

Alzheimer's and the Aging Process: Disease or Continuum?

by

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ABSTRACT

This investigation examined whether Dementia of the Alzheimer's type (DAT) and normal aging are two distinct processes (i.e., disease model) or differ only in level of severity, forming one continuum (i.e., continuum model). According to Huppert and Brayne (1994), whether DAT is considered a disease or part of the normal aging process will consequently shape research strategy, prevention, treatment, social attitudes, and social policies. A disease model approach contends that prevention and successful treatment are theoretically possible and efforts should be focused on reducing incidence and prevalence rates; however, a continuum model approach would expand existing services to include those that display milder forms of cognitive impairment in addition to those with severe cognitive impairment. Previous research has provided supporting evidence for both positions, with recent studies lending increasing support to the continuum model; the conclusions drawn by these studies however are limited by small sample sizes and sampling bias. This investigation was conducted with data collected from the Canadian Study of Health and Aging (CSHA), a nationwide, longitudinal study following the changing health status of more than 10,000 elderly Canadians over a 10-year period (1991-2001). Cases selected from the study had classifications of either no cognitive impairment (NCI) or DAT. Data from the first two of three assessments (CSHA-1 & CSHA-2), assessing performance on neuropsychological measures of memory, attention, language, and visuospatial skills were compared between NCI and DAT groups. Four hypotheses were explored: 1) persons with DAT will perform more

poorly on measures of memory, attention, language and visuospatial ability than persons classified as NCI; 2) persons in the early stages of DAT will perform more poorly on measures of attention and language than very old non-demented persons; 3) healthy elderly persons who perform poorly on measures of sustained attention and semantic ability are more likely to develop DAT; and 4) change in cognitive ability over time will appear in different domains in persons with DAT and persons classified as NCI. Using various regression techniques, it was observed that: 1) individuals with DAT performed more poorly in memory, attention, language, and visuospatial domains; 2) individuals in the early stages of DAT performed more poorly on measures of attention and language than very old healthy elderly individuals; 3) poor sustained attention and semantic ability may be associated with DAT onset; and 4) over time, changes in the four domains occur for both the DAT and NCI groups but declines were steeper for the DAT group. The results support a disease model approach to DAT with effects sizes ranging from small to robust. Future considerations discussed include: 1) the opportunity for replication studies to increase the size of the DAT group and the number of measures administered; 2) exploring differences between NCI and DAT groups on specific features of memory, attention, language, and visuospatial abilities, in addition to between these four domains as performed in this investigation; and 3) exploring differences between normal aging and other populations affected by pathological processes similar to DAT, thus extending the DAT disease model to encompass other pathological aging disorders.

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ALZHEIMER'S AND THE AGING PROCESS: DISEASE OR CONTINUUM?

INTRODUCTION

It has been demonstrated that cognitive domains differ with respect to stability across the adult life span; some cognitive domains may show a marked decline during the early stages of adulthood, others do not exhibit decline until the later stages of adulthood, and yet others may remain relatively stable well into old age (Ivnik, Smith, Malec, Petersen, & Tangalos, 1995). Smith and Ivnik (2003) argue that variation in the stability of cognitive areas leads to complications in making a clinical distinction between disease-related and normal cognitive change. They surmise that parallels between disease-related and normal cognitive change make a clear distinction difficult as some aspects of cognitive change are associated with both normal aging and pathological aging. Further compounding matters, according to these researchers, is that cognitive change is insidious in degenerative dementias. Consequently, the absence of a clear distinction has led some researchers to suggest that dementia and normal aging are not discrete processes; in particular, it is debated whether dementia of the Alzheimer's type (DAT) and normal aging have qualitative differences and thus are distinct processes or are simply quantitatively different, differing only in level of severity. The present investigation will seek support for the position that DAT can be distinguished from normal aging processes. The proposed investigation will present evidence for this position by outlining the changes that occur within each cognitive process. Included in the study will be a critical appraisal of the literature supporting both sides of the issue, highlighting the strengths

and limitations of previous research surrounding this debate. Finally, there will be a description of the investigation undertaken.

Background

Historically, pathological aging has been regarded as distinct from normal aging processes. Kral (1962) first made this distinction when he described benign and malignant senescent forgetfulness. Benign senescent forgetfulness was described as those modest changes in memory functions that do not sufficiently interfere with daily life, whereas malignant senescent forgetfulness was that seen as part of a degenerative disease process. According to literature describing normal or healthy aging, some amount of cognitive decline is inevitable. Crook et al. (1986) proposed criteria for Age-Associated Memory Impairment (AAMI) to describe the types of difficulties experienced by individuals aged 50 years or older, specifically complaints and objective measurement of memory loss in the absence of other medical conditions. AAMI however was criticized as a useful construct describing changes that occur during healthy aging, as it relies on comparison of performance between elderly and young people and hence may inadvertently be describing individuals displaying early signs of pathology (Rediess & Caine, 1996). Moreover, the AAMI construct implies that intervention is necessary for the normal aging process (Bamford & Caine, 1988) because this construct views memory as being impaired and therefore needs to be treated. Among the critics, Blackford and La Rue (1989) suggested that AAMI should be further decomposed into Age-Consistent Memory Impairment (ACMI), and Late-Life Forgetfulness (LLF) to distinguish between the types of cognitive decline seen in adults between 50 and 79 years. In both cases, comparisons on memory tests are made with similarly aged persons, but LLF describes

abnormal or pathological changes in memory associated with aging whereas ACMI represents normal aging.

Age-Consistent Memory Impairment

The earliest change in cognitive function associated with aging appears to occur in secondary or long term memory, followed by visuospatial, linguistic, and attentional domains. These changes have been observed in both longitudinal and cross-sectional studies (Hoyer, Rybash, & Roodin, 1999). Specifically, changes in these cognitive domains do not appear to arise solely due to cohort effects that can exaggerate results of cross-sectional studies, or attrition which can underestimate results of longitudinal studies.

Secondary or long-term memory refers to an individual's ability to retain information over a period of time and can be measured with tasks requiring recall or recognition of newly presented information. Deficits in recall, freely recalling large amounts of novel information over a delay, can be seen as early as 50 years of age (Albert, 1988). Performance on recall tasks declines at a more rapid rate than on recognition tasks involving verbal and visual stimuli (Erber, 1974; Howell, 1972). Deficits typically remain even when cues are provided during these tasks (Rabinowitz, 1986), suggesting that poor performance may reflect inadequate encoding (Albert, 1988; Hoyer, Rybash, & Roodin, 1999). Primary or short term memory refers to the immediate repetition of new information and, in contrast, is relatively stable over time. For example, no significant age differences are typically reported on tasks requiring the repetition of words (Talland, 1965).

Visuospatial ability, an individual's ability to manipulate objects and figures in space, shows substantial decline with age. Elderly individuals demonstrate difficulty on production and recognition of two- and three- dimensional figures. Performance on constructional tasks such as the Block Design subtest of the WAIS, identification of incomplete figures, recognition of embedded figures, and figure drawing are poorer for older adults in comparison to younger adults (Albert, 1988).

Some aspects of language processing also decline with age, but are not manifested until relatively late in life. Phonological (Bayles & Kaszniak, 1987), lexical and syntactic (Albert, 1988) knowledge remain relatively intact over time. Phonological knowledge refers to the knowledge of speech sounds and pronunciation (*Webster's universal college dictionary*, 1997). Lexical and syntactic knowledge refers to knowledge of vocabulary and rules of formation of grammatical sentences (*Webster's universal college dictionary*, 1997). A more prominent language-related problem among older individuals occurs with semantic knowledge. Albert (1988) documents that on word retrieval tasks, particularly around 70 years of age, errors in naming ability resulting from semantic association, circumlocutions, and nominalizations increase. Semantic fluency as measured by verbal fluency tasks seems to decline with age as well (Obler & Albert, 1981; Spreen & Benton, 1969).

Attention remains relatively stable in later life. According to Albert (1988), sustained attention, the ability to focus on simple tests (e.g., digit span forward) shows excellent performance into old age, and Albert (1988) reports results from several studies demonstrating less than 1 SD difference in performance for subjects between 20 and 80 years of age. Selective attention on the other hand is somewhat variable (Connelly &

Hasher, 1993; Plude & Hoyer, 1986); poorer performance on tasks of selective attention however may be attributable to perceptual problems rather than actual attentional difficulty (Albert, 1988).

Although decline from previous levels of function are evident, it should be noted that cognitive changes associated with normal aging are subtle and have minimal impact on daily living (Caine, 1993).

Dementia

In contrast, a progressive impairment of cognitive functioning that affects the ability to engage in social, occupational, and daily functions has been identified as dementia. Dementia, a behavioral diagnosis, has been defined in a number of ways but the most commonly used criteria are those described in the American Psychiatric Association's Diagnostic and Statistical Manuals. The third revision of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-III-R) describes a diagnosis of dementia as being appropriate when memory impairment and at least one other area of cognitive disturbance—impairment in abstract thinking, impaired judgment, other disturbances of higher cortical function (e.g., aphasia, apraxia, agnosia), or personality change, is present and these areas of cognitive impairment sufficiently interfere with social and occupational functioning (American Psychiatric Association, 1987). The term dementia is a broad category encompassing many subtypes resulting from a wide range of etiologies; common subtypes include cerebral disorders such as DAT and Pick's disease, vascular disorders such as vascular dementia, and metabolic disorders such as alcoholism (Greenberg, Aminoff, & Simon, 1999). Each dementia subtype presents with particular symptomatology. For example, Lewy body dementia is

characterized by deficits in attention, verbal fluency and visuospatial processing which reflect frontal lobe dysfunction (Salmon & Galasko, 1996). Neuropsychological profiles of dementia subtypes however may exhibit some degree of overlap with one another.

Presently, 8% of Canadians aged 65 and older meet the criteria for dementia (Canadian Study of Health and Aging Working Group, 1994). Within this group, substantially higher rates are reported among those 85 years of age and older; 34.5% of individuals in this age group meet criteria for dementia compared to 2.4% of individuals between 65 and 74 years of age (Canadian Study of Health and Aging Working Group, 1994). 60,150 new cases of dementia are reported to arise each year (21.8 women, 19.1 men per 1,000 non-demented persons; Canadian Study of Health and Aging Working Group, 2000). If prevalence and incidence rates remain constant, it is predicted that the number of Canadians meeting criteria for dementia will rise from 252,600 in 1990, to 592,000 by 2021 (Canadian Study of Health and Aging Working Group, 1994). Among the dementias, DAT is the most prevalent. Approximately 5 percent of Canadians meet the criteria for DAT while approximately 1.5% of Canadians meet criteria for vascular dementia, the second most prevalent form (Canadian Study of Health and Aging Working Group, 1994).

