as a prominent marker for the early stage of DAT (Bäckman, Small, & Fratiglioni, 2001). However, the attention impairment in DAT has not been recognized until recent decades (Baddeley, 1986; Baddeley et al., 1991) because attention decline usually manifested as memory problem and it is difficult to differentiate the attention-related deficit from the memoy deficit till the availability of appropriate methodology (e.g., tests specific to detect attention; for a review, see Balota & Faust, 2001; Perry & Hodges, 1999) and related theoretical underpinning in recent years.

Based on the increasing number of psychological models on attention proposed in recent decades, specific tests have been developed and designed to measure attention more accurately (Baddeley, 1986; Norman & Shallice, 1986; Posner & Petersen, 1990; Shiffrin & Schneider, 1977). More evidence suggested the early DAT might actually be attention impairment (Everitt & Robbins, 1997; Silveri, Reali, Jenner & Puopolo, 2007).

3.2.2 Impairment in Selective Attention and Divided Attention

It is critical to point out that not all subcomponents in attention are equally affected by DAT (Amieva et al., 2004; Parasuraman & Haxby, 1993; Perry et al., 2000). Specifically, divided attention (Baddeley et al., 2001; Perry et al., 2000; but see Crossley, Hiscock, & Beckie-Forman, 2004; Lonie, 2008) and selective attention are

believed to be relatively vulnerable impairments among DAT patients while sustained attention remains relatively intact at least among the milder DAT patients (Amieva et al., 2004; Collette, & Van der Linden, 2000; Foster, 2001).

As has been noted by some researchers, memory relies heavily on attention-related processes (e.g., maintaining some information and inhibiting others in encoding) and is so closely related to memory that it is difficult to differentiate attention from memory. Various theoretical models have been proposed to clarify the relations among the subcomponents of attention (e.g., Norman & Shallice, 1986; Posner & Petersen, 1990; Shiffrin & Schneider, 1977). However, no unified theory of attention exists; researchers usually employ a combined framework in which attention could be subdivided into three subtypes, namely, sustained attention, selective attention and divided attention (e.g., Amieva et al., 2004; Balota & Faust, 2001; Perry & Hodges, 1999).

Selective attention refers to the ability to allocate and concentrate one's cognitive capacity on the input information. Specifically, it refers to the ability to ignore certain parts of the stimuli and other distracting information so as to concentrate on the target information at any given point. It contains a series of processes and manipulations such as orientation, detection, filtering, and selection of target as the priorities while inhabiting the distractors (Perry & Hodges, 1999).

One of the most investigated aspects in selective attention is inhibitory functioning, which is mainly responsible for the resistance to interference and irrelevant stimuli and the suppression of inappropriate intention or inertia (Amieva et

al., 2004; Bjorklund, & Harnishfeger, 1995). The inhibitory mechanisms play a fundamental role in other cognitive domains such as selective attention and working memory by suppressing irrelevant information so as to attend to the targeted information (Houghton & Tipper, 1994; Zacks & Hasher, 1994). People with an early DAT exhibit reduced capability of inhibiting distractors in spatial negative priming task, suggesting that both inhibition and activation function have been affected among patients with DAT (Vaughan, Hughes, Jones, Woods, Tipper, 2006).

Divided attention refers to the ability to pay attention on more than one stimulus or tasks simultaneously. The most common paradigm to measure divided attention is the dual-task procedure in which one is required to perform two tasks simultaneously (Baddeley et al., 1983). *Sustained attention* is the ability to focuse on a specific task over a period of time (Wilkins, Shallice, & McCarthy, 1987).

People with early DAT have been found to have difficulties in dividing their attention and allocating cognitive recourses into two concurrent tasks. The most often used paradigm to measure such ability and to tap the executive component of working memory is the dual task paradigm (Baddeley et al., 1983). Practically, the poor performance in dual tasks has been interpreted as a decline of the attentional component of the working memory system, namely, the central executive component (Baddeley, 1986; Baddeley et al., 1991; Borgo et al., 2003; Sebastian, Menor & Elosua, 2006).

In one study (MacPherson, Della Sala, Logie, 2004), though people with DAT performed well in individual tasks, they experienced more difficulties in dual-tasks

than their normal aging counterparts. This might be attributed to the patients' deficiency in allocating cognitive resources into two tasks simultaneously and the impairment in the executive component of their working memory system. Consistently, the DAT-related dual task impairment has been also demonstrated in the paper-and-pen version of dual task (Della Sala, Baddeley, Papagno, & Spinnler, 1995, Sebastian et al., 2006).

It is intriguing that the DAT-related impairment in divided attention found in previous studies often occurs at the early stage of DAT. This impairment also becomes more salient with increasing severity despite the uncertainty when the patients begin to exhibit this problem (Crossley et al., 2004; Lonie et al., 2007; Perry & Hodges, 1999). Furthermore, the dual task paradigm might not be sufficiently sensitive to the attention changes at the early stages of DAT (Lonie et al., 2007). It has also been shown that the dual task impairment is common in more effortful and taxing tasks but less so in those relatively automatic tasks (Crossley et al., 2004).

3.4 Brief Summary and Implications

As summarized above, although memory impairment has long been recognized as the early manifestation of DAT, researchers have become realized that it is important to investigate the attention performance as earlier marker before any memory impairment being detected (Balota &Faust, 2001; Twamley et al., 2006). In light of the availability and facility of various attention tasks, the present thesis attempted to investigate the sensitivity of attention task that are proper for Chinese

elderly with relatively lower level of education in discriminating very mild DAT from normal aging.

Chapter 4 Literature Review -- Assessment and Screening: Neuropsychological Tests

In general, screening tests refer to instruments that used to detect the onset of dementia, while diagnostic instruments refer to assessments that evaluate the severity of the disease. Though these two types of instruments are not necessarily mutually exclusive, the present study was limited to the neuropsychological tests used in screening procedure among Chinese population.

Various screening tests originally designed in Western population have been translated and adapted for use in Hong Kong and mainland China. The adaptation has to take language and cultural differences into consideration so as to cater for the large proportion of elder adults with little formal education and the unavailability of standardized clinical testing settings (vs. residential environment) in China. Special cautions should be paid on the educational background of Chinese population in practice. A number of neuropsychological tests have been validated with satisfactory psychometric properties and have been recommended by different researchers for use with Hong Kong Chinese (see Table 3).

The present chapter reviewed three types of tests that are designed to measure the functions limited to certain aspects, namely, cognitive aspect, behavioral and psychiatric aspect, and functional aspect. In addition, the tests and methods appropriate for population with less education were noted as well.

Table 3

Psychometric characteristics of the Chinese version of Instruments

Instruments and reference	Reliability	Validity	Sensitivity %	Specificity %	Other findings
Cognitive Assessment					
CMMSE (Chiu, Lee, Chung, & Kwong., 1994)	Cronbach's α = .78	Canonical corr = .94	97.5	97.3	cut-off score 19/20 recommended
ADAS-Cog	Cronbach's α: 0.91, 0.88 and 0.65 for whole group, AD and normal group; test-retest reliability = .96, .86, .86; inter-rater reliability =.95, .91,.65		90	94.7	test-retest reliability (Spearman's rho) correlation for the whole group, AD and normal subjects
C-EXIT25 (Chan, Chiu, & Lam, 2006)	Cronbach's α = .80; inter-rater reliability r = .91				feasible and valid bedside for assess the executive cognitive functions
Behavioral & psychiatric assessment					
NPI (Leung, Lam, Chiu, Cummings, Chen, 2001)	> .90 for all subscale	concurrent validity with BEHAVE-AD, ρ=.71			
CMAI (Choy et al., 2001)	Cronbach 's α = .75; inter-rater reliability r = .98	concurrent validity: with BEHAVE-AD, ρ=.76			factor analysis yielded 3 subtypes of agitation: physically, aggressive, physically nonaggressive, verbally agitated

			behaviors.
Functional assessment			
CADA (Mok et al., 2005)	Cronbach's α = .91; test-retest reliability (ICC = 0.99); inter-rater reliability ICC = 0.98	Construct validity: corr with ADLS, r = .94; corr with CMMSE, r = .60	suitable for community-residing elderly adults
EdFED (Lin, Watson, Lee, Chou, & Wu, 2008)	Inter-rater ICC = .76, .84 and .74 for groups with 'never', 'sometimes' or 'often' response to the symptoms.		

Note. corr = correlation

4.1 Cognitive Tests

The Mini-Mental State Examination (MMSE, Folstein et al., 1975) is one of the most widely used as a preliminary cognitive screening tool for dementia (Nelson, Fogel, & Faust, 1986; Uhlmann, Larson, & Buchner, 1987). It comprises 6 subtasks of items (e.g., naming dates, day of the week, place, and short-term memory tasks) in a scale. More specifically, the items include: recalling the time (year, season, month, day, and date; i.e., MMSE1) and the place (county, town, hospital, and floor; i.e., MMSE2), registration (naming three objects, i.e., MMSE3), attention and concentration (continually subtracting 7 from 100; i.e., MMSE4), recall (recalling three previously named objects; i.e., MMSE5), and language (naming two objects, repeating a phrase, reading aloud and understanding a sentence, writing a sentence,

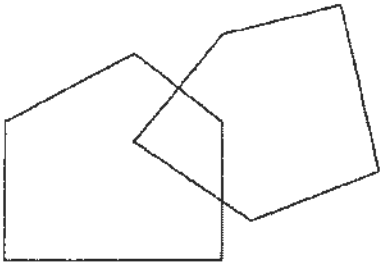
following a three-stage command, and copying a design; i.e., MMSE6).

Chinese versions of the MMSE (C-MMSE) have been developed and used in mainland China (Li et al., 1989) and Hong Kong (Chiu, Lee, Chung, & Kwong, 1994; Chiu et al., 1998) respectively, in which satisfactory reliability and validity had been shown in clinical applications (Lam, Tam, Lui, & Chan, 2008; Poon, Lam, & Wong, 2008; Tsang & Man, 2006). As Chiu et al. (1998) suggested, most of the items, other than the cultural or educational related one, on the MMSE could be directly translated and used for the Hong Kong population. Thus, for example, the item requiring people to repeat "No ifs, ands, or buts" was replaced with a Cantonese alliteration "uncle going to buy fish intestine" (in Chinese, "姨丈买鱼肠"). The other item that originally requires to read and follow the instruction "Please close your eyes" has been changed to "Clap your hands" (in Chinese, "拍手"). It is because the original phrase "close your eyes" might be misinterpreted as "death" in the Chinese culture which should be avoided as much as possible for older adults. Furthermore, due to the large population of older adults with no or little education, the task requiring them to "*write* a sentence" has been replaced with to "*tell* a sentence". More detailed modifications are summarized in Table 4. This revised instrument has been widely used as a screening tool or as an assessment of cognitive impairment in dementia in various studies (e.g., Lam et al., 2008; Poon et al., 2008).

Table 4

MMSE and Chinese (Cantonese) version of MMSE (C-MMSE)

MMSE	C-MMSE
Recall	Recall
1 What is the	依家係乜嘢日子
Year?	年份？
Season?	季節？
Date?	月份？
Day?	幾號？
Month?	星期幾？
2 Where are we	我哋依家係邊度？
State?	九龍/新界/香港？
County?	九龍/新界/香港 嘅邊度？
Town/city?	醫院/診所/邊條街/邊個屋村？
Floor?	邊層樓/診所名字/邊一座/中心名字？
Address/nave of building?	病房/邊層樓/邊層樓/邊層樓？
Registration	Registration
3 Name 3 objects, taking one second to say each	依家我會講三樣嘢嘅名，講完之後，請你重複一次。請記
Then ask the patient all 3 after you have said them	住佢地，因為我幾分鐘後，會教你再講番畀我聽。
Repeat the answers until the patient learns all 3	"蘋果" "報紙"、"火車"。依家請你講番哩三樣嘢畀我聽。
	（以第一次所講嚟計分）
Attention and Calculation	Attention and Calculation
4 Serial sevens Give one point for each correct answer	請你用一百減七，然後再減七，一路減落去，直至我教你
Stop after 5 answers Alternative spell word	停為止。
backward	（減五次後便停）
Recall	Recall
5 Ask for names of 3 objects learned in question 3	我頭先教你記住嘅三樣嘢係乜嘢啊？
Give	
one point for each correct answer	
Language	Language
6 Point to a pencil and a watch Have the patient	哩樣係乜嘢？ （鉛筆）（手錶）
name them as you point	請你跟我講句說話"姨丈買魚腸"。
7 Have the patient repeat "No ifs, ands, or buts"	依家台上面有一張纸。用你嘅右手拿起張纸，用兩隻手一
8 Have the patient follow a 3-stage command "Take	起講纸折成一半，然後放番張纸係台上面。
The paper in your right hand Fold the paper in ball	
Put the paper on the floor"	請讀出哩張纸上面嘅字，然後照住去做。（"拍手"）
9 Have the patient read and obey the following "Close	請你講任何一句完整嘅句子畀我聽。例如 "我係一個人"、
your eyes"	"今日天氣好好"。
10 Have the patient write a sentence of his or her	

	own choice (The sentence should contain a subject and an object and should make sense Ignore spelling errors when scoring)	哩處有幅圖，請你照住黎畫啦。
11	Enlarge the design printed below to 1-5 cm per side And have the patient copy it	
12	(Give 1 point if all the sides and angles are preserved and if the intersecting sides form a quadrangle)	

Note Taken from Folstein et al (1985) and Chiu et al (1994)

Recently, researchers have also developed the telephone version of the C-MMSE (T-CMMSE, Wong & Fong, 2009) based on Newkirk et al.'s work (2004). It could be used as an alternative to the C-MMSE for people who have difficulty in attending a face-to-face assessment in a clinic setting. The Mattis Dementia Rating Scale (DRS; Mattis, 1988) is a relative more global cognitive assessment that could be used to assess five cognitve domains, namely, attention, preservation, construction (reproduction of stimulus designs), conceptualization and memory. A Chinese version (CDRS) has been constructed with necessary adaption for cultural differences and language requirements (Chan, Lam, Choy, Leung, & Li, 2001). Thus, for example, the original materials used in the counting task (i.e., English alphabets) have been replaced with numbers which are more familiar to the Chinese participants. Similarly, the words (*"fish, car, train"*) used in the other question testing has been replaced with *"fish, car, ship"*. Because in Chinese, the word "*train*" (火車) consists of 2 characters, one of which is the character for *car* （車）. To avoid confusion, it is better to replace "train" with "ship". It has been demonstrated that the CDRS is a suitable tool in detecting early cognitive impairment in the Hong Kong Chinese population (Lam et al., 2008).

Verbal fluency tests have also been used to assess the semantic memory and executive function. There are two popular verbal fluency tests, namely, the Letter Verbal Fluency Test (LVFT; to generate new words starting with a certain letter) and the Category Verbal Fluency Test (CVFT; to list exemplars of a certain category). The former is relatively more restrictive and it is difficult to be adapted into an equivalent test due to the very distinct characteristics between the English and Chinese languages. In contrast, the CVFT has been adapted into a Chinese version (Chiu et al., 1997; Mok, Lam, & Chiu, 2004).

As to the assessment of memory deficits, Lui, Lam and Chiu (2006) have developed

the Memory Inventory for Chinese (MIC) to assess memory deficits by interviewing both the patients and their caregivers. Similarly, the Alzheimer's disease Assessment Scale cognitive subscale (ADAS-Cog, Rosen et al., 1984) has also been designed to assess cognitive function for DAT. It consists of 11 items with a maximum score of 70 to assess cognitive domains such as memory, orientation, language and praxis functioning. Its Chinese version has been validated with satisfactory psychometric properties (Chu et al., 2000).

The Fuld Object Memory Evaluation (FOME) evaluates the function of the episodic memory and has been validated as a screening tool for dementia (Fuld, 1981). In conventional memory assessment, participants have to use their auditory or visual modalities for information coding. In contrast, the FOME requires participants to identify objects through multi-sensory channels (touch, vision and hearing) to encode information. This will greatly facilitate people who have potential visual or auditory disabilities to complete the task. Importantly, it has been demonstrated that the performance in the FOME would not be unnecessarily influenced by educational background (Wall, Deshpande, MacNeill, & Lichtenberg, 1998). The Chinese version of this test has been adapted by Chung (2009) with satisfactory psychometric properties, and has been successfully used with residents at Chinese nursing home (see Chung & Ho, 2009).

Another popular screening test is the Clock drawing test (CDT) which aims to measure the cognitive functions, which include visual spatial organization, orientation and conceptualization of time. It has been shown that the test is useful in detecting dementia (Shulman et al., 1993; Rouleau et al., 1996) and has been validated for people with mild DAT in Taiwan (Chiu, Li, Lin, Chiu, & Liu, 2008).

4.2 Behavioral and Psychiatric Tests

People with dementia may also suffer from behavioral problems (e.g., aggression), psychiatric problems (e.g., delusions), or mood disorders (e.g., depression). To this end, the Neuropsychiatric Inventory (NPI) has been designed to evaluate a wide range of behavioral disturbances of dementia including delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, and aberrant motor activity (Cummings, 1997). This instrument has three major advantages. Firstly, it saves the administration time by assessing and scoring only those behavioral domains which respond positively to the screening questions. Secondly, information for the NPI is mainly obtained from one close relative or a caregiver who is familiar with the patient's behavior, which facilitates the assessment of patients who have language disabilities or are not available to attend the test in the clinic setting. The Chinese version of NPI was developed by Leung, Lam, Chiu, Cummings and Chen. (2001) and had been demonstrated to be applicable for the Hong Kong population.

Another instrument based on similar construct as NPI is the Chinese version of the Cohen-Mansfield Agitation Inventory (CCMAI) (Choy et al., 2001). It has been translated from the Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield, Marx, & Rosenthal, 1989) and has been used to quantify the frequency of agitated behavior such as inappropriate verbal or behavioral activities (e.g., aggression, keeping asking questions).

4.3 Functional Tests

Functional assessment is used to assess a number of aspects in mental and behavior that are related to the dependence in daily activities. The Disability Assessment for Dementia (DAD) was originally developed by Gelinas, Gauthier, McIntyre and Gauthier

(1999) and has been translated into Chinese with language polishing into more idiomatic style (Mok et al., 2005). The Chinese version of DAD (CDAD) has been found to have satisfactory reliability and validity in assessing the functional disabilities among Chinese population, and the test is especially useful for community-residing older adults. CDAD (Mok et al., 2005) is an interview-based assessment and, therefore, well trained interviewers and assessors are required.

Chu and Chung (2008) developed the Chinese version of Activities of Daily Living Questionnaire (ADLQ, Johnson, Barion, Rademaker, Rehkemper, & Weintraub, 2004) (ADLQ-CV) which consists of 25 items and assesses the impairments in daily life basic activities. It is a convenient assessment that enables patients' caregivers to complete the questionnaire on their own without the help of a trained interviewer.

Some effort has also been devoted to combine various types of assessments that are complementary in their strengths so as to enhance the screening power of the tools. For example, a recent attempt (Narasimhal, Lee, Auchus, & Chen, 2008) have tried to build a more effective screening by combining MMSE with IQCODE.

4.4 Assessing Populations with Low-level Literacy

It has been documented that the cognitive performance of older adults in screening test could be unnecessarily affected by their education background (e.g., Schmitt et al., 2000). Older adults with lower education are likely to get lower scores in some screening tests and thus would be wrongly classified as having dementia-related deficit (e.g., Borkowski et al., 1967).

One method to minimize the possible bias is to reduce the task demand on cognitive skills such as reading and writing, which are typically advantageous for people who have gone through proper schooling. Therefore, the Chinese version of Fuld Object

Memory Evaluation (FOME) mentioned above, which relies much less on language proficiency, is preferable for older adults with little education. Another effort was the Chinese version of ADAS-Cog, in which words are replaced with pictures in recall and recognition tasks. The test has been used to assess the cognitive deficit among Taiwan Chinese population with lower level of education (e.g., Lin et al., 2002). Similarly, in Hong Kong, the Clock-face test (Lam et al., 1998) has been designed for individuals with limited education. The test consists of three parts. The first is a drawing task which requires participants to draw the numbers and arms inside a clock face to indicate a certain specific time. Then, the participants are asked to tell and set the time using a toy clock.

An alternative approach is to use the informant-based assessment or combine the informant-based interview with traditional screening tests. The Chinese version of the Community Screening Instrument for Dementia (CSID, Chan, Choi, Chiu, & Lam, 2003) is a good example of combining cognitive assessment with informant-based interview and is targeted at individuals with heterogeneous educational and cultural background. Previous studies supported the use of an informant-based assessment as a supplement to the cognitive screening test (e.g., MMSE; Mackinnon & Mulligan, 1998; Narasimhalu, Lee, Auchus, & Chen, 2008).

4.5 Brief Summary and Implications

This chapter reviewed the psychometric tests that are used in Chinese community for screening dementia. It should be noted that almost all the screening tests are developed in the West in which education attainment in old population is essentially different from that in mainland China and Hong Kong. As discussed in Chapter Two, education plays an essential influence on the performance of older adults. The present

thesis aimed to investigate the impact of education on the performance of a set of psychometric tests among Chinese older adults with different level of education and furthermore, to identify the tasks that are more appropriate for Chinese population.

Chapter 5 Literature Review -- Response Time Distributionand Intraindividual Variability

5.1 Beyond Normal Distribution and Mean Comparison

5.1.1 Problems of Traditional Approaches

Response time has been a central focus of analyses in cognitive psychology for a long time (e.g., Luce, 1986; Matzke & Wagenmakers, 2009; Ratcliff & McKoon, 2008; Townsend & Ashby, 1983). In these analyses, mostly quantitative in nature, inferential tests such as ANOVA and t-test on a central tendency measure (e.g., means) of the performance of different groups are compared. Based on the same statistical principles, slightly more sophisticated analyses including regression and factor analyses may also be used. They will be able to reveal the differences of the mean performance of groups or other contrast effects as beta coefficients.

The above analytical approaches are simple to conduct and readily available in commercial software. These methods are popular because means are generally stable and not easily affected by isolated deviant data points, whereas skewness and kurtosis estimates are comparatively less reliable and can hardly be used for comparisons (Balota et al., 2008). The irony is that exactly due to the features of means aforementioned, mean comparisons have their limitations because they may miss important underlying effects, mask possibly crucial information, and not be sensitive enough to capture changes at the tails or in other characteristics of the distribution (e.g., Heathcote, Popiel, & Mewhort, 1991).

Recently researchers have advocated the use of more detailed characteristics of the response time distribution, such as in Balota et al.'s (2008) chronometric (time-measuring) studies of language and memory processing. They used the

advancement in greater magnification of observation in astronomy, biology, or neuroimaging as analogies, and argued that similar development has already been made in psycholinguistic and other response time related research. Time has come, therefore, to move beyond the analyses of the means as the main characteristics of the response time distribution.

Analyses of means are unsatisfactory in particular for neuropsychological assessment because the normality distribution assumptions are generally not met in that (e.g., Balota et al., 2008; Heathcote et al., 1991):

a. In mean comparisons using t-test or ANOVA designs, it is assumed that the distributions in the different conditions are similar and are both symmetrical so that the means are good indicators of the respective distributions. This assumption, however, is not valid because a lot of reaction time (RT) responses are positively skewed with a heavier tail at the high value end (slower response time) (Luce, 1986).
b. The model (peak) and tail parts of the distribution may shift or change in shape and cannot be appropriately reflected by their respective means (Balota et al., 2008).
c. The problem of deviant data points or outliers on response time analyses has long been identified (e.g., see review Ratcliff, 1993). Thus, these deviant points may lead to misleading conclusions when using ANOVA type of analyses. Different solutions to this problem using deletion, transformations, cutoffs, and fitting functions are useful but have their limitations. In brief, the analyses of deviated data points may provide additional rich and important information beyond that captured by the comparisons of means.

To fully reflect the characteristics of the distribution, it is necessary, therefore, to develop stable indicators of the higher-order moments of the distribution. Furthermore,

this may also involve the collection of 50 to 100 trials of observation, much more than the standard 10 to 20 trials. Here, the present chapter will basically follow and the previous investigations by Balota et al. (2008), Ratcliff (1978, 1979), Bielak, Hultsch, Strauss, MacDonald, & Hunter (2010a), Hultsch, Strauss, MacDonald, & Hunter (2010b), and Hutlsch et al. (2008).

There are two recent directions of development that move beyond the analyses of the means. Both approaches challenge that the mean of performance over repeated trials on the same or similar task (e.g., 50 responses in a Stroop task) cannot fully capture and reflect the main characteristics of the distribution. In the first advancement, one could use the ex-Gaussian function to capture the abnormal characteristics of the response time distribution. In the other advancement, the present research will mainly focus on and analyze the fluctuations in performance within an individual (i.e., intraindividual variability) over an identical task.

For the former approach, one can put together the responses of all trials to build a distribution. The main interest is the shape of the distribution and the order of the data points in the actual assessment, which had not been taken into consideration in building the cumulative distribution. Then the ex-Gaussian model will be used to capture the degree of positive skewness in the distribution. In the latter intraindividual variability approach, the order of the data points will be entered into the analyses to see the possible practice or fatigue effects. The regression equation will take into consideration various affecting factors so as to predict participants' performance at each trial. The residuals in the regression will then be used as a measure of the variability across trials.

5.1.2 Visual Presentation and Mathematical Modeling

At one end of the extreme, probably the simplest solution to reflect and capture the change and difference in the distribution is to visually inspect the data plotted on graphs

(see below, e.g., vincentile analyses). At the other extreme, sophisticated and dedicated mathematical models, presumably capturing the data distribution in a certain research problem can be used in the analyses of the change in the distribution. Thus, the researchers' work is to test the fit of the mathematical models to the empirical data and examine the changes or differences reflected in these models. More details of both approaches will be discussed in the sections on skewed distribution and intraindividual variability below.

5.2 Analyses of the Skewed Distribution

The analyses of the positively skewed distribution of response time can be achieved through the visual vincentile approach or the mathematical ex-Gaussian function approach. For the latter, while the most popular models will be introduced, elaborated discussion on the development and comparison of various general mathematical functions is beyond the scope of the present dissertation (e.g., see review, Van Zandt, 2000). Here for the capturing of memory retrieval and cognitive functioning, the present section will narrow down and concentrate on the most popular ex-Gaussian approach (as advocated by Balota et al., 2008, Ratcliff, 1978, 1979).

5.2.1 The Ex-Gaussian Distribution

For a sample of response time data, the fitting of a mathematical model to the data refers to the process in identifying a theoretically reasonable mathematical function. This function associated with a certain set of estimated parameters (mu, sigma, tau as in the case of the ex-Gaussian distribution) will have a theoretical distribution match to the empirically observed distribution. Obviously different distributions will be generated from different sets of estimated parameters. The set of parameters producing the best matching behavior will be chosen.

Operationally, theoretically reasonable functions can be fitted with empirical samples obtained from diversified experimental conditions and backgrounds of participants (Cousineau, Brown, & Heathcote, 2004; van Zandt, 2000). In choosing the best function, the common assessment criteria are: (i) a minimal bias -- the parameters obtained from the theoretical function do not over- nor under-estimate the characteristics of the empirical distributions), and (ii) the highest efficiency -- the deviation or variance of the parameters in the matching between the theoretical function and the empirical distributions repeated over different samples is minimal.

