Walden University
A higher degree. A higher purpose.

Walden University
ScholarWorks

Walden Dissertations and Doctoral Studies

Walden Dissertations and Doctoral Studies Collection

2016

Comparative Memory/Behavioral Symptoms of Alzheimer's disease: EOAD vs. LOAD

Marcia Gale Roberson
Walden University

Follow this and additional works at: https://scholarworks.waldenu.edu/dissertations

 Part of the Clinical Psychology Commons, Cognitive Psychology Commons, and the Family, Life Course, and Society Commons

This Dissertation is brought to you for free and open access by the Walden Dissertations and Doctoral Studies Collection at ScholarWorks. It has been accepted for inclusion in Walden Dissertations and Doctoral Studies by an authorized administrator of ScholarWorks. For more information, please contact ScholarWorks@waldenu.edu.

Walden University

College of Social and Behavioral Sciences

This is to certify that the doctoral dissertation by

Marcia G. Roberson

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. David Yells, Committee Chairperson, Psychology Faculty
Dr. Annemarie Murphy, Committee Member, Psychology Faculty
Dr. John Astin, University Reviewer, Psychology Faculty

Chief Academic Officer
Eric Riedel, Ph.D.

Walden University
2016

Abstract

Comparative Memory/Behavioral Symptoms of Alzheimer's disease: EOAD vs. LOAD

by

Marcia G. Roberson

MBA, American Intercontinental University - June 2008

BS, University of Houston Central Campus - May 1985

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Clinical Psychology

Walden University

November 2016

Abstract

Alzheimer's disease (AD) is a fatal disorder with no apparent cure. Early-onset AD (EOAD) occurs in individuals before the age of 65, and late-onset AD (LOAD) occurs in individuals age 65 and older. Past studies have proven that AD is fatal among Americans age 65 and older. The disease is characterized by impairments in memory and executive function as well as other cognitive and behavioral problems. The research questions addressed by this sequential, mixed-method study compared EOAD and LOAD by exploring common behavioral/cognitive symptoms and stage levels of AD. Research participants were recruited from the Alzheimer's Association who were members of caregiver support groups and cared for an individual with AD. The qualitative component of this study consisted of a qualitative interview given to caregivers (N = 6), which was audio-recorded and transcribed verbatim using the 6-phase thematic analysis. Sequentially, the quantitative component of this study consisted of the BEHAVE-AD and Short IQCODE instruments, which were filled out and completed by caregivers (N = 20) on behalf of patients with probable AD. These data were analyzed using 1-way ANOVA, with the alpha set at 0.05. Integration of qualitative and quantitative results indicated no differences in cognitive or behavioral symptoms of either EOAD or LOAD care recipients. These findings have implications for positive social change by continually involving caregiver participants in future studies. Doing so can ensure that care recipients, whether they have been diagnosed at EOAD or LOAD, have a voice.

Comparative Memory/Behavioral Symptoms of Alzheimer's disease: EOAD vs. LOAD

by

Marcia G. Roberson

MBA, American Intercontinental University - June 2008

BS, University of Houston Central Campus - May 1985

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Clinical Psychology

Walden University

November 2016

Dedication

I dedicate this dissertation to my late parents, Travis J. and Willie M. Smith.

Acknowledgments

I would like to thank my committee chairperson, Dr. David Yells, committee member, Dr. Annemarie Murphy, and URR person, Dr. John Astin, for the help and guidance on my dissertation. Thanks to my loving husband, Glenn Roberson, for giving me moral and financial support; as well as being so patient and understanding. My two sons and daughter-in-laws for stepping in and giving me their love, support and understanding throughout this long process. I would like to also acknowledge my sisters, brother, and cousins for listening and cheering me on when I was running out of energy; and thanks to all the caring friends who gave me that ray of sunshine when the clouds seem to take over at times. Without all of these individuals, I could not have reached this point in my academic career.