Dementia of the Alzheimer Type (DAT)

According to Grady et al. (1988), patients with mild DAT first experience impairment in secondary memory, followed by impaired attention to complex cognitive sets, deficits in language, and visuospatial abilities. Other findings have supported secondary memory as the most susceptible cognitive area and language ability being more resistant to impairment (Sulkava & Amberla, 1982). Deficits in secondary memory

occur in encoding (Kopelman, 1992) and retrieval (Martin, Brouwers, Cox, & Fedio, 1985) of information; accelerated rates of forgetting are also characteristic of patients with DAT (Larrabee, Youngjohn, & Sudilovsky, 1993), and become increasingly rapid as the disease progresses. Patients demonstrating severe deficits in secondary memory have difficulty recalling over-learned information such as their birthday or occupation (Zec, 1993).

Conflicting results surrounding attentional impairment have been reported, with some studies supporting attentional deficits during the early stages of DAT (Almkvist & Backman, 1993) and others not finding any evidence of impairment in this domain (Lines, Dawson, Preston, Reich, Foster, & Traub, 1991). Almkvist (1996) suggests that these differences can be attributed to the type of tasks administered; performance on tasks placing greater demands on executive ability seem to be more impaired than performance on simpler tasks.

Becker, Huff, Nebes, Holland, and Boller (1988) propose that the language deficit in DAT occurs in two modalities: lexical/semantic ability involved in word production, and syntactic ability. Crossley, D'Arcy, and Rawson (1997) noted that category fluency, while relatively insensitive to the effects of education, age, and gender, may be particularly sensitive to DAT, even during the earliest stages.

Visuospatial impairments have been demonstrated on tasks including drawing (Ober et al., 1991) and on constructional tasks such as the Wechsler Adult Intelligence Scale Block Design subtest (Almkvist & Backman, 1993). Persons with DAT show impairment in attention to details, accuracy of details, and poor configuration of objects (Ober et al., 1991).

As DAT progresses, the severity of impairment increases in the areas of memory, attention, language, and visuospatial ability, impeding independent living (Almkvist, 1996).

Discontinuity or Continuity?

The similarities seen between the cognitive areas affected in normal aging and DAT has led researchers to question whether DAT and normal aging are really distinct, or lie along a continuum of severity, with DAT exhibiting more severe symptoms than is evident in normal aging. Consequently, researchers have been divided into two schools of thought: 1) those advocating a disease model approach to DAT, and 2) those advocating a continuum model approach to DAT.

The foundation of the disease model rests on several tenets. According to Huppert and Brayne (1994), support for the disease model demands identification of qualitative differences between disease processes and normal processes; they also advocate that disease be identified through demonstration of bimodality, that the condition labeled as 'diseased' should display a separate distribution of symptoms (i.e., discontinuous) from what is considered typical when observed in a large community. Conversely, in a continuum model approach, DAT and normal aging are considered to differ only in range of severity, and would be represented by a unimodal distribution of symptoms (i.e., continuous).

Debates over whether disorders present as continuous versus discontinuous are not unique to DAT. Studies in depression provide evidence supporting opposing views on whether depression is a homogeneous, discrete entity or represents a broad category representing a spectrum of disorders (Fleiss, 1972; Kendel & Brockington, 1980; Parker

& Hadzi-Pavlovic, 1993). Critics of depression representing a spectrum of disorders posit that studies that do not find evidence supporting separate forms of depression result from inclusion of variables that are not characteristic of a particular form of depression and do not distinguish between groups in the analysis, thus reflecting and building towards an overriding severity dimension (Parker & Hadzi-Pavlovic, 1993).

Similarly, in the learning disabilities literature, the issue as to whether dyslexia represents an extreme form of reading ability, or whether it represents a distinct form of reading ability is still debated. Yule, Rutter, Berger, and Thompson (1974) demonstrated that, after administration of tests of non-verbal intelligence and reading, the number of children with reading difficulties was greater than predicted from the normal distribution of reading ability, creating a "hump" at the lower end of the normal distribution. Others however, were unable to replicate this finding (Dobbins, 1988). The conflicting results found in dyslexia studies may arise as a consequence of the focus on the lower end of the normal distribution. Tails of distributions are especially sensitive to small effects as the number of observations is low compared to the number of observations in the middle of the distribution (Shaywitz, Escobar, Shaywitz, Fletcher, & Makuch, 1992). Therefore, the presence or absence of a "hump" could be a reflection of certain characteristics of the study undertaken (Shaywitz, Escobar, Shaywitz, Fletcher, & Makuch, 1992); methodological issues such as administration of measures with ceiling effects may increase the number of observations at the lower end of the distribution (Shaywitz, Escobar, Shaywitz, Fletcher, & Makuch, 1992).

Differences in study design and sample characteristics may have led to the conflicting results reported in the literature in the areas of dyslexia and depression.

Similarly, study design and sample characteristics correspondingly may be responsible for some of the results that support a disease or continuum model of DAT. This will be explored in the following sections.

DAT—Disease Model

Advocates of the disease model assert that DAT has been demonstrated to be best described by the disease model. Brinkman, Lergen Jr., Gerganoff, and Pomara (1983) differentiated performance on the Wechsler Memory Scale-Revised (WMS-R) of 25 participants with DAT and 31 normal participants matched with the DAT participants for age and education. The normal group performed significantly better on all WMS-R variables, and patients with probable DAT showed particular deficits in semantic and figural memory. In further support of the disease model, delayed recall scores from the DAT group were found to be bimodally distributed; these patients either performed well or performed poorly, suggesting that performance may represent a critical stage of worsening of delayed recall processes as the disease progresses.

Carlesimo et al. (1998) examined the relationship between memory changes, physiological aging, and memory impairment resulting from DAT, and attempted to determine the point at which memory deficit occurs in the course of the disease. They assert that sampling from the very old population is appropriate in order to determine whether brain degeneration in DAT is an anticipation of what occurs in physiological aging or is fundamentally different from normal aging; if the continuum hypothesis is true, and DAT is simply an exaggerated form of normal aging, younger persons in the mild stage of DAT and non-demented persons in the very old population should display a similar level of performance on neuropsychological tests. Participants, screened for

history of severe head trauma, alcoholism, serious and prolonged psychiatric illness, neurological diseases, and major systemic medical illnesses (n=124) were classified in the following groups: Probable DAT (N=29, 55-75yrs), Elderly (N=37, matched for age and years of education), Young (N=39, 20-40yrs), and Very Old (N=19, 80-93yrs). All participants were administered a neuropsychological test battery assessing short term, implicit, episodic, and semantic memory. The relationship between memory change occurring as function of physiological aging and memory impairment in DAT assumed three different patterns; 1) a memory function unaffected by both aging and dementia, 2) a progressive deterioration in performance from young, to healthy elderly, to DAT, 3) a memory function affected by both aging and DAT such that performance declines occur across all age groups and in individuals with DAT with greater declines demonstrated by individuals with DAT. They concluded that different aspects of memory function can either support the continuity or discontinuity theories. However, pertinent to the present investigation is the performance of the DAT group on Digit Span, the measure of short term memory and tasks measuring verbal episodic memory. The DAT group had severe difficulty reproducing span sequences in reverse order, and failed to utilize the semantic relatedness of items on verbal memory tasks to improve retention. This led the researchers to conclude that these deficits appear early and should be considered a direct result of pathological changes in the disease.

The implications of considering DAT from the perspective of the disease model, or discontinuous approach have some distinct advantages. By regarding DAT as distinct from normal aging, prediction of the clinical course and treatment options could be better articulated. Distinguishing between processes allows for identification of specific

etiological factors, and facilitates prediction of the clinical course of the pathological process. Accurate prediction of the clinical course would focus treatment plans to consider only the most appropriate forms of treatment such as pharmacological interventions, for persons in this group (Fleiss, 1972). A disease model is also advantageous as it suggests that theoretically, DAT prevention and successful treatment is possible (Goodwin, 1991). However, to date, results supporting the discontinuous approach to DAT were obtained from small samples; small samples may not have sufficient statistical power to detect significant effects which may inadvertently lead to spurious results.

DAT—Continuum Model

Other studies have challenged the idea that DAT is best described by the disease model and report results that are more consistent with a continuous model of DAT. The basic tenet of the continuum model is that DAT and normal aging differ in levels of severity. The strongest evidence in favour of this model is the lack of qualitative differences that have been found between DAT and normal aging. Brayne and Calloway (1988) administered a comprehensive cognitive and psychiatric assessment to a sample of elderly women, aged 70 to 79 years, from both community and institutional settings; they found that frequency distributions of cognitive function and behaviour were highly skewed, but unimodal and smooth. Similarly, Brayne, Gill, Paykel, Huppert, and O'Connor (1995), after a two-wave administration of the Mini-Mental State Examination (MMSE) to a large sample of subjects aged 75 years and older who did not receive a diagnosis of dementia during the first wave, showed that MMSE scores were normally

distributed; score distribution remained unaltered following exclusion of subjects with physical, visual or hearing disabilities.

An advantage to adopting the continuous approach is the implication that information on etiology, prognosis, and treatment is best provided by a person's position on that continuum rather than assignment to an arbitrary 'disease' category (Fleiss, 1972); in this manner, greater benefits will be acquired from treatment specifically tailored according to individual needs. Consequently, considering etiology, prognosis, and treatment for each individual may be more costly and time consuming, particularly for those bearing the financial responsibility.

Despite the results reported that are consistent with the continuum model, further evidence challenges the adoption of the continuum approach. Studies in support of the continuum approach report results that are potentially influenced by confounding factors. These studies may be affected by sampling bias. Many of the apparently healthy individuals used in controlled studies may have sub-clinical DAT, increasing the likelihood that unimodal results would be found (Hodges, 1994). For example, control subjects with mild aphasia may produce lower scores on recall tasks than otherwise healthy subjects, causing the control group to appear to have more deficits and be less distinguishable from the DAT group (Miller, 1971). Similarly, Brayne and Calloway (1988) who attempted to represent a "full range of possible function", likely included individuals with confounding factors such as other medical or psychological conditions that may affect cognitive function and ultimately mask bimodality. Control subjects may have concurrent medical or psychological conditions with possible effects on cognitive abilities thus underestimating the performance of the control group and causing them to

appear more closely in ability to the impaired group. Alternatively, results reported by Brayne, Gill, Paykel, Huppert, and O'Connor (1995) appear biased toward higher MMSE scores. The group of individuals examined in this study was healthier and thus not representative of the elderly population as most demented individuals were initially excluded and considerable attrition occurred due to the age of the population studied (75+ years). This would reduce the likelihood of finding bimodal results as differences in performance between the cognitively impaired and unimpaired individuals would appear smaller due to the presence of fewer individuals actually being impaired. In addition to excluding the most demented individuals by sampling from very old healthy individuals, Forbes and Hirdes (1993) would also argue that the sampling from the very old population is not appropriate as the very old population is not representative of the general population; very old participants tend to have lower MMSE scores than younger participants, and thus would further increase the likelihood of producing unimodal results.

The studies supporting a continuum model may have been affected by inadequate measurement techniques. Studies that have reported findings of unimodal, skewed distributions suggesting a continuous relationship between entities, likely are reporting distributions composed of aggregate distributions. Roth (1994) argued that the unimodal distribution discovered by Brayne and Calloway (1988) is the result of using a measure that is too crude to quantify differences in mental competence among severely demented individuals. Their results, he states, are based on the assumption that the correlation between the Blessed-Roth dementia scale and DAT-type changes is linear, which he asserts is curvilinear. Using a Poisson model, Reischies, Schaub, and Schlattmann (1996)

were able to decompose the unimodal distribution of Brayne and Calloway (1988) showing that a two component Poisson model best fit their data. The studies supporting the continuum model on reanalysis actually support the disease model.