Among various mathematical models, the ex-Gaussian distribution is one of the most commonly used functions to fit reaction time response distributions in cognitive psychology (Hockley, 1984; see summary in Cousineau et al., 2004; for uses in other domains, e.g., Staub, White, Drieghe, Hollway, & Rayner, 2010, on eye-fixation duration measures). In advocating its use, Balota and Spieler (1999) have provided a number of reasons, namely, (i) mu from the ex-Gaussian distribution can be easily understood, (ii) the exponential and Gaussian components nicely reflected the central tendency and the skewness of the distribution, and (iii) these characteristics of the ex-Gaussian distribution are relatively stable across participants over diversified tasks.

In simple terms, the ex-Gaussian function can be seen as the convolution or merging of the Gaussian (normal) distribution and an exponential distribution (or exponential decay). The distribution can then be described by three parameters, μ (mu), σ (sigma) and τ (tau). The first two parameters are identical to those used to describe the mean and standard deviation of the Gaussian distribution, while the last one represents the skewness of the tail at the positive end and is the single parameter capturing the mean and standard deviation of the exponential function.

Mathematically, the density of the ex-Gaussian can be expressed either as (Ratcliff,

1993; Van Zandt, 2000),

$$f(t)=\frac{1}{\tau}e^{-\frac{t}{\tau}+\frac{\mu}{\tau}+\frac{\sigma^2}{2\tau^2}}\Phi\left(\frac{t-\mu-\sigma^2/\tau}{\sigma}\right),$$

where Φ is the standard normal cumulative density function (CDF), and as:

$$f(t)=\frac{e^{-[(t-\mu)/\tau]+\sigma^2/(2\tau^2)}}{\tau\sqrt{2\pi}}\int_{-\infty}^{\{[(t-\mu)/\sigma]-\sigma/\tau\}}e^{-y^2/2}dy.$$

or as a cumulative density function as:

$$F(t)=e^{-\frac{t}{\tau}+\frac{\mu}{\tau}+\frac{\sigma^2}{2\tau^2}}\Phi\left(\frac{t-\mu-\sigma^2/\tau}{\sigma}\right)+e^{\frac{\mu}{\tau}+\frac{\sigma^2}{2\tau^2}}\Phi\left(\frac{-\mu-\sigma^2/\tau}{\sigma}\right)+\Phi\left(\frac{t-\mu}{\sigma}\right)-\Phi\left(\frac{-\mu}{\sigma}\right).$$

As regards the relations between the parameters and the distribution in an ex-Gaussian distribution, mathematically its mean is equal to $\mu + \tau$. When $\tau = 0$, this reduces to the typical normal distribution. For cases when $\tau \neq 0$, the tail becomes thicker than that of a normal distribution, the new mean will be shifted and will be equal to $\mu+ \tau$.

A certain experimental factor can have (i) an effect on μ only – shifting the distribution, (ii) an effect on τ only – affecting (e.g., thickening when $\tau > 0$) the tail of the distribution, (iii) an counteracting (tradeoff) effect on both μ and τ — e.g., while reducing μ and increasing τ, the net effect on the mean of the distribution can be close to zero and would be masked in traditional mean comparisons (see Figure 1). All these effects can be delineated and detected if the above three parameters can be estimated for each of the conditions or groups in the experiment.

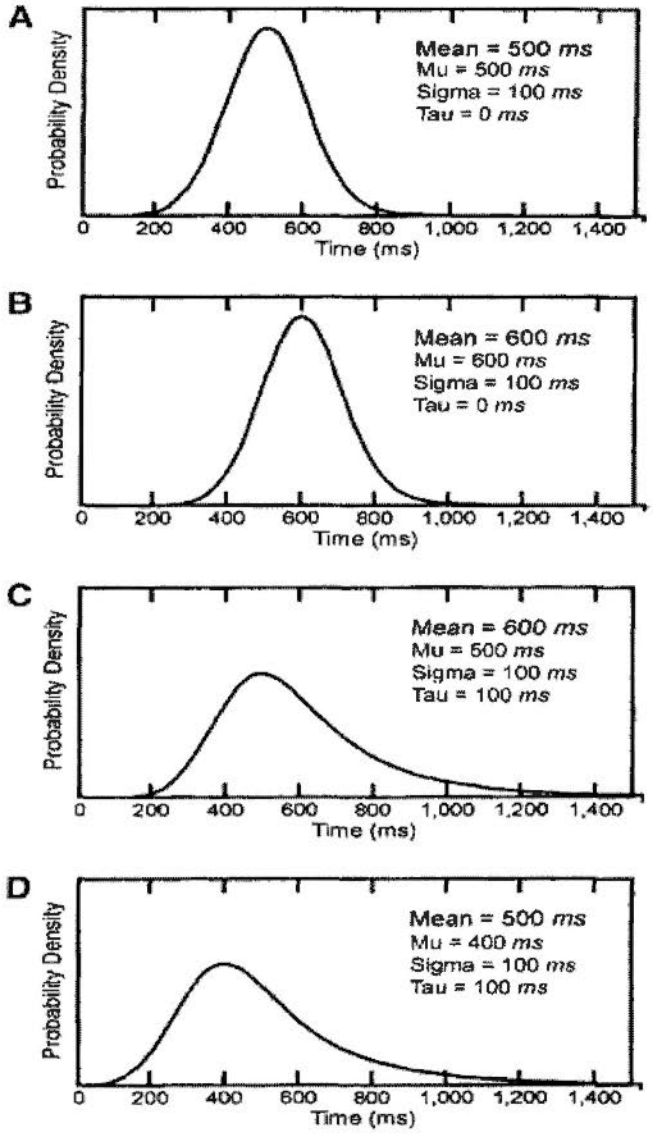


Figure 1. Relation between mu, sigma, tau and the distribution (from Balota et al., 2008, Figure 3).

5.2.2 Estimation Methods

Operationally, the estimation of the parameters in the ex-Gaussian distribution can be obtained using different software (e.g., QMPE 2.18, an open-source program, Cousineau et al., 2004; Heathcote, Brown, & Mewhort, 2002; Brown & Heathcote, 2003) and algorithms (e.g., QMP, see review in Cousineau et al., 2004).

Importantly, the estimation of the three parameters (mu, sigma, tau) is not trivial

particularly when the problem of noise is serious (e.g., large measurement errors) and the sample size is small (Heathcote, Brown, & Mewhort, 2000). The maximum likelihood and the quantile maximum probability methods, among other less popular ones, have been found to perform relatively well (Heathcote et al., 2000; Van Zandt, 2000). As regards the computational procedures, in brief, in the maximum likelihood (ML) method, a set of parameters $\hat{\theta}$ of the function that maximized the likelihood of the observed distribution will be searched. The difference of the QMP approach was that the continuous distribution was collapsed into categories first and the set of parameters was expressed as a function of these quantiles (Cousineau et al., 2004; Speckman & Rouder, 2004). It was noted that these estimation methods when implemented in different packages produced similar optimal solutions.

In comparing a few most widely used estimation methods in response time research, Van Zandt (2000) evaluated the maximization of likelihood and least square fits of the theoretical distributions to empirical estimates of simulated distributions. Results supported the maximum likelihood methods to be outperforming the least square methods. Though in general, the ex-Gaussian function behaved quite well, parameter recovery is still a concern unless the sample size is reasonably large.

The quantile maximum propability (QMP) method performed quite well. In a direct comparison of the ML and the QMP method, the latter has been shown to be superior in terms of its bias and efficiency on the ex-Gaussian distribution (Cousineau et al., 2004; see also Heathcote, 2004; Heathcote & Brown, 2004; Heathcote, Brown, & Cousineau, 2004; Heathcote et al., 2000; Speckman & Rouder, 2004). Heathcote and Brown (2004) have concluded that the QMP fitting performs much more effectively than maximum likelihood estimation particularly for small sample sizes (e.g., as few as 40; see also Speckman & Rouder, 2004). When the response time data are contaminated by other

factors such as practice or fatigue (which might be prevailing in psychological studies), the parameters of the distributions will change over time. In such cases, the QMP calculations might be more robust to the effects of outliers and measurement noise than the standard maximum likelihood estimation (Cousineau et al., 2004).

More interestingly, Speckman and Louder (2004) have shown that although QMP does not have an exact theoretical basis in likelihood asymptotically, QMP may perform better than the more theoretically justified maximum likelihood approach under nonasymptotical situations when the sample size is small (see also Heathcote & Brown, 2004).

Possible explanations of the above observations have been proposed. The original intuition was that one would lose information in compressing the scores into quantiles (scores within a narrow inter-quantile range collapsed into categories). Interestingly, there are benefits in return in using appropriately chosen quantiles because the effects of disturbing outliers can be reduced (Cousineau et al., 2004). The QMP approach is believed to retain the efficiency and consistency of the maximum likelihood estimation, yet enjoying the benefits of the robustness of the quantiles derived from the samples.

In real rather than simulated data, when outliers may be more common, the advantage of the robustness of QML may be more obvious at a small cost in its bias and efficiency. The possible drawback, nevertheless, is that the QMP method is computationally intensive and is difficult to be implemented.

On the choice of the number of quantiles, there is a trade-off between estimation accuracy and robustness ---- less quantiles are more robust and protective against outliers, while more quantiles compatible with sample size produce smaller bias and maximum efficiency. In the specific simulation condition as used by Heathcote et al. (2000), it has been found that QML is still well behaved for as many as 16 observations

(thus, generally not more) per inter-quantile range and at least ten quantiles (thus, generally not less). One strategy as recommended by Heathcote et al. is to have larger number of observations in the two ends (first and last intequantile ranges) than in the middle part of the distribution.

5.2.3 Vincentile Analyses

Ex-Gaussian analyses can be supported or supplemented by plotting the quantiles or vincentiles. The advantage of plotting the raw data is that one does not have to make any assumption about the distribution nor summarize the characteristics of the distributions with parameters in mathematical models. The graphical display has a direct visual image but generally do not have any post-hoc significant test on the interesting trends identified. In some situations, researchers (e.g., Balota et al., 2008, Figure 7 and relevant analyses on p.505) did conduct follow-up analyses (e.g., ANOVA) of the trends displayed.

In the Vincentile analyses, one could begin with plotting the raw data in groups and drew conclusions based mainly on the visual patterns. Thus, for example, for a certain group or condition in the study, one could arrange the response time data (e.g., from fast to slow) and then compute the mean of the first 10%, the second 10%, etc. The plots of these means against the ten interval points, or the plots of the differences of the means across two different conditions can be used to reveal where the impacts are in the distribution. Typical changes of the μ or τ are shown in Figure 2 (Balota et al., 2008).

In vincentile analyses, one can plot the means of vincentile against the deci-points (the 10 points, see Figure 2). But, perhaps easier to interpret is the plot of the differences of the vincentile graphs in the two experimental conditions. For example, if the treatment does not affect the three parameters (μ, σ and τ), then the two lines will overlap with each other, with zero difference between the two plots (i.e., a plot of the

difference versus the 10 deci-x-axis points will be a horizontal line with y = 0). If the treatment changes the μ value by 100 units, the differences of the two plots will result in a horizon line with y = 100 (the solid line in the top panel of Figure 2). If there is a shift in τ after the treatment, it will result in the dotted line in the top panel in Figure 2. Change in σ will result in the dotted plots corresponding to the difference between two Vincentile plots, as shown in the lower panel in Figure 2. In empirical situations with shifts in all three parameters, these plots will be reflected accordingly in more complicated trends.

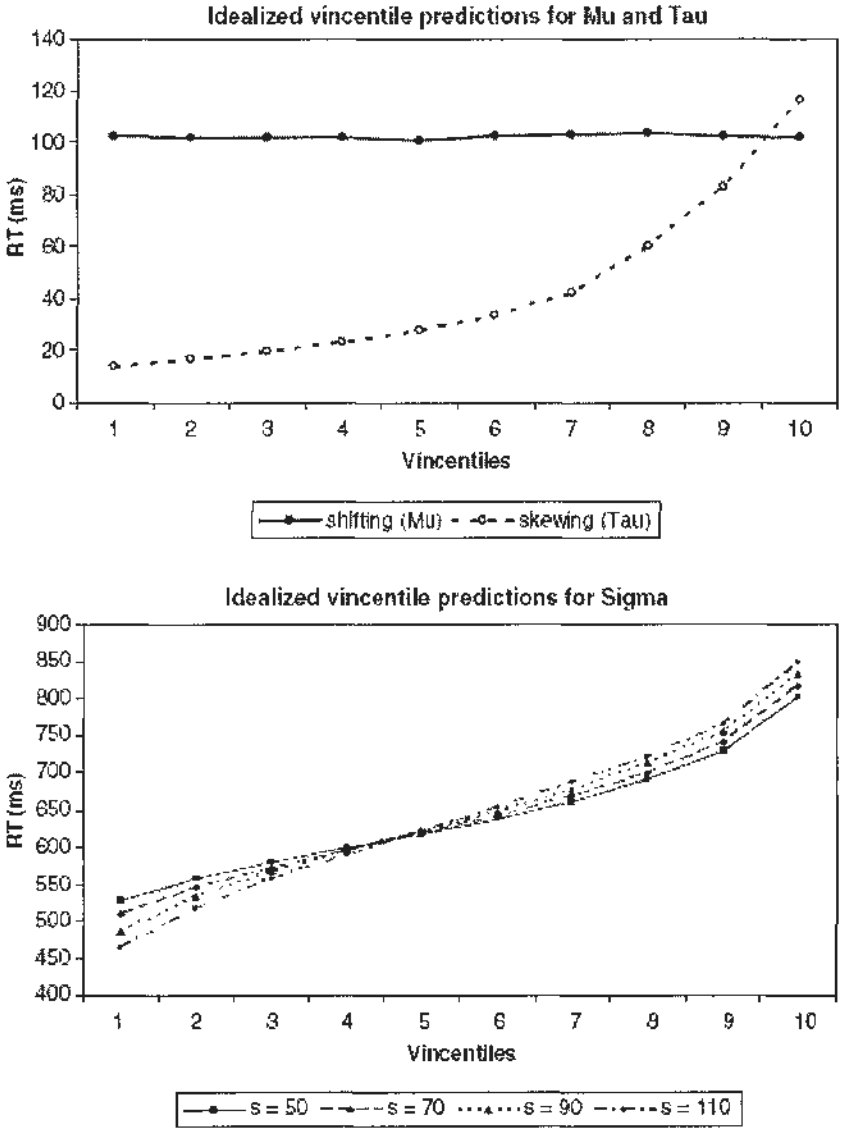


Figure 2. Vincentile analyses comparing vencentile plots across different distributions (from Balota et al., 2008, Figure 4).

5.3 Analyses of Intraindividual Variability

Sensitive instruments and measures for early identification of potential Alzheimer's disease patients are critical (Duchek et al., 2009), particularly when early interventions are more promising than treatment at the latter stages. There has been great interest in using and examining intraindividual variability — differences, inconsistencies in performance over repetitive trials on similar tasks (see other kinds of variability below), so much that theme-focused conferences have been held (e.g., Martin & Hofer, 2004) and special issues in academic journals were devoted to the topic (e.g., in psychology and aging; Ram, Lindenberger, & Blanchard-Fields, 2009).

In typical neuropsychological tasks, participants' performance over multiple repetitions of the same tasks is obtained. In traditional analyses of the performance across these repetitions, variations are seen as measurement errors and are typically ignored. Accumulated research evidence, however, suggests that the intraindividual variability across a number of trials can be a more useful and powerful predictor of targeted health status or problems, on and above the variance and prediction power based on the mean level performance (Dixon et al., 2007; Duchek et al., 2009; Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000; Hultsch, MacDonald, & Dixon, 2002; Strauss, Bielak, Bunce, Hunter, & Hultsch, 2007).

As pointed out in the earlier discussion in this chapter, the mean reaction time of these multiple trials across individuals in different groups or experimental treatment conditions were compared and analyzed. The present research also concentrated on the distribution analyses, in particular the examination of skewness through the ex-Gaussian distribution analyses. In this section, the main interest is on the intraindividual

variability and how appropriate analyses can be conducted on these characteristics of the data collected over multiple trials.

While in the above discussion and in this research project, the focus is on participants' performance on multiple trials over repetitive measurement on the same or very similar task, it is also noted that other researchers (Holtzer, Verghese, Wang, Hall, & Lipton, 2008; Kliegel & Sliwinski, 2004; Rapp, Schnaider-Beeri, Sano, Silverman, & Haroutunian, 2005) might focus on the variations in relative performance over multiple tasks or subscales of the same tests. Understandably the variability in different contexts might reflect totally different constructs and aspects of mental activities. Thus, as pointed out by Martin and Hofer (2004), "We might consider sampling moment to moment (attentional lapses), within-test (fatigue, practice), within-session (fatigue, order effects, motivation), within day (time of day effects), across days or weeks (environmental perturbations, physical health, practice), months or years (characteristic change trajectory)" (Martin & Hofer, 2004, p.10). In this research, the main interest was the moment to moment variation in repetitive performance for the same or similar tasks.

5.3.1 Intraindividual Variability and Cognitive Functioning

An increase in within task variability has been found to be related to important indicators of cognitive functioning in general and of dementia in particular, the latter of which is the central interest of the present research (see reviews, e.g., Bielak et al., 2010a, 2010b; Hultsch et al., 2008, Schmiedek, Lövdén, & Lindenberger, 2009; see also Christensen, Lindberg, & Andersen, 2005; Hultsch et al., 2000). Sophisticated theories have also been proposed to explain the relationship between intraindividual variability and cognitive impairment, and why the variability of performance may be reflecting the central nervous system (CNS) functioning (see extensive review by Hultsch et al., 2008).

In particular, relevant to the discussion of dementia assessment, one can differentiate variability affected by neurobiological level or affective (or somatic) state. The former may influence the neural transmission speed or neurotransmitter systems and might induce the rapid variability of performance in repeated trials in typical neuropsychological (e.g., Simon Task) assessment. The latter kind (affective, somatic) is not the source of effects that leads to the variability of performance within such a short time span.

As summarized by Bielak et al. (2010a), "Although the precise neurological cause of inconsistency is still unknown, intraindividual variability in response speed is believed to be a behavioral indicator of neurological integrity.... consequently, intraindividual variability may be an early marker of impending disease and behavioral impairment" (p. 732). Thus, for example, intraindividual variability has been found to be related to poor cognitive ability, brain disorders, mild cognitive impairment, and the white matter hyperintensities in the frontal lobe is likely reflecting the deterioration in attentional control or executive control across time (e.g., Bunce et al., 2007). Similarly, de Frais et al. (2007) showed that Parkinson disease patients not only had a slower response speed, but a larger variability in response time on complex tasks than healthy patients. On the tasks that are most discriminating, research results suggest that intraindividual variability is very accurate when predicting cognitively complex and speed related tasks that demand heavily executive functioning or involve working memory (Bielak et al., 2010a, 2010b; Dixon et al., 2007; Strauss et al., 2007).

Despite the seemingly promising predictive power of intraindividual variability on subsequent decline of the cognition condition, there is still concern and research that questions whether the level of performance (mean score) is as useful or more important than variability (Bielak, Hughes, Small, & Dixon, 2007; Christensen et al., 2005;

Lövdén, Li, Shing, & Lindenberger, 2007; Salthouse, Nesselroade, & Berish, 2006; see Whitehead, Dixon, Hultsch, & MacDonald, 2011 on predicting diabetes). Thus, it is paramount that one investigates the relative predictive power of intraindividual variability in the Chinese context and for a wide range of psychoneurological tests.

5.3.2 Components in Intraindividual Variability

Research on intraindividual variability usually concentrates on the amount (rather than form, trends, etc.) of variability, most usually indicated by the standard deviation across time/trials of the raw responses. The comparison of these raw standard deviations across groups is, however, complicated because the total intraindividual variation contains various components, including: (i) systematic (e.g., practice effect, fatigue) and unsystematic within-subject components (the targeted most interesting variability under discussion), (ii) systematic between-group (e.g., between dementia and normal aging groups) and residual within-group components (variations across dementia group individuals) (Hultsch et al., 2008). Simply put, one major challenge researchers have long been aware of is that the means and standard deviation are highly correlated (Faust, Balota, Spieler, & Ferraro, 1999) and the means in repeated measurement have to be controlled in the comparison of intraindividual variability. Thus, it would be wrong to conclude a standard deviation of 10 implies a larger variability than another of 5, if the former is associated with a mean of 100 while that of the latter is only 10.

It is further noted that in the computation of the intraindividual standard deviation, as the number of errors in response time is generally low, the standard deviation computed over all items (or responses) whether by including or excluding the incorrect responses will not affect much the conclusion so obtained (Bielak et al., 2010a, 2010b; Burton, Strauss, Hultsch, Moll, & Hunter, 2006; Dixon et al., 2007).

The development as well as the characteristics of a few commonly used indicators of

intraindividual variability will be discussed below.

5.3.3 ANCOVA vs. Regression

In the analyses of the intraindividual variability, one easy way to control for the difference in mean across participants is to put the mean level as a covariate in the between-group (e.g., dementia group vs. normal aging group) comparisons (ANCOVA type) or as one of the predictors in the regression equations. This method, however, has a number of limitations, including (Hultsch et al., 2008; Schmiedek et al., 2009): (i) the grouping variable (e.g., dementia vs. normal aging) and the covariate (i.e., mean of performance) are obviously not uncorrelated (independent) as assumed in ANCOVA, (ii) the grouping effect is partialed out in the ANCOVA or regression making it hard to be interpreted (i.e., the effects of interest has been removed in the ANCOVA); (iii) the systematic (e.g., practice effect, fatigue) and unsystematic within-subject variations have not been disentangled; (iv) the assumed linear relation between mean and standard deviation is reasonable in some conditions, but is not necessarily always true, and (v) the relation between mean and standard deviation assumed to be invariant across time and individuals may not be true.

Coefficient of variation. Another simple and common indicator of variability is the coefficient of variation (CoV), computed as the individual's standard deviation divided by its respected mean (SD/M) (e.g., Duchek et al., 2009). The logic is simple in that as the raw unit of standard deviation becomes larger with increasing mean across groups, dividing SD by mean will provide a more comparable index for comparison. The use of the coefficient of variation approach has also been empirically supported. For example, Wagenmakers and Brown (2007) have shown over a wide range of tasks and experimental paradigms that the response time mean and standard deviation can be approximated by a linear relation. Their results, therefore, support the use of the

coefficient of variation (SD/M) in the comparison of variability (SD) where the effects due to the changing baseline rate (mean) can be controlled.

Similar to ANCOVA, however, this coefficient still has a number of drawbacks, such as (Hultsch et al., 2008): (i) as SD/M is a cross-product term, one have to include the main effects (SD, mean) in the same analyses, which often are missing and missspecified in the analyses and (ii) one still could not disentangle the systematic and unsystematic within-subject variability.

Residualized Intraindividual Standard Deviation. In the coefficient of variation approach, the effect due to the mean will be controlled. This will solve and handle the problem due to substantial differences in the mean levels across two treatment (comparison) groups (e.g., DAT vs. normal aging). Further control may also be necessary to partial out the systematic effects due to the changing means across trials (practice or fatigue effects), age (older participants are slower), or other related effects (Dixon et al., 2007).

Using procedures developed by Hultsch et al. (2000, 2005), these groups and time-related (trial) effects can be removed or controlled prior to the computing of the individual standard deviation. Operationally this can be achieved through spilt-plot ANOVA for more balanced designs or by controlling for the effects of age (or age group) and trials (e.g., practice or fatigue effects), these variables and their interactions are first partialled out to generate residual response time scores (Bielak et al., 2010a; see de Frais et al., 2007):

$Y = a + b$ (age group) $+ c$ (trial) $+ d$ (Age Group $\times$ Trial) $+ e$.

In this process, for research involving more than one task, the dependent variable response time across different tasks can be further standardized into T-scores (e.g., M = 50, SD = 10) to generate a common metric for easy comparison.

Alternatively, potential confounding effects due to age group and the within-level time-related effects (practice or fatigue trial effects modeled with linear and quadratic terms) can be modeled in multilevel regression equations. As the multiple data points from the same individuals on certain tasks are obviously not independent, multilevel regression can be used as the analytic method (Hoffman, 2007; see also Almeida, Piazza, & Stawski, 2009). In brief, the multiple observations for each individual at a certain wave or time are treated as level 1, while individual characteristics (background variables) are treated as level 2 or 3 variable depending on the specific set up of the research question (Hoffman, 2007; Hultsch et al., 2008, p.530, see also Almeida et al., 2009; Bielak et al., 2010b):

$$Y_{jik} = \mu + g_i + t_k + (gt)_{ij} + p_{k(i)} + e_{ijk}$$

where

Y_{jik} = performance of person k, in group i, on j-th trial,

μ = grand mean,

g_i = effect of group i,

t_k = effect of time,

$(gt)_{ij}$ = interaction effect of group i and time j,

$p_{k(i)}$ = individual difference for subject k within group i,

e_{ijk} = residual for subject k in group i at time j.

Here, intraindividual variability is defined as the standard deviation of the unsystematic part (i.e., e_{ijk}), and is called residualized intraindividual standard deviation (residual-ISD).

In the choice of a single or multi-level regression model for the present research, one has to consider the results by Bielak et al. (2010b). They showed that the individualized

standard deviations in single- and multilevel models are highly correlated and the results so produced are hence nearly identical. Despite the attractiveness that the multilevel method can provide a flexible assessment of the interactions among the various components across levels (e.g., how the slope changes with certain background variables) and the direct examination on the residual variance at individual level (i.e., intraindividual variability), there are more stringent assumptions to be met in these multilevel regression analyses. The process is computationally demanding and may lead to estimation problems, particularly when the number of assessment is small, and that the individual variability at level 1 may also include the misfit to the regression equation in addition to intraindividual differences (Hoffman, 2007). Thus, in this particular study, due to the small sample size and the interest being more on the psychometric properties of the instruments, the single-level regression approach was adopted in main analyses of intraindividual variability analyses.

Importantly, it is also noted that the above model can be further generalized to include and control for more relevant potential variables in the regression analysis. Operationally these variables will be put in a regression analysis and regress the response time on its components (contributing factors) in either single- or multi-level regression models (e.g., Bielak et al., 2010a, 2010b). The standard deviation of the residuals in these equations will be used as the intraindividual standard deviation. The analyses of the residuals from the above single- or multi-level regression will effectively remove any systematic within- (i.e., trial) and between-subjects (between different age, or between DAT group and normal aging group) source of variance in the effect of mean response time on the intraindividual variability. Previous studies (e.g., Hunter & Bielak, 2005) suggested that the effects due to trial and its interactions seem to be substantially larger than those due to between groups.

Chapter 6 Study One -- Use of Attention Tasks and Working Memory Tasks in Early DAT Discrimination among Chinese

6. 1 Background

6.1.1 Memory Deficit vs. Attention Deficit

The presence of memory deterioration has been well noted as a prominent clinical symptom of earliest stages of DAT in previous studies (Bäckman et al., 2001). Memory decline has been included in nearly all kinds of diagnosis criteria for DAT (e.g., DSM-IV criteria, American Psychiatric Association, 1994). Conversely, there have been relatively less studies investigated the attention deficit in early stage of DAT (see Twamley et al., 2006). Some proposed that attention-related deficit might also be a neuropsychological marker but later than memory impairment in early stage of DAT (Perry et al., 2000), whereas others argued that impairment in attention could also be an earliest sensitive predictor together with memory decline in DAT (Albert, 1996; Balota & Spieler, 1999). People advocating the latter view argued that previous studies might have failed to detect the attention deterioration in early DAT (Balota & Faust, 2001; Twamley et al., 2006).