Table of Contents

List of Tables

Chapter 1: Introduction to the Study

Introduction

Alzheimer's disease (AD) is the sixth leading cause of death in the United States (Alzheimer's Association, 2016). AD is also the fifth leading cause of death among Americans age 65 and older. Approximately 5.4 million Americans suffer from this neurodegenerative disease (AA, 2016). The financial and medical cost to treat AD is between $200 and $600 billion, annually. The average age of diagnosis is 65 (Duke University Medical Center, 2002). In the next decade there will be 10 million more individuals diagnosed with AD due to the baby boomer generation—those born between 1946 and 1964—turning 65 and older. By the year 2050, the annual cost to treat this population will increase to well over $1 trillion (Okie, 2011). Diagnosis of AD increases significantly with age. The Alzheimer's Association Report (2012) indicated that there are about 53 new cases per 1000 individuals aged 65 to 74 years, 170 new cases per 1000 individuals aged 75 to 84 years, and 231 cases per 1000 individuals 85 and older (the oldest old).

According to the Alzheimer's Association (2012), aging baby boomers will increase the percentage of Americans living longer and being amongst the oldest old (85 and older). Therefore, this increases their chances of developing AD. Age is a consistent risk factor for AD (Kalaria et al., 2008). The oldest baby boomer turned 65 years old in 2011 and the youngest baby boomer will turn 65 years old in 2029. The Centers for Disease Control and Prevention and the U.S. Census Bureau estimate that by 2030, those

aged 65 and older will double in population and these 71 million "older" Americans will account for 20% of the entire population (AA, 2012).

Background

Alzheimer's disease (AD) is a neurodegenerative brain disorder of unknown cause with neuropathological and neurochemical features. The disorder is usually harmful in onset and increases slowly, but steadily, over a period of several years (Jongbloed et al., 2013). Once individuals have been diagnosed with AD, they can live with the disease, on average, 4 to 8 years before death (AA, 2013). However, there are those who may live as long as 20 years after being diagnosed with AD.

A significant number of researchers and scientists are in agreement that vital processes are interrupted by amyloid plaques and neurofibrillary tangles, which are considered to be the two hallmarks of AD (Braak & Tredici, 2012; Cummings, Golde, Sano, & Tariot, 2007; Jongbloed et al., 2013; Kar et al., 2004; Yu et al., 2013). The role these microscopic abnormal structures play in the terminal disease are not clear. However, once these abnormalities spread, causing shrinkage of the brain, certain memory components suffer. Jongbloed et al. (2013) explained that amyloid plaques contain a 42-amino acid-long isoform of amyloid β ($A\beta_{42}$) and that neurofibrillary tangles consist mainly of hyper-phosphorylated forms of the microtubule-associated protein tau (TAU). Formations of these abnormal proteins are thought to contribute to the loss or degeneration of neurons in the brain and the ensuing symptoms of Alzheimer's disease.

Duara et al. (2013) summarized the importance of amyloid in AD. They hypothesized that amyloid deposition in the brain may be the earliest detectable biomarker among subjects destined to develop AD. Brain amyloid levels increase from 6% in 50- to 59-year-old individuals to 50% in those 80-years and older. Elevated brain amyloid load has been associated with memory decline, increased risk for progression to mild cognitive impairment (MCI), and dementia among elderly individuals who are non-demented, but not among AD patients in whom amyloid levels have stabilized. Brain amyloid load is also associated with hippocampal (HP) volume loss and cognitive impairment among elderly, healthy subjects and patients with MCI. These atrophic changes, which may be present for many years before clinical symptoms appear or cognitive decline occurs, represent the neurodegenerative element of AD, and the possible cause of cognitive impairment and eventual progression to the disease (Duara et al., 2013). Amyloid plaques are considered an initial event in AD, which is followed by neurofibrillary tangle formation, neuronal loss and dysfunction, and ultimately dementia.

Hyman et al. (2012) further explained the neuropathology of AD. As mentioned above, neurofibrillary tangles (NFTs) are intraneuronal fibrils primarily composed of abnormal tau. NFTs are commonly observed in the limbic regions early on in AD, but depending on the stage of the disease, NFTs can also be present in other regions of the brain. Both amyloid plaques and NFTs are widely distributed throughout the neocortex. However, it must be noted that these two biomarkers of AD do not reflect the complete molecular pathology of the disease.