Implications of Discontinuous versus Continuous Models

Whether DAT is distinct from or part of the normal aging process has implications for research strategy, prevention, treatment, social attitudes, and social policies. Huppert and Brayne (1994) contend that if the continuum model is valid, then research should examine representative samples of elderly people, and should be directed towards prevention rather than treatment, as treatment of the entire elderly population would be impractical. They further assert that adoption of a continuum model of DAT would shift the focus of service provision, prevention, and treatment from being restricted to the extreme lower end of the continuum to now include those in the middle who show milder signs of cognitive impairment. However, there exist potential dangers of regarding DAT as simply a manifestation of an aging brain. This may encourage a lack of respect for elderly, discourage expansion of federal funding for research on aging related issues, and potentially encourage a sense of fatalism and an avoidance of health-promoting activities among the elderly (Goodwin, 1991). Alternatively, if the disease model is valid, the possibility exists that striving to identify age related diseases may initiate a preoccupation with successful aging, potentially leading to devaluation and neglect of the frail elderly (Forbes & Hirdes, 1993).

Based on the review of the literature, there is a compelling argument for the disease model approach to DAT. In addition to qualitative differences that have been discovered that distinguish between DAT and normal aging (e.g., semantic memory,

figural memory), the continuum model has been subject to many criticisms. These criticisms primarily assert that poor measures and sample selection are masking underlying current evidence supporting the disease model.

In addition, failure to demonstrate bimodality does not automatically discount the existence of multiple separate distributions (Dunn, Sham, & Hand, 1993; Fleiss, 1972; Kendell & Brockington, 1980), despite the assertion by Huppert and Brayne (1994) that the disease model be substantiated by demonstration of bimodally distributed variables. Failure to obtain an overt bimodal distribution may be due to high overlap of cognitive abilities between healthy older individuals and persons with mild DAT. As stated previously, this may be due in part to sampling from the very old population. This might be improved by employing measures with high discriminative validity (Reischies et al., 1996). Although Forbes and Hirdes (1993) argue that the very old population is not representative of the general population, it is relevant to investigate a wide age range, especially subjects over 80 years of age, in view of the fact that the prevalence of DAT increases with age, increasing the probability of detecting distinctions from normal aging (Reischies, Schaub, & Schlattmann, 1996).

Moreover, bimodality could be obscured by persons experiencing certain medical and/or psychiatric conditions. Cognitive decline accompanying certain medical and psychiatric problems may be the consequence of these problems and not attributable to DAT (Bassett & Folstein, 1991), giving DAT the appearance of continuity with normal aging. Depressed individuals in particular perform more poorly on memory tests than non-depressed healthy individuals (Niederehe, 1986). The presence of these medical or psychiatric conditions may mask co-existing or preclinical DAT (Huppert, 1994). It is

important to make a distinction between individuals with normal decline and individuals with cognitive decline that may be linked to other conditions as, although the latter group may be at greater risk of developing DAT, the decline may not be the type that will develop into DAT. Due to this uncertainty, individuals with cognitive decline accompanying certain medical conditions have appropriately been excluded from previous studies.

The Investigation

If DAT is distinct from normal aging, neuropsychological profiles of DAT and healthy elderly individuals will differ both in cross-section and longitudinally. Therefore this investigation intended to explore the following hypotheses:

Cross sectional- 1) In accordance with neuropsychological characteristics described in the literature, at any one period in time, persons with DAT will perform more poorly on measures of secondary memory, attention, language, and visuospatial ability than non-demented elderly persons of a similar background.

2) Comparison of very old, non-demented persons and younger individuals with mild DAT on measures of attention and language are predicted to reveal differences in performance between the two groups according to the theory put forward by Carlesimo et al. (1998). If the discontinuity hypothesis is true, a discontinuation of performance on neuropsychological tests (i.e., difference in mean performance) from healthy elderly, very old healthy elderly, to individuals with DAT should be demonstrated. Conversely, if a continuum model is more appropriate, then very old, non-demented persons and persons with mild DAT will perform similarly on cognitive tests. Reportedly, very little difference in performance on attention tasks occurs between young adults and older

individuals (Albert, 1988); it so follows that performance of very old healthy individuals on these tasks is likely to be superior to that of individuals with DAT.

Longitudinal- 3) Cognitive domains that distinguish between healthy elderly persons and persons with DAT may predict which healthy individuals will further decline to DAT.

Individuals that show poorer performance on measures of sustained attention and semantic ability involved in word production, with time, are predicted to develop DAT as decline in these areas, if present, only occurs later in normal aging (Albert, 1988).

4) Over time, not only will persons with DAT perform more poorly on cognitive tests, but the change in cognitive ability over time will appear in different domains than for healthy elderly persons. In relation to individuals with DAT, healthy elderly persons are expected to show some decline in secondary memory and visuospatial ability, but modest if any decline in cognitive domains of language and attention later in life, domains that have been demonstrated to be more stable (Albert, 1988).

METHODS

Canadian Study of Health and Aging—Procedure

The Canadian Study of Health and Aging (CSHA) is a national, longitudinal study of the epidemiology of dementia in Canada, and provides estimates of prevalence, and incidence for Alzheimer's disease and dementia (Canadian Study of Health and Aging Working Group, 1994, 2000). The CSHA involves 10,263 people aged 65 or over, seen in 18 study centres across Canada; representative samples were drawn from the community and from institutions, and participants were assessed at 5-year intervals (CSHA-1, 1991; CSHA-2, 1996; CSHA-3, 2001). Equal sized samples were selected across the five geographic regions across Canada (i.e, British Columbia, the Prairie provinces, Ontario, Quebec, the Atlantic region) and were stratified by age (i.e., 65-74, 75-84, 85+) and gender. To obtain comparable samples sizes across strata and to compensate for underrepresented age groups in the general population, the sampling ratios for the 85+ age group and the 75-84 age group were 2.5 and 2 times greater that of the 65-74 age group, respectively.

Subjects from the community received a screening interview that included administration of the Modified Mini-Mental State Examination (3MS; Teng & Chui, 1987), collection of demographic information and a health status questionnaire. Those scoring below 78 on the 3MS, a random sample of those scoring 78 and above, those who could not be screened, and all institutionalized subjects were invited for a clinical assessment. The clinical assessment consisted of a nurse's evaluation, a physical examination, laboratory blood work, and a neuropsychological assessment.

Subsequently, a case conference was held to obtain a consensus decision on the

diagnosis; criteria and differential diagnoses for dementia and DAT were based on the third revision of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-III-R; American Psychological Association, 1987) and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann et al., 1984).

Differential diagnosis for DAT included diagnoses of probable and possible DAT. Probable DAT is defined by a diagnosis of dementia established by a clinical examination, including a progressive decline in memory and deficits in two or more areas of cognition (McKhann et al., 1984); the diagnosis must be made in the absence of other conditions that could account for the progressive decline in memory and other areas of cognition (McKhann et al., 1984). Similarly, possible DAT is defined by a diagnosis of dementia established by a clinical examination, including a progressive decline in memory and deficits in two or more areas of cognition (McKhann et al., 1984); however, individuals may present with variations in onset, presentation or clinical course of dementia, and a diagnosis may be made in the presence of other conditions that are sufficient to produce dementia but are not considered to be the cause of the dementia (McKhann et al., 1984). The tenth edition of the International Classification of Diseases (ICD-10) was used to identify depression and other specific dementias. Participants were classified with No Cognitive Impairment (NCI) or Cognitive Impairment No Dementia (CIND) if they did not meet the DSM-III-R criteria for dementia. This distinction was derived from clinical judgment and without application of any specific diagnostic criteria. CIND diagnoses were made based on the clinical impression that some form of cognitive impairment was present, but did not warrant a diagnosis of dementia (Tuokko et al.,

2003). It is from the CSHA study that data for a particular set of participants were chosen to investigate the proposed hypotheses.

Participants

Cases for the investigation were selected based on the following criteria: 1) Completion of a neuropsychological assessment at CSHA-1, in English; 2) classification of NCI, possible DAT, or probable DAT following the CSHA-1 case conference; and 3) absence of a co-existing condition that may have influenced the development or course of DAT (Table 1) as determined by the examining physician.

Table 1

The Number of Cases with Co-existing Diseases Contributing to Dementia

| Co-existing disease contributing to dementia | Number of Cases |
|--|-----------------|
| Hypothyroidism | 8 |
| B12 deficiency | 10 |
| Alcoholism | 19 |
| Other | 63 |

The criteria yielded 682 cases classified as NCI ($N = 570$) and DAT ($N = 112$) at CSHA-1. Individuals identified with either possible or probable DAT were selected to maximize the sample size in the DAT group (see McKhann et al., 1984 for a description). Co-existing conditions that were identified by the examining physician in these groups as not contributing to DAT are listed in Table 2.

Table 2

Frequency of Various Types of Diagnoses that Physicians Identified as not Influencing Dementia Diagnoses

| Disease | Number of Diagnoses |
|---|---------------------|
| No coexisting disease | 1600 |
| Infectious and parasitic diseases (e.g., tuberculosis; colitis; gastroenteritis) | 12 |
| Neoplasms (e.g., malignant neoplasm of the respiratory & intrathoracic organs; benign neoplasm of the skin) | 49 |
| Endocrine, nutritional & metabolic diseases, & immunity disorders (e.g., disorders of the thyroid gland; disorders of lipid metabolism; gout) | 107 |
| Diseases of the blood & blood-forming organs (e.g., iron deficiency anemias; other deficiency anemias) | 15 |
| Mental disorders (e.g., psychoses; neurotic disorders; independent abuse of drugs) | 47 |
| Diseases of the nervous system & sense organs (e.g., Parkinson's disease; epilepsy; glaucoma) | 152 |
| Diseases of the circulatory system (e.g., chronic rheumatic heart disease; cerebrovascular disease; atherosclerosis) | 378 |
| Diseases of the respiratory system (e.g., chronic obstructive pulmonary disease & allied conditions; diseases of the upper respiratory tract) | 51 |
| Diseases of the digestive system (e.g., diseases of the esophagus; duodenal ulcer; hernia of abdominal cavity) | 46 |
| Diseases of the genitourinary system (e.g., chronic renal failure; hyperplasia of prostate; inflammatory diseases of prostate) | 34 |
| Diseases of the skin & subcutaneous tissue (e.g., inflammatory conditions of skin & subcutaneous tissue) | 13 |
| Diseases of musculoskeletal system & connective tissue (e.g., rheumatoid arthritis & other inflammatory polyarthropathies; intervertebral disc disorders; rheumatism) | 159 |
| Congenital anomalies (e.g., congenital anomalies of the heart) | 2 |
| Symptoms, signs & ill-defined conditions (e.g., syncope & collapse; non-specific abnormal findings; general symptoms) | 33 |
| Injury & poisoning (e.g., fractures; poison by drugs, medicinal & biological substances; dislocation) | 30 |
| Total | 2728 |

Note. Clinicians were permitted to provide a maximum of four diagnoses per individual.