More specifically, there might be two underlying reasons for the lack of attention studies. On the one hand, as to the nature of attention, it might be difficult to measure attention on its own by separating attention engagement from other cognitive processing (Balota & Faust, 2001). More importantly, in previous studies, there has been relative paucity of attention theories available and according tests for detecting specific component of attention appropriately, which might subsequently restrict the investigation of attention (see Parasuraman & Greenwood, 1998; Twamley et al., 2006). Until recent several decades' years, newly developed attentional theory (e.g., Baddeley,

1986; Baddeley et al., 1991; Balota & Faust, 2001; Norman & Shallice, 1986) and according testing approaches become available, through which specific aspects of attention could be tapped by appropriate measurement (Foldi, Lobosco & Schaefer, 2002; Spinnler, 1991).

On the other hand, the deterioration in attention is often manifested as poor memory performance. In other words, breakdowns in memory in early stage of DAT might be partly attributed to attention deficit (Balota & Faust, 2001). Though the critical role of attention process underpinning in memory task might has been well recognized (Fernandes & Moscovitch, 2002; Jacob, 1999), the magnitude of the attentional demands in memory task seemed to have not been appropriately manipulated or controlled in earlier studies (e.g., Simone & Baylis, 1997a). Since attention is of vital importance to other cognitive functions, the general process of memory is inevitably influenced from selecting and attending to the selected information to encoding, storage and later retrieval (Craik, Govoni, Naveh-Benjamin, & Anderson, 1996; Everitt & Robbins, 1997; Fernandes & Moscovitch, 2002; Hasher, Zacks, & May, 1999). For example, even healthy people have been found to experience difficulties in free recall of unrelated words if attention is divided to distracting task simultaneously during the processing of encoding and retrieval (Fernandes & Moscovitch, 2002). Similarly, researchers have suggested that the impairment in attention could at least partially account for cognitive impairment that is traditionally attributed to deficit in other cognitive domains, such as memory and language deficits (Amieva et al., 2004; Castel, Balota, & McCabe, 2009; Gernsbacher & Faust, 1991).

Given the above evidence that attention involved greatly in memory, the impairment of attentional function might help to explain the poor memory performance observed in DAT (Balota & Faust, 2001; Castel et al., 2007; Castel et al., 2009). As suggested by

recent studies (e.g., Belleville, Chertkow, & Gauthier, 2007; Twamley et al., 2006), it is imperative to investigate the potential attention deficits preceding the emergence of memory impairment in very early DAT.

6.1.2 Attention-related Tasks

The attentional control on the participants as evoked by Stroop tasks (e.g., Spieler et al., 1996; Balota et al., 2010), switching tasks (e.g., Duchek et al., 2009; Sinai, Phillips, Chertkow & Kabani, 2010), and Stroop switching tasks (i.e., a paradigm combining Stroop and switching tasks; e.g., Eppinger, Kray, Mecklinger, & John, 2007) have been used to examine cognitive control deficits among older adults. In the present thesis, the main interest was to examine the utility of two attention tasks, namely, Number Stroop Switching task and Face-number Switching task, in detection of early stages of DAT among Chinese older adults. Specifically, the discrimination power of two attention tasks would be examined among participants with very mild dementia and normal control.

Stroop task. Stroop color naming (Macleod, 1991; Spieler et al., 1996) and switching task (Mayr & Keele, 2000) are frequently used experimental paradigms in detecting the attention aspect in DAT. Similarly, these tasks are usually used in vaious theoretical framework to detect different notions related to attention. The Stroop task (Stroop, 1935), for an example, has been used as "golden standard" measures to investigate the selective attention for a long time (MacLeod, 1991, 1992; Melara & Algom, 2003; McGuinness, 2010). Meanwhile, it is often used as a test of executive function (Kramer, Reed, Mungas, Weiner, & Chui, 2002) and attentional control (Balota et al., 2010; Hutchison, Balota & Duchek, 2010), or even a test of inhibitory function (Bélanger, Belleville, & Gauthiera, 2010; also see Amieva et al., 2004).

As Balota and Faust (2001) noted, comparing to the conventional paper and pen

tests, computerized tests are developed basing upon advanced attentional theory, which is convenient for narrowing down the specific components of attention and detecting various components accurately by appropriate task. Moreover, variables in the computer-based tests are well designed and manipulated and accuracy performance and response times could be accurately recorded. It has been found that the computer-based version of Stroop task might be more sensitive than the card-reading version of this task in predicting the conversion of DAT (Perlstein et al., 1998; also see Balota et al., 2010).

It is critical to note that attention deficit is not always found in all attention tasks (see Baddeley et al., 2001; Perry & Hodges, 1999). For example, people with DAT performed poorly in tasks that require rules switching or inertia inhabitation but survived in tasks that involved little cognitive loading (Perry et al., 2000).

More recently, the Stroop switch paradigm has been shown to be sensitive for the early detection of AD (e.g., Hutchison et al., 2010). However, the commonly used standard stimuli in the Stroop tasks are simple words (e.g., red, green, blue and yellow) in four different colors and the corresponding Chinese words (紅，綠，藍，黃) might be not appropriate or easy enough for Chinese older adults who had practically no or very limited education. As such, it seemed necessary to modify the materials considering the lower level of education attainment of Chinese older adults.

Pilot studies showed that the even people without any education experience were competent in reading and writing the Arabic numerals which they had been using in their daily life activities. That is, the Arabic numbers might be proper and easy enough for Chinese older population who were either illiterates or had very limited education.

Switching task. Switching task paradigm has been developed for a long time (Jersild, 1927). Until recent years, however, with the growing research interests in attention, it has become popular as a measurement of components of executive function

such as shifting, inhibition and the working memory updating (Minear & Shah, 2008; Miyake et al., 2000). There are two types of paradigm of switching sequences, predictable switching and random switching. In predictable switching, the switching sequence is presented in a fixed, alternating order (e.g., alternating in every two trials as AABBAABB… Rogers & Monsell, 1995) and participants could predict the type of next trial during performing the task. In random switching paradigm, the sequence is randomized and participants are supposed to conduct the next trial based on the cues precede each trial. Previous studies have proposed that the cognitive demand in predictable switching is greater than in random switching (Milán et al., 2005; Monsell et al., 2003; but see Tornay & Milán, 2001).

Practically, this task has been used to tap the control process in set-shifting between two distinct trials (e.g., Duchek et al., 2009; Meiran, Chorev, & Sapir, 2000; Minear & Shah, 2008). The nature of this task allows detecting the switching ability with taking the non-switch block as baseline. Two types of measures have been proposed to quantify the performance of RTs and errors in switching task, namely, the switch cost and the mixing cost. The switch cost refers to the differences between switch and nonswitch trials within a mixed block (i.e., AABBAABB…), while the mixing cost is defined as the difference between the pure blocks of trials (e.g., AAAA…or BBBB…) and the mixed block of trials (AABBAABB…). Despite the ongoing debate about the essential of the cognitive processing underlying these two costs, researchers usually interpret the cost as follows.

Typically, the switch cost represents the ability of reconfiguration across trials by proper goal activation and rule activation (Rogers & Monsell, 1995; Meiran et al., 2000, for alternative explanation see Allport & Wylie, 2000), while the mixing cost reflects the ability to keep or maintain two types of tasks in working memory. Previous studies have

found a larger age-related difference on switch cost than mixing cost (Kray, Li, & Lindenberger, 2002) and dementia-related effect in switch cost (Sinai, Phillips, Chertkow & Kabani, 2010).

In conventional switching task (Minear & Shah, 2008), the stimuli are letter-number pairs (e.g., B 5) and the textual cues indicating the nature of the task are English words (e.g., "consonant", "vowel", "odd", "even"), which might be not appropriate for Chinese older adults who are not familiar with English Alphabets. The task used in the present thesis has been modified by replacing the letters with hand-drawing pictures of faces (i.e., face-number pairs), in which participants were required to judge whether the face is happy or sad in face trials and whether the number is odd or even in number trials. Also, the textual cues have been updated by picture cues which have been found to be easy to understand for older adults with limited education in pilot studies.

The pilot study preceding the experiments always confirmed that (a) each of the participants had no potential disability (e.g., vision disabilities) that might lead them to fail to recognize the numbers and pictures on the computer screen, (b) they could successfully differentiate the numerical and physical magnitude of single-digit Arabic numbers, and (c) they could recognize the pictures of hand-drawing faces and differentiate the happy faces from the sad faces without difficulties.

Working memory tasks. As has been discussed in Chapter Three, some researchers have proposed that the central executive component in working memory is similar to attentional control (Baddeley, 1986; Engle, 2002). The active inhibition processes of central executive abilities (Baddeley & Hitch, 1974; Baddeley, 2000) have been found to be impaired very early in the course of DAT (Albert et al., 2001; Baddeley et al., 2001; Collette et al., 1999b; Belleville et al., 2007; Huntley & Howard, 2010; Perry & Hodges, 1999). The present study would also examine the utility of two working memory tasks in

discriminating very mild DAT from normal aging among Chinese population. Specifically, the digit suppression task is used to tap the inhibition processes, in which participants had to reproduce a sequence of verbally presented digits while suppressing every second ones in the digit sequence. Counting span task is used to assess the ability of coordinate two concurrent activities which is one important subcomponents of working memory fractionated by Baddeley (1996). Particularly, in this task, one is needed to perform a counting task while remembering the counting results. More details about the above tasks would be addressed in the method section.

6.2 Objectives

Based on the findings of previous studies using similar tasks (Hutchison et al., 2010; Duchek et al., 2009; Tse Balota, Yap, Duchek, & McCabe, 2010), in general, it was predicted that age-related and DAT-related effect difference should be found in performance on the attention tasks and working memory capacity across groups. Specifically, larger RTs and higher error rates in attention tasks would be expected for very mild DAT patients compared to healthy older adults. Similar pattern should be found between healthy older adults and young adults. For working memory tasks, performance is predicted to be relatively poorer for very mild DAT group than for normal aging group, and in turn for young adults group. Lastly, the investigation on the relation of working memory capacity and attention performance is expected to show a link of lower working memory capacity and poorer performance on attention tasks (i.e., larger tau and greater intraindividual variability).

6.3 Methodology

6.3.1 Participants

A total of 88 older adults were recruited from an epidemiology survey on the prevalence of dementia in Hong Kong (Lam et al., 2008a, 2008b). All participants were community-dwelling older adults, about half (N = 40) being very mild DAT (CDR = 0.5) and half (N = 48) being normal aging (CDR = 0) according to the Clinical Dementia Rating (CDR) Scale (Morris, 1993; Morris et al., 1988) (see demographic details in Table 5).

Another batch of young adults (N=51) were also recruited as a comparison group. This gave a total of 139 participants in the present analyses. There were approximately equal number of males and females and their basic demographic background were tabulated (see Table 5). It should be noted that the sample sizes in different analyses might be slightly different across tasks because a small number of participants might not be able to finish all tasks in this study.

Participants with depression, untreated hypertension, stroke, or disorders that might be associated with cognitive impairment were excluded from the study first. Then, the inclusion and exclusion criteria for diagnosis of DAT were set according to the major criteria for the "possible Alzheimer's disease" of the National Institute of Neurological and Communications Disorders and Stroke–Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984).

The severity of dementia was categorized basing on the Clinical Dementia Rating (CDR) Scale (Morris, 1993; Morris et al., 1988). According to the scoring of this scale, CDR 0, 0.5, 1, 2, and 3 represents no dementia, very mild dementia, mild dementia, moderate dementia, and severe dementia, respectively. Specifically, as suggested by Morris, McKeel, and Storandt (1991; Morris et al., 2001), a CDR of 0.5 might represent the earliest symptomatic stage of DAT. The CDR has good inter-rater reliability, concurrent validity (e.g., autopsy, 93% diagnostic accuracy; Burke et al., 1998), and

other psychometric properties (Welsh, Butters, Hughes, Moh, & Heyman, 1991). Furthermore, the score has been found to be robust across cultures (Morris et al., 1995) and have been used with the Chinese population with good face validity (e.g., Lai et al., 2003).

Results showed that the normal aging group and the very mild DAT group ranged from 66 to 95 years old and had zero to 20 years of education, with the normal aging group being slightly younger (M = 73.33 years) and with more education (M = 7.12 years) than the very mild DAT group (M = 76.83 years old, M = 4.63 years of education); t (97) = 2.63, 2.59, p = .010, .011, respectively (see Table 5). In all subsequent analyses, sex, age, and years of education would be controlled either as covariates in the ANCOVA or as predictors in regression analyses.

Table 5

Background information of participants in Study One

	Gender			Age		Year of Education	
	Male	Female	total	*M* (range)	*SD*	*M* (range)	*SD*
Older adults							
Normal aging	26	22	48	73.33 (66 - 90)	5.70	7.13 (0 - 20)	4.56
Very mild DAT	18	22	40	76.83 (67 - 95)	6.74	4.63 (0 - 16)	4.47
Young adults	15	36	51	20.73 (19 - 27)	1.86	14.96 (14 - 19)	1.28

6.3.2 Procedure and Design

The data for this study came from a supplementary study to a much larger epidemiology survey on the prevalence of very mild dementia in Hong Kong (see Lam et al., 2008a, 2008b for details). For each participant, the individually administrated tasks were administered over two sessions. While clinical assessments (e.g., CDR) were

completed in Session 1, the cognitive tasks (e.g., Number Stroop switching task and Face-number switching task) used in the present study were administered in Session 2, with an interval of less than two weeks. The researchers in administrating the cognitive tasks in the second session were different from those in the first session, and thus were unaware of the CDR scores of the participants while they were administering the cognitive tasks. As such, the study was double-blinded, in the sense that both the participants and the researchers were kept blind about their dementia status till the data analyses. All assessments and experiments were conducted in a quiet setting either at the participants' home or at elderly activities centre near their home.

For each of the tasks, after building up rapport with the participants, clear instructions were first presented on the screen with examples of experimental stimuli being shown along with the demonstration. The examiner always verbally explained the instruction. All participants were asked to repeat the task instruction in their own words to ensure their full understanding before the practice trials. If a participant fails to understand the instruction, the examiner would repeat and explain the task and the instruction again, if necessarily, together with the practice trials to ensure the participants' full understanding of the task instruction before the actual test trials. After the test, the participants were asked to repeat the task instruction again so as to understand whether the participants still remembered what they were expected to do right after the test. This provided additional information, if necessary, for the interpretation of the participants' responses or failure to respond during the experiment.

More detailed information of the tasks used specifically for the present research is provided below. These tasks had been chosen or modified from earlier studies that measured attentional selection and switching (see e.g., Duchek et al., 2009; Tse et al., 2010) and had been piloted before the actual implementation for the present research.

In contrast to earlier Western studies, the present research had modified the tasks by replacing the English alphabets with pictures that are proper to Chinese older adults with minimal level of education.

6.3.2 Apparatus and Tasks

Face-number switching task, number Stroop switching task and counting span task were programmed using E-Prime software (Version 2.0, Schneider, Eschman, & Zuccolotto, 2002) and administrated on a HP laptop (Intel core (TM) I5) with a 30 by 23 cm screen size.

Face-number switching task. The tasks and design here followed and modified after the Letter-Number pair task as used in previous studies (Minear & Shah, 2008; Duchek et al., 2009). In those studies, the experimental materials included a set of displays of letter-number pairs (e.g., A 3). Depending on the cue shown, the participants were required to tell whether the letter was a vowel (or a consonant) or the number was odd (or even). Consider the fact that the less educated older Chinese participants in this research would not be able to recognize the letters and distinguish vowels from consonants, it was necessary to modify the task and replace the letter with happy and sad faces.

Specifically in each trial, a display of face-number pair (e.g., "☺ 3" or "☹ 3") was shown at the centre of the screen with cues at the top right and left corners to instruct the participants whether it was a face- or number trial. In the face trial, a picture of a blooming rose () (representing happy) and that of a wilted rose () (representing sad) were presented as cues at the top right- and left-corners of the screen respectively. For all three blocks, the picture cues were always presented with the face-number pairs simultaneously to reduce working memory demands (see Miner & Shah, 2008).

Participants had to judge whether the face in the Face-Number pair at the centre of

the screen was a happy or a sad face, and then they had to press the d (sad face) or k (happy face) key as quickly as possible in correspondence with the respective rose at the top corners. The pictures used in the face trials were 8 black and white hand-drawing pictures (half happy faces and half sad faces).

Similarly, in the Number-trials, the cues at the top right and left corners were a pair of shoes (representing even) and one shoe (representing odd) respectively. Participants had to judge whether the number in the face-number trial was odd or even by pressing the d (odd) and k (even) keys respectively.

The sequencing of the tasks was identical across all participants in the order "FFNNFFNN…" (F = face trial, N = number trial) starting with face trials, and switching after two consecutive face- (or number-) trials. Before the formal testing session, it was first confirmed that the participants were proficient in (i) recognizing the single-digit Arabic numbers and (ii) discriminating odd and even numbers. They had 10 practice trials with feedback before the 48 pure Face-trials (FFFF…) and 48 pure number-trials (NNNN…). Then they were given 10 practice trials before the block of 96 trials with switching (FFNNFFNN…).

Both switch cost and mixing cost in RTs and accuracy have been computed respectively to test the attentional performance in switching.

Number Stroop switching task. The numerical Stroop switching task was similar to typical Stroop switching tasks (Hutchison et al., 2010; Kaufmann et al., 2006), except that the stimuli are different. Due to the concerns mentioned earlier in this Chapter, in contrast to four color words being used in the more commonly used Stroop task studies, numbers (digits) were used in the present task instead.

In each of the trials, the stimulus consisted of a pair of single-digit Arabic numbers from 1 to 9 (except 5) was shown at the centre of the screen, with the numerical value

distance being 4 (difference in numeric value is four, e.g., "2 6", or "8 4") and the physical distance being Arial font size 55 vs. 73 (see Figure 3). This numerical value and physical size differences were chosen from pilot trials that supported the appropriateness their use with older adults.

At the beginning of this task, participants were told that they would be cued prior to each trial as to whether they should make response based on the numerical value (hereafter, N-trial) or the physical size (P-trial) of each pair of numbers. Specifically in the N-trials, participants had to compare the numerical values of the two Arabic numbers, whereas in the P-trial, they had to compare the physical sizes instead.

Participants were told that when the stimuli (2 Arabic digits) were presented simultaneously inside a red square at the centre of the screen, it would be an N-trial and they were required to select the numerically larger digit while ignoring their physical sizes. In contrast, when the pair of digits was put inside a red ellipse, the participants needed to chose the physically larger digit while ignoring their numerical value. Participants were instructed to indicate whether the left- or right-hand side number was numerically (in N-trials) or physically (in P-trials) larger as quickly as possible by pressing the d key (left-side) or the k key (right-side) correspondingly.

Both congruent and incongruent trials were involved. In the congruent trials, one of the pair of numbers (e.g., the left-hand side digit) was both numerically and physically larger than the other number (thus, the other digit is both numerically and physically smaller, see Figure 3). In contrast, in the incongruent trials, one of the two numbers (e.g., the left-hand side digit) was numerically larger but physically smaller than the other number (see Figure 4).

Figure 3. An Example of Congruent Trials.

Figure 4. An Example of Incongruent Trials.

The N- and P-trials with pairs of numbers inside square and ellipse respectively, were presented in an alternating order (NNPPNNPP…, see Rogers & Monsell, 1995), such that it would be the same N (or P) trials twice (non-switching) followed immediately with a switch to P (or N). The pattern of the trials was further nested with the congruence/incongruence conditions. Assume NC, NI, PC, NI stand for number-congruent, number-incongruent, physical size-congruent, and physical size-incongruent trials. A switching was said to occur when "NC, NC" was followed and switched PC; or similarly "NI, NI" was switched to PI; "PC, PC" was switched to NC; or when "PI, PI" was switched to NI.

The pair of number stimulus was shown at the centre of the screen. It would disappear immediately and show the next stimulus once the participants made a response by pressing either the d or k key. Participants were required to respond and press the corresponding keys as quickly and as accurately as possible.

The whole task consisted of a block of 20 practice trials (10 each of N-trials and P-trials) and a block of 240 test trials. A 60 seconds break was given after they finished the first half (120) of the trials. The sequence of trials was pseudo-randomized in the sense that the sequence was identical across participants but otherwise appeared to be

randomized to each participant. Thus, for example, whether the numerically (or physically) larger number was placed on the left- or right-side of the screen was randomized. Switching to P-trials (or N-trials) occurred at every third trials in the sequence (NNPPNN…).

An overall 100 switch trials were generated based on manipulation of the sequence of trials (25 for each of the four types of switch trials, namely, NC → PC (NC trial switched to PC trial), NI → PI, PC → NC, or PI → NI) and 120 nonswitch trials (30 for each of four types of pure trials: PI → PI, PI trial followed by PI trial), PC → PC, NI → NI, NC → NC.

The sequence in this research paradigm allowed us to compare participants' performance on switching and the immediately preceding non-switching trials. That is, the increase in RT and error rates on the switching trials as compared to the non-switching trials was taken as the cognitive cost in switching.

Counting Span task. This task has been adapted from the Counting Span task as used in a previous study (Engle, Tuholski, Laughlin, & Conway, 1999; Unsworth, Heitz, Schrock & Engle, 2005). In brief, in each set of tasks, participants had to count the number of targets in several displays shown in sequence (e.g., 3, 7, 6 targets in three displays in sequence). Then they had to recall these numbers (3, 7, 6 in this case).

More specifically, sets of displays were shown in a sequence. In each display, the stimuli were pictures consisting of randomly arranged dark blue circles (3 to 9 in number), dark blue squares (1 to 5), and light blue circles (1 to 5). Participants were instructed to count aloud the number of the dark blue circles one by one without pointing to the circles and repeat the total number to indicate the end of counting. For example, in a display with three targeted dark blue circles, participant was supposed to count aloud, "one, two, three, three". Once the participant repeated the count result

("three"), the experimenter would present the next display by pressing a key and the participant continued to count aloud for the new display immediately.

The number of target (dark blue circles) varied randomly but systematically in the sense that there was in a roughly ascending order from 3 to 9 with the numbers of distractors also increasing accordingly. As such, the task was conducted in an order of increasing difficulty. The number of displays within each set (i.e., number of digits to be recalled) varied from 2 to 6. There were 3 sets for each display size and thus, with overall 15 displays being presented. After each set of displays, a recall cue in Chinese ("please recall") was presented on the screen to instruct the participants to recall the numbers of dark blue circles in each of the previous displays and in the original order they had been presented. Thus, for example, in a set of 4 displays with 5, 3, 6, 8 targets in the displays in sequence, the participant had to recall the number sequence 5, 3, 6, 8.

The experimenter monitored the counting performance and recorded all of the participant's counting results by pressing the corresponding number keys. The number of displays in each set, and hence the number of digits to remember for the recall at end of each set, was taken as a proxy measure of digit-span. The digit count task was purposely made more difficult by asking the participants to count the targets in each display.

The order of the 18 sets was fixed and the displays within in each set were arranged in an ascending order of difficulty (i.e., from least to most difficult) with the number of targets and distractors in each display being increased accordingly. For each digit-span number (e.g., 5), three sets of displays were shown. The tasks were in an increasing difficulty arrangement for two reasons. Firstly, the pilot study showed that an ascending order of difficulty would provide sufficient successful experience at the beginning of the test to motivate and engage the participants. Secondly, participants would not get extra

benefit in their performance even if they were aware of the ascending difficulty in which a predictable number of items were presented.

There were several advantages in using of Counting Span tasks in this research as a measure of working memory capacity. Firstly, the stimuli used in this task were literacy-free and the operation processing needed was just counting. This would be simple enough for older adults especially for those with no or limited education. Secondly, the underlying structure of this task has been found to be identical to the reading span or the operation span tasks that are widely used to assess working memory span (Conway et al., 2005).

As a check for the minimal competence for the tasks, participants were confirmed before the experiment that they could successfully count from one to ten and recognize different colors and shape correctly.

Digit suppression test. The digit suppression test has been designed and used as a measure of verbal working memory (Beblo, Macek, Brinkers, Hartje, & Klaver, 2004). Participants would have to repeat digit sequence while suppressing or inhibiting other interfering information. It was a simple task and is easy to understand, which required at most 10 minutes to complete.

In each of the trials, a sequence of digits would be presented orally, with the examiner reading aloud these digits. The participants were requied to repeat every second digit in the sequence (e.g., if the examiner read aloud "2-7-8-3-5", the participant had to say "2-8-5"). For each set with the same digit-span (i.e., sequence of the same length), two trials with different number sequences would be presented.

The sequences of digits (digit-span) would be presented in an ascending order of difficulty (with increasingly more digits in the sequences). The first and shortest sequence consisted of 4 digits, in which 2 digits were expected to be repeated, whereas

the longest sequence had 14 digits, among which 7 digits should be repeated. The length of digit sequences ranged from 4 to 14 digits and the respective lengths to be repeated ranged from 2 to 7. If participants failed in both sequences of the same digit lengths, testing would end.

Overall three scores would be derived for further analyses. The longest sequence of digits that participants could successfully reach in the correct order would be recorded as the *trial span*. Whereas, the number of all successfully performed sequences with all digits being correctly recalled would be recorded as the *total trials*, and the total number of digits being successfully recalled would be marked as the *total digits*.

6.3.3 General Strategies in Statistical Analyses

Controlling variables. In all analyses, age, sex, and years of education were routinely included as control variables. For example, in the analyses of the effects of CDR (very mild DAT vs. normal aging) on response time (i.e., criterion variable) in regression analyses, CDR status was entered as a predictor with the effects of age, sex, and years of education controlled simultaneously. Analogously, in analyses of variance, age, sex, and years of education were routinely included as covariates in the analyses of other main effects (e.g., CDR).

Two-group comparison as the main analyses. As there were drastic differences in the characteristics between older adults and young adults, taking factors such as age, years of education as covariates might not be a fully satisfactory solution in the simultaneous comparison of the three groups (normal aging group, very mild DAT group, young adults). Generally the analyses would therefore concentrate on the comparison between the normal aging group and the very mild DAT group. This would constitute the main analyses of the conclusion. Then, if appropriate, further similar analyses would be conducted with the young adults being included.

Response time and accuracy. In all response time analyses, as discussed earlier and in line with the general practice (Schmiedek, Oberauer, Wilhelm, Süß, and Wittmann, 2007; Balota et al, 2010), trials with outliers in response time (3 SD from the respective means), extremely short response (faster than 200ms), and incorrect responses (e.g., wrong key being pressed accidentally) had been excluded. This eliminated about 4-5% of the correct responses in most cases (except for the mixed tasks).

Analyses of interactions in regression. For regression analyses involving interaction terms, following the procedures as recommended by Marsh, Hau, Wen, Nagengast and Morin (in press), with all variables being standardized first. Appropriate product terms representing the interactions were then formed and included as predictors in the regression analyses accordingly.