As further research is conducted on AD, more questions continue to be raised. The Consensus Committee (Hyman et al., 2012), which involved a panel from the United States and Europe, recommended an "ABC" staging protocol for AD neuropathologic changes, based on three morphological characteristics of AD: amyloid plaques (A), NFTs (B), and neuritic plaques (C). The neuritic plaques were most closely associated with neuronal injury. They were characterized by occurrence of dystrophic neuritis, greater local synapse loss, and glial activation (Hyman et al., 2012).

Research studies conducted on Alzheimer's disease have investigated memory loss/impairment and how it affects patients' behavior. Castel, Balota, and McCabe (2009) examined whether aging and AD influenced patient selection of what is important to recall, attending to information, and later retrieving the information. The pattern suggested that relative to healthy aging, AD leads to impairments in strategic control at encoding and value-directed recall, crucial elements of executive control of cognitive processes. The National Institute of Aging (2009) provided background information for causes, signs, and symptoms of AD relating to memory loss and thinking skills.

This study examined cognitive/behavioral symptoms of AD patients comparing those with EOAD to those with LOAD. A more accurate understanding of the progression of the disease may contribute to efforts at prevention and treatment.

Problem Statement

This study explored collaboration on the part of many scientists, researchers, and neuropsychologists. There is no known cure for AD (AA, 2013). There are numerous

research studies that have been conducted on AD patients regarding cognitive functioning related to a variety of phenomena such as memory impairment (Berwig, Leicht, Hartwig, & Gertz, 2011; Gagnon & Belleville, 2011; Mathias & Burke, 2009), personality traits (Duberfstein et al., 2011), emotion perception (Phillips et al., 2010), motivation (Forstmeier, et al., 2011), and attentional control (Coubard et al., 2011). The fact still remains that those most significantly affected by AD are individuals ranging from age 65 years to 85 years. This risk factor will most likely affect a significant number of future baby boomers (AA, 2013). As a result, in January 2011, President Barack Obama passed the National Alzheimer's Project Act (NAPA). With the help of the U.S. Department of Health and Human Services (HHS), this law was created to reduce the prevalence of or find a cure for Alzheimer's disease by: (a) coordinating research and services across all federal agencies regarding AD; (b) speeding up treatment developments that would slow down, prevent, or overturn the course of the disease; (c) improving coordination of care, treatment, and early diagnosis of AD; (d) improving outcomes for demographic populations who are at risk for AD; and (e) forming collaborative efforts globally with international bodies to fight AD (NAPA, 2011). Therefore, comparing symptoms and stages of groups with diagnosis of EOAD to that of LOAD may contribute to a greater increase in our understanding of the progression of the disease. Such an increase in understanding may contribute to more effective efforts at prevention, diagnosis, and treatment.

Aging changes

The National Institutes of Health (NIH, 2013) explained that as individuals age the brain and nervous system go through natural changes. The brain and spinal cord lose nerve cells and weight (atrophy). Nerve cells may begin to pass messages more slowly than in the past. Waste products can collect in the brain tissue as nerve cells break down, causing abnormal brain changes such as formation of amyloid plaques and neurofibrillary tangles. Breakdown of nerves can affect human senses. Reduced or lost reflexes or sensation can lead to problems with movement and safety.

Cells are the basic building blocks of tissues (Feng & Gao, 2011) and all cells experience changes with aging (NIH, 2013). They become larger and are less able to divide and multiply. Many cells begin to function abnormally and progressive loss of neural cells can occur, especially in the case of AD patients (Feng & Gao, 2011). Waste products build up in tissues with aging. Therefore, many AD patients loose oxygen and nutrients in brain cells; as well as the ability to remove carbon dioxide and wastes (Cheung & Ip, 2011). Mass loss occurs in these tissues, causing them to become lumpy or more rigid, which results in a process called atrophy (NIH, 2013). Feng and Gao (2011) suggested cell replacement as an alternative option for fighting neurodegenerative disorders such as AD.