The cases selected from CSHA-1 consisted of more females (63.2% vs. 36.8% males), and primarily resided in the community (81.5% vs. 18.5% in institutions).

Independent sample t-tests were performed to compare NCI and DAT groups on age and education (Table 3). The DAT group was significantly older than the NCI group

$[t(680) = -6.34, p < .05]$ and had fewer years of education than the NCI group $[t(675) = 4.01, p < .05]$; gender composition did not differ between groups $[\chi^2(1, N = 682) = 3.91, p = .05]$.

Table 3

Age and Education of NCI and DAT Groups at CSHA-1 & 2

| | CSHA-1 | | CSHA-2 | |
|--------------------|-----------------------|-----------------------|-----------------------|---------------------|
| | NCI | DAT | NCI | DAT |
| | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) |
| Age | N = 570 79.2 (6.7) | N = 112 83.6 (6.2) | N = 160 81.6 (5.8) | N = 9 86.7 (3.4) |
| Years of Education | N = 566 10.4 (3.8) | N = 111 8.8 (3.5) | N = 166 11.3 (3.9) | N = 12 8.7 (4.0) |

NCI and DAT groups at CSHA-2 consisted of all persons classified as NCI that met selection criteria at CSHA-1 who were alive at the beginning of the second wave of assessments ($N = 451$); 282 individuals completed the neuropsychological assessment at CSHA-2. The individuals that underwent neuropsychological assessment primarily resided in the community (80.1% vs. 7.8% in institutions, 12.1% unknown). Independent sample t-tests showed that the DAT group was significantly older than the NCI group $[t(167) = -2.58, p < .05]$ and had fewer years of education than the NCI group $[t(176) = 2.26, p < .05]$. Although most individuals at CSHA-2 were female (60.6% vs. 39.4% males), groups did not differ in gender composition $[\chi^2(1, N = 178) = 0.41, p = .52]$.

Measures

The measures selected for use in this study were administered at both CSHA-1 and CSHA-2 (Table 4). Measures of memory, attention, language, and visuospatial ability were selected so that comparisons could be made between groups across time intervals.

Table 4

Measures and Scores Accessed from CSHA-1 & 2

| | Measure | Scores |
|--------------|--|---|
| Memory | Buschke Cued Recall | Delayed free recall (max=12) |
| | Wechsler Memory Scale—Information Subtest | Total (max=6) |
| | Rey Auditory Verbal Learning Test | A6 (max=15) True Positive Recognition (max=15) |
| | Benton Visual Retention Test Revised—Multiple Choice Version | Correct (max=15) |
| Attention | Wechsler Adult Intelligence Scale Revised—Digit Symbol | Total (max=93) |
| Language | Wechsler Adult Intelligence Scale Revised—Similarities | Total (max=14) |
| | Word Fluency | Total (max=64) |
| | Animal Naming | Total (max=30) |
| Visuospatial | Wechsler Adult Intelligence Scale Revised—Block Design | Total (max=30) |

Note. From "Development and validation of a demographic correction system for neuropsychological measures used in the Canadian study of health and aging," by H. Tuokko and T.S. Woodward, 1996, *Journal of Clinical and Experimental Neuropsychology*, 18, p. 491. Copyright 1996 by Swets & Zeitlinger. Adapted with permission.

Memory

Buschke Cued Recall (Buschke, 1984): This test provides a measure of verbal memory.

Individuals are presented with a sheet of pictures of common objects. They are required to search for, point to, and name the objects that correspond with the semantic category provided (e.g., "Which one is a piece of clothing?"). Individuals are prompted to provide the correct response if there is no response (e.g., "What is that called?"), or an inaccurate response, such as a synonym, is given (e.g., "What is another name for that object?"); incorrect responses are automatically corrected (e.g., "We call that a sweater").

Following a 60-second delay, during which individuals are asked to count backward from 100, individuals are required to recall the previously presented objects; category cues are provided for objects not freely recalled (e.g. "One of the pictures was of an animal");

O'Connell & Tuokko, 2002). The same pictures are presented again if individuals respond incorrectly or fail to respond to the category cue (O'Connell & Tuokko, 2002). The sequence (i.e., recall of the pictures, presentation of category cues for objects not freely recalled and subsequent presentation of pictures following incorrect or no response to the category cue) is repeated for a total of three learning trials (Kristjansson, 1996). Individuals are not informed to recall the pictures over a 15 minute delay. Subsequent to the delay, individuals are required to recall the previously presented pictures (O'Connell & Tuokko, 2002); as in the learning trials, individuals are presented with category cues for objects not freely recalled. This test yields 5 measures of performance (Kristjansson, 1996): 1) Immediate recall (i.e., total number of words freely recalled on trial 1); 2) Retrieval (i.e., sum of the words freely recalled over the three learning trials); 3) acquisition (i.e., sum of words from free recall and cued recall over the three learning trials); 4) delayed free recall (i.e., total number of words freely recalled following 15 minute delay); and 5) retention (i.e., sum of words from delayed free recall and cued recall). Analyses were conducted using the raw scores of the delayed free recall trial. This performance measure was selected because free recall of information over a delay involves the retrieval information from secondary memory (Albert, 1988).

Wechsler Memory Scale-Information Subtest (WMS-I; Wechsler, 1981): This test is a measure of rote memory, the ability to freely recall information that individuals are likely to have been exposed to repeatedly. Individuals are asked questions concerning personal facts (e.g., "When were you born?") and government officials (e.g., "Who is the prime

minister of Canada"; Spreen & Strauss, 1998). Analyses were conducted using the total raw score.

Rey Auditory Verbal Learning Test (RAVLT; Rey, 1964): This test assesses immediate memory span, new learning, susceptibility to interference, and recognition memory (Spreen & Strauss, 1998). In each of five consecutive learning trials, individuals are presented with a 15-word list (List A) then asked to recall as many of the words as possible. Subsequently, an interference list of 15 words is presented (List B), and individuals are asked to recall as many words from the new list of words as possible. Immediately after the free recall test of List B, without additional presentations of the word list, individuals are asked to freely recall the words from List A (Kristjansson, 1996). A recognition test is completed following the free recall test of List A; the recognition task requires individuals to identify the words from List A from a list of 30 words presented orally (Kristjansson, 1996). The following measures of performance are obtained (Kristjansson, 1996): 1) free recall trials A1-A5 (i.e., number of words freely recalled on each learning trial of List A); 2) free recall B1 (i.e., total number of words freely recalled from List B); 3) delayed free recall A6 (i.e., total number of words freely recalled from List A after free recall of List B); 4) true positive recognition (i.e., the number of words correctly identified from List A); and 5) true negative recognition (i.e., the number of new words correctly identified as not belonging to List A).

Analyses were conducted using the raw scores of 1) the delayed free recall trial A6 and 2) true positive recognition, the number of correctly identified targets. These performance measures were selected as recall and recognition of information, two measures of secondary memory, have been demonstrated to distinguish between NCI and DAT. Non-

demented elderly individuals have difficulty with encoding information and thus have better performance on recognition than recall tasks (Albert, 1988; Erber, 1974); individuals with DAT have difficulty encoding and retrieving information (Kopelman, 1992; Martin, Brouwers, Cox, & Fedio, 1985) and thus do not show differences in performance on recall and recognition tasks.

Benton Visual Retention Test Revised—Multiple Choice Version (BVRTR-MC; Benton, 1974): This test measures visual perception and memory (Spreeen & Strauss, 1998).

Individuals are presented with 15 cards depicting one to three geometric figures, and are instructed to maintain their focus on each card that is exposed for 10 seconds, after which it is removed (Spreeen & Strauss, 1998). Immediately following presentation of each card, individuals are presented with a multiple-choice card depicting four similar geometric figures, and are asked to identify the figure that is identical to the figure previously shown (Spreeen & Strauss, 1998); incorrect, mirror image choices are recorded (Kristjansson, 1996). The test is discontinued if individuals miss 6 out of the last 8 items (Kristjansson, 1996). The following measures of performance are obtained (Kristjansson, 1996): 1) Total correct responses; and 2) The number of mirror-image choices. Analyses were conducted using the raw scores of the total number of correct responses. This performance measure was selected as the total number of correct responses is a measure most commonly employed in other studies to measure recognition.

Attention

Wechsler Adult Intelligent Scale Revised—Digit Symbol Subtest (WAIS R—DS; Wechsler, 1981): This test is a measure of sustained attention, examining an individual's

visual scanning and tracking abilities (Sattler, 2001). Individuals are provided with a sheet consisting of rows of blank squares with the numbers 1 through 9 randomly printed in a box above each square; a key with the numbers 1 through 9 is printed at the top of the page, each number associated with a particular symbol (Spreeen & Strauss, 1998). Individuals are required to fill in the blanks with the appropriate symbol as quickly as possible, in the order as they appear on the sheet, up to a maximum time of 90 seconds (Kristjansson, 1996). Analyses were conducted using the total raw score.

Language

Wechsler Adult Intelligence Scale Revised—Similarities Subtest, Short Form (WAIS R-S; Wechsler, 1981): This test is a measure of verbal concept formation. Individuals are presented with two words and asked how they are alike (Spreeen & Strauss, 1998). This requires individuals to find relationships between objects and events, organizing information into meaningful groups (Sattler, 2001). An example of 2-point responses (i.e., any general classification that is primarily important to each member of the pair) is provided on the first item if individuals provide a 1-point response (i.e., less pertinent, general classifications of both members of the pair; a specific property or function that is common to both members of the pair and represents a relevant similarity; Kristjansson, 1996). The test is discontinued after three consecutive 0-point responses (e.g., properties specific to each member of the pair; incorrect or irrelevant generalizations; clearly incorrect responses). The test was abbreviated from the original version (Satz & Mogel, 1962) by administration of the odd numbered questions. Analyses were conducted using the total raw score.

Word Fluency (Spreen & Benton, 1977): This test evaluates the spontaneous production of words in a limited amount of time (Spreen & Strauss, 1998). Individuals are required to produce as many words that begin with the letters F, A, and S. A one minute interval is allotted for each letter. Analyses were conducted using the total number of responses across the F, A, and S trials as the total number of responses would provide a more robust measure of verbal fluency than any individual trial. Analyses were conducted using the total raw score.

Animal Naming (Read, 1980): This is a measure of semantic language fluency. A subtest of the word fluency test, it evaluates the spontaneous production of animal names within a one minute interval (Spreen & Strauss, 1998). Individuals are not given credit for producing category names (e.g., mammals, insects), producing variations of the same species (e.g., humpback whale, blue whale), or producing variations of the same animal (e.g., cat, kitten). Analyses were conducted using the total raw score.