6.4 Results

6.4.1 Face-number Switching Task

a. Response time

The means and SDs of response time of three groups (normal aging, very mild DAT, young) are shown in Table 6. The effects of participant grouping (CDR status) on response time were examined with regression analyses. Response time was used as the dependent variable while the other relevant variables were entered as the predictors. The interaction term (CDR × Time) was also included in the regression so as to investigate how the effect of CDR on performance varied across time, and the regression analysis could be represented as the following equation:

$$\text{Response time} = \beta_0 + \beta_1\,(\text{CDR}) + \beta_2(\text{Sex}) + \beta_3\,(\text{Age}) + \beta_4\,(\text{Education}) + \beta_5\,(\text{Trial}) + \beta_6\,(\text{CDR} \times \text{Trial})\,(+ e)$$

or simplified as:

Response time = CDR + Sex + Age + Education + Trial + CDR × Trial.

The respective beta coefficients are shown in Tables 7, 8, and 9 for the pure face block, pure number block and mixed block, respectively. As discussed in the method section, the analyses were repeated for the 2 groups (aging, very mild DAT, Columns 2, 3) and the 3 groups (aging, very mild DAT, young adults, Columns 4, 5) separately. The results of two pure blocks (i.e., pure face trials and pure number trials) were very similar and are reported below.

In the analyses involving the normal aging group and very mild DAT group only (Tables 7, 8, 9; Column 2), participants with very mild DAT (b = .343, 277, for face and number trials respectively, both $p < .001$), older (b = .129, .175, both $p < .001$), with less education (b = -.119, -.175, both $p < .001$), or in the earlier trials (b = -.176, -.161, both $p < .001$) had relatively longer response time. The trial effect suggested a practice effect in that response time decreased along the trials.

To understand the significant interaction of CDR × Trial (b = -.095, -.071 for two pure trials respectively, both $p < .001$), further separate analyses was conducted for the two older adults group (normal aging vs. very mild DAT). A larger trial effect was observed for the very mild DAT group (b = -.281, -.245, both $p < .001$) relative to the normal aging group (b = -.088, -.098, both $p < .001$), suggesting that very mild DAT individuals improved more through practice than the normal aging group did relatively to their initial performance in the earlier trials.

To further understand whether there was any change in the practice effect across trials (along the testing), a non-linear (square) term of Trial was included in the regression in further analyses (see Columns 3, 5 in Tables 7, 8, 9). The results showed that beta values of the other variables were almost identical to those without this square term. The effect of this nonlinear term (Trial × Trial) was relative minor despite its

significant (b = .032, .071 for face and number trials; p = .007, p < .001 respectively). The positive coefficient suggested a diminishing return in that the practice effect decreased slightly and became smaller in the trials towards the end of the observation. The above analyses were repeated by including the young adults group as well. The results were almost identical to those reported above (see Columns 4, 5 in Tables 7, 8, 9).

For the mixed block, due to the potential difference in task difficulty between the switch and non-switch trials, the means and SDs were presented for each of these modes separately in Table 6. In the regression analyses (see Table 9), the following factors were also included, namely, Switch [switch (coded as 1) vs. non-switch (0)], Stimulus Type [face (0) vs. number (1) trials], and their interaction term, as three additional variables in the regression analyses. These three terms would enable us to explore (i) whether switch trials were more difficult than non-switch ones, (ii) whether face trials were more difficult than number ones, (iii) whether the difference in the difficulty between face and number trials changed with the switch status (switch vs. non-switch), (iv) the effects of other variables (e.g., very mild DAT vs. normal aging) after controlling for the above effects.

The examination of the beta values in regression weights showed that very mild DAT individuals had a longer response time than normal aging group (b = .085, p < .001) in mixed block (Table 9, Column 1), suggesting a smaller effect than those in the corresponding pure blocks (b = .343, .277, for face and number trials respectively, Tables 7 & 8). Actually the total R^2 [.158 in mixed block vs. .470, .493 in pure (non-switching) face and number trials respectively; Tables 7, 8, 9] and other beta weights in the mixed block were much smaller than those in the pure face and pure number blocks. Apparently, the power of the switch and non-switch trials in mixed block

to discriminate very mild DAT from normal aging was much weaker than those of the pure face and number trials. That is, the mixed block appeared to be a less effective task in discriminating very mild DAT.

The separate set of analyses with three participant groups (young, normal aging, very mild DAT) are shown in Tables 6, 7, and 8. The trends and conclusion from these analyses were similar to those with the two groups (normal aging vs. very mild DAT). The only possible difference was that with the three groups, the effect of age on response time was much larger (.245 vs. .129 in 3 and 2 groups respectively for pure face trials and .311 vs. 175 for pure number trials).

Table 6

Means and SDs of RT in face-number switching task

Grouping Characteristics	Response time (ms)		Accuracy	
	M	*SD*	*M*	*SD*
Pure Face Block				
Older adults				
Normal Aging (CDR = 0)	1397.19	367.46	.922	.086
Very Mild DAT (CDR = 0.5)	2682.46	1421.39	.842	.184
Young adults	603.50	68.43	.961	.084
Pure Number Block				
Older adults				
Normal Aging (CDR = 0)	1037.69	154.29	.976	.064
Very Mild DAT (CDR = 0.5)	1484.83	559.19	.921	.142
Young adults	654.61	82.59	.964	.034
Mixed Block: Nonswitch, Face trials				
Older adults				
Normal Aging (CDR = 0)	2607.27	1007.47	.810	.183
Very Mild DAT (CDR = 0.5)	2825.59	1342.02	.736	.204
Young adults	1014.31	325.96	.964	.082
Mixed Block: Nonswitch, Number trials				
Older adults				
Normal Aging (CDR = 0)	2543.56	933.46	.820	.182
Very Mild DAT (CDR = 0.5)	2802.20	1192.03	.793	.188
Young adults	1179.84	319.26	.954	.085
Mixed Block: Switch, Face trials				
Older adults				
Normal Aging (CDR = 0)	2818.43	1235.06	.789	.172
Very Mild DAT (CDR = 0.5)	3081.59	1318.73	.722	.181
Young adults	1522.65	344.14	.955	.080
Mixed Block: Switch, Number trials				
Older adults				
Normal Aging (CDR = 0)	2776.99	1175.43	.830	.162
Very Mild DAT (CDR = 0.5)	2963.12	1367.01	.792	.191
Young adults	1546.57	326.98	.952	.085

Table 7

Regression analyses (beta) on RT of pure face block

	beta weights			
	very mild DAT + normal aging		very mild DAT + normal aging + young	
Predictors	Linear Effects of Trial	Quadratic Effect of Trial	Linear Effects of Trial	Quadratic Effect of Trial
CDR	.343***	.343***	.364***	.364***
Gender (M =1, F=2)	-.022	-.023	.000	-.001
Age	.129***	.129***	.245***	.245***
Year of Education	-.119***	-.119***	-.127***	-.127***
Trial	-.176***	-.179***	-.124***	-.126***
CDR × Trial	-.095***	-.096***	-.118***	-.119***
Trial × Trial		.032**		.026**
Multiple R	.470***	.471***	.632***	.633***

*$p < .05$, **$p < .01$, ***$p < .001$.

Table 8

Regression analyses (beta) on RT of pure number block

	beta weights			
	very mild DAT + normal aging		very mild DAT + normal aging + young	
Predictors	Linear Effects of Trial	Quadratic Effect of Trial	Linear Effects of Trial	Quadratic Effect of Trial
CDR	.277***	.276***	.285***	.284***
Gender (M =1, F=2)	.143***	.144***	.120***	.120***
Age	.175***	.175***	.311***	.312***
Year of Edu	-.175***	-.174***	-.187***	-.186***
Trial	-.161***	-.168***	-.118***	-.121***
CDR × Trial	-.071***	-.068***	-.079***	-.078***
Trial × Trial		.071***		.039***
Multiple R	.493***	.501***	.663***	.665***

*$p < .05$, **$p < .01$, ***$p < .001$.

Table 9

Regression analyses (beta) on RT of mixed block

	beta weights			
	very mild DAT + normal aging		all 3 groups	
Predictors	Linear Effects of Trial	Quadratic Effect of Trial	Linear Effects of Trial	Quadratic Effect of Trial
CDR	.085***	.084***	.053***	.053***
Gender (M =1, F=2)	.035**	.035**	.003	.003
Age	-.051***	-.051***	.394***	.394***
Year of Education	.022	.022	-.028*	-.028*
Trial	-.115***	-.113***	-.094***	-.093***
CDR × Trial	-.035**	-.002	-.022**	-.022*
Switch (1) vs. non-switch (0)	.052***	.056***	.091***	.095***
Face (0) vs. Number (1) trials	-.035	-.035**	-.011	-.011
Switch × (Face/Number)	.007	.009	-.005	-.003
Trial× Trial		.032**		.025***
Multiple R	.158***	.164***	.469***	.470***

*$p < .05$, **$p < .01$, ***$p < .001$.

b. Response Accuracy

The accuracy of responses was analyzed by ANCOVA, with the response accuracy being the dependent variable, the dementia status (normal aging vs. very mild DAT) as between-subject independent variable, and sex, age, years of education, and trial as the covariates (see Columns 2, 3 in Table 10). The analyses were also repeated with the young adults group included (see Columns 4, 5 under "All 3 participant groups" in Table 10). Similar analyses were conducted respectively for two pure blocks and the mixed block (see Table 10).

In general, after controlling for the appropriate covariates, there were practically no differences in the response accuracy between males and females (η^2 = .003, .000, .000

for both pure and mixed block, Table 10). In contrast, accuracy decreased slightly with increasing age (η^2 = .009, .027, .009 for pure face trials, pure number trials and trials in mixed block, respectively) but increased slightly with years of education (η^2 = .011, .003, .012). Results also showed that response accuracy did not improve nor deteriorate along the trials (i.e., the serial numbers of trials increased) (η^2 = .000, .004, .001).

Though the very mild DAT participants were slightly less accurate, their difference from the normal aging group was not substantial (η^2 = .004, .003, .000 on the pure face, pure number and mixed trials; see Columns 2, 3 in Table 10). When young adults group was included, it was obvious that the young adults were more accurate in their responses than the other two older adults (η^2 = .014, .027, .004).

Table 10

ANCOVA of accuracy in face-number switching task

Covariates /Main Effects	Very mild DAT + normal aging		All 3 groups	
	F	η^2	*F*	η^2
		Pure Face Block		
Covariates				
Sex (M=1, F=2)	10.56**	.003	4.81*	.001
Age	38.01***	.009	46.83***	.007
Yr of Edu	47.32***	.011	50.42***	.008
Trial	.04	.000	.57	.000
Main Effect				
Group	18.76***	.004	46.54***	.014
		Pure Number Block		
Covariates				
Sex (M=1, F=2)	0.85	.000	.223	.000
Age	116.70***	.027	119.99***	.018
Yr of Edu	14.61***	.003	18.47***	.003
Trial	16.70***	.004	11.03**	.002
Main Effect				
Group	14.94***	.003	89.73***	.027
		Mixed Block		
Covariates				
Sex (M=1, F=2)	.301	.000	.24	.000
Age	73.76***	.009	99.77***	.007
Yr of Edu	104.69***	.012	136.78***	.010
Trial	9.46**	.001	11.33**	.001
Main Effect				
Group(Gp)	.31	.000	29.93***	.004
Switch (Swi)	.40	.000	.93	.000
Face(F)/Num(N)	24.70***	.003	20.17***	.001
Interaction				
Gp × Swi	.034	.000	.024	.000
Gp × N/F	3.88*	.000	10.93***	.002
Switch × N/F	2.21	.000	2.77	.000
Gp×Swi×N/F	.37	.000	.51	.000

Note. $*p < .05$, $**p < .01$, $***p < .001$.

c. Intraindividual Variability

In light of previous research (Duchek et al., 2009; Hultsch et al., 2000), it was predicted that intraindividual variability would be larger for the very mild DAT group (relative to normal aging group). This hypothesis was examined by computing the coefficient of variation (CoV) and the Residualized Intraindividual standard deviation (Residual-ISD) (Bielak et al., 2010a; Hultsch et al., 2008; see Chapter 5 for detailed discussion). It was posited that the very mild DAT individuals would show larger CoV and Residual-ISD than their normal aging counterparts.

Coefficient of variation (CoV). The means and standard deviation (SD) of the coefficient of variations across participant groups are shown in Table 11 (Columns 2, 3). The two older adults groups were compared by ANCOVA with sex, age and year of education being controlled. The very mild DAT individuals (M = 0.444, 0.304 for face and number trials, and 0.464, 0.544, 0.504, 0.458 for various modes of switch trials, see Table 11, Columns 2, 3) had a significantly larger CoV than the normal aging group (M = 0.321, 0.204 for face and number trials, 0.431, 0.468, 0.406, 0.424 for various modes of mixed trials); $F(1, 87) = 13.26, 25.16, 8.32$; $p < .001, p < .001, p = .004$; $\eta^2 = .127, .227, .023$ for face, number, mixed trials respectively (see Table 11, Columns 2, 3). A similar analysis including the young adults group showed almost identical results with the young adults having the smallest coefficient of variation (M = 0.188, 0.214 for pure face and number trials, 0.412, 0.422, 0.341, 0.317 for various modes of trials in mixed block); $F(2, 138) = 11.26, 18.09, 5.61$; $p < .001, p < .001, p = .004$; $\eta^2 = .089, .202, .018$ respectively (see Table 11, Columns 4, 5).

Residualized intraindividual standard deviation (Residual-ISD). In the first step, the residuals of the following regression were computed across trials, with potential influences eliminated.

Response time = CDR + Sex + Age + Edu + Trial + CDR × Trial (+ e)

The corresponding mean (hereafter called "residualized intraindividual mean", residual-IMn) and standard deviation (i.e., residual-ISD) over 48 trials for each individual in the pure face and number trials were computed respectively. For the 96 trials in the mixed block, the face/number, switch/nonswitch mode and their interaction terms were also included in the regression:

Response time = CDR + Sex + Age + Edu + Trial + CDR × Trial
+ switch(1)/nonswitch(0) + face(0)/number(1) + Swi/n-Swi × Face/Num

It was predicted that (see literature review, Chapter 5) that the residual-ISD of very mild DAT participants would be larger than those of normal aging participants. To achieve this, the mean and SD of residual-IMn and residual-ISD were computed and compared respectively for each participant group (see Table 11, last 4 columns). This was conducted through ANOVA with the residual-IMn and residual-ISD as the dependent variable and the participant groups (normal aging, very mild DAT, young) as the independent variable (see Table 12, last 8 columns).

For the ANOVA comparing the participant groups (normal aging vs. very mild DAT), there were no significant differences in the residual-IMn among the two or three groups, F (1, 86) = .632, .423, .000 for face, number and switch trials respectively; p = .429, .517, .998). The residuals were computed with the effects of sex, age, year of education, and trials being controlled, therefore, in the analyses of these residual-IMn (or residual-ISD), these covariates were not included again in the ANOVA (see Table 12, last 8 columns).

Most importantly, results showed that while the means of the residual-IMn were not significantly different across the two or three groups, there were significant differences in the means of residual-ISD across different participant groups for the face and number trials; F(1, 86) = 54.91, 52.02 for face and number trials, both $p < .001$; η^2 = .390, .377. These effects were similar in the three group analyses in which the young adults were

also included.

For the mixed block, there was no difference in residual-ISD between the normal aging group and very mild DAT group; F (1, 87) = 3.00, p = .087. This finding was in line with similar non-significant results on response time with the mixed block. In sum, the mixed block did not perform any better than the pure face or pure number blocks in discriminating the very mild DAT from normal aging.

It might be worth noting that an examination of the effect size (η^2) between the normal aging group and very mild DAT group suggested that the residual-ISD was more sensitive (η^2 = .390, .377, Table 12, third column from the right) than the coefficient of variation (η^2 = .127, .227; Table 12, column 3). Based on the present sample, the latter (residual-ISD) is a better choice in discriminating the very mild DAT from normal aging.

Table 11

Means and SDs of CoV and Residual-ISD in face-number switching task

	Intraindividual Variability Analyses					
	Coef of variation		Residual -IMn		Residual-ISD	
Grouping Characteristics	*M*	*SD*	M^1	*SD*	M^2	*SD*
Pure Face Block						
Older adults						
Normal Aging	0.321	0.091	0.003	0.291	0.358	0.139
Very Mild DAT	0.444	0.188	0.155	1.132	0.913	0.501
Young adults	0.188	0.040	0.021	0.064	0.101	0.022
Pure Number Block						
Older adults						
Normal Aging	0.204	0.051	-0.006	0.312	0.409	0.107
Very Mild DAT	0.304	0.116	0.124	1.032	0.849	0.408
Young adults	0.214	0.045	0.033	0.181	0.280	0.062
Mixed Block: non-Switch Face Trials						
Older adults						
Normal Aging	0.431	0.142				
Very Mild DAT	0.464	0.154				
Young adults	0.412	0.133				
Mixed Block: non-Switch Num Trials			**Mixed Block: all trials (2 groups)**			
Older adults						
Normal Aging	0.468	0.150	-0.009	0.568	0.674	0.281
Very Mild DAT	0.544	0.228	-0.009	0.705	0.785	0.318
Young adults	0.422	0.100				
Mixed Block: Switch Face Trials			**Mixed Block: all trials (3 groups)**			
Older adults						
Normal Aging	0.406	0.131	0.011	0.649	0.753	0.311
Very Mild DAT	0.504	0.197	-0.020	0.796	0.873	0.352
Young adults	0.341	0.073	-0.020	0.182	0.322	0.081
Mixed Block: Switch Number Trials						
Older adults						
Normal Aging	0.424	0.152				
Very Mild DAT	0.458	0.186				
Young adults	0.317	0.071				

Note. [1, 2] The means (residual-IMn) and standard deviation (residual-ISD) of the residuals (from regressions) over all trials in the pure face block (similarly for pure number, and other kinds of blocks) for each individual participant were first computed. The means and SD of these residual-IMn and residual-ISD were further calculated for the participants within each group.

Table 12

ANCOVA of CoV and residual-ISD in face-number switching task

	Intraindividual Variability Analyses											
	Coefficient of Variation				Residual -IMn				Residual-ISD			
	Very Mild DAT + Normal Aging		All 3 Groups		Very Mild DAT +Normal Aging		All 3 Groups		Very Mild DAT +Normal Aging		All 3 Groups	
Covariates /Main Effects	*F*	η^2	*F*	η^2	*F*	η^2	*F*	η^2	*F*	η^2	*F*	η^2
Face Block												
Covariates												
Sex	0.02	.000	0.01	.000								
Age	2.76	.026	4.09*	.016								
Yr of Edu	1.63	.016	2.44	.010								
Main Effect												
Between gps	13.26***	.127	11.26***	.089	.632	.007	0.743	.011	54.91***	.390	95.84***	.585
Number Block												
Covariates												
Sex	.022	.000	0.03	.000								
Age	.072	.001	0.14	.001								
Yr of Edu	.034	.000	0.11	.001								
Main Effect												

Between gps	25.16***	.23	18.09***	.202	.423	.005	0.544	.001	52.02***	.377	72.63***	.516
					Mixed Block							
Covariates												
Sex	1.66	.005	.334	.001								
Age	.002	.000	.001	.000								
Yr of Edu	.066	.000	.313	.001								
Main Effect												
Group[1] (Gp)	8.32**	.023	5.61**	.018	.000	.000	3.00	.034	3.00	.034	55.60***	.450
Switch (Swi)	2.58	.007	15.14***	.024								
Face(F)/Num(N)	1.56	.004	1.02	0.002								
Interaction												
Gp × Swi	.097	.000	2.63	.008								
Gp × F/N	.065	.000	.73	.002								
Swi ×F/N	4.09*	.011	5.78*	.009								
Gp×Swi×F/N	2.19	.006	1.66	.005								

Note. [1]Group Effect:
2 groups: Very mild DAT group vs normal aging group;
3 groups: very mild DAT group, normal aging group, young adults.
Sex: M=1, F=2.
*$p < .05$, **$p < .01$, ***$p < .001$.

d. Mixing Cost

In the face-number switching task, both pure blocks (face trials and number trials) and mixed block were included. Particularly, in the mixed block, the switching sequence is presented in an alternating manner AABBAABB… (Rogers & Monsell, 1995). This allowed us to examine the mixing cost (nonswitch trials in the mixed block vs. pure trials) and switch cost (switch vs. nonswitch trials within the mixed block) in response time and accuracy (e.g., Duchek et al., 2009; Meiran et al., 2000). This section concentrates on the mixing cost, while switch cost will be analyzed in the next section.

Response time. Table 13 shows the means and SDs of response time and accuracy by switch and mixing conditions. Mixing cost was analyzed in the following regression analysis with a focus on the effect of the Mixing condition (mixing (1)/pure (0)]:

Response time = CDR + Sex + Age + Yr of Edu + Trial
+ Stimulus type [face(0)/number(1)] + Mixing condition [mixing (1)/pure(0)]
+ CDR × Trial + Mix × Stimulus + Mix × CDR + Mix × Trial
+ Trial × Trial

Similar to the preceding section, the effects of CDR, sex, age, year of education, trial, and stimulus type [face(0)/number(1)] had been controlled. Furthermore, interaction terms were included so as to control and address issues including: (i) whether the time effect (i.e., practice effect or fatigue effect across trials) changed with CDR status, (ii) whether the mixing cost changed with stimulus type, CDR status, or time (Trial), and (iii) whether the practice effect diminished along the testing (non-linear practice effect).

The results of the analyses involving the very mild DAT group and normal aging group are shown in Table 13. In line with the earlier findings, the very mild DAT participants (b = .175, p < .001), females (b = .026, p = .002), older adults (b = .048, p

< .001), and those with less education (b = -.050, p < .001) tended to have a longer response time. The response time in face trials were slightly longer than those with number trials (b = -.084, p < .001). There was a substantial mixing cost (b = .621, p < .001), suggesting reaction times increased greatly in mixed trials relative to pure trials.

Two interaction effects were perhaps worth further examination, namely, b (CDR × Trial) = -.156, b (Mix × Trial) = .124 (see Table 14). For the first interaction, further separate analyses for the normal aging group and very mild DAT group showed that the practice effect (Trial) was larger for the very mild DAT individuals (b = -.410, p < .001) than the normal aging group (b = -.176, p < .001). For the second interaction, similar separate analyses for the mixed and pure blocks showed that the positive practice effect was stronger with the pure trials (b = -.633, p < .001) than with the mixed trials (b = -.314, p < .001). This suggested that in the mixing trials with both face and number stimuli, participants would not be able to respond much faster with more practice, while in the pure (non-switch) trials, participants did make greater progress and respond faster across the trials.

The regression involving three participant groups (very mild DAT, normal aging, young) were almost identical (see Table 14, Column 3) with the possible exception that the effect due to age increased substantially (b = .048, .305, for the 2- and 3-group analyses, both p < .001) due to the inclusion of the young adults group.

Accuracy. The mixing cost in participants' accuracy was analyzed using ANCOVA with the respective sex, age, year of education and time effect (i.e., trial) being controlled as covariates (see mean, SD in Table 13, ANCOVA in Table 15).

For the analyses involving the very mild DAT group and normal aging group only, the effects (beta weights) of the controlled covariates and a careful examination

of the subgroup respective means showed that the older (η^2 = .010), more educated participants (η^2 = .008), and very mild DAT group (η^2 = .001) made slightly more mistakes. It was also noted that the participants made slightly more mistakes in the face trials than in the number trials (η^2 = .004). There was also a small mixing cost in that accuracy was a bit lower for mixing than pure (non-mixing) trials (η^2 = .011). The small interactions suggested that the above effects did not change with CDR status or stimulus type (face/number). The results of the three group (very mild DAT, normal aging, young) analyses were very similar. In general, results in all analyses suggested that the mixing cost on accuracy was small, despite some of them might be statistically significant.

Table 13

Means and SDs of RT and accuracy in pure and mixed blocks

Mixing/Switching Condition	Response time (ms)		Accuracy	
	M	*SD*	*M*	*SD*
Face Trials				
Pure block				
Pure Trials	1365.34	1240.65	.915	.279
Mixed block				
nonswitch Trials	2022.53	1619.76	.846	.361
switch Trials	2344.05	1623.49	.830	.376
Number Trials				
Pure block				
Pure Trials	996.24	498.96	.958	.201
Mixed block				
nonswitch Trials	2053.27	1568.59	.862	.345
switch Trials	2319/29	1599.08	.864	.342

Table 14

Regression analyses (beta) on RT in mixing cost in face-number switching task

	Beta weights	
Predictors	Very Mild DAT + normal aging	All 3 groups
CDR	.175***	.183***
Gender (M =1, F=2)	.026**	.017**
Age	.048***	.305***
Yr of Edu	-.050***	-.071***
Trial	-.255***	-.196***
Face(0)/Number(1)	-.084***	-.043***
Mixing cost[1]	-.621***	-.522***
CDR×Trial	-.156***	-.210***
Mix × Face/Num	-.026*	-.030***
Mix × CDR	-.039**	-.165***
Mix ×Trial	.124*	.115**
Trial × Trial	.079***	.063***
Multiple R	.513***	.606***

Note. [1] Mixing cost: mixing trial=0, pure trials=1.
*p < .05, **p < .01, ***p < .001.

Table 15

ANCOVA of accuracy in mixing cost in face-number switching task

Covariates /Main Effects	Very Mild DAT + Normal Aging		All 3 Groups	
	F	η^2	*F*	η^2
Covariates				
Sex (M=1, F=2)	3.55	.000	.46	.000
Age	134.21***	.010	33.03***	.003
Yr of Edu	109.99***	.008	67.72***	.042
Trial	1.05	.000	.25	.000
Main Effect				
Grouping	13.64***	.001	83.67***	.052
Mixing cost[1]	143.80***	.011	136.81***	.084
Face(0)/Num(1)	53.97***	.004	64.93***	.040
Interaction				
Mixing × Face/Num	3.97*	.000	5.20*	.003
Mixing × CDR	1.67	.000	31.98***	.020
Face/Num × CDR	8.65**	.001	33.77***	.020
Mix×Face/Num×CDR	.79	.000	.09	.000

Note. [1]Mixing cost: pure (0) vs. mixed (1).
*$p < .05$, **$p < .01$, ***$p < .001$.

e. Switch Cost

The analyses for the switch cost were very similar to that with the mixing cost. As noted in the earlier section, the interest would be on the cost on trials that require one to switch between different tasks (e.g., when a face trial followed a number trial or vice versa). Specifically, the focus was on the comparison between non-switch trials (e.g., a face trial following a face trial, coded as 0) versus switch trials (e.g., a face trial following a number trial, coded as 1). Similarly, for number trials, it would be the comparison between a number trial that followed a number trial (non-switch trial) against a number trial that followed a face trial (switch trial).

Response time. Table 13 showed the means and SDs of response time and accuracy by switch and mixing conditions. Switch cost was analyzed in the following regression analysis with a focus on the effect of the switch condition (switch (1)/non-switch (0)]:

Response time = CDR + Sex + Age + Yr of Edu + Trial
+ Stimulus type [face(0)/number(1)] + Switch condition [switch (1)/non-switch(0)] + CDR × Trial + Switch × Stimulus Type + Switch × CDR + Switch × Trial + Trial × Trial

As before, the effects due to CDR, sex, age, year of education, trial, and stimulus type [face(0)/number(1)] had been controlled. Furthermore, interaction terms were included to control and address issues including: (i) whether the practice effect across time (i.e., Trial) changed with CDR status, (ii) whether the switch cost changed with stimulus type, CDR status, or practicing (Trial), and (iii) whether the practice effect diminished along the testing (non-linear practice effect).

The results of the analyses involving the very mild DAT group and normal aging group are shown in Table 16. In congruent with the earlier findings, the very mild DAT group (vs. normal aging group, $b = .084$, $p < .001$) and females (vs. males, $b = .035$, $p = .005$) tended to have slightly longer response times. Interestingly, younger

participants also tended to be slightly slower (b = -.051, p < .001).

The switch cost (b = .053, p < .001), though significant, was relatively much smaller than the mixing cost (see last section on mixing cost, b = .621, p < .001) with participants spending slightly longer response times when switch occurred (vs. non-switch trials). That is, for face trials following number trials (vs. following face trials) and number trials following face trials (vs. following number trials), the response time was a bit longer.

The interactions between switch (from face to number, or from number to face) and other factors were all nonsignificant. This suggested that the switch cost did not vary with other major factors in the study. Similar to earlier analyses, there was a small positive Trial ×Trial interaction (b = .041, p < .001) suggesting the practice effect would decrease with increasing trials, or the practice effect had a diminishing return with the increase in practice.

The regression involving three participant groups (very mild DAT, normal aging, young) were almost identical (see Table 16, Column 3) with possibly the only exception that the effect due to age increased substantially (b changed from -.051 to .394) because of the much smaller age in the young adults group. This effect showed that the young adults had a much shorter response time for these switch trials.

Accuracy. The switch cost in participants' accuracy was analyzed using ANCOVA with the respective sex, age, year of education and trial being controlled as covariates (see means, SDs in Table 15, ANCOVA in Table 17). For the analyses involving the very mild DAT group and normal aging group only, the effects (beta weights) of the controlled covariates and a careful examination of the subgroup respective means showed that older (η^2 = .009) and less educated participants (η^2 = .012) made slightly more mistakes (lower accuracy). It was also noted that the

participants made slightly more mistakes in the face trials than in the number trials (η^2 = .003).

Importantly the switch cost for accuracy was non-significant (η^2 = .000) and in general most of the effects on accuracy were generally tiny even when they were significant. The results of the three groups (very mild DAT, normal aging, young) analyses were very similar. Thus, in conclusion, in general switch cost effects and their interaction on response accuracy were small despite some of them might be significant.

Table 16

Regression analyses (beta) on RT in face-number switching task

	Beta weights	
Predictors	Very Mild DAT + Normal Aging	All 3 Groups
CDR	.084***	.053***
Gender (M =1, F=2)	.035**	.003
Age	-.051***	.394***
Yr of Edu	.021	-.028*
Trial	-.137***	-.112***
Face(0)/Number(1)	-.031*	-.009
Switch cost[1]	.053***	.091***
CDR×Trial	.010	-.010
Switch×Face/Num	.005	-.006
Switch×CDR	.001	-.019*
Switch×Trial	.005	.006
Trial × Trial	.041***	.034***
Multiple R	.157***	.469***

Note. [1] Switch cost: nonswitch trial = 0, switch trials=1.
*p < .05, **p < .01, ***p < .001.

Table 17

ANCOVA of accuracy in switch cost in face-number switching task

Covariates /Main Effects	Beta weights: Very Mild DAT + Normal Aging F	η^2	Beta weights: All 3 groups F	η^2
Covariates				
Sex (M=1, F=2)	.30	.000	2.75	.000
Age	73.74***	.009	108.73***	.008
Yr of Edu	104.75***	.012	97.26***	.007
Trial	3.34	.001	4.10*	.000
Main Effect				
Participant gp	.32	.000	6.16*	.000
Switch cost	.49	.000	1.00	.000
Face(0)/Number(1)	25.46***	.003	29.40***	.002
Interaction				
Switch × Face/Num	1.93	.000	1.74	.000
Switch × CDR	.04	.000	.02	.000
Face/Num × CDR	3.90*	.000	16.03***	.001
Switch×Face/Num×CDR	.37	.000	.06	.000

Note. $*p < .05$, $**p < .01$, $***p < .001$.

f. Response Time Distribution Analyses

In line with early research that showed a positively skewed distribution of response time, response time data in the present study was fitted to the ex-Gaussian Distribution (e.g, as suggested by Balota et al., 2008). The raw response time of individual trial was used in the ex-Gaussian distribution analyses (see details in the literature review). Three parameters (mu, sigma, and tau) obtained for each participant would be compared across groups after controlling for their age, sex and years of education (e.g., using ANCOVA).

In the ex-Gaussian distribution analyses, the widely used and publicly available software QMPE (version 2.18, Cousineau et al., 2004; Heathcote et al., 2002) was

used. An error (exit) code was produced for each participant indicating possible problems (e.g., less trustworthy standard error and correlation estimates). In general, as recommended in the manual and adopted by some researchers (Brown, S., Cousinau, D., & Heathcote, 2004), runs with error codes less than 128 would probably be useful. However, anomalies with some trials with error codes less than 128 were noticed. Thus, a more conservative approach was adopted by including runs that ended with full convergence only (error code = 1). This would result in 85% and 88% of trials being retained for the face and number trials (each participant would contribute 48 trials). The analyses with error codes less than 128 were also repeated with the results being practically identical.

As the face and number trials might invoke different response time, in order to get more accurate estimate, response time data for each pure block were fitted separately to the ex-Gaussian distribution. For the switch trials in the mixed block, due to the distinct nature of task, the performance in each combination of stimulus type (face/number) and switch condition (switch/non-switch) might be not the same. A more proper procedure, therefore, would be separate analyses for each of the Stimulus Type × Switch Condition combination. However, as there were only as few as 24 trials for each combination, the analyses for each condition led to unstable ex-Gaussian parameters. Based on the above concerns, the analyses on the pure face and number trials would be the main focus, while those switch and non-switch trials in the mixed block would be used for reference only.

In Table 18, the means and SDs of the estimated mu, sigma and tau for three groups (normal aging, very mild DAT, young) and stimulus types (face, number, switching) are shown. The participant group effects for each different stimulus types were examined with ANCOVA using sex, age, and years of education as the covariate

(see results in Tables 19, 20).

The results were clear and consistent, (i) for both pure face and number trials, the effects of sex, age, and year of education on mu, sigma, and tau were either non-significant or small ($\eta^2 < .05$), (ii) there was little difference among the participant groups in their mu and sigma values (see Table 19, η^2 = .060, .068, .052, .050 for mu in face and number trials; η^2 = .013, .052, .018, .053 for sigma); (iii) in contrast, the young adults had substantially smaller tau (mean = 102.34, 131.21, SD = 40.07, 38.66 for face and number trials respectively, see Table 18) than those of the normal aging group (mean = 412.82, 191.02, SD = 189.73, 67.35), which in turn were smaller than those of the very mild DAT group (mean = 1002.70, 361.42, SD = 681.02, 156.97), and (iv) the effects and differences with the much fewer switch/non-switch trials (24 trials only) were all tiny and often unstable and unsystematic.

Most importantly for the whole analyses was that the differences in the tau values between the normal aging group and very mild DAT group (as well as against the young adults) in pure face and number trials (η^2 = .207, .169, .273, .226) were very large relative to all other effects being examined in this study. This further supported the use of tau as an indicator in differentiating very mild DAT from normal aging.

Table 18

Means and SDs of ex-Gaussian parameters in face-number switching task

	mu		sigma		tau	
Condition	*M*	*SD*	*M*	*SD*	*M*	*SD*
Pure Face Block						
Normal Aging	981.87	324.25	123.34	119.54	412.82	189.73
Very mild DAT	1510.08	819.45	250.94	343.80	1002.70	681.02
Young	496.74	61.10	48.63	20.23	102.34	40.07
Pure Number Block						
Normal Aging	846.35	142.59	74.70	36.34	191.02	67.35
Very mild DAT	1082.19	442.14	110.19	104.47	361.42	156.97
Young	516.92	53.38	48.11	26.78	131.21	38.66
Mixed Block: Non-Switch, Face Trials						
Normal Aging	1585.00	705.52	413.71	370.83	1052.21	546.21
Very mild DAT	1630.18	894.99	365.08	347.74	1059.93	524.76
Young	622.21	229.67	76.28	47.39	390.24	192.04
Mixed Block: Non-Switch, Number Trials						
Normal Aging	1529.82	545.30	368.55	341.66	1215.66	605.39
Very mild DAT	1935.13	1129.41	562.63	714.23	1479.61	631.83
Young	714.60	257.98	153.20	128.13	433.69	212.81
Mixed Block: Switch, Face Trials						
Normal Aging	1753.76	752.56	485.10	389.46	1014.83	604.82
Very mild DAT	1966.97	1130.39	594.84	618.42	1361.05	653.39
Young	1069.08	299.53	210.83	158.14	478.71	160.36
Mixed Block: Switch, Number Trials						
Normal Aging	1433.24	982.75	557.17	478.94	834.23	522.20
Very mild DAT	1180.18	1043.76	368.86	375.83	1151.15	797.57
Young	1845.09	322.81	216.90	196.66	446.95	212.46

Table 19

ANCOVA of ex-Gaussian parameters in pure face and number blocks

	Mu		Sigma		Tau	
	F	η^2	*F*	η^2	*F*	η^2
Pure Face Block (2 groups)						
Covariate						
Sex	.17	.002	.68	.008	.18	.002
Age	2.22	.024	1.86	.024	.80	.008
Yr of Ed	6.28*	.069	5.09*	.064	.02	.000
Grouping Effect[1]	5.42*	.060	.99	.013	19.73***	.207
Pure Face Block (3 groups)						
Covariate						
Sex	.29	.001	.74	.005	.19	.001
Age	3.96*	.018	3.44	.024	1.16	.005
Yr of Ed	10.40**	.046	8.01**	.055	.02	.000
Grouping Effect[1]	7.63**	.068	3.80*	.052	18.65***	.169
Pure Number Block (2 groups)						
Covariate						
Sex	4.44*	.044	2.28	.026	.055	.000
Age	4.39*	.043	3.44	.040	1.71	.014
Yr of Ed	4.59*	.045	1.77	.020	.480	.004
Grouping Effect[1]	5.34*	.052	1.59	.018	32.45***	.027
Pure Number Block (3 groups)						
Covariate						
Sex	5.32*	.021	3.70	.025	.140	.001
Age	7.01**	.028	6.03*	.040	2.58	.011
Yr of Ed	7.09**	.028	2.25	.015	.586	.002
Grouping Effect[1]	6.24**	.050	3.99*	.053	26.66***	.226

Note. [1]Grouping Effect:
2 groups: Very mild DAT group vs normal aging group;
3 groups: very mild DAT group, normal aging group, young adults.
*$p < .05$, **$p < .01$, ***$p < .001$.

Table 20

ANCOVA of ex-Gaussian parameters in mixed block

	Mu		Sigma		Tau	
	F	η^2	*F*	η^2	*F*	η^2
Non-Switch Face Trials (2 groups)						
Covariate						
Sex	.30	.006	1.36	.025	1.03	.019
Age	.39	.007	.21	.004	.04	.001
Yr of Ed	.47	.009	.01	.004	.51	.009
Grouping Effect[1]	.01	.000	.30	.006	.00	.000
Non-Switch Face Trials (3 groups)						
Covariate						
Sex	.34	.002	1.25	.011	.73	.006
Age	.77	.006	.26	.002	.08	.001
Yr of Ed	.95	.007	.01	.000	.71	.005
Grouping Effect[1]	.18	.003	1.54	.028	.67	.010
Non-Switching Number Trials (2 groups)						
Covariate						
Sex	.86	.016	1.41	.027	.30	.006
Age	.00	.000	.00	.000	.00	.000
Yr of Ed	.91	.017	.44	.008	.96	.018
Grouping Effect[1]	2.13	.039	1.21	.023	1.53	.029
Non-Switching Number Trials (3 groups)						
Covariate						
Sex	.78	.007	1.13	.013	.10	.001
Age	.01	.000	.01	.000	.00	.000
Yr of Ed	1.14	.010	.66	.007	1.35	.010
Grouping Effect[1]	1.63	.027	.89	.020	1.38	.021
Switch Face Trials (2 groups)						
Covariate						
Sex	.04	.001	1.22	.021	.08	.001
Age	1.62	.029	2.79	.048	.02	.000
Yr of Ed	.14	.003	.18	.003	.07	.001
Grouping Effect[1]	1.37	.025	.83	.014	3.64	.063
Switch Face Trials (3 groups)						
Covariate						
Sex	.08	.001	1.26	.012	.01	.000
Age	2.51	.023	4.16*	.039	.04	.000
Yr of Ed	.24	.002	.30	.003	.07	.001
Grouping Effect[1]	3.20*	.058	3.16*	.060	2.85	.044
Switch Number Trials (2 groups)						
Covariate						

Sex	.60	.011	1.05	.018	.07	.001
Age	.09	.002	.01	.000	1.00	.017
Yr of Ed	.06	.001	.73	.012	.00	.000
Grouping Effect[1]	.00	.000	2.55	.043	2.65	.045
Switch Number Trials (3 groups)						
Covariate						
Sex	.48	.004	.35	.003	.01	.000
Age	.07	.001	.06	.001	1.53	.012
Yr of Ed	.07	.013	1.80	.016	.01	.000
Grouping Effect[1]	.73	.013	2.56	.046	2.95	.047

Note. [1]Grouping Effect:
2 groups: Very mild DAT group vs normal aging group;
3 groups: very mild DAT group, normal aging group, young adults.
*$p < .05$, **$p < .01$, ***$p < .001$.

6.4.2 Number Stroop Switching Task

a. Response Time and Accuracy

In this task, as noted in the method section, there were congruent trials (coded as 1 in analyses) and incongruent trials (coded as 0). Specifically, one of the pair of numbers (e.g., the left-hand side digit) was both numerically and physically larger than the other number (thus, the other digit is both numerically and physically smaller). In contrast, in the incongruent trials, one of the two numbers (e.g., the left-hand side digit) was numerically larger but physically smaller than the other number (see details in the method section).

Making the analyses a bit more complicated was that there were two types of switch. In the first type, trials were differentiated into those that Switch in Stimulus Type (coded as 1) and non-Switch in Stimulus Type (0). In the former, the trial immediately preceding was different in Stimulus type to the current trial. As such, for example, a N-trial emphasizing numerical value changed to a P-trial that emphasized physical size difference (see details in method section), or vice versa. A non-Switch type was one that remained a P-trial (or N-trials) in the preceding and the current trials.

In the second type of switching, trials were differentiated into those that Switch in Congruence (coded as 1) and non-Switch in Congruence (0). In the former, there was a change from the preceding congruent (or incongruent) trial to the current incongruent (or congruent) trial.

Response time. Means and SDs of participants' response time and accuracy are tabulated by the above types in Table 21. Similarly, a regression was conducted with the variables (age, gender, year of education) controlled, main effects due to design (Stimulus type, Congruence, Switch in Congruence, Switch in Stimulus type), and various potential interactions between the above main effects used as predictors, and the response time as the criterion variable (see Table 22).

There were obvious effects on the stimuli being used, with longer response times for judgments on numerical value (vs. physical size) (b = .055, p < .001), incongruent (vs. congruent) trials (b = -.150, p < .001), and when there was a switch in Stimulus Type (vs. non-switch) (b = .107, p < .001).

Very mild DAT individuals (vs. normal aging group), older participants, and interestingly those with more years of education responded slower. There was also a practice effect (b = -.127, p < .001) with response time decreased with increasing trials. The results were similar with the analyses involving three participant groups (very mild DAT individuals, normal aging adults, young adults), except the effect due to age increased substantially (b = .578, p < .001) in the three group analysis.

Response accuracy. The means and SDs of response accuracy are shown in Table 21. ANCOVA analyses were conducted with sex, age, year of education and trial being the covariates and accuracy being the dependent variable (see Table 23).

Accuracy increased with decreasing age, increasing years of education, and increasing trial numbers (η^2 = .003, .014, .002 respectively), though the effects were

not great. The accuracy of numerical value (vs. physical size) and incongruent (vs. congruent) trials was slightly lower (η^2 = .009, .070 respectively), though again the differences were also small. There was no difference in the accuracy between very mild DAT individuals and normal aging adults after controlling for various background variables (η^2 = .000).

b. Intraindividual Variability Analyses

Similar to the earlier analyses, intraindividual variability analyses were also conducted on the response time of the Stroop task. Though there were totally 240 trials in the Stroop task, as mentioned above there were different congruent and switching conditions, leaving only 24 trials for each unique combination of mode only. This rendered the distribution analyses quite difficult and gave rise to unstable estimates. Nevertheless, basic analyses were conducted on their coefficient of variations and residual-ISD (and mean) (see Tables 24, 25).

As can be seen from the results in Table 24, 25, in general, there was no significant difference in the coefficient of variation, nor in the residual-ISD between the various participant groups. This again supported that any intraindividual analyses had to be based on more trials than had been used in these analyses.

c. Ex-Gaussian distribution Analyses

To understand the ex-Gaussian distribution of participants' response time, their raw response time was fitted with the QMPE program (version 2.18, Cousineau et al., 2004; Heathcote et al., 2002). As before the present study used conservative solutions, namely, the runs that terminated with the fully converged solutions (error/exit code=1), which constituted 87.5% of all data. A separate analysis using error/exit code < 128 generated identical patterns of results.

Similar to the problem encountered in intraindividual variability analyses above,

there were not sufficient observations (only 24 trials for individual conditions) for the analyses, with all effects of mu, sigma, and tau being either non-significant or tiny (see Tables 26 & 27).

Table 21

Means and SDs of RT, accuracy in number Stroop switching task

Switch from Congruence Stimulus	Switch from P/N	Congruence/ Incongruence	Response time (ms)		Accuracy	
			M	*SD*	*M*	*SD*
P-Trials						
No	No	No	1461.93	1013.73	.861	.346
No	Yes	No	1915.65	1082.90	.844	.362
No	Yes	Yes	1942.75	1072.59	.839	.368
Yes	No	No	1412.35	935.77	.939	.238
Yes	No	Yes	1601.62	1039.47	.947	.225
N-Trials						
No	No	No	1729.58	1102.83	.783	.412
No	Yes	No	1844.06	989.37	.747	.435
No	Yes	Yes	1955.38	1108.93	.685	.465
Yes	No	No	1523.04	968.78	.937	.242
Yes	No	Yes	1646.12	931.33	.914	.280

Table 22

Regression analyses (beta) on RT in number Stroop switching task

	Beta weights	
Predictors	Very Mild DAT +Normal Aging	All 3 Groups
CDR	.040***	.025***
Gender (M =1, F=2)	.009	.003
Age	.034***	.578***
Yr of Edu	.078***	.095***
Trial	-.127***	-.097***
Stimulus type [Size(0)/Value(1)]	.055***	.046***
Congruent(1)/Incongruent (0)	-.150***	-.104***
Switch (1) in Stimulus type/non-Switch(0)	.107***	.133***
Switch (1) in Congruence/non-Switch(0)	.028**	.031***
Stimulus Type × Congruence	-.049***	-.036***
Stimulus Type × Switch Stimulus Type	-.060***	-.058***
Stimulus Type × Switch Congruence	-.005	-.002
Congruence × Switch Stimulus Type	.000	-.006
Congruence × Switch Congruence	.016	.014
CDR × Stimulus Type	-.023**	-.011
CDR × Congruence	.010	-.024
CDR × Switch Stimulus Type	-.005	-.020
CDR × Switch Congruence	-.010	-.009
Multiple R	.252***	.558***

Notes. **p < .01, ***p < .001.

Table 23

ANCOVA of accuracy in number Stroop switching task

Covariates /Main Effects	Very Mild DAT + Normal Aging		All 3 Groups	
	F	η^2	*F*	η^2
Covariates				
Sex (M=1, F=2)	7.65**	.000	8.49**	.000
Age	56.50***	.003	85.86***	.002
Yr of Edu	305.99***	.014	459.29***	.012
Trial	52.59***	.002	36.12***	.001
Main Effect				
Participant Gp	1.38	.000	24.20***	.001
Stimulus Type	193.95***	.009	215.02***	.006
Congruence	1544.96***	.070	1857.30***	.050
Interaction				
Stimulus Type × Congruence	150.24***	.007	185.23***	.005
Stimulus Type × Gp	13.03***	.001	57.76***	.003
Congruence × Gp	119.19***	.005	357.23***	.019
Stimulus Type×Cong× Gp	13.69***	.001	39.21***	.002

Notes. $*p < .05$, $**p < .01$, $***p < .001$.

Table 24

Means and SDs of CoV and residual-ISD in number Stroop switching task

	Intraindividual variability analyses					
	Coef of Variation		Residual -IMn		Residual-ISD	
Grouping Characteristics	*M*	*SD*	*M*	*SD*	*M*	*SD*
Older adults						
Normal Aging	.422	.081	-.011	.242	.487	.181
			(.003	.434	.815	.209)
Very Mild DAT	.424	.104	.020	.460	.823	.207
			(-.006	.585	.842	.259)
Young adults	.501	.111	-.016	.580	.851	.261

Table 25

ANCOVA of CoV and residual-ISD in number Stroop switching task

	Very Mild DAT + Normal Aging		All 3 Groups	
Covariates /Main Effects	*F*	η^2	*F*	η^2
Coefficient of Variation				
Covariates				
Sex	.52	.006	.13	.001
Age	.18	.003	.09	.001
Yr of Ed	2.12	.026	2.25	.014
Main Effect				
Between groups	.24	.003	.94	.013
Residual Intraindividual Analyses				
Residual-IMn				
Between Participant Group	.01	.000	.091	.001
Residual-ISD				
Between Participant Group	.28	.003	42.01	.387

Note. Sex: M=1, F=2

Table 26

Means and SDs of ex-Gaussian parameters in number Stroop switching task

	mu		sigma		tau	
Condition	*M*	*SD*	*M*	*SD*	*M*	*SD*
Normal Aging	1209.61	293.29	201.11	106.08	864.22	284.24
Very Mild DAT	1318.24	606.92	290.93	313.43	842.13	322.93
Young	528.92	165.70	95.02	56.43	527.13	206.26

Table 27

ANCOVA of ex-Gaussian parameters in number Stroop switching task

	mu		sigma		tau	
	F	η^2	*F*	η^2	*F*	η^2
			2 groups			
Covariate						
Sex	1.51	.020	2.64	.033	3.00	.041
Age	1.24	.016	2.48	.031	.14	.002
Yr of Ed	3.20	.041	2.26	.028	.00	.000
Grouping Effect[1]	1.42	.018	2.93	.036	.13	.002
			3 groups			
Covariate						
Sex	1.27	.006	2.71	.018	1.93	.012
Age	2.19	.010	3.98*	.027	.04	.000
Yr of Ed	5.95*	.026	3.44*	.030	.00	.000
Grouping Effect[1]	1.14	.010	3.23*	.044	1.25	.016

Note. [1]Grouping Effect:
2 groups: Very mild DAT group vs normal aging group;
3 groups: very mild DAT group, normal aging group, young adults.
*$p < .05$.

6.4.3 Counting Span Task

For counting span task, as suggested by other investigators (Conway et al., 2005), four closely related indexes of performance were computed, namely, the partial-credit-unit, the all-or-nothing-unit, the partial-credit-load-unit, and the all-or-nothing-loaded-unit. While the full scoring procedures for each score were given in the method section, their basic differences were outlined here. In the first main difference, scores/credits were still assigned for partially correct responses for a certain item (digit-span) in the partial-credit scores, while only items with all individual digits being answered completely correctly could be given credits for the all-or-nothing scores.

In the second main difference, the loaded versus unloaded scores differed in that the responses were weighted with the digit span in the loaded scores. That is, getting correct answers at the longer digit-span item would lead to a greater increase in the total score because of the heavier weight added to the individual digits scores.

In Table 28, the means and SDs of the above four scores for three groups (normal aging, very mild DAT, young) are shown. Understandably, these four different scores were highly correlated (see Table 29, for very mild DAT and normal aging); correlations ranged from .90 to .98. The simple correlations between these scores with age, sex, year of education and CDR are also shown in Table 29. In general, the partial-credit and all-or-nothing scores were more highly correlated with CDR (-.36, -.32 respectively, see Table 29).

Separate regressions were conducted for each of these indexes (scores) as the criterion with age, sex, year of education and CDR as the predictors. Furthermore, the analyses were repeated for the two (normal aging vs. very mild DAT) and three (normal aging, very mild DAT, young) groups respectively (see Table 30). The results

were consisted showing that counting performance was worse with increasing age and less years of education. None of these scores however, were discriminating enough for the two participant groups (CDR 0 vs. CDR 0.5). In general, Partial-credit unit performed marginally better with a stronger negative relation with CDR (-.205 in 2 groups, -.117 in 3 groups).

Table 28

Means and SDs of Scores in Counting Span task

Predictors	Scores							
	Partial-Credit		All-or-Nothing		Partial-Credit Loaded		All-or-Nothing Loaded	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Old Adults								
Normal Aging	.48	.13	.34	.14	.37	.12	.24	.13
Very Mild DAT	.36	.18	.23	.18	.29	.16	.16	.15
Young Adults	.90	.09	.76	.14	.88	.11	.70	.17

Note. $*p < .05$, $**p < .01$, $***p < .001$.

Table 29

Correlations among various scores by groups in Counting Span task

Scores	1	2	3	4	5	6	7
1. Partial-credit	1						
2. All-or-Nothing	.93***	1					
3. Partial-credit-loaded	.99***	.91***	1				
4. All-or-Nothing-loaded	.90***	.98***	.91***	1			
5. Age	-.31**	-.34**	-.31**	-.34**	1		
6. Sex (1=M, 2=F)	-.17	-.17	-.17	-.16	-.15	1	
7. Year of Education	.39**	.40***	.39**	.42***	-.081	-.16	1
8. CDR	-.36**	-.32**	-.29**	-.26*	.27*	.12	-.29**

Note. $*p < .05$, $**p < .01$, $***p < .001$.

Table 30.

Regression analyses (beta) on various scores in Counting Span task

Predictors	Criterion			
	Partial-Credit	All-or-Nothing	Partial-Credit Loaded	All-or-Nothing Loaded
	Normal Aging + Very Mild DAT			
Age	-.222*	-.260*	-.237*	-.279*
Sex	-.068	-.062	-.062	-.048
Year of Education	.297**	.329**	.320**	.369**
CDR	-.205	-.152	-.129	-.075
Multiple R	.518***	.529***	.494***	.526***
	Normal Aging + Very Mild DAT + Young			
Age	-.642***	-.613***	-.718***	-.660***
Sex	.015	.017	.033	.040
Year of Education	.214**	.227**	.194**	.215**
CDR	-.117*	-.094	-.056	-.040
Multiple R	.892***	.860***	.914***	.867***

Note. $*p < .05$, $**p < .01$, $***p < .001$.