Visuospatial

Wechsler Adult Intelligence Scale Revised-Block Design, Short Form (WAIS R-BD; Wechsler, 1981): This test is a measure of visual organization and visual-motor coordination. It can be considered to measure non-verbal concept formation (Sattler, 2001). With red and white blocks provided, individuals are required to replicate as quickly as possible, constructions built by the examiner (the top side of the blocks only), or pictures of designs presented by the examiner (Spreen & Strauss, 1998). Points are awarded for correct designs produced within the time limit permitted for each item, and for quick completion times. The test is discontinued after two consecutive failures (i.e.,

incorrect reproduction of a design, rotated reproduction of a design, or designs not completed during the allotted time). The test was abbreviated from the original version (Satz & Mogel, 1962) by administration of the odd numbered items (Kristjansson, 1996). Analyses were conducted using the total raw score.

RESULTS

Analyses were performed using SPSS version 8.0 statistical software (SPSS Inc, Chicago, Ill). Memory, attention, language, and visuospatial domains were created based on the sum of raw scores of all tests administered at CSHA-1 that measured a respective domain. The sum of raw scores measuring each domain represented the global domain score. Global scores were standardized by converting the scores to z-scores in order to allow comparison across domains. This procedure was repeated to create these domains from the tests administered at CSHA-2. From a correlation matrix, low to moderate correlations among the measures were identified from which the dependent variables were created (.084 - .641). The assumption of multicollinearity was met in a satisfactory manner.

1) Persons with DAT perform more poorly on measures of secondary memory, attention, language, and visuospatial ability than healthy elderly persons

A one-way, between-subjects multivariate analysis of covariance (MANCOVA) was performed to compare NCI ($N = 465$) and DAT ($N = 75$) groups on four dependent variables: the standardized global scores measuring memory, attention, language and visuospatial abilities. Group sizes were smaller than the initial groups consisting of individuals who underwent the neuropsychological assessment at CSHA-1, as certain individuals did not complete all of the measures administered and thus all four global domain scores could not be computed for these individuals. Age and years of education were entered as covariates. Attribute variables such as age and years of education have been identified as possibly influencing neuropsychological performance, as these are

factors that cannot be manipulated under test conditions (Tupper & Rosenblood, 1984). Consequently, it is unclear whether resulting levels of performance are due in part to the attribute variables (Tupper & Rosenblood, 1984).

Two techniques are often employed to account for attribute variables. Matched-Groups design aims to control these variables prior to carrying out analyses (Tupper & Rosenblood, 1984). By matching pairs of subjects on the attribute variables, it is believed that the variables are held constant (Tupper & Rosenblood, 1984). However, matching subjects posed two difficulties for the present investigation: 1) matching pairs of subjects likely would reduce sample size; and 2) matching may obscure relationships that would otherwise emerge from measurement of the dependent variables (Tupper & Rosenblood, 1984). Alternatively, MANCOVA is a method used to statistically control attribute variables by removing the variance of the attribute variables that is correlated with the dependent variables (Tupper & Rosenblood, 1984). The application of this technique has been criticized in the literature. One of the reasons it has been criticized is that it has been applied beyond the appropriate conditions. Tupper and Rosenblood (1984) report that studies have disregarded the major requirement of a covariance analysis: that an orthogonal relationship must exist between the attribute and independent variables, conveying that the attribute and independent variables must not be significantly correlated with one another. In addition Adams, Brown, and Grant (1985) affirm that this technique should not be used to 1) produce an effect by controlling for covariates in a demographically unmatched group, when an initial analysis of variance showed an insignificant effect; and 2) disregard the influence of demographic variables when an effect has been produced in a demographically unmatched group. Entering age and years

of education as covariates was believed to be appropriate under the conditions of the investigation. As the DAT group was significantly older and had fewer years of education in comparison to the NCI group at CSHA-1, age and years of education were entered as covariates not to remove their contribution to performance on measures reflected by the global domain scores thus ignoring their influence on the dependent variables, but to determine whether significant results were obtained above the influence of the attribute variables.

The overall relationship between the independent variable (i.e., groups) and dependent variables (i.e., global domains) was significant [$F(4,533) = 117.54$, $p < .05$], indicating that group membership influenced performance on measures in the four cognitive domains. Analysis of the between-group main effects on individual global scores revealed that the DAT group had significantly poorer performance on tasks measuring memory [$F(1,536) = 458.15$, $p < .05$], attention [$F(1,536) = 80.80$, $p < .05$], language [$F(1,536) = 68.46$, $p < .05$], and visuospatial [$F(1,536) = 54.64$, $p < .05$] skills than the NCI group above the influence of differences in age and education between the groups. The strength of the relationship between the dependent variables and group membership can be represented in terms of effect size. Cohen's criteria for effect sizes describe small, medium, and large effect sizes as correlations of .10, .30, and .50 respectively (Cohen, 1992); taking the square of these correlations (i.e., .01, .09, and .25) reflects the magnitude of the effect, the amount of variance in the dependent variables that is attributed to group membership. Similarly, eta squared (η^2), an alternative measure of the magnitude of an effect, measures the amount of variance in the dependent variables that is accounted for by group membership (Howell, 2004). In accordance with

Cohen's criteria, a strong relationship exists between group membership and each of the four domains (memory, $\eta^2 = .56$; attention, $\eta^2 = .46$; language, $\eta^2 = .35$; visuospatial, $\eta^2 = .23$).

2) Comparison of very old non-demented persons and individuals with mild DAT on measures of attention and language are predicted to reveal differences in performance between the two groups

At CSHA-1, the very old non-demented group ($N = 135$) consisted of individuals 85 years of age or older, in accordance with the sampling strategy of the CSHA study; these individuals largely resided in the community (community, $N = 114$; institution, $N = 21$). In contrast, the mild DAT group ($N = 45$), all community dwellers, consisted of individuals who were classified as having DAT but performed above the ninth percentile on the 3MS in comparison with the CSHA-1 participants included in the present study; all 3MS scores were standardized by converting the scores to z-scores to generate percentiles. Percentiles are commonly used to express performance according to varying levels of ability ranging from Very Poor, Borderline, Low Average, Average, High Average, Superior, to Very Superior classifications (Spreeen & Strauss, 1998). The ninth percentile is considered to represent the lower limit of the Low Average range (Lezak, 1995). The intent of using the lower limit of the Low Average range as a cut-off level of performance and not the range of percentiles that are considered to fall within the low Average range (9th - 24th percentile) is to capture higher functioning individuals classified as DAT. The very old NCI group was significantly older than the mild DAT group (88.1 years vs. 82.4 years respectively, $t(51.82) = 6.11, p < .05$, but the groups did not differ in

their level of education (10.4 years vs. 9.2 years respectively, $t(177) = 1.79, p > .05$), nor in gender composition, $\chi^2(1, N = 180) = .13, p = .72$.

A one-way, between-subjects multivariate analysis of variance (MANOVA) was conducted to compare NCI and mild DAT groups on attention and language ability using the standardized global scores previously computed to represent the domains at CSHA-1. Age was not entered as a covariate as the oldest individuals from the NCI group were specifically selected for this analysis, and thus an age difference was expected between NCI and mild DAT groups.

The overall relationship between the independent variable (i.e., groups) and dependent variables (i.e., attention and language domains) was significant, $F(2,146) = 13.18, p < .05$, indicating that group membership influenced performance on measures in these cognitive domains. Analysis of the between-group main effects revealed that performance of the mild DAT group on tasks measuring attention and language skills was significantly poorer than the older NCI group (attention, $F(1,147) = 17.37, p < .05$; language, $F(1,147) = 24.07, p < .05$). The magnitude of the difference in performance between these groups was modest (attention, $\eta^2 = .11$; language, $\eta^2 = .14$).

3) Healthy elderly individuals who perform poorly on measures of sustained attention and semantic ability are more likely to develop DAT

Performance on measures of sustained attention (i.e., WAIS R-DS) and semantic ability (i.e., Word Fluency, Animal Naming) administered at CSHA-1 were expected to predict group membership at CSHA-2. Scores on WAIS R-DS, Word Fluency, and

Animal Naming were standardized by converting the scores to z-scores in order to compare performance across the three measures.

A sequential logistic regression analysis was performed to determine whether the degree of sustained attention or semantic ability of individuals classified as NCI at CSHA-1 predicted group membership at CSHA-2, specifically whether performance of individuals classified as NCI at CSHA-1 on these measures could predict who would be classified as DAT at CSHA-2. A total of 198 individuals classified as NCI at CSHA-1 were classified at CSHA-2 as NCI or DAT from the consensus diagnosis, and had scores for all predictor variables. Age and years of education were also entered as predictors before any measure predictor(s) was entered, to determine whether sustained attention and semantic ability were able to predict group membership once influences of the attribute variables were considered. Age and years of education were previously determined to differ between NCI and DAT groups at CSHA-2 (Table 3).

When age and years of education were entered first, age was a predictor of group membership, when all other predictors (i.e., education, Word Fluency, Animal Naming, WAIS R-DS) were entered ($N = 198$; odds ratio [OR], 1.24; 95% CI, 1.07 – 1.43), but years of education did not remain significant once the measure predictors were entered ($p > .05$). Age and years of education alone, without the measure predictors, classified 91.4% individuals correctly (98.9% NCI, 6.2% DAT). Poor performance on Word Fluency was associated with group membership at CSHA-2 ($N = 208$; OR, 0.33; 95% CI, 0.16 – 0.74) when age and years of education were the only other predictors entered; 92.8% of individuals were correctly classified (99% NCI, 23.5% DAT). This association did not remain significant in the presence of the other measure predictors that

were entered separately (i.e., Animal Naming, WAIS R-DS). Similarly, poor performance on WAIS R-DS was associated with group membership at CSHA-2 ($N = 200$; OR, 0.23; 95% CI, 0.07 – 0.71), when age and years of education were the only other predictors entered; 92% of individuals were correctly classified (98.4% NCI, 18.8% DAT). This association however did not remain significant in the presence of the other measure predictors that were entered separately (i.e., Word Fluency, Animal Naming). Performance on Animal Naming was not associated with group membership when all other predictors were entered, nor when age and years of education were the only other predictors ($N = 209$; $p > .05$). These results are summarized in table 5.

Table 5

Summary of Logistic Regression Analyses

| Model | Predictors | Model R ² | OR (95% CI) |
|-------|---|----------------------|--|
| 1 | 1 Age & Education 2 Word Fluency 3 Animal Naming 4 WAIS R-DS | .006* | 1.07-1.43 0.83-1.19 0.19-1.14 0.45-2.20 0.1-1.24 |
| 2 | 1 Age & Education | .028* | 1.12-1.43 0.70-0.98 |
| 3 | 1 Age & Education 2 Word Fluency | .008* | 1.11-1.44 0.77-1.07 0.16-0.74 |
| 4 | 1 Age & Education 2 Animal Naming | .024* | 1.11-1.43 0.73-1.02 0.30-1.11 |
| 5 | 1 Age & Education 2 WAIS R-DS | .002* | 1.05-1.37 0.81-1.16 0.08-0.71 |

*overall model, $p < 0.05$.