6.4.4 Digit Suppression Task

For the digit suppression task, three closely related indexes of performance were computed (see Table 31), trial span, total digit and total trials (see method section for details). As can be seen from their zero-order correlations (Table 32), trial-span was more highly correlated with total-digit (.92), and less so with total trials (.85). In general, the suppression span as measured by any of these three indicators would decrease with increasing age, and with less education. Most importantly, all these indicators could effectively discriminating the CDR=0 and CDR=.5 group (r = -.57, -.49, and -.50 respectively).

Separate regressions were conducted for each of these indexes as the criterion and age, sex, year of education and CDR as the predictors. Furthermore, the analyses were repeated for these

two (normal aging vs.very mild DAT) and three (normal aging, very mild DAT, young) groups separately (see Table 33). The results were consistently showing that recall performance decreased with increasing age and less years of education, reconfirming the findings with zero-order correlations. Importantly again, trial span could effectively discriminate the CDR=0 and CDR=0.5 group after controlling for other demographic variables (age, sex, years of education). Specifically, the very mild DAT participants had a significantly lower trial-span score (b = -.243, p = .013). The regression results were very similar for the two or three participant groups, both supporting the superior performance of trial-span scores and the use of suppression span to identify very mild DAT participants. In general, the suppression span performed better than the Counting span task which was otherwise more traditional and more widely used.

Table 31

Means and SDs of scores in digit suppression task

Participant group	Trial span		Total digit		Total trials	
	M	*SD*	*M*	*SD*	*M*	*SD*
Old Adults						
Normal Aging	5.96	1.74	15.79	12.01	4.50	2.92
Very Mild DAT	3.88	2.78	8.13	8.86	2.55	2.55
Young Adults	8.94	1.58	39.18	14.75	10.53	3.48

Table 32

Correlations among various scores by groups in digit suppression task

Scores	1	2	3	4	5	6
1. Trial span	1					
2. Total-digit	.92***	1				
3. total trials	.85***	.87***	1			
4. Age	-.70***	-.74***	-.74***	1		
5. Sex (1=M, 2=F)	.10	.19*	.21*	-.18*	1	
6. Year of Education	.63***	.64***	.70***	.74***	.090	1
7. CDR	-.57***	-.49***	-.50***	.52***	-.033	-.52***

Note. $*p < .05$, $**p < .01$, $***p < .001$.

Table 33

Regression analyses (beta) on RT in digit suppression task

Predictor	Criterion		
	Trial-Span	Total-digit	total trials
	Normal Aging + Very Mild DAT		
Age	-.376***	-.312**	-.305**
Sex	-.043	.004	.027

Year of Ed	.260***	.296**	.355***
CDR	-.243*	-.175	-.159
Multiple R	.600***	.520***	.543***
	Normal Aging + Very Mild DAT + Young		
Age	-.443***	-.531***	-.444***
Sex	-.004	.071	.104
Year of Ed	.182*	.182*	.306***
CDR	-.242**	-.122	-.110
Multiple R	.750***	.764***	.788***

Note. $*p < .05$, $**p < .01$, $***p < .001$.

6.4.5 Relationships between ex-Gaussian Parameters and working memory Performance

In order to understand the relationships between the ex-Gaussian parameters (i.e., mu, sigma, tau) and working memory task competence, a structural equation model was constructed using the three parameters to predict the working memory competence. Specifically, mu, sigma and tau values were extracted from pure face and number trials as indicators for the three factors (mu, sigma, tau), and four observed indicators from the counting span task and digit suppression task were used as measures of working memory performance (see Figure 3). Similar to Schmiedek et al. (2007), these observed indicators in the face and number tasks were modeled using the multi-trait-multi-method analyses. As suggested by Marsh, Martin and Hau (2006) and related research, the frequently encountered non-convergence problem in this kind of model was solved by specifying the multi-method effects as correlated uniqueness. This strategy was adopted in the present analyses (not fully shown in the Figure for brevity).

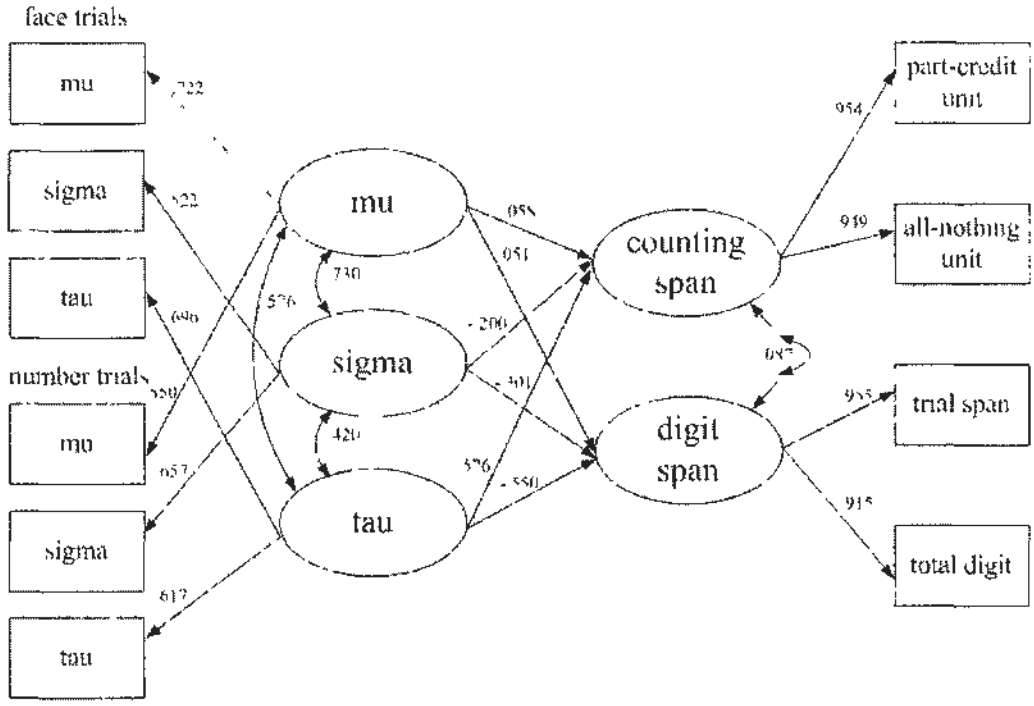


Figure 5. Structural relationships between ex-Gaussian parameters and working memory tasks

In this structural equation model imitating that by Schmiedek et al. (2007), the present study tested the structure of the three parameters of ex-Gaussian distribution as related to two working memory tasks. Furthermore, in contrast to regression analyses, the factorial structure of ex-Gaussian parameters (mu, sigma, tau) was examined simultaneously with their interrelations to the working memory factors. Understandably due to the relatively small sample size, the parameter estimates in the model might not be stable and hence leading to large standard errors of measurement. The present study had adopted the recommendation by Marsh and Hau (1999) for small sample analyses in forcing some of the paths to be equivalent (e.g., the two loadings relating the two observed tau indicators to the tau factor were forced to be equivalent). This would slightly increase the chi-square values sacrificing the fit (i.e., fit looked worse), but would stabilize the paths in the model for analyses involving small sample sizes.

In order to examine the relations by controlling sex, age, and year-of-education effects, the

covariance matrix was used after partialling out the effects of the above variables. Furthermore, similar to other parts in this research, the present study focused on analyses with the older adults (very early DAT group vs. normal aging group) only, but the structural equation model analyses were replicated with all participants (normal aging group, very early DAT group, young adults), and without controlling for the covariates. The results were very similar displaying almost identical patterns of relations.

The fit of the model using the indexes as recommended by Marsh, Hau, and Grayson (2005) was reasonably good when considering that a lot of equality constraints had been imposed to get a more stable solution, $\chi^2(27) = 82.14$, RMSEA = 0.145, NNFI = 0.858, CFI = 0.915. The respective fits for all participants (including young adults) and for the model without covariates were similarly good; $\chi^2(27) = 142.23, 85.09$; RMSEA = 0.166, 0.151; NNFI = 0.903, 0.849; CFI = 0.942, 0.909 respectively.

The loadings of the indicators to respective factors were reasonably high, ranging from .522 to .850 for the mu, sigma, and tau factors, and .915 to .955 for the digit-span and suppression tasks. In general, the factors mu, sigma and tau were positively correlated, suggesting longer response times were related to a larger SD and a larger positive skew (thicker tail).

Most importantly and most crucial to the analyses was the finding that tau was negatively related to cognitive performance in both two working memory tasks; $b = -.576, -.550$, $p = .011, .013$. That is, participants with thicker positively skew tail in the response time had weaker performance in both counting span task and digit suppression task. Similar patterns were observed with the analyses with all participants and for the model without controlling for the covariates; $b = -.552, -.555$, respectively for digit-span; $b = -.567, -.552$, respectively for suppression tasks ($p = .001, .001, 011, .013$ respectively). In contrast, mu and sigma factors were not related to the Counting Span task and Digit Suppression task performance at all.

In conclusion, similar to Schmiedek et al. (2007), the results showed that among the

Chinese, the tau factor (skewed response time) was substantially and significantly related to poor performance in cognitive tasks (Counting Span and Digit Suppression task) while mu, sigma were not. This reaffirms the analyses in other parts of this research that tau and intraindividual variability were more sensitive indicators for very early DAT.

6.5 Discussion

The present thesis investigated the performance of young adults, normal aging adults and older adults with very mild DAT in attention tasks and working memory tasks. More specifically, the overarching objective was to effectively discriminate very mild DAT and normal aging through examining (a) the characteristics of the parameters in ex-Gaussian distribution (mu, sigma, and tau) and intraindividual variability in performance in two typical attention tasks (number Stroop switching task and face-number switch task), (b) the performance of two working memory tasks (Counting Span task and digit suppression task) and (c) the relationships between working memory capacity and attentional control performance.

There have been various foci of interests under different frameworks or theories to capture the poor performance in people at early stages of DAT, one of which is to measure RT in attention or similar tasks. This is on the underlying theoretical assumption that people with very mild DAT are more likely to take longer time due to the breakdown in attentional control to overcome distraction and concentrate on the task demands (Balota & Faust, 2001), . Given the close relation of working memory and attention (see literature review in Chapter 3), it is not surprising to relate very mild DAT individuals' poor performance in working memory task to the deterioration in their divided attention or other executive controls (Baddeley, 1986; Belleville et al., 2007).

It should also be noted that the present study mainly aimed to investigate the discrimination power of two attention tasks and working memory tasks. Due to the limited scope of the study, a

generic term "attentional control" was used in this study rather than attempting to differentiate and attend to the detailed structure of attention. Future studies can refine this structure and explore the effects of different components of attention.

The present study mainly concentrated on the comparison between two groups, normal aging group and very mild DAT group (i.e., DAT-related effect). Specifically, the present study explored potentially useful task for early detection of DAT among Chinese older adults. The present research showed that with factors such as age, year of education, sex being considered, the tasks on attentional control ability and working memory capacity could effectively differentiate individuals with very mild DAT from normal aging adults. Face-number switch task and digit suppression task performed particularly well in this aspect.

6.5.1 Effective Tasks and Sensitive Indicators

a. Intraindividual variability and ex-Gaussian distribution in attention tasks

For attention tasks, the most sensitive indicator for very mild DAT would be a measure of intraindividual variability (*Residual-ISD*) and tau value of ex-Gaussian distribution in pure trials (face trials and number trials) in Face-number switch task. It is intriguing that there is no difference in the residual-IMn across groups, whereas both age-related effect and DAT-related effect are found with the *Residual-ISD*.

In line with previous findings, the results affirm intraindividual variability in response time can effectively discriminate individuals' groups (young adults vs. normal aging group vs. very mild DAT) independent of mean-level performance (e.g., Dixon et al., 2002; Hultsch et al., 2002; Hultsch et al., 2008). In the pure face and number trials, residual-ISD has been found to be a better indicator of both CDR status (η^2 = .390, .377) and aging groups (η^2 = .585, .516) than the mean of residuals.

In the comparison between residual-ISD and coefficient of variation, the results show the residual-ISD has a much larger effect size (η^2) (η^2 = .390, .377, see Table 12) and is thus more

sensitive than measure than the coefficient of variation (eta^2 = .127, .227, see Table 12). This finding is in line with Hultsch et al. (2008). Thus, the present research reaffirms that *Residual-ISD* is a better indicator of intraindividual variability than coefficient of variation in discriminating the very mild DAT individuals from the normal aging ones.

In the utility of ex-Gaussian distribution analyses in detecting early stage of DAT, it has been found that very mild DAT individuals have much larger tau values than normal aging ones in pure face and number trials (η^2 = .207, .169, .273, .226, see table 19). This again is in line with the findings in Schmiedek et al. (2007) which demonstrate the parameter tau in ex-Gaussian distribution is substantially related to the working memory performance. This further supported previous investigations in the use of tau as a sensitive indicator in differentiating individuals with very mild DAT from the normal aging participants.

b. Working memory tasks

Digit suppression task outperforms the counting span task as a measure of attentional control capacity, with better power to discriminate individuals with CDR 0.5 from normal aging older adults with CDR 0.

The main purpose of the counting span task is to capture the recall performance rather than that of the processing or storage. The performance in the latter two have been found to be ceiling due to the simplicity of the counting process (Conway et al., 2005; Kane et al., 2004). As suggested by Conway et al. (2005), it is useful to examine whether the better recall performance is at the expense the poor counting processing. Operationally, the processing (counting) accuracy can represent the processing component of working memory, while the recall score can represent the "storage component" (Conway et al., 2005). In this research, consistent with previous findings (e.g., Kane et al., 2004), a generally positive correlation was found between the processing accuracy and the recall score (all *r*s ranged from .33 to .55), suggesting that there has not been any counting/recall trade-off and that the analysis of the recall score would be valid.

There might be similar concerns on the DAT-related effect in the pure face and number trials. A generally negative correlation between tau and accuracy has been found in each of the participant group (for normal aging group, r = -.082, n.s, p = .580 for face trial, r = -.261, n.s., p = .073 for number trials; for very mild DAT group, r = -.379, p = .016; r = -.574, p < .001 respectively), indicating that very mild DAT individuals have spent longer time but have also been less accurate in their response. Therefore, DAT-related effect on tau value in pure face and number trials could not have been due to speed-accuracy trade-offs.

6.5.2 Task Complexity

The task-switching paradigm used in present study did not perform any better than the purely face or purely number trials in discriminating the very mild DAT participants from the normal aging adults.

Previous studies have found that divided attention performance in DAT might be mediated by the task complexity in dual task paradigm (Lonie et al., 2008; Crossley et al., 2004). For example, impaired performance in AD patients has only been found in dual tasks that include complex and novel tasks that involve greater efforts (Crossley et al., 2004). Similarly, it has been shown that impaired performance in patients with DAT could only be detected in dual tasks with more effort and cognitive loading but not in relatively automatic tasks otherwise (Crossley et al., 2004). In other words, the DAT-related attention deficit might not be detected when the task involves insufficient cognitive loading in attentional processes. Similarly, Kramer, Hahn, and Gopher (1999) have compared the performance in switching task between young and old adults and found the age-related effect on switch costs in task could be observed only if cognitive demanding has been increased in the task by removing the explicit cues,

The present findings suggest that the switch paradigm seemed not as effective as it has done in previous work (e.g., Duchek et al., 2009; Hutchison et al., 2010; Tse et al., 2010). Both the switch trials in face-number switch task and the number Stroop switch task have not

outperformed the pure blocks in face-number switch task in discriminating the very mild DAT participants from the normal aging adults. For the number Stroop switch task, one obvious limitation is limited number of observations (only 24 replicates) in each combination of conditions.

Alternatively, another explanation can be the over-complexity due to the increased cognitive loading with the use of symbol cues in the task. The face-number switch task requires participants to make proper response according to different rules (representing by cues). For example, in pure number trials, the cues (pictures of a pair of shoes and one single shoe) are presented at the left- and right- corners of the screen simultaneously with the stimulus (face-number pair) in the middle of the screen. This indicates that the present task is a number trial and the participant has to press the k-key if the digit is even or press the d-key if it is odd. When compared to the direct cues used in earlier studies (e.g., the word cues "odd" and "even" in number trials, see Minear & Shah, 2008; Duchek et al., 2009), the present paradigm demands one to maintain the association/mapping between the symbol cues and its expected meanings (e.g., in number trials, a pair of shoes represents "even", while one single shoe represents "odd") while making proper response according to the stimuli. The extra effort needed for the task might make it too difficult even to the normal aging adults, and subsequently, masking the difference between very mild CDR and normal aging. In pure blocks, however, the cognitive loading might be more appropriate to capture the breakdowns in attention in very mild DAT. Task difficulty is definitely an important factor that affects the discriminating power in differentiate the very mild DAT from healthy older adults that researchers in this field and needs to be taken into consideration in future work.

Chapter 7 Study Two -- Bias in Assessment of Very Mild Dementia: Differential Screening Power for High and Low Education Groups

7.1 Objectives

Study Two examined the differential power of various screening tasks with older adults diagnosed as CDR 0 or 0.5, who might have varying years of education. The main purpose of this study was to identify tasks with potential bias for those who have minimal or no education. The screening tasks were commonly used in Hong Kong in which various cognitive functions are involved, including the Cantonese version of the Mini-Mental State Examination (C-MMSE, Chiu et al., 1994; Chiu et al., 1998), the Chinese version of Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog, Chu et al., 2000), Abstract Thinking (adapted from the Wechsler Adult Intelligence Scale, Wechsler, 1999), Verbal Fluency Test (Chiu et al., 1997) and forward and backward digit and visual span tasks (also adapted from Wechsler Adult Intelligence Scale, Wechsler, 1999). The set of neuropsychological and cognitive screening tests were selected to test the main areas of cognition including attention, semantic memory, language ability, visual-constructional ability and so on.

We examined the CDR in both global and subscale levels and the screening tasks down to item level so as to reveal the specific influence of education bias on each of the items or subscales in these commonly used screening tasks. To our knowledge, this has only been done in very few studies (e.g., Yassuda et al., 2009) and no other study has investigated the differentiating power of individual items of various dementia screening tests with Chinese population. The data in the following analyses were collected in a much larger 6-year longitudinal study conducted by Lam et al. (2008a, 2008b).

7.2 Methodology

7.2.1 Participants

The participants were from an epidemiology survey on the prevalence of very mild dementia in Hong Kong (Lam et al., 2008a, 2008b). As shown in table 34, among the 788 participants (364 males, 424 females), 405 (51.4%) had very mild dementia (CDR = 0.5) while 383 (48.6%) were normal control (CDR = 0), based on the Clinical Dementia Rating (Morris, 1993; Morris et al., 1988). The mean age was 72.08 (*SD* = 7.27) and ranged from 57 to 96.

7.2.2 Material and Design

While details of the methodology of the data collected were reported elsewhere (Lam et al., 2008a, 2008b), it is suffice to say that all participants were community-dwelling older adults and individually assessed by a geriatric psychiatrist and a research assistant. The geriatric psychiatrist conducted assessment for global cognitive status using the CDR scale (Morris, 1993; Morris et al., 1988), with 0, 0.5, 1, 2, and 3 representing no dementia, very mild dementia, mild dementia, moderate dementia, and severe dementia, respectively. The reliability and validity of CDR in Asian populations have been shown to be sensitive to the level of education in Hong Kong older adults (Lam et al., 2008a; Lim et al., 2007).

The CDR was determined by a semi-structured clinical interview that assessed the participants and obtained collateral information from informants. The scoring of the CDR emphasized the changes in participants' cognitive and functional abilities in memory, orientation, judgment/problem solving, home/hobbies, community affairs, and personal care relative to their previous behavior (used as benchmark). This CDR status obtained through an interview was determined without reference to older adults' psychometric performance. When necessary, the participants' CDR status was corroborated with the diagnoses of mild cognitive impairment (Lam et al., 2008a, 2008b).

Under supervision and guidance of a geriatric psychiatrist, the research assistant conducted a number of psychometric tasks (see Table 35) to assess participants' cognitive functions (e.g., attention, memory and language) that are considered central to the diagnosis of dementia, which included (see Table 35 for more description of the instruments):

a) the Mini-Mental State Examination (MMSE, Folstein et al., 1975), which has been widely used as a preliminary cognitive screening tool for dementia (Nelson et al., 1986; Uhlmann et al., 1987),
b) the Chinese versions of the MMSE, which has been developed and utilized in mainland China (Li et al., 1989) and Hong Kong (Chiu et al., 1994; Chiu et al., 1998) and showed good reliability and validity in clinical applications (Lam et al., 2008; Poon et al., 2008; Tsang & Man, 2006),
c) the Cantonese version of the MMSE (Chiu et al., 1998; Chiu et al., 1994), which is developed on the basis of MMSE with necessary modification for the language and cultural concern; it consists of 30 subtasks/items (e.g., naming dates, day of the week, place, short-term memory tasks) that can be categorized into 5 main aspects: recalling the time (year, season, month, day, and date; i.e., MMSE1) and the place (county, town, hospital, and floor; i.e., MMSE2), registration (naming three objects, i.e., MMSE3), attention and concentration (serially subtracting 7, beginning with 100; i.e., MMSE4,), recall (recalling the previously named three objects; i.e., MMSE5), language (naming two objects, repeating a phrase, reading aloud and understanding a sentence, writing a sentence, and following a three-stage command, and copying a design; i.e., MMSE6),
d) The Chinese version of ADAS-Cog (Chu et al., 2000), which consists of 11 items with a maximum total score of 70 to assess memory, orientation, language and praxis function,
e) the Abstract Thinking task, which requires people to point out in what way two objects (that

look different) are similar,

f) the digit and visual span tests, which include digits/visual forward and backward span test to assess the working memory and attention, and

g) the Verbal Fluency Test (VFT, Chiu et al., 1997), which is taken as a measure of executive function which requires a directed search processing for target words within a restriction of 30 seconds or 60 seconds

Table 34

Background information of participants in Studies Two and Three

	Gender			Age		Year of Education	
	Male	Female	total	*M* (range)	*SD*	*M* (range)	*SD*
Normal aging	191	173	364	72.38 (61 - 90)	6.39	6.32 (0 - 20)	4.69
Very mild DAT	192	232	424	76.83 (61 - 100)	7.03	3.20 (0 - 18)	3.96

Table 35

Description on all screening tasks used in Study Two

Screening Tasks	Subscale	Task to be completed
CDR	*Memory*	Ability to encode and remember events
	Orientation	Ability to reason about the time/place relationship
	Judgment	Ability to solve problems, similarities, and differences
	Community	Ability to function independently at job, shopping, volunteer and in social groups
	Home	Ability to function at home
CMMSE	*CMMSE1(recall 1)*	To describe the current date
	CMMSE2(recall 2)	To describe his/her current location (home address, hospital address, etc.)
	CMMSE3(registration)	To repeat names of 3 objects that he/she has been told several minutes ago.
	CMMSE4(attention and calculation)	To count downward from 100 by sevens or to recite backward a series numbers.
	CMMSE5(recall3)	Recall and repeat names of 3 objects learned in CMMSE3.
	CMMSE6(language)	Name objects, repeat a short phrase, follow a 3-step command, read and obey a short sentence, copy a design.
ADAS-Cog	*1.Word recall*	Read after the interviewer a list of words, and remember them.
	2.Naming objects and fingers	Name 12 objects and fingers of one hand.
	3.Commands	Follow a set of commands/actions.
	4.Constructional praxis	Draw and copy a figure.
	5.Delayed recall	Recall and repeat the10 objects in question1.
	6.Ideational praxis	Follow a 5-step command.
	7.Orientation	Speak out his/her name, the current year/week day/season/date/time/month and location.
	8.Word recognition	Read (or just listen to) loudly 12 words and then tell/recognition whether he/she had read/heard it by showing the word list and do the recognition again.
	9.Remembering testing instructions	(By the interviewer) evaluate and rate the memory ability of the interviewee.
	10.Spoken language ability	(By the interviewer) evaluate and rate the spoken language ability of the interviewee.
	11.word-finding difficulty in spontaneous speech	(By the interviewer) evaluate if the interviewee has the difficulty in selecting words in speech.
	12.Comprehension of speech	(By the interviewer) evaluate the comprehension ability of the interviewee.
Abstract thinking	*Similarity* *Difference*	To point out in what way two objects are similar or dissimilar. The object pairs for the similarity test are apple-banana, desk-chair, and boat-car. The object pairs for the difference test are sugar-vinegar, ball-orange, and escalator-elevator.
Digit and visual span	*Digits forward span & score Digits backward span & score* *Visual forward span & score* *Visual backward span & score*	To assess participants' short-term/working memory and attention (for the backward ones)
Verbal fluency test	total 30s total 60s	Measured by the number of target words within a established restriction (30 seconds or 60 seconds) and is considered a measure of executive function.

7.2.3 Analyses

Education was measured by the years of education completed by each participant. Dementia was assessed by the CDR with a global score (*CDR-global*), as well as six subscale scores used as dependent variables. As the present study focused on the difference between CDR 0 and 0.5 in the analyses, some items were dropped and low frequency codes were collapsed when necessary. More specifically, one CDR subscale and one C-MMSE component were non-discriminating and therefore were discarded due to ceiling effects [99.7% of the participants score 0 (non-dementia) in CDR-care; 94.3% of participants scored 3 (full score) in C-MMSE3]. In addition, for those participants who scored 0.5 in CDR-global, there were about 1.4%, 0.5%, 3.2%, 0.8%, and 0.6% of them scoring 1 (i.e., mild dementia) in CDR-memory, orientation, judgment, community, and home, respectively. Due to the few cases in these items, these scores were collapsed with CDR 0.5 in the analyses. The pattern of findings remained identical when they were deleted, instead of being collapsed into the current dataset.

Binary logistic regression analyses were performed with CDR global or subscale scores (0.5 vs. 0) being used as the dependent variable. It was predicted that CDR scores (dementia) with task performance (screening item), education (years of education), and their interaction (screening item × education). A significant interaction term would suggest that the effect of screening item on CDR would change with years of education (see Table 36). In order to obtain a more interpretable solution, all predictor variables were mean-centered (i.e., subtracting with their respective means) (Jaccard, 2001) and the product term was computed by multiplying the mean-centered education and screening item variables. When the interactions were significant, the main effects were the odds ratios of the respective variable (e.g., effect of screening item) at the mean values of the other variables (e.g., education and age). Furthermore, to visualize the significant interactions more easily, the participants were devided by median split based on their

years of education [0-3 years (Mean=.96, *SD*=1.21) vs. 4 or more years of education (Mean=8.37, *SD*=3.63)] and conducted logistic regression analyses (screening item predicting dementia) for the high vs. low education groups separately (last two columns).

Table 36 shows the odds ratio of the effect. For example, the value 0.451 (first row, "Screening Item" column) is the multiplying factor of MMSE1 score on CDR-memory subscale score. For each unit increase in the MMSE1 score, the odds ratio of CDR 0.5 vs. CDR 0 in CDR-memory decreased by 0.451. Whether the expected odds ratio should be larger or smaller than 1 depends on whether high or low scores indicate high performance. Significant odds ratios in the "Screening Item" column could suggest the sensitivity of screening items on discriminating very mild dementia from healthy aging. While some screening items would be equally sensitive whether older adults had high or low education when its relations with CDR scores were similar, a significant interaction term ["Interaction (1) x (2)" column] would suggest that the discriminating power of screening items on CDR scores was not identical for high and low education groups. The findings of follow-up analyses, as shown in "Screening Item (Low/High-Ed group)", further revealed whether those screening items were particularly sensitive for older adults with high or low education.