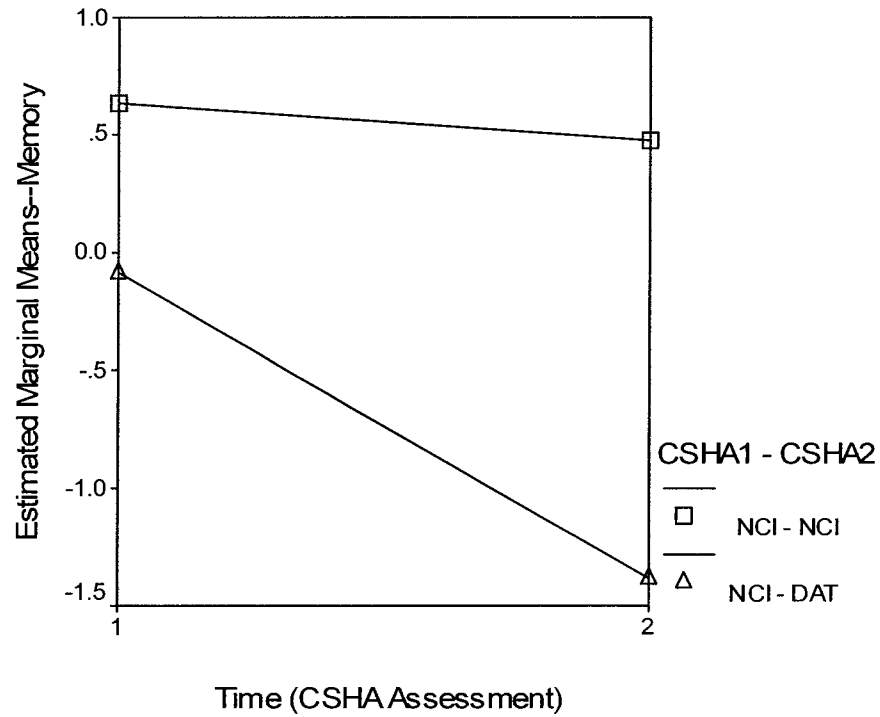
4) *Over time, not only will persons with DAT perform more poorly on cognitive tests, but the change in cognitive ability over time will appear in different domains than healthy elderly persons*

Using the standardized global scores representing the memory, attention, language and visuospatial domains, a 2 (group) x 2 (time) x 4 (domains) MANCOVA was performed to examine the cognitive profiles of those individuals classified as NCI at CSHA-1 and CSHA-2 ($N = 133$), and those individuals classified as NCI at CSHA-1 who developed DAT at CSHA-2 ($N = 7$). Groups were compared on global domain scores obtained from tests administered at CSHA-1 and global domain scores obtained from tests administered at CSHA-2. Individuals that developed DAT at CSHA-2 were significantly older than those who did not decline, $t(209) = -4.47, p < .05$, and had fewer years of education, $t(209) = 2.76, p < .05$; no gender differences were observed, $\chi^2(1, N = 211) = 2.16, p = .14$. As performed previously, age and years of education were entered as covariates to determine whether significant effects occurred above the influence of these attribute variables.

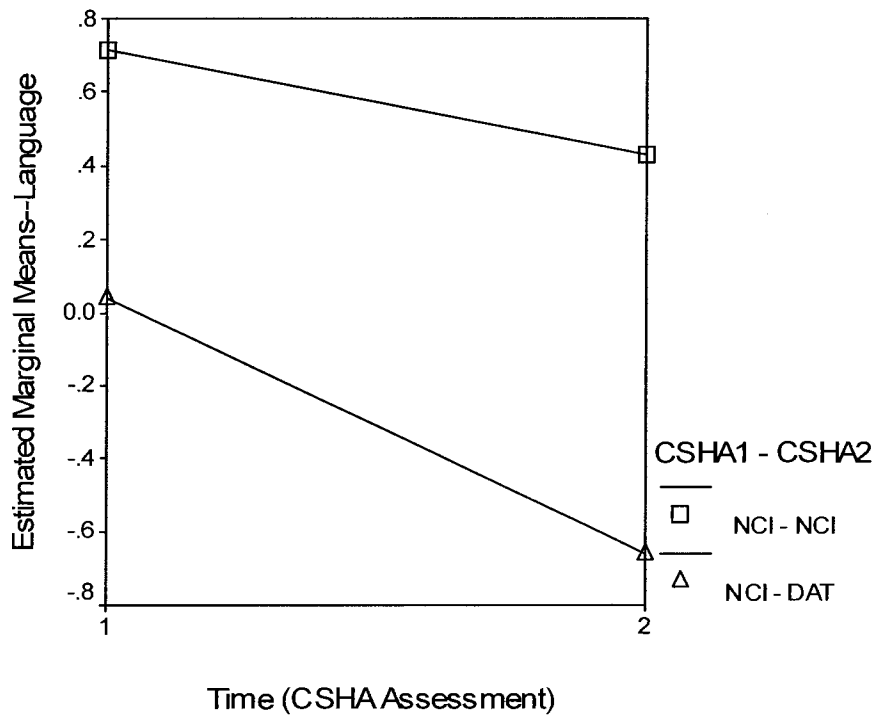
The overall relationship between the independent variable (i.e., groups) and dependent variables (i.e., global domains) was significant, $F(4,133) = 9.23, p < .05$, indicating that group membership influenced performance at CSHA-1 and CSHA-2 on measures in the four cognitive domains above the influence of age and education. Analysis of the between-group main effects revealed that performance by individuals who did not develop DAT at CSHA-2 was significantly better across all domains than that of individuals who developed DAT (memory, $F(1,136) = 36.56, p < .05$; attention, $F(1,136) = 5.31, p < .05$; language, $F(1,136) = 7.34, p < .05$; visuospatial, $F(1,136) = 4.71,$

$p < .05$). Performance in the memory domain was strongly associated with group membership ($\eta^2 = .21$), but performance in the other domains was weakly associated with differences between the groups (attention, $\eta^2 = .04$; language, $\eta^2 = .05$; visuospatial, $\eta^2 = .03$).

A significant interaction effect between group membership and global domain scores indicate that cognitive profiles differed between NCI individuals who did not develop DAT at CSHA-2 and NCI individuals who developed DAT at CSHA-2 [$F(4,133) = 7.41, p < .05$] above the influence of age and education. A relationship was found between group membership and performance within memory [$F(1,136) = 24.49, p < .05$] and language [$F(1,136) = 4.60, p < .05$] domains. Profile plots demonstrated that NCI individuals who developed DAT at CSHA-2 showed a much steeper decline on memory measures than NCI individuals who did not develop DAT; the latter group showed a modest decline in the memory domain between CSHA-1 and CSHA-2 (Figure 1a). Similarly, on measures of language, NCI individuals who developed DAT showed a much steeper decline in performance between CSHA-1 and CSHA-2 than NCI individuals who did not develop DAT. Decline between CSHA-1 and CSHA-2 in the latter group was modest, however was greater than decline on measures of memory (Figure 1b). The strength of these relationships however were small to modest (language, $\eta^2 = .03$; memory, $\eta^2 = .15$).



(a)



(b)

Figure 1. Estimated marginal means of performance in (a) memory and (b) language domains at CSHA-1 & 2 for individuals classified as NCI at CSHA-1 & 2 and individuals classified as NCI at CSHA-1 who developed DAT at CSHA-2.

DISCUSSION

The results of this investigation lend support to the position that the cognitive changes occurring during DAT and normal aging are not solely quantitatively different but also are qualitatively different. This supports the disease model of DAT that suggests normal aging and DAT are distinct processes. Differences in neuropsychological profiles between DAT and NCI groups have been demonstrated in cross-section and longitudinally through exploration of four hypotheses.

Hypothesis 1 demonstrated that persons with DAT performed more poorly on measures of secondary memory, attention, language, and visuospatial ability than healthy elderly persons. The strength of association among performance and group membership, according to Cohen's criteria was robust with each of the memory, attention, language and visuospatial domains. These results could be considered to lend support to the DAT continuum model because the DAT group performed poorly in all domains in relation to the NCI group, suggesting that the groups differ only in level of severity of cognitive decline. Carlesimo et al. (1998) from their results, concluded that the relationship between memory change occurring as function of physiological aging and memory impairment in DAT may assume three different patterns, one supporting the continuity hypothesis of a progressive deterioration in performance from young, to healthy elderly, to DAT. The results related to hypothesis 1 are consistent with this conclusion in that poorer performance was demonstrated by the DAT group in comparison to the NCI group on all domains measured. More pertinently, however, the results establish a basis for investigation of qualitative differences between normal aging and DAT processes because differences in level of performance have been established.

Hypothesis 2 demonstrated that comparison of very old non-demented persons and individuals with mild DAT on measures of attention and language revealed poorer performance on these measures by the latter group. Carlesimo et al. (1998) hypothesized that if DAT is simply an exaggerated form of normal aging, consistent with the DAT continuum model, then younger individuals with mild DAT and non-demented individuals in the very old population should display a similar level of performance on neuropsychological tests. In contrast, if cognitive decline associated with DAT diverges from the pattern of cognitive decline associated with normal aging, consistent with the DAT disease model, then performance in the very old population should not be similar to performance in the DAT population. It was revealed that performance on neuropsychological tests in the domains of attention and language differed between very old NCI and mild DAT groups and thus support the DAT disease model. This finding is consistent with the pattern of decline in normal aging and in DAT reported in the literature. In normal aging, attentional capabilities remain relatively stable in later life. Studies report greater stability of sustained attention (Albert, 1988), and some variability in performance on selective attention tasks (Connelly & Hasher, 1993). Language capabilities do demonstrate some decline in normal aging, the skills in which decline occurs, such as semantic knowledge (Obler & Albert, 1981) only appearing in later life. Other aspects of language such as phonological (Bayles & Krasziak, 1987), lexical, and syntactic (Albert, 1988) knowledge in normal aging remain relatively intact. Conversely, in DAT, attentional (Almkvist & Backman, 1993) and language (Becker et al., 1988) deficits have been documented during the early stages. However, only a modest association according to Cohen's criteria, was found between attention, language skills,

and group membership reported in this study. The association between attentional skills and group membership may be the consequence of having only one measure of attention; more measures would have increased the robustness of this domain, perhaps demonstrating poorer performance by the mild DAT group on more measures of attention and thus increasing the strength of association with group membership. The association between language skills and group membership may reflect the pattern of cognitive decline in both normal and pathological process specific to DAT and thus a stronger relationship between language and group membership may not exist. Both processes incur deficits in language skills; however deficits appear during the early stages of DAT as experienced by the mild DAT group in this study, and only during later life in normal aging as experienced by the very old, non-demented group.

Hypothesis 3 demonstrated that poorer performance by healthy elderly individuals on measures of either sustained attention or semantic ability was associated with group membership, specifically those with poorer performance were more likely to be classified as DAT at CSHA-2. This was demonstrated above the influences of age and years of education variables. However, the sizes of the odds ratios indicate that neither sustained attention nor semantic ability were strongly associated with development of DAT when age and education variables are controlled. This is further supported by the observations that neither cognitive predictor was associated with development of DAT when all other attribute predictors were entered into the model, and that these factors made small contributions in correctly identifying individuals who developed DAT. However it is possible that age could have influenced the results because age was identified as a key predictor of group membership. Sustained attention and semantic ability may not have

predicted development of DAT if only older elderly in this sample performed poorly on these measures and developed DAT as deficits in attention and language in normal aging only appear during later life. Taking age into account, a sample consisting of younger individuals with difficulties in the areas of attention and language may support a relationship between sustained attention, semantic ability and development of DAT. If sustained attention and semantic ability can be demonstrated to predict development of DAT, these abilities could be markers of the onset of DAT. This is consistent with one of the tenets of the disease model put forward by Huppert and Brayne (1994), that qualitative differences between disease processes and normal processes must be identified. However it should be noted that neither test of semantic ability was associated with group membership; specifically, Animal Naming, a measure of category fluency (Crossley, D'Arcy, & Rawson, 1997) and Word Fluency in the present study were not found to be associated with group membership.

This appears to contradict the conclusions reported by Crossley, D'Arcy, and Rawson (1997) that category fluency is particularly sensitive to DAT, even during the earliest stages. These authors suggest that this measure may be useful in predicting the course of cognitive impairment in DAT because they demonstrated differences between healthy elderly and individuals in the early stages of DAT. However, as shown in this investigation, this measure may not be effective in longitudinal analysis where performance at one point in time is used to predict who will develop DAT. Thus in accordance with the DAT disease model, poor sustained attention and semantic ability may possibly be particular qualitative differences distinguishing normal aging and DAT processes, with poorer performance on measures of these abilities being associated with

an increased likelihood of developing DAT. Additional robust measures of sustained attention and semantic ability, in addition to a sample of younger elderly individuals who demonstrate difficulty in these areas, may demonstrate a stronger dissociation of these abilities between normal aging and DAT processes, providing compelling support that this dissociation is a distinct, qualitative difference between these processes.

Hypothesis 4 demonstrated that over time, not only did persons who developed DAT perform more poorly on cognitive tests, but in addition showed steeper declines in memory and language skills than persons who did not develop DAT. These results also lend support to the disease model put forward by Huppert and Brayne (1994), the tenet that requires identification of qualitative differences between disease processes and normal processes. Decline in performance on memory and language tasks, as demonstrated by these results, was more gradual in normal aging than in DAT. These differences in memory and language skills could also be markers for the onset of DAT, providing that a critical level or rate of decline separating DAT from normal aging can be identified. However, the effect sizes measuring the strength of the relationship between group membership and performance on measures of memory and language at CSHA-1 and CSHA-2, according to Cohen's criteria, were small to modest. The effect sizes found may be due to the size of the DAT group ($N = 7$); it is possible that with a larger DAT group larger effect sizes may have been found. Moreover, with a larger DAT group, differences in attentional and visuospatial skills may have been significant. The weak association between attentional skills, visuospatial skills and group membership may also be the consequence of having only one measure of attention and visuospatial ability; more measures would have increased the robustness of these domains. A pattern of

performance between individuals who developed DAT and individuals who did not, across more measures of attention and visuospatial ability, may have been evident and thus increase the strength of association with group membership.

The results of the four hypotheses lend support to the disease model approach to DAT because not only were quantitative differences between non-demented and DAT groups found but qualitative differences between the groups were also shown. The qualitative differences between the groups ranged from small to robust, the strongest relationship demonstrated between group membership and memory, where individuals with DAT were outperformed on measures of memory. The small and modest effect sizes are likely the result of having a small number of measures representing the four cognitive domains examined in this study, particularly the attention and visuospatial domains, obscuring a clear, distinguishable pattern of performance between groups. Another pertinent factor that may be influencing the results of this investigation is the differences in age and education between the groups. The present study attempted to control the influence of these attribute variables by controlling their contribution to the domain scores through the use of MANCOVA statistical procedure. However, doing this does not preclude their influence on group membership, therefore, the results found may be indirectly influenced by these attribute variables through their relationship with group membership.

Although Tupper and Rosenblood (1984) advocate against using a covariance analysis when covariates and independent variables are correlated, it was deemed necessary in order to demonstrate differences in performance between NCI and DAT groups on the dependent variables above the influence of attribute variables. Controlling

the influence of the attribute variables on group membership was regarded as inappropriate because controlling this interaction may have obscured meaningful relationships between the attribute and independent variables that may influence performance on the domains measured.

The results of this investigation preclude confirmation of unequivocal qualitative differences between DAT and normal aging. Although modest and robust effects were found small effect sizes were also demonstrated and in particular no qualitative differences in visuospatial ability were found; this is likely consequence of the limitations identified in this study. The results however do illustrate areas where qualitative differences could be found. Increasing the sample size of the DAT group and increasing the number of robust measures administered, particularly attention and visuospatial tasks, may improve results in replication studies, demonstrating explicit qualitative differences between normal aging and DAT.

In addition, this study focused on demonstrating differences between four global domains; stronger support for the DAT disease model could be sought by demonstrating qualitative differences between normal aging and DAT groups within these domains. For example, studies have demonstrated that healthy elderly individuals have difficulty with encoding information, performing better on recognition than recall tasks (Albert, 1988; Erber, 1974); individuals with DAT have difficulty encoding and retrieving information (Kopelman, 1992; Martin, Brouwers, Cox, & Fedio, 1985) and do not show a difference in performance on recall and recognition tasks. Differential performance on recall and recognition tasks could be supported by comparing healthy and DAT groups on differences scores created from performances on recall versus recognition memory tasks.

Identification of other qualitative differences such as differential performance on recall and recognition tasks may lead to the discovery of cognitive markers that may assist in earlier detection of DAT.

Subsequent research could also address the issue of attribute variables. This investigation attempted to account for age and education differences between NCI and DAT groups using MANCOVA analysis, however, could not conclude that significant results were solely the result of group differences. With adequate samples of NCI and DAT individuals, the matching technique, matching pairs of individuals between groups on age and level of education before analyses are performed, could be utilized to determine whether the results from this investigation can be replicated and attributed exclusively to differences in group membership.

Future considerations may also include additional longitudinal investigation if adequate sample sizes could be obtained. Assessment at two intervals is sufficient to evaluate change in cognition, however to establish patterns of cognitive decline requires assessment at more than two intervals (Brayne, Gill, Paykel, Huppert, & O'Connor, 1995). Participants from the CSHA study who were alive following CSHA-2, and who agreed to continue to participate, underwent a third clinical examination, including a neuropsychological assessment (CSHA-3). The number of new and pre-existing individuals with DAT however was anticipated to be too small for analyses to be conducted. Finally, future research could seek to support the hypotheses explored in this investigation, or hypotheses exploring other qualitative differences in populations affected by similar pathological processes. Vascular disorders such as vascular dementia, and metabolic disorders such as alcoholism (Greenberg, Aminoff, & Simon, 1999), are

among the most common subtypes of dementia that share similar symptomatology with DAT. Progeria, a condition defined as an “Accelerated aging syndrome in which most of the characteristic stages of human senescence are compressed into less than a decade” (*The On-Line Medical Dictionary*, 2004), may also present with symptoms that distinguish this condition from normal aging processes (Berg, 1985). Identification of qualitative differences within other populations will serve to support the position that normal and pathological aging processes are discrete, thus extending the DAT disease model to encompass other dementias and other pathological aging disorders.

REFERENCES

- American Psychological Association. (1987). *Diagnostic and statistical manual of mental disorders (3rd, rev. ed.)*. Washington, DC: Author.
- Albert, M.S. (1988). Cognitive Function. In M.S. Albert & M.B. Moss (Eds.), *Geriatric neuropsychology* (pp.33-56). New York: The Guilford Press.
- Almkvist, O. (1996). Neuropsychological features of early Alzheimer's disease: Preclinical and clinical stages. *Acta Neurologica Scandinavica*, 165, 63-71.
- Almkvist, O., & Backman, L. (1993). Detection and staging of early clinical dementia. *Acta Neurologica Scandinavica*, 88, 10-15.
- Bamford, K.A., & Caine, E.D. (1988). Does "benign senescent forgetfulness" exist? *Clinics in Geriatric Medicine*, 4, 897-915.
- Bassett, S.S., & Folstein, M.F. (1991). Cognitive impairment and functional disability in the absence of psychiatric diagnosis. *Psychological Medicine*, 21, 77-84.
- Bayles, K.A., & Kraszniak, A.W. (Eds.). (1987). *Communication and cognition in normal aging and dementia*. Boston: Little, Brown.
- Becker, J.T., Huff, J. Nebes, R.D., Holland, A. & Boller F. (1988). Neuropsychological function in Alzheimer's disease. *Archives of Neurology*, 45, 263-268.
- Berg, L. (1985). Does Alzheimer's disease represent an exaggeration of normal aging? *Archives of Neurology*, 42, 737-739.
- Blackford, R.C., & La Rue, A. (1989). Criteria for diagnosing age-associated memory impairment: Proposed improvements from the field. *Developmental Neuropsychology*, 5, 295-306.
- Benton, A. L. (1974). *Revised Visual Retention test: Clinical and experimental applications (4th ed.)*. New York: Psychological Corporation.
- Benton, A. L., & Hamsher, K. (1989). *Multilingual aphasia examination (2nd ed.)*. Iowa City, Iowa USA: AJA Associates.
- Brayne, C., Best, N., Muir, M., Richards, S.J., & Gill, C. (1997). Five-year incidence and prediction of dementia and cognitive decline in a population sample of women aged 70-79 at baseline. *International Journal of Geriatric Psychiatry*, 12, 1107-1118.
- Brayne, C., & Calloway, P. (1988). Normal ageing, impaired cognitive function, and senile dementia of the Alzheimer's type: A continuum? *Lancet*, 1, 1265-1267.

- Brayne, C., Gill, C., Paykel, E.S., Huppert, F., & O'Connor, D.W. (1995). Cognitive decline in an elderly population—a two wave study of change. *Psychological Medicine*, 25, 673-683.
- Brinkman, S.D., Lergen, J.W., Gerganoff, S., & Nunzio, P. (1983). Russell's revised Wechsler memory scale in the evaluation of dementia. *Journal of Clinical Psychology*, 39, 989-993.
- Buschke, H. (1984). Cued recall in amnesia. *Journal of Clinical Neuropsychology*, 6, 433-440.
- Caine, E.D. (1993). Should aging-associated cognitive decline be included in the DSM-IV? *Journal of Neuropsychiatry and Clinical Neurosciences*, 5, 1-5.
- Canadian Study of Health and Aging Working Group. (1994). Canadian study of health and aging: Study methods and prevalence of dementia. *Canadian Medical Association Journal*, 150, 899-913.
- Canadian Study of Health and Aging Working Group. (2000). The incidence of dementia in Canada. *Neurology*, 55, 66-73.
- Carlesimo, G.A., Mauri, M., Graceffa, A.M.S., Fadda, L., Loasses, A., Lorusso, S., et al. (1998). Memory performance in young elderly, and very old healthy individuals versus patients with Alzheimer's disease: Evidence for discontinuity between normal and pathological aging. *Journal of Clinical and Experimental Neuropsychology*, 20, 14-29.
- Cohen, J. (1992). A power primer. *Psychological Bulletin*, 112, 155-159.
- Connelly, S.L., & Hasher, L. (1993). Aging and inhibition of spatial location. *Journal of Experimental Psychology: Human Perception and Performance*, 19, 1238-1250.
- Crook, T., Bartus, R.T., Ferris, S.H., Whitehouse, P., Cohen, G.D., & Gershon, S. (1986). Age-associated memory impairment: Proposed diagnostic criteria and measures of clinical change—Report of a National Institute of Mental Health Work Group. *Developmental Neuropsychology*, 2, 261-276.
- Crossley, M., D'Arcy, C., & Rawson, N.S.B. (1997). Letter and category fluency in community-dwelling Canadian seniors: A comparison of normal participant to those with dementia of the Alzheimer or Vascular Type. *Journal of Clinical and Experimental Neuropsychology*, 19, 52-62.
- Dobbins, D. (1988). Yule's "hump" revisited. *British Journal of Educational Psychology*, 58, 338-344.
- Dunn, G., Sham, P., Hand, D. (1993). Statistics and the nature of depression.