Table 36

Predicting CDR subscales with screening tasks – differential effects in high and low education groups

Screening Tasks	Dependent Variable CDR subscale	Effects of Age (Odds Ratio)	Effects of Age (10-years Odds Ratio)	Effects on Dependent Variable (Odds Ratio)					
				Education (1)	Education (10-yr)	Screening Task (2)	Interaction (1) × (2)	Screening Task (Low-Ed Group)	Screening Task (High-Ed Group)
MMSE1	*Memory*	1.068***	1.93	0.890***	0.31	0.451***	1.028		
	Orientation	1.045**	1.55	0.940*	0.54	0.370***	1.034		
	Judgment	1.034**	1.40	0.868***	0.24	0.820	1.045		
	Community	1.066***	1.90	0.966	0.70	0.647**	1.032		
	Home	1.078***	2.12	0.977	0.79	0.751	1.054		
	Total	1.074	2.03	0.884***	0.29	0.412***	1.061		
MMSE2	*Memory*	1.079***	2.14	0.878***	0.27	0.584***	0.982		
	Orientation	1.072***	2.01	0.894***	0.33	0.476***	0.977		
	Judgment	1.041***	1.49	0.865***	0.23	0.791	0.990		
	Community	1.077***	2.12	0.940*	0.54	0.588***	0.924*	0.841	0.392***
	Home	1.088***	2.34	0.963	0.68	0.687**	0.967		
	Total	1.086***	2.27	0.877***	0.27	0.556***	1.001		
MMSE4	*Memory*	1.078***	2.11	0.891***	0.32	0.757***	1.009		
	Orientation	1.068***	1.93	0.924**	0.45	0.702***	0.998		
	Judgment	1.041*	1.49	0.890***	0.31	0.709***	1.035*	0.590***	0.753**
	Community	1.077***	2.10	0.967	0.71	0.808**	1.007		
	Home	1.087***	2.32	0.986	0.87	0.798**	1.007		
	Total	1.084***	2.25	0.886***	0.30	0.743***	1.027		
MMSE5	*Memory*	1.072***	2.01	0.867***	0.24	0.580***	0.967		
	Orientation	1.066***	1.90	0.886***	0.30	0.946	0.962		
	Judgment	1.040***	1.40	0.862***	0.23	0.976	0.976		

	Community	1.074***	2.05	0.941*	0.54	0.771*	0.975		
	Home	1.085***	2.25	0.954	0.63	0.765*	0.944*	1.026	0.551***
	Total	1.078***	2.12	0.869***	0.25	0.648***	0.973		
MMSE6	*Memory*	1.073***	2.01	0.887***	0.30	0.670***	1.055*	0.477***	0.754
	Orientation	1.063***	1.84	0.900***	0.35	0.871	1.039		
	Judgment	1.034**	1.40	0.880***	0.28	0.725**	1.064*	0.500***	0.811
	Community	1.069***	1.95	0.970	0.74	0.700**	1.030		
	Home	1.080***	2.16	0.982	0.84	0.763*	1.070*	0.586***	0.870
	Total	1.079***	2.14	0.882***	0.28	0.650***	1.080**	0.418***	0.792
ADAS-Word Recognition	*Memory*	1.063**	1.84	0.892***	0.32	0.685***	0.957**	0.802**	0.577***
	Orientation	1.039	1.46	0.900**	0.35	0.885*	0.979		
	Judgment	1.018	1.20	0.866***	0.24	0.915	0.977		
	Community	1.059**	1.79	0.958	0.65	0.897	0.965*	1.027	0.813*
	Home	1.066**	1.90	0.998	0.98	0.945	0.953*	1.178	0.811*
	Total	1.072***	2.01	0.877	0.27	0.680***	0.966*	0.773**	0.581***
ADAS-Delay Recall	*Memory*	1.042**	1.51	0.895***	0.33	0.530***	0.980		
	Orientation	1.049**	1.62	0.893***	0.32	0.837***	0.986		
	Judgment	1.019	1.21	0.874***	0.26	0.804***	0.977**	0.858**	0.757***
	Community	1.056***	1.73	0.955	0.63	0.782***	0.979*	0.863*	0.712***
	Home	1.068***	1.93	0.979	0.81	0.812***	0.985		
	Total	1.051***	1.65	0.896***	0.33	0.556***	0.979		
ADAS-Word Recall	*Memory*	1.037**	1.45	0.913***	0.40	0.438***	0.961*	0.497***	0.384***
	Orientation	1.050**	1.63	0.901**	0.35	0.748***	0.974		
	Judgment	1.020	1.21	0.886***	0.30	0.742***	0.972*	0.782**	0.698***
	Community	1.056***	1.72	0.966	0.70	0.638***	0.954*	0.756**	0.582***
	Home	1.067***	1.90	1.006	1.06	0.676***	0.993		
	Total	1.044**	1.82	0.913***	0.40	0.451***	0.963*	0.494***	0.411***
ADAS-Orientation	*Memory*	1.072***	2.01	0.868***	0.24	0.528**	1.052		
	Orientation	1.037	1.43	0.938	0.53	0.392***	0.993		
	Judgment	1.019	1.21	0.868***	0.24	0.795	1.082		
	Community	1.063**	1.84	0.972	0.75	0.581*	0.972		
	Home	1.061*	1.82	1.017	1.19	0.535**	0.947		

	Total	1.080***	2.16	0.849***	0.19	0.397***	1.138(marginal)		
ADAS-Constructional Praxis	*Memory*	1.073***	2.01	0.885***	0.30	0.543***	1.034		
	Orientation	1.045*	1.55	0.915*	0.41	0.733	1.066		
	Judgment	1.018	1.20	0.859***	0.22	0.876	1.058		
	Community	1.061***	1.80	0.947	0.58	0.938	1.041		
	Home	1.060***	1.79	0.980	0.82	0.989	1.070		
	Total	1.082***	2.20	0.877***	0.27	0.482***	1.045		
ADAS-Ideational Praxis	*Memory*	1.076***	2.08	0.877***	0.27	0.408***	0.922		
	Orientation	1.040	1.48	0.906*	0.37	0.513**	0.924		
	Judgment	1.018	1.20	0.873***	0.26	0.534**	0.941		
	Community	1.064**	1.86	0.957	0.64	0.562*	0.878*	0.863	0.432*
	Home	1.066**	1.88	0.999	1.00	0.641	0.871*	0.996	0.464
	Total	1.085***	2.27	0.864***	0.23	0.376***	0.928		
ADAS-Naming Objects and fingers	*Memory*	1.073***	2.05	0.877***	0.25	0.734***	1.011		
	Orientation	1.042*	1.57	0.910**	0.35	0.826*	1.006		
	Judgment	1.018	1.23	0.871***	0.23	0.854*	0.994		
	Community	1.066**	1.90	0.957	0.62	0.911	0.995		
	Home	1.070**	2.01	0.995	0.95	0.926	0.999		
	Total	1.082***	2.22	0.866***	0.22	0.716***	1.005		
ADAS-Commands	*Memory*	1.078***	2.11	0.869***	0.24	0.503***	0.981		
	Orientation	1.044	1.54	0.901**	0.35	0.717*	1.018		
	Judgment	1.021	1.22	0.864***	0.23	0.727*	1.018		
	Community	1.067**	1.92	0.952	0.61	0.824	0.919		
	Home	1.074**	2.03	0.992	0.92	0.951	0.899*	1.339	0.800
	Total	1.088***	2.32	0.855***	0.21	0.498***	1.001		
Abstract Thinking Banana-Apple	*Memory*	1.065***	1.88	0.884***	0.29	0.578***	1.022		
	Orientation	1.055***	1.70	0.909**	0.38	0.529***	0.974		
	Judgment	1.027*	1.31	0.885***	0.30	0.447***	0.967		
	Community	1.069***	1.93	0.967	0.72	0.583***	0.954		
	Home	1.081***	2.18	0.980	0.82	0.722*	1.010		
	Total	1.071***	1.97	0.883***	0.29	0.559***	1.034		

Abstract Thinking Desk-Chair	*Memory*	1.065***	1.88	0.913***	0.40	0.462***	0.977		
	Orientation	1.056***	1.73	0.927*	0.47	0.514***	0.980		
	Judgment	1.027*	1.31	0.925**	0.46	0.248***	0.939		
	Community	1.069***	1.95	0.999	1.00	0.430***	0,968		
	Home	1.081***	2.18	1.005	1.05	0.553**	1.009		
	Total	1.072***	1.99	0.918***	0.42	0.410***	0.981		
Abstract Thinking_ Boat-Bus	*Memory*	1.061***	1.80	0.909***	0.38	0.466***	1.001		
	Orientation	1.054***	1.68	0.918**	0.43	0.637**	1.006		
	Judgment	1.022	1.23	0.915***	0.41	0.337***	0.935*	0.432***	0.249***
	Community	1.066***	1.90	0.986	0.87	0.539***	0.956		
	Home	1.079***	2.14	0.992	0.92	0.680*	1.044		
	Total	1.066***	1.90	0.912***	0.40	0.422***	1.004		
Abstract Thinking_ Sugar-Vinegar	*Memory*	1.068***	1.93	0.875***	0.26	0.798	0.962		
	Orientation	1.057***	1.73	0.909**	0.39	0.306***	0.999		
	Judgment	1.031*	1.35	0.874***	0.26	0.346***	0.952		
	Community	1.070	1.97	0.962	0.68	0.572*	1.033		
	Home	1.082***	2.20	0.979	0.80	0.589*	1.061		
	Total	1.074***	2.03	0.876***	0.27	0.771	0.968		
Abstract Thinking_ Ball-Orange	*Memory*	1.066***	1.90	0.882***	0.28	0.592**	0.953		
	Orientation	1.056***	1.73	0.910**	0.39	0.411***	0.998		
	Judgment	1.029*	1.32	0.878***	0.27	0.351***	0.948		
	Community	1.070***	1.95	0.964	0.69	0.581**	1.004		
	Home	1.082***	2.20	0.983	0.84	0.572**	1.052		
	Total	1.072***	2.01	0.882***	0.28	0.601**	0.967		
Abstract Thinking Lift-Escalator	*Memory*	1.065***	1.88	0.881***	0.28	0.628***	0.965		
	Orientation	1.056***	1.72	0.876***	0.27	0.386***	0.896*	0.551**	0.305***
	Judgment	1.029*	1.32	0.874***	0.26	0.481***	0.977		
	Community	1.070***	1.95	0.957	0.64	0.647**	0.949		
	Home	1.082***	2.18	0.979	0.80	0.648**	1.009		
	Total	1.071***	1.99	0.881***	0.28	0.620***	0.987		
Digit_forward_ Span	*Memory*	1.077***	2.10	0.862***	0.23	0.818**	1.010		
	Orientation	1.044*	1.54	0.898**	0.34	0.820*	0.995		

	Judgment	1.028	1.31	0.863***	0.23	0.862*	0.984
	Community	1.074**	2.05	0.944	0.56	0.830*	0.966
	Home	1.075**	2.08	0.980	0.82	0.868	0.969
	Total	1.087***	2.29	0.852***	0.20	0.757***	1.008
Digit_foward_ Score	*Memory*	1.077***	2.10	0.865***	0.23	0.866**	1.007
	Orientation	1.043*	1.54	0.901**	0.35	0.885*	0.999
	Judgment	1.027	1.31	0.866***	0.24	0.900*	0.992
	Community	1.074**	2.03	0.946	0.57	0.879*	0.981
	Home	1.074**	2.05	0.982	0.84	0.914	0.985
	Total	1.087***	2.29	0.854***	0.21	0.833***	1.005
Digit_backward_ Span	*Memory*	1.074***	2.03	0.892***	0.32	0.694***	1.001
	Orientation	1.043*	1.52	0.912*	0.40	0.773*	0.972
	Judgment	1.024	1.27	0.903**	0.36	0.682***	1.007
	Community	1.072**	1.99	0.972	0.76	0.791	0.978
	Home	1.074**	2.03	0.994	0.94	0.909	0.979
	Total	1.083***	2.20	0.886***	0.30	0.635***	1.008
Digit_backward_ Score	*Memory*	1.073***	2.03	0.895***	0.33	0.800***	1.002
	Orientation	1.042*	1.50	0.909*	0.39	0.860*	0.980
	Judgment	1.023	1.26	0.905**	0.37	0.795***	1.003
	Community	1.070**	1.97	0.978	0.80	0.836*	0.987
	Home	1.073**	2.01	1.002	1.02	0.909	0.993
	Total	1.082***	2.20	0.889***	0.31	0.765***	1.004
Visual_forward_ Span	*Memory*	1.083***	2.23	0.858***	0.22	0.653***	1.031
	Orientation	1.047*	1.58	0.889**	0.31	0.721*	0.970
	Judgment	1.033	1.38	0.895***	0.23	0.716**	1.035
	Community	1.076**	2.08	0.950	0.59	0.782	0.985
	Home	1.068**	1.93	0.986	0.86	0.942	0.950
	Total	1.091***	2.39	0.844***	0.18	0.701**	1.027
Visual_forward_ score	*Memory*	1.084***	2.23	0.870***	0.25	0.758***	1.002
	Orientation	1.048*	1.60	0.901**	0.35	0.787*	0.980
	Judgment	1.032	1.36	0.875***	0.26	0.794**	1.017
	Community	1.079**	2.14	0.966	0.70	0.751**	0.976

	Home	1.072**	2.01	0.998	0.98	0.876	0.975		
	Total	1.092***	2.41	0.855***	0.21	0.779**	1.004		
Visual_backward span	*Memory*	1.076***	2.10	0.877***	0.27	0.638***	1.013		
	Orientation	1.044*	1.54	0.911*	0.39	0.708*	1.002		
	Judgment	1.026	1.30	0.885***	0.30	0.652***	1.009		
	Community	1.072**	1.99	0.972	0.75	0.660**	0.978		
	Home	1.068***	1.93	1.000	1.00	0.816	0.986		
	Total	1.085***	2.27	0.869***	0.24	0.578***	1.016		
Visual_backward score	*Memory*	1.078***	2.12	0.883***	0.29	0.784***	0.988		
	Orientation	1.045*	1.55	0.911*	0.39	0.831*	0.989		
	Judgment	1.028	1.31	0.885***	0.30	0.810**	0.990		
	Community	1.074**	2.03	0.975	0.77	0.788**	0.976		
	Home	1.069**	1.95	1.001	1.01	0.914	0.985		
	Total	1.087***	2.32	0.876***	0.27	0.743***	0.992		
Verbal Fluency Total 30s	*Memory*	1.061***	1.80	0.887***	0.30	0.861***	0.999		
	Orientation	1.051**	1.65	0.894**	0.33	0.891***	0.996		
	Judgment	1.023	1.26	0.871***	0.25	0.883***	0.991*	0.907***	0.870***
	Community	1.062***	1.82	0.954	0.63	0.874***	0.992		
	Home	1.071***	1.99	0.984	0.85	0.892***	0.997		
	Total	1.067***	1.92	0.886***	0.30	0.830***	0.998		
Verbal Fluency Total 60s	*Memory*	1.059***	1.77	0.890***	0.31	0.888***	1.000		
	Orientation	1.052**	1.67	0.888***	0.30	0.924***	0.996		
	Judgment	1.023	1.25	0.876***	0.27	0.919***	0.995		
	Community	1.063***	1.84	0.951	0.60	0.900***	0.992*	0.934***	0.862***
	Home	1.072***	1.99	0.980	0.82	0.919***	0.995		
	Total	1.066***	1.90	0.889***	0.31	0.861***	1.000		

7.3 Results

Participants had an average of 4.71 years of education (*SD*=4.60). About a quarter (27.8%) had no formal education and only 5% had more than 14 years of education. This is in contrast to the studies reported in Western countries (e.g., the U.S.A.) where older adults who obtained more than 14 years of education are typical, rather than as exceptional in the current Hong Kong samples. However, consistent with previous research (e.g., Jones & Gallo, 2001), dementia, as quantified by CDR-global scores, increased with age, $r = .318$, $p < .001$, but decreased with education, $r = -.340$, $p < .001$.

7.3.1 Effect of Age

Consistent with previous studies, the findings in the logistic regression analyses showed that the chance of developing very mild dementia in CDR-global and subscales increased with age. For example, one year increase in age resulted in 6.8% (i.e., 0.068 x 100) increase in the chance of being diagnosed as 0.5 vs. 0 in CDR-memory subscale (Table 36, "Effect of Age" column). As these effects were not linear, we computed the percentage increase in the odds ratio of 0.5 vs. 0 for each 10-year increase in age. For example, the odds ratio of CDR-memory (from 0 to 0.5) increased by 93% for every 10-year increase in age. Given the substantial effect of age on predicting the CDR status, participants' age was controlled in all of the following analyses.

7.3.2 Effect of Education

The ratios in the "Education" column (Table 36) showed that the chance of being diagnosed as 0.5 vs. 0 tended to be smaller as the participants had more education (years of education increased). For example, one year increase in education led to 11% [i.e., (1 - 0.89) x 100] drop in the chance of being diagnosed as 0.5 vs. 0 in CDR-memory subscale. Also, the ratios in "Education (10-yr)" column showed the chance of being diagnosed as 0.5 vs. 0 for each 10-year

increase of education. The odds ratio of CDR-memory (from 0 to 0.5) decreased by 69% for each 10-year increase of education. The multiplying factor for each 10-year increase of education varied across screening items. It ranged from 0.22 to 1.19 (mean = 0.50) on CDR subscale scores and ranged from 0.18 to 0.42 (mean = 0.28) on CDR global scores. In line with earlier research (e.g., Stern et al., 1994), these figures showed that the ratio of the chance being diagnosed as very mild dementia (CDR = 0.5) vs. healthy old (CDR = 0) as measured by CDR-global or subscales would likely decrease by a multiplying factor of 0.3 to 0.5 for every 10 additional years of education.

Differential screening power of instruments in high and low education groups was not identical across items and tests. According to significant level of the "education × screening item" interaction term and the relative sizes screening-item effects in the high and low education groups, screening items can be classified as follows (see Table 37 for a summary):

a) tasks or items that are useful for screening high education group only — that is, with a significant "education × screening item" interaction *and* a much larger effect of screening items for high education group than for low education group, e.g., MMSE2 (for CDR-community);
b) tasks or items that are useful for screening low education group only — that is, with a significant "education × screening item" interaction *and* a much larger effect of screening items for low education group than for high education group, e.g., MMSE6 (for CDR-global);
c) tasks or items that are not useful as a screening task in general — that is, with the main effect of screening item *and* the "education × screening item" interaction were both nonsignificant, e.g., Sugar-Vinegar in Abstract Thinking (for CDR-global); and
d) tasks or items that are useful as screening task for all education groups — that is, with a significant effect of screening item *and* a non-significant "education × screening item"

interaction, e.g., Naming objects and fingers in ADAS-Cog (for CDR-global).

Table 37

Categories of screening tasks for different education groups

Category	edu × screen task interaction	effect due to Screen tasks (low edu group)	effect due to Screen tasks (high edu group)	Name of Task (in specific CDR subscales)	Targeted Population
A	√	×	√	MMSE2 (community) ADAS-Word Recognition (community, home) ADAD-Ideational Praxis (community) MMSE5 (home)	high education group
	√	√ (smaller)	√ (stronger)	ADAS-Word Recognition (memory, total) ADAS-Delay Recall (judgement, community) ADAS-Word Recall (memory, judgement, community, total) Abstract Thinking Boat-Bus (judgement) Abstract Thinking Lift-Escalator (orientation) Verbal Fluency Total 30s (judgement) Verbal Fluency Total 60s (community)	high education group
	√	×	×	ADAS Commands (home)	not discriminating enough
B	√	√	×	MMSE6 (memory, judgement, home, total)	low education group
	√	√(stronger)	√ (smaller)	MMSE4 (judgement)	low education group
C	×	× (nonsignificant main effect due to task)		ADAS Constructional Praxis (orientation, judgement, community, home) ADAS Naming Objects(orientation, judgement, community, home) Abstract Thinking-sugar-vinegar (total)	not discriminating enough
D	×	√ (significant main effect due to task)		MMSE1 (memory, orientation, community, total) MMSE2 (memory, orientation, home, total) MMSE4 (memory, orientation, community, home, total) MMSE5 (memory, total) ADAS-delay recall (memory, orientation, home, total)	for both high and low education groups

	ADAS-word recall (orientation, home) ADAS-orientation (memory, orientation, community, home, total) ADAS-constructional Praxis (memory, total) ADAS-ideational Praxis (memory, orientation, judgement, total) ADAS-naming objects (memory, total) ADAS-commands (memory, judgement, total) Abstract Thinking Banana-apple (memory, orientation, judgment, community, home, total) Abstract Thinking desk-chair (memory, orientation, judgment, community, home, total) Abstract Thinking-boat-bus (memory, orientation, judgment, community, home, total) Abstract Thinking-sugar-vinegar (orientation, judgment, community, home) Abstract Thinking-ball-orange (memory, orientation, judgment, community, home, total) Abstract Thinking-lift-escalator (memory, judgment, community, home, total) Digit-forward-span (memory, orientation, judgment, community, total) Digit-forward-score (memory, orientation, judgment, community, total) Digit-backward-span (memory, orientation, judgment, total) Digit-backward-score (memory, orientation, judgment, community, total) Visual-forward-span (memory, orientation, judgment, total) Visual-forward-score (memory, orientation, judgment, community, total) Visual-backward-span (memory, orientation, judgment, community, total) Digit-backward-score (memory, orientation, judgment, community, total)

	Verbal Fluency 30s (memory, orientation, community, home, total)
	Verbal Fluency 60s (memory, orientation, judgment, home, total)

$\surd$ = effect significant

7.4 Discussion

Many dementia-screening tasks were developed in countries where the elderly population had much longer education than that in Hong Kong. Thus, these tasks developed for the Western more educated older adults could have a bias against people with low education in Hong Kong (e.g., Koepsell et al., 2008). To our knowledge, this is the first study that investigates the differential power of the screening tasks (down to the item level) among the healthy old (CDR 0) vs. very mild DAT (CDR 0.5) older adults with heterogeneous educational background in Hong Kong. This line of research is of special importance in developing countries like China where a very high proportion of the older adult population is illiterate (about one third, see National Bureau of Statistics of China, 2005; also see *Hong Kong Council of Social Service, 2002*). The results showed that some items were equally effective in discriminating very mild DAT individuals from healthy older adults, irrespective of their education, whereas some had discriminating power only for high education group (see Table 37).

Previous studies showed inconsistent findings as regards the effect of education levels on the ADAS-Cog performance. According to some researchers (e.g., Hannesdottir & Snaedal, 2002; Tsolaki, Fountoulakis, Nakopoulou, Kazis, & Mohs, 1997; Zec et al., 1992), ADAS-Cog was minimally related to the education attainment and was considered as an effective instrument in detecting cognitive impairment, while others (e.g., Doraiswamy et al., 1997; Pena-Casanova, Blesa, Sol, Hernandez, & Aguilar, 1997) might think the contrary. The discrepancies in findings might be due to the different ranges of educational levels or spectrum being involved in these studies. It has also been suggested that the effect of education on cognitive function might have a nonlinear relation in that education started to have a positive impact on cognitive test performance at the low end of the education scale (1 or 2 years or 0 to 6 years of education in different studies, see Liu et al., 2002), but it had a much bigger improvement on cognitive test

performance with more years of education received. This positive benefit of education diminished, however, beyond 12 years of education and possibly reflected a ceiling effect of education (Ardila, 2005; Brucki & Nitrini, 2008).

As indicated in the findings (Table 37), word recognition in ADAS-Cog was only suitable for older adults with high education. It is possible that the word recognition task was so heavily loaded with skills that were heavily drilled or practiced in schools. In fact, in Taiwan, word recognition tests replaced word with pictures in ADAS-Cog recall in order to accommodate the older adult population with low literacy (Lin et al., 2002).

The Verbal Fluency task also indicated a stronger screening power for the group with more education than the group with less education (see Table 37). Thus, the instrument might become biased if one uniform benchmark or assessment criterion is used for all older adults irrespective of their educational level. This finding was consistent with findings in previous studies (Brucki & Rocha, 2004; Kempler, Teng, Dick, Taussig, & Davis, 1998; Kosmidis et al., 2004; Mathuranath et al., 2003; Ratcliff, G. et al., 1998; but see Harrison Buxton, Husain, & Wise, 2000).

Previous studies examining the education effect on WISC suggested that the abstract thinking subtest performance was related to education (Sudo et al., 2010). In congruence, in the present study, some items in the Abstract Thinking task might not be as sensitive to the older adults with lower education as those with higher education. Hence, these tasks might similarly become problematic if one assessment criterion and standard is being used for both high and low educational groups.

Given the high proportion of illiterates in developing countries like China, it is imperative to develop and adopt screening tasks which are equally suitable and discriminating for low and high educational groups Thus, the Clock-face test (Lam et al., 1998), for example, was one of these endeavors designed for Chinese individuals with limited literacy. The test consists of three

parts. In the drawing test, participants are asked to fill inside a circle the numbers of a clock face with the arms indicating a certain position. Then they are asked to read the time from a toy clock in the clock-face reading test. In the last part, the clock-face setting test, participants are asked to set the time of the same toy clock to a certain time of the day. Similarly, the Chinese version of Fuld Object Memory Evaluation (FOME) is another test to be used for older adults with minimal education. In that test, participants are required to identify the objects by touch, vision and hearing instead of to read heavily language intensive materials such as words or sentences. Also, the Chinese version of the Community Screening Instrument for Dementia (CSID, Chan et al., 2003) was an example of a special assessment that combined cognitive assessment and informant-based interview and was independent of education and cultural background.

While more appropriate instruments are to be developed, the present study examined the CDR in both global and subscale levels and the dementia screening tasks down to individual items so as to identify the tasks and items which might be biased for people with minimal education. More caution should be paid during the interpretation of results using these instruments. These findings could also provide insight into the development of *more* sensitive instruments for screening older adults with different educational backgrounds for dementia. Further studies are needed to develop dementia screening tests with sufficient and similar differential power across participants with different educational backgrounds.

Chapter 8 Study Three -- Effects of Education on Very Mild Dementia: Potential Mediators in the Cantonese Mini-Mental State Examination Tasks

8.1 Objectives

Given that education might moderate the decline of cognitive abilities in older adults, it is important to test the relationship between education and risk of DAT in developing countries that have a large population of people with limited literacy (e.g., China). To determine how education might protect older adults from dementia, it is also useful to identify cognitive abilities that might mediate the link between education and the risk of DAT in older adults.

The present study was based on the data collected in a community-based survey collected by Lam et al. (2008). The goal is to identify potential cognitive abilities that mediate the link between education and DAT risk in older adults who are diagnosed as 0 (free from dementia) or 0.5 (the earliest stage of DAT) in Clinical Dementia Rating scale (CDR, Lam et al., 2008). These two groups are most difficult to discriminate (e.g., Storandt, 2008). By drawing community-based samples (N=788) in the Hong Kong older adult population, in which only about 21% have finished their high-school education (Hong Kong Council of Social Service, 2002), the present study investigated how performance in the Cantonese version of the Mini-Mental State Examination (C-MMSE, Chiu et al., 1994) could mediate the link between the education (as quantified by the number of years of education) and dementia (as diagnosed by the CDR scale). In particular, by examining the performance in individual C-MMSE components, the present study identified specific types of cognitive abilities that may serve as beneficial mediators for protecting older adults from dementia.