Psychological Medicine, 23, 871-889.

Erber, J. T. (1974). Age differences in recognition memory. *Journal of Gerontology*, 29, 177-181.

Forbes, W.F., & Hirdes, J.P. (1993). The relationship between aging and disease: Geriatric ideology and myths of senility. *Journal of the American Geriatrics Society*, 41, 1267-1271.

Fleiss, J.L. (1972). Classification of the depressive disorders by numerical typology. *Journal of Psychiatric Research*, 9, 141-153.

Goodwin, J.S. (1991). Geriatric ideology: The myth of the myth of senility. *Journal of the American Geriatric Society*, 39, 627-631.

Grady, C.L., Haxby, J.V., Horwitz, B., Sundaram, M. Berg, G., Schapiro, et al. (1988). Longitudinal study of the early neuropsychological and cerebral metabolic changes in dementia of the Alzheimer Type. *Journal of Clinical and Experimental Neuropsychology*, 10, 576-596.

Greenberg, D.A., Aminoff, M.J., & Simon, R.P. (Eds.). (1999). *Clinical neurology, fifth edition*. New York: McGraw-Hill Companies, Inc.

Hodges, J.R. (1994). Neurological aspects of dementia and normal aging. In F.A. Huppert, C. Brayne, & D.W. O'Connor (Eds.), *Dementia and normal aging* (pp. 118-129). Cambridge: Cambridge University Press.

Howell, D.C. (2004). *Fundamental statistics for the behavioral sciences* (5th ed.). Belmont, CA: Brooks/Cole.

Howell, S.C. (1972). Familiarity and complexity in perceptual recognition. *Journal of Gerontology*, 27, 364-371.

Hoyer, W.J., Rybash, J.M., & Roodin, P.A. (Eds.). (1999). *Adult development and aging, fourth edition*. New York: The McGraw-Hill Companies, Inc.

Huppert, F.A. (1994). Memory function in dementia and normal aging—dimension or dichotomy? In F.A. Huppert, C. Brayne, & D.W. O'Connor (Eds.), *Dementia and normal aging* (pp. 291-329). Cambridge: Cambridge University Press.

Huppert, F.A., & Brayne, C. (1994). What is the relationship between dementia and normal aging? In F.A. Huppert, C. Brayne, & D.W. O'Connor (Eds.), *Dementia and normal aging* (pp. 3-15). Great Britain: Cambridge University Press.

Ivnik, R., Smith, G., Malec, J., Petersen, R., & Tangalos, E. (1995). Long-term stability

and inter-correlations of cognitive abilities in older persons. *Psychological Assessment*, 7, 155-161.

Kendel, R.E., & Brockington, I.F. (1980). The identification of disease entities and the relationship between schizophrenic and affective psychoses. *British Journal of Psychiatry*, 137, 324-331.

Kopelman, M.D. (1992). Storage, forgetting, and retrieval in the anterograde and retrograde amnesia of Alzheimer's dementia. In L. Backman (Ed.), *Memory functioning in dementia* (pp. 45-71). Amsterdam: North Holland.

Kristjansson, B. (1996). *Canadian Study of Health and Aging-2 Neuropsychological Manual*. Ottawa, ON.: University of Ottawa.

Kral, V.A. (1962). Senescent forgetfulness: Benign and malignant. *Canadian Medical Association Journal*, 86, 257-260.

Larrabee, G.J., Youngjohn, J.R., & Sudilovsky, A. (1993). Accelerated forgetting in Alzheimer-type dementia. *Journal of Clinical and Experimental Neuropsychology*, 15, 701-712.

Lezak, M.D. (Ed.). (1995). *Neuropsychological assessment, third Edition*. New York: Oxford University Press.

Lines, C.R., Dawson, C., Preston, G.C., Reich, S., Foster, C., & Traub, M. (1991). Memory and attention in patients with senile dementia of the Alzheimer type and in normal elderly subjects. *Journal of Clinical and Experimental Neuropsychology*, 13, 691-702.

Martin, A., Brouwers, P., Cox, C., & Fedio, P. (1985). On the nature of the verbal memory deficit in Alzheimer's disease. *Brain and Language*, 25, 323-341.

Mckhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E.M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*, 34, 939-944.

Miller, E. (1971). On the nature of the memory disorder in presenile dementia. *Neuropsychologia*, 9, 75-81.

Niederehe, 1986. Depression and memory impairment in the aged. In L.W. Poon & T. Crook (Eds.), *Handbook for clinical memory assessment of older adults* (pp. 226-237). Washington, DC, US: American Psychological Association.

Ober, B.A., Jagust, W.J., Koss, E., Delis, D.C., & Friedland, R.P. (1991). Visuoconstructive performance and regional cerebral glucose metabolism in Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology*, 13,

752-772.

- Obler, L.K., & Albert, M.L. (1981). Language and aging: A neurobehavioral analysis. In D.S. Beasley & G.A. Davis (Eds.), *Aging: Communication processes and disorders* (pp. 107-121). New York: Grune & Stratton.
- O'Connell, M., & Tuokko, H. (2002). The 12-item Buschke memory test: Appropriate for use across levels of impairment. *Applied Neuropsychology*, 9, 226-233.
- Parker, G., & Hadzi-Pavlovic, D. (1993). Old data, new interpretation: A re-analysis of Sir Aubrey Lewis' M.D. thesis. *Psychological Medicine*, 23, 859-870.
- Plude, D.J., & Hoyer, W.J. (1986). Age and the selectivity of visual information processing. *Psychology and Aging*, 1, 4-10.
- Rabinowitz, J.C. (1986). Priming in episodic memory. *Journal of Gerontology*, 41, 204-213.
- Read, D. E. (1980). *Neuropsychological Assessment of Memory in Early Dementia: Normative data for a new battery of memory tests "Animal Naming"*. Victoria, Canada.
- Rediess, S., & Caine, E.D. (1996). Aging, cognition, and DSM-IV. *Aging, Neuropsychology, and Cognition*, 3, 105-117.
- Reischies, F.M., Schaub, R.T., & Schlattmann, P. (1996). Normal ageing, impaired cognitive functioning and senile dementia—a mixture distribution analysis. *Psychological Medicine*, 26, 785-790.
- Rey, A. (1964). *L'examen clinique en psychologie*. Paris: Presses Universitaires de France.
- Roth, M. (1994). The relationship between dementia and normal aging of the brain. In F.A. Huppert, C. Brayne, & D.W. O'Connor (Eds.), *Dementia and Normal Aging* (pp. 57-76). Cambridge: Cambridge University Press.
- Salmon, D.P., & Galasko, D. (1996). Neuropsychological aspects of Lewy body dementia. In R. Perry, I. McKeith, & E. Perry (Eds.), *Dementia with Lewy bodies* (pp. 99-113). Cambridge: Cambridge University Press.
- Sattler, J.M. (2001). WAIS-III Subtests and Interpreting the WAIS III. Ch. 13 in *Assessment of Children Cognitive Applications, fourth edition*. Jerome M. Sattler, Publisher Inc. La Messa, California.
- Satz, P., & Mogel, S. (1962). An abbreviation of the WAIS for clinical use. *Journal of Clinical Psychology*, 18, 77-79.

- Shaywitz, S.E., Escobar, M.D., Shaywitz, B.A., Fletcher, J.M., & Makuch, R. (1992). Evidence that dyslexia may represent the lower tail of a normal distribution of reading ability. *New England Journal of Medicine*, 326, 145-150.
- Smith, G.E., & Ivnik, R.J. (2003). Normative Neuropsychology. In R.C. Petersen (Ed.), *Mild cognitive impairment: Aging to Alzheimer's disease* (pp. 63-88). London: Oxford University Press.
- Spreeen, O., & Benton, A. (1969). *Neurosensory center comprehensive examination for aphasia*. Victoria, BC: Neuropsychology Laboratory, Department of Psychology, University of Victoria.
- Spreeen, O., & Benton, A. L. (1977). *Neurosensory center comprehensive examination for aphasia*. Victoria, British Columbia: University of Victoria.
- Spreeen, O., & Strauss, E. (Eds.). (1998). *A Compendium of Neuropsychological Tests*. New York: Oxford University Press.
- SPSS for Windows, Rel. 8.0.0. 1997. Chicago: SPSS Inc.
- Sulkava, R. & Amberla, K. (1982). Alzheimer's disease and senile dementia of Alzheimer's type: A neuropsychological study. *Acta Neurologica Scandinavica*, 65, 651-660.
- Talland, G.A. (1965). Three estimates of the word span and their stability over the adult years. *Quarterly Journal of Experimental Psychology*, 17, 301-307.
- Teng, E.L., & Chui, H.C. (1987). The Modified Mini-Mental State (3MS) Examination. *Journal of Clinical Psychiatry*, 48, 314-318.
- The On-Line Medical Dictionary*. 2003. Retrieved November 29, 2004, from <http://cancerweb.ncl.ac.uk/omd/>
- Tuokko, H., Frerichs, R., Graham, J., Rockwood, K., Kristjansson, B., Fisk, J., et al. (2003). Five-year follow-up of cognitive impairment with no dementia. *Archives of Neurology*, 60, 577-582.
- Tuokko, H., & Woodward, T.S. (1996). Development and validation of a demographic correction system for neuropsychological measures used in the Canadian Study of Health and Aging. *Journal of Clinical and Experimental Neuropsychology*, 18, 479-616.
- Webster's universal college dictionary*. (1997). New York: NY: Gramercy Books.

- Wechsler, D. (1981). *Manual for the Wechsler Adult Intelligence Scale - Revised*. New York: Psychological Corporation.
- Yule, W., Rutter, M., Berger, M., & Thompson, J. (1974). Over- and under-achievement in reading: Distribution in the general population. *British Journal of Educational Psychology*, 44, 1-12.
- Zec, R.F. (1993). Neuropsychological functioning in Alzheimer's disease. In R.W. Parks & R.F. Zec (Eds.), *Neuropsychology of Alzheimer's disease and other dementias* (pp. 3-80). London: Oxford University Press.