8.1.1 Education and MMSE

Modified from the original version of MMSE (Folstein et al., 1975; Tombaugh & Mcintyre,

1992), C-MMSE has been used as a preliminary screening tool for DAT, as diagnosed in a CDR scale in Hong Kong (Chiu et al., 1998; Chiu et al., 1994). The fixed-order questions (scores, 30 units in total, indicated in parentheses) are about responding to *when* (year, season, month, day, and date) (5 units) and *where* (county, town, hospital, and floor) (5 units) of the task being conducted, a vocal repetition of three object names (3 units), a serial subtraction beginning from 100 *or* the backward repetition of a 5-digit string (5 units), the recall of the previous three object names (3 units), and several language tasks and motoric tasks: identifying and naming two objects (2 units), repeating a phrase (1 units), a three-stage command of paper folding (3 units), reading aloud a word (1 units) and creating and reading aloud a sentence (1 units), and copying a simple figure (1 units). The C-MMSE takes about 5-10 min. to administer and shows good reliability and validity in clinical applications (Lam et al., 2008; Poon et al., 2008; Tsang & Man, 2006).

Previous studies reported that education has an impact on the MMSE scores during dementia screening (e.g., Anderson et al., 2007; Anthony et al., 1982; Crum, Anthony, Bassett, & Folstein, 1993; Ishizaki et al., 1998; Jones & Gallo, 2001; Jorm, Scott, Henderson, Kay, 1988). While some studies found the impact of education on the total MMSE scores (e.g., Fraser, Singh, & Bennett, 1996), others reported that the effect of education might not be the same for all MMSE components (e.g., O'Connor, Pollitt, Treasure, Brook, & Reiss, 1989). Using the samples from individuals without dementia, Lindeboom, Launer, Schmand, Hooyer and Jonker (1996, see also Weiss, Reed, & Kligman, 1995) reported that MMSE scores were highly correlated with the Dutch version of the National Adult Reading Test, also highlighting that the scores may be sensitive to some specific cognitive abilities (i.e., language in this case). Similar to other versions of MMSE, the total score of C-MMSE is also sensitive to the educational level of the samples (e.g., Lam et al., 2008).

As MMSE is not unidimensional (e.g., Folstein et al., 2001, but see Jones & Gallo, 2000). In

order to pinpoint the cognitive abilities that are the most sensitive to the effect of education on dementia, the present study examined the mediating effect of the scores of the C-MMSE total as well as their components. Previous studies have confirmed there are six components in the MMSE factor structure: orientation to when (MMSE1) and where (MMSE2), repeating three object names (MMSE3), attention (serial subtraction or backward repetition, MMSE4), recalling the previous object names (MMSE5), language and motoric skills (MMSE6) (e.g., Castro-Costa, et al., 2009; Jones & Gallo, 2000; Banos & Franklin, 2002; but see Baekhus, Laake & Engedal, 1992; Commenges et al., 1992). Accordingly, the present study adapted this structure in order to examine the effects of education on dementia mediated through various C-MMSE components. This provides insight on the components that are more vulnerable to education and the cognitive abilities that education could enhance and thus protect individuals from dementia.

8.1.2 Mediation Analyses

For education (X) to affect the CDR (Y) mediated through some C-MMSE components (mediator, M), the following effects had to be demonstrated (MacKinnon, 2008): education on CDR (X → Y); education on C-MMSE (X → M); C-MMSE on CDR (M → Y). Importantly the effect of education on CDR should be substantially decreased in the presence of the effects in the C-MMSE component (X, M → Y). Apart from C-MMSE scores, the CDR subscales were also analyzed to examine the effect of education on each of six subscales: memory, orientation, problem solving/judgment, community affairs, home/hobbies, and personal care. As in all examinations of causal relationships that use correlation data, it is worth noting that an association between the C-MMSE and CDR scores did not demonstrate the direction of causation.

8.2 Methodology

8.2.1 Participants

The data were collected in an epidemiology survey on the prevalence of very mild dementia in Hong Kong (see Lam et al., 2008a, 2008b for details). Among 788 participants (364 males, 424 females), 405 (51.4%) had very mild dementia (CDR=0.5) while 383 (48.6%) were normal control (CDR=0). The mean age was 72.08 (SD = 7.27), ranging from 57 to 96.

8.2.2 Material and Design

Details of the methodology were reported elsewhere (e.g., Lam et al., 2008a, 2008b). It is suffice to say that all participants were community-dwelling older adults and individually assessed by a geriatric psychiatrist and a research assistant. The geriatric psychiatrist assessed them for the presence of dementia using the CDR scale (Morris, 1993; Morris et al., 1988), with CDR 0, 0.5, 1, 2, and 3 representing no dementia, very mild dementia, mild dementia, moderate dementia, and severe dementia, respectively. The CDR was based on a 90-minute semi-structured clinical interview that assessed the participants and obtained information from their family members. This interview assessed potential changes in participants' cognitive and functional abilities in memory, orientation, home and hobbies, judgment and problem solving, community affairs, and personal care relative to previous behavior. The determination of a CDR status for each participant at baseline and at each annual assessment thereafter was made without reference to his/her psychometric performance. The CDR was established for its reliability and validity in Asian populations (e.g., Lim et al., 2007) and demonstrated to be sensitive to the educational background in Hong Kong older adults (e.g., Lam et al., 2008a). It is noteworthy that the participants' CDR status was corroborated with the diagnoses of mild cognitive impairment (see Lam et al., 2008, for the psychometric cutoffs). Under clinical neurologists' direction, the research assistant conducted a series of psychometric tasks including the C-MMSE (Chiu et al., 1994) and Chinese version of the Alzheimer's Disease Assessment Scale Cognitive subscale (Chu et al., 2000). The present study focussed on the C-MMSE total as well as component scores in order to identify the cognitive abilities that are sensitive to the effect of

education on the earliest stage of DAT, as defined by the CDR (i.e., CDR 0.5).

8.2.3 Analyses

Education was measured by the year of education that each participant completed. Dementia was assessed by CDR with its total scores and six subscale scores being used as dependent variables. As the present study focused on the difference between CDR 0 and 0.5 individuals, some items had been dropped in the analyses and low frequency codes were collapsed when necessary. That is, one CDR subscale and one C-MMSE component were non-discriminating and discarded due to ceiling effects [99.7% of the participants score 0 (non-dementia) in CDR-care; 94.3% of participants scored 3 (full score) in C-MMSE3]. In addition, for those participants who scored 0.5 in CDR-total, there were about 1.4%, 0.5%, 3.2%, 0.8%, and 0.6% of them scoring 1 (i.e., mild dementia) in CDR-memory, orientation, judgment, community, and home, respectively. Due to the low proportion, these scores were collapsed with CDR 0.5 in analyses. The pattern of results remained the same when these exceptional cases were taken out, instead of being collapsed into the current dataset. Binary logistic regression analyses were performed with CDR (0 vs. 0.5) being used as a dependent variable.

8.3 Results

8.3.1 Preliminary Analyses

Participants had an average of 4.71 years of education (SD = 4.60). About a quarter of them (27.8%) had no formal education and only 5% had more than 14 years of education. This is in contrast to the studies reported in Western countries (e.g., the U.S.) where older adults who obtained more than 14 years of education are typical, rather than as exceptional as in the current samples in Hong Kong. However, in agreement with previous research (e.g., Jones & Gallo, 2001), dementia, as quantified by CDR-total, increased with age, r=.318, p<.001, but decreased with education, r = -.340, p < .001.

As demonstrated in logistic regression analyses, the CDR-total and three subscale scores increased with age (see Table 38). For example, the odd ratio of CDR-memory was 1.058, indicating that the odd ratio of 0.5 vs. 0 in CDR-memory increased by 5.8% for each additional year in age. As these effects were not linear, we computed the percentage increase in the odd ratio of 0.5 vs. 0 for each 10 years' increase in age. For example, the odd ratio of CDR-memory increased by 77% for every 10 - year increase in age. With an increase in age, CDR-home deteriorated the fastest, followed by CDR-community, memory, and orientation, while the negative effect of age on CDR-judgment being the smallest. Finally, for each 10 - year increase in age, the CDR-total increased (i.e., from 0 to 0.5) by about 90%, replicating the pattern reported in previous studies (e.g., Lam et al., 2008b). The present study also examined how the effect of age on CDR scores (total and subscales) was individually mediated with each of the C-MMSE component scores. The overall pattern was consistent with the results when all C-MMSE component scores were treated as mediators. Since the effect of education is correlated with age, $r = -.257$, $p < .001$, to control for the effect of age in delineating the effect of education, age was used as a covariate and its effect was partialled out in the following analyses.

8.3.2 Mediation Effects

First, the present study examined the direct effects of education on CDR-total and subscale scores. Education was negatively related to CDR-memory, orientation, and judgment only. For example, the odd ratio of education on CDR-memory was 0.87 indicates that for every one more year of education, the ratio of 0.5 vs. 0 in CDR-memory decreased by 13% (odd ratio less than 1 indicating decrease; see Columns 5 and 6 in Table 38). In other words, education has a protective effect on dementia in the domain of memory, orientation, and judgment (e.g., impairment in solving problems, similarities, and differences). The correlations between CDR-total and CDR-subscale were .896, .388, .513, .399, and .330 for memory, orientation, judgment, community, and home, respectively; all $ps<.001$.

Second, the effects of education on C-MMSE component scores (i.e., mediators) was also examined. Among the five component scores, education had direct effects on C-MMSE1, C-MMSE2, C-MMSE4, and C-MMSE6 (b=.245, .145, .312, and .337, respectively, all ps<.001), but not on C-MMSE5 (b=.043, p=.244). There was also a direct effect of education on C-MMSE-total (b=.404, p<.001). This showed that with age being controlled, older adults with more education performed better in C-MMSE1, C-MMSE2, C-MMSE4, C-MMSE6, and C-MMSE-total, but not in C-MMSE5.

Third, this study examined how C-MMSE component scores were associated with the scores in CDR-total and memory, orientation, and judgment subscales (see five rightmost columns in Table 38). The odd ratio being smaller than 1 means that for each unit increase in C-MMSE, the scores in CDR subscales decreased by a certain percentages. The effects of C-MMSE components (other than one value of C-MMSE5, i.e., 1.019) on CDR-total and subscale scores were mostly negative—an increase in C-MMSE component scores means a decrease in the likelihood that participants were rated as CDR 0.5 (very mild DAT) in the CDR-total and most of the subscales in CDR.

Finally, the study examined whether the direct effect of education on scores in CDR-total and subscale would drop when the effect of education was allowed to mediate through C-MMSE components (i.e., statistically, the effect of C-MMSE components was controlled in the analyses of the effect of education on CDR scores). Logistic regressions were conducted for scores in CDR-total and each of five CDR subscales with both education and *all* C-MMSE component scores being simultaneously entered. As shown in Table 38 (Column 6 vs. 8-12) that the effects of education on CDR-memory, orientation, judgment, and total dropped by 6.8% (from -13.0% to -6.2%), 10.4% (from -11.4% to -1.0%), 6.1% (from -13.9% to -7.8%), and 7.3% (from -13.1% to -5.8%), respectively when all C-MMSE component scores were included in the analyses. After taking into account the effects of all C-MMSE component scores, only the direct effect of

education on CDR-judgment remained significant (b=.922, p<.001). Averaged across the odd ratios (for which smaller values mean stronger mediating effects) across CDR subscales in each of Columns 8-12, the order of mediating effects was C-MMSE1 (.607) > C-MMSE2 (.673) > C-MMSE4 (.765) > C-MMSE5 (.772) > C-MMSE6 (.814). The analyses were also repeated by using each of the C-MMSE component scores to examine how the effect of education on CDR scores (total and subscales) was individually mediated with each of the C-MMSE component scores. The results were in line with those when all the C-MMSE component scores were considered simultaneously.

Table 38

Mediation effects of education on CDR-subscales through C-MMSE component scores

CDR	Effects of Age (controlled for years of education and *all* MMSE mediators)			Effects of Education on CDR: Alone (Direct Effect) (controlled for age)		Effects of Education on CDR: Controlling for age and *all* MMSE mediators		Effects of Mediators on CDR (odd ratio)				
	Odd Ratio	% Change per year	% Change per 10 years	Odd Ratio	% Change per Yr of Ed	Odd Ratio	% Change per Yr of Ed	C-MMSE1 (Orientation to when)	C-MMSE2 (Orientation to where)	C-MMSE4 (Attention)	C-MMSE5 (Recall)	C-MMSE6 (Language & Motoric)
Memory	**1.058***	+5.8	+77	**0.870***	-13.0	0.938	-6.2	**0.469***	**0.635***	**0.758***	**0.536***	**0.688***
Orientation	1.053	+5.3	+68	**0.886***	-11.4	0.990	-1.0	**0.370***	**0.486***	**0.720***	1.019	0.964
Judgment	1.032	+3.2	+36	**0.861***	-13.9	**0.922***	-7.8	0.832	0.827	**0.694***	0.965	0.743
Community	**1.059***	+5.9	+78	0.943	-5.7	1.017	+1.7	**0.652***	0.673	0.836	0.768	0.719
Home	**1.071***	+7.1	+99	0.960	-4.0	1.028	+2.8	0.712	0.742	0.819	0.783	0.747
Total[1]	**1.066***	+6.6	+90	**0.869***	-13.1	0.942	-5.8	**0.423***	**0.601***	**0.737***	**0.598***	**0.673***
Total[2]	**1.064***	+6.4	+86	**0.869***	-13.1	0.938	-6.2	---------- CDR-total (odd ratio) = **0.654***----------				

[1] In this analysis, CDR-total is used as the criterion (dependent) variable, while MMSE subscales are used as mediators.

[2] In this analysis, CDR-total is used as the criterion (dependent) variable, while MMSE-total is used as the mediator.

*$p < .001$.

8.4 Discussion

To our knowledge, this is the first study that examines the relationship of education and the severity of dementia, with C-MMSE as the mediator, for healthy older adults with CDR 0 or 0.5 in Hong Kong. The C-MMSE component scores were used as mediators to find out the cognitive abilities underlying the protective effects of education on very mild DAT (as defined by CDR 0.5). The older-adult population in this study had an overall lower level of education, relative to those reported in Western countries, as supported by the mean years of education at 4.7 (*SD*=4.6). Consistent with prior studies (e.g., Caamaño-Isorna et al., 2006), education has a protective effect on dementia in CDR-total. The effect was larger in the subscales of memory, orientation, and judgment. Moreover, in the current dataset, some C-MMSE components were associated with more CDR subscales, including C-MMSE1 (whether participants are aware of the current time), C-MMSE2 (whether participants are aware of the current location), and C-MMSE4 (whether they are able to subtract 7 from 100 continuously *or* repeat a 5-digit string backward after encoding the three object names that would then be recalled). Questions in C-MMSE1 and 2 are related to the older adults' ability to orient in reality, including *when* and *where*. Consistent with this finding, Cushman, Stein and Duffy (2008) used virtual reality simulation techniques and showed that healthy older adults and very mild DAT individuals showed particular difficulty in self-orientation and scene localization tests (see Braekhus, Laake, & Engedal, 1992; Fillenbaum, Heyman, Wilkinson, & Haynes, 1987; Ringman et al., 2007, for similar results, and Mishina et al., 2007, for neurological basis for the effects of dementia on time and place disorientation).

The question in C-MMSE4 may reflect how well participants were able to

rehearse the encoded words (i.e., from C-MMSE3 question) at the time when they need to do another task (e.g., keep subtracting 7 from 100). Participants who were more educated were more likely to balance the attentional resources for these two simultaneous tasks than those who were less educated. This highlights the importance of attentional control in the detection of early-stage DAT. In fact, the sensitivity of the attention component was congruent with previous studies using the original version of MMSE in English (e.g., Jones & Gallo, 2000). Also, Xu et al. (2003) reported that the attention component was the only discriminator of literates vs. illiterates for older adults without dementia in Northwest China. Hence, in addition to episodic memory (e.g., Albert, Moss, Blacker, Tanzi, & McArdle, 2007), attention may also be one of the vulnerable cognitive abilities in the clinical manifestations of early stage of DAT (see Balota et al., 2000; Perry & Hodges, 1999; Tse, Balota, Yap, et al., 2010 for additional evidences).

After controlling for the scores of C-MMSE components, almost all of the effect of education on dementia was eliminated, suggesting that the C-MMSE questions were sensitive to participants' level of education. That is, a better performance in C-MMSE might only reflect better test-taking skills (e.g., Koepsell et al., 2008). Perhaps education helps in the performance of these tests as the test incorporates skills that may be typical of tasks routinely performed at school. Of course, effects due to occupation are usually confounded with those of education and are therefore difficult to untangle. Apart from the elimination of the effect of education on dementia, as quantified by CDR-total scores, after taking the scores of C-MMSE components into account, it is important to consider the effect of C-MMSE components on scores in some specific CDR subscales (i.e., the rightmost columns in Table 38). Note that the smaller the scores in CDR subscales, the larger the relationship between the

performance in C-MMSE components and CDR subscales. First, as the questions in C-MMSE1 and C-MMSE2 inquire about the orientation to date/time and location, it is not surprising that the performance in these questions were associated with CDR-orientation (.370 and .486). Second, the questions in C-MMSE1 and C-MMSE5 require the participants to recall current date/time and what they had just encoded in C-MMSE3 question, respectively, so the performance in these questions were more associated with CDR-memory (.456 and .536). Finally, the question in C-MMSE4 requires the participants to perform multiple tasks with attentional demands. That is, participants need to subtract 7 from 100 repeatedly (or try to repeat the 5-digit string in a backward order), while rehearsing the words that they had been told to remember in C-MMSE3 question. This is closely related to various aspects of abilities as quantified by CDR subscales, including memory, orientation, and judgment. Overall, these results showed that questions in C-MMSE1, C-MMSE2 and C-MMSE4 might tap a wider range of cognitive abilities than those in C-MMSE3, C-MMSE5, and C-MMSE6.

There are some limitations to the interpretation of the results in the present study. Similar to other correlational studies, casual effects are difficult, if not impossible, to be demonstrated unequivocally. On the one hand, education may enhance some types of cognitive processing (e.g., coordinating the attentional resources for two tasks, i.e., C-MMSE4) that may have a life-long protective effect on dementia when people become old. On the other hand, more developed brains could also increase the chance of receiving more education as well as protect people from dementia at old age. Further research is needed to delineate the causal relationship between education and dementia. Because recent studies showed that more education was found to be associated with higher MMSE scores only among those with no or mild pathological

DAT (e.g., Koepsell et al., 2008), future research should include participants with wider range of severity of dementia, instead of only very mild cases as in the current study, in order to further clarify the linkage between education and dementia.

In conclusion, the current study demonstrates the effect of education on mild cases of dementia in the Hong Kong population. Such effect was measured using the C-MMSE task, including orientation to time and location (C-MMSE1 and C-MMSE2) and multi-tasking; that is, participants' abilities in rehearsing the encoded words and continuously subtracting 7 from 100 (or report a 5-digit string backward) (C-MMSE4). Given that most of the questions in C-MMSE are sensitive to education, it is important to take this into account when researchers and clinicians use this task to do the preliminary screening for the sample. Previous research has noted that appropriate cutoff scores should be determined with respect to the educational level of samples (e.g., Kukull et al., 1994, but see Jones & Gallo, 2001). Indeed, several modifications have been done in the MMSE in order to reduce the education bias (e.g., Mungas, Marshall, Weldon, Haan, & Reed, 1996; Molloy & Standish, 1997). Indeed, the calibration of C-MMSE scores has been done in some recent research (e.g., Chan et al., 2010). It is important to modify C-MMSE so as to provide a more suitable preliminary screening measure for older Hong Kong adults who have a relatively low educational level.

Chapter 9 Overall Summary, Discussion, and Conclusion

The whole research in this thesis can be considered as three related studies. In Study One, the overarching research objective is to adapt and examine various attention-related tasks that are potential useful to identify every early DAT participants. Studies Two and Three are supplementary in providing more characteristics on a wide range of instruments as well as delineating possible mediators in the effect of education on dementia.

9.1 Education and CDR

The CDR was developed to stage the severity of dementia. In the present research, the CDR scores were used as a measure to define participants' dementia status of participants. One might argue that the CDR scores of participants is be biased by the levels of their education because the assignment of a CDR is dependent upon the interview with the participant and informant. This issue could be addressed in two ways. On the one hand, as the scoring of the CDR emphasizes change in cognitive ability over time (e.g., one year) from individuals' baseline rather than in their absolute performance at anytime. For example, one question for the informant is to get the information about the recent change of the patient in memory performance in last year (i.e., Question 4 "Has there been some decline in memory during the past year?", Lim, Chong, & Sahadevan, 2007). As such, the assessment will be based on changes of each patient from a given time point onwards. The possible bias will be minimized when changes are being measured. On the other hand, if the CDR were biased against individuals with lower level of education, the majority of the fair instruments would have appeared to be disadvantaged for those with more education.

However, the present study showed no finding of this, suggesting that CDR might be free of educational bias. As a caution, further investigation of the concurrent validity of the CDR is required in the future.

9.2 Utility of Cognitive Tasks

9.2.1 Most discriminating tasks

Importantly, in Study One, two traditional attention task (Stroop task and switching task) and working memory tasks (digit suppression task and Counting Span task) are adapted and examined that would be potentially useful for participants with minimal education. Among these tasks, the pure face/number trials in face-number switching task and the digit span suppression task performed the best in having the best discrimination power for very mild DAT participants. In comparison, the mixed block in the face-number switch task, the number Stroop switching task and the Counting Span task were comparatively less discriminating. While age-related effect was found in Counting Span task performance (decrease performance with increasing age), the task could not discriminate very early DAT from normal aging.

There were a number of potential explanations to the poor performance of these tasks. Firstly, insufficient power might due to the small sample size in this study and relatively less data points for analyses within each degradation condition. Secondly, the type of tasks might be inherently not discriminating enough. Last but not least, the task could be too difficult even for normal aging participants, which lead to the failure of detecting DAT-related effect on performance in these tasks.

In this research, the main purpose was to investigate the utility of the attention-related tasks to discriminate the very mild DAT participants from normal aging adults. Understandably, these tasks are specific to the range of severity in DAT

that the present research is targeting to discriminate. Thus, logically, if more severe DAT participants have to be discriminate, then the tasks have to be even simpler than the present set. In general, task difficulty is an issue for consideration and has to be thoroughly piloted according to the targeted group to be discriminated.

9.2.2 Most discriminating indicators

In Study One, in agreement with emphases in more recent research, the results showed that (i) the parameter tau outperformed the other two parameters (mu, sigma) in ex-Gaussian distribution analyses and was a sensitive indicator to differentiate very mild DAT from normal aging by capturing the positive skewness (thicker tail) of the distribution and (ii) the intraindividual variability, in particular the intraindividual standard deviation (vs. coefficient of variation) were much more sensitive than the traditional mean comparisons in discriminating the very mild DAT. The possible drawback was the insufficient trials (only 24 trials) within each degradation condition, which might be attribute to the unstable estimation of parameter. In this research, 48 trials per condition performed satisfactorily and produced relatively stable and useful parameters. Accuracy in response and mean comparison of response time (e.g., using the sigma parameter) were generally much weaker indexes, if at all useful, in discriminating very early DAT.

9.2.3 Other correlates

In all three studies, in line with the literature, older and less educated participants performed worse than their younger and more educated counterparts. In general, for tasks with many trials in repetition, there was a positive practice effect with slight diminishing of this practice effect along the testing (with more trials).

9.3 Utility of Neuropsychological Tests

9.3.1 Discriminating power and potential bias of popular measures

By examining the performance of popular instruments down to subscale level, Study Two identified instruments that are effective for all kinds of participants with or without formal education, as well as popular measures that may be biased and disadvantage participants with minimal education. More caution should be paid in using these tests for screening purposes particularly when their limitations are not obvious to the examiners.

9.3.2 Mediators in the protective role of education

As education is a protective factor for older adults to prevent them from dementia, it is always interesting to find how education helps. Study 3 attempted to tease out some potential pathways using the CMMSE subscales as indicators of different dimensions of performance. The study shows that the education has a stronger protective effect on memory, orientation and judgment, and possibly through enhancing some specific skills (e.g., C-MMSE1, C-MMSE2, C-MMSE4). Of course, these are correlates rather than definite causal relationships. Further work should include a much wider range of education related activities so as to rule out how many years of education in early life may protect one from dementia in later life.

9.4 Implications and Future Directions

Foremost, to minimize the cultural and educational bias, future work has to employ tests and tasks that are nonverbal and demand little or no academic abilities such as reading and writing. For example, in the present study, given the large number of Chinese old population who have only little or no education, the stimuli used in

original version of switching task (i.e., letter-number pairs) have been replaced with face-number pairs. The nonverbal stimuli used in present study might be more appropriate for people with minimal education or those who are from countries where English is not their mother tongue language.

It might also be necessary for older adults to routinely monitor their cognitive changes. This will help to keep one informed about the potential cognitive function change and abnormal memory loss of individuals who are at risk of developing dementia. Tests and tasks that are sensitive and easy to administer (e.g., computerized version of cognitive tasks) will be very useful for these routine screening.

Moreover, ex-Gaussian distribution analyses could be used as a sensitive indicator of attention deficit especially for people with various educational backgrounds. One intriguing finding is that while the mean of RT in attention tasks was substantially affected by particpants' educational background, the tau value in ex-Gaussian distribution was immune and therefore could discriminate very mild DAT from normal aging.

In addition, early detection has to be triangulated with assessments of cognitive abilities using self-report and performance-based measures. There are a number of neuropsychological tests and assessment procedures that are dependent on interview with the elders and their informants. As previous studies noted, however, self-report measures might be subjective and are prone to be influenced by cultural factor. For example, to save face, people in developing countries are less likely to report the disorder of their elders during interview. On the one hand the patients and their relatives might fail to acknowledge the impairment or disabilities their elderly were experiencing due to their limited knowledge about dementia. People might recognize the symptoms for severe dementia yet fail to perceive or acknowledge the sign at the

early stages of this disease.

In the present research, several participants who reported that they "had no problem with their memory in daily living" were unfortunately to be scored as being very mild dementia (CDR 0.5) and they performed poorly in all four cognitive tasks. This is an example to demonstrate the usefulness ofperformance-based measures as a supplement to the assessment of cognitive functions.

9.5 Conclusion

There are three major conclusions from the present findings. First, the pure number and face trials in face-number switching task and the digit span suppression task perform the best in discriminating very mild DAT from normal aging among Chinese older adults with minimal education. In line with previous studies, the individual standard deviation (vs. coefficient of variation) and the tau value estimated from ex-Gaussian distribution analyses are more discriminating indicators than traditional mean level indicators. Second, neuropsychological tests have been identified that are effective for all kinds of participants with or without formal education. Popular measures that may be biased and disadvantage Chinses participants with minimal education have also been identified. Third, education has a stronger protective effect on memory, orientation and judgment, and possibly through enhancing some specific skills.

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