Because of cell and tissue changes, organs (e.g., the brain) also change as individuals age. Aging organs slowly lose function. Most people do not notice this loss, because human organs are not used to their fullest ability (NIH, 2013). Conducting

research studies that explored cognitive/behavior symptoms of groups diagnosed with AD and comparing AD patients diagnosed before age 65 to those diagnosed age 65 and over, can help better understand the progression of this disease.

This study allowed me to explore the connection of cognitive/behavioral symptoms of AD to time of onset, which was beneficial. AD patients are considered to be early onset (EOAD) before the age of 65 and late onset (LOAD) at 65 years and older. LOAD is the most common type of AD. These factors allowed me to form two research groups. I compared both cognitive and behavioral symptoms of individuals with EOAD and LOAD. Then once I conducted statistical analysis, cognitive and behavioral symptoms scores were determined for each group. As a result of my research, future treatment, possible prevention, and early intervention/screening can be managed and shared across all professional disciplines (academic, scientific, private, public, government, etc.). This, in turn, could lead to more collaboration, which could increase the probability of finding a cure or at least more effective treatment for AD.

Purpose of the Study

This study explored Alzheimer's disease (AD), which is the most common form of dementia (Alzheimer's Association, 2009), has no known cure, and is fatal to those who have it. In particular, this study examined whether there is a difference in progression of the disease based upon early-onset AD (EOAD) or late-onset AD (LOAD). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition ([DSM-V] APA, 2013), lists Alzheimer's disease under the category *neurocognitive*

disorders (NCDs). The criteria for various NCDs are based on specified cognitive domains such as complex attention, executive function, learning and memory, language, perceptual-motor function, and social cognition. Criteria are met for either probable or possible Alzheimer's disease with or without behavioral disturbance and severity. By definition, major or mild NCDs affect functioning, given the central role of cognition in human life. Thus the criteria for the disorders and the threshold for differentiating mild from major NCD are based in part on functional assessment. These domains and descriptors in the DSM-V are slightly different from those included in the DSM-IV. For the diagnostic criteria for Major or Mild Neurocognitive Disorder due to Alzheimer's disease see Appendix A.

Vanderstichele et al. (2012) indicated that accurate clinical diagnostic criteria for AD are poor because the disease is a complex disorder with overlapping profiles. The authors posit that depending on the research, clinical diagnoses of AD are correct only 63% to 90% of the time. Clinical diagnosis made at first visit in confirmed cases of AD results in only 68% of AD cases being straightforward and correct. In remaining cases, 16% of clinical diagnoses made at first visit are incorrect or doubtful. In the early stages of the disease, diagnostic accuracy is much lower. Vanderstichele et al. (2012) stated that the development of revised diagnostic criteria that included biomarkers could improve diagnostic accuracy of AD significantly.

Shoji et al. (2000) and Sunderland et al. (2003) confirmed the relevance of the neurofibrillary tangles and amyloid plaques associated with AD by using these

biomarkers for AD present in cerebrospinal fluid (CSF). This research and other studies revealed that combined use of these markers (Blennow & Hampel, 2003; Engelborghs et al., 2008; Fagan et al., 2003; Sjogren, Andreasen, & Blennow, 2003) resulted in higher sensitivity and specificity and met the requirements for discriminating AD from other specific neurological disorders and normal aging (Vanderstichele et al., 2012). Vanderstichele et al. (2012) posited that biomarker assessments were helpful in addressing the AD etiological diagnosis in nonamnestic presentations of AD. In most cases of posterior cortical atrophy, typical biological AD patterns have low amyloid deposits with low tau levels, confirming initial reports of underlying AD pathology in posterior cortical atrophy after autopsy. In addition, low amyloid deposit levels together with high levels of tau are reliable signatures of an underlying pathology of AD (Braak & Tredici, 2012; Kawas et al., 2013; Vanderstichele et al., 2012).

It has been more than 100 years since AD was first identified (AA, 2012), but only within the last 30 years has research by scientists, academics, government programs, and private and public sectors gained financial-momentum and exposure. Research into AD symptoms, risk factors, causes, and treatment has uncovered a considerable amount of information in regards to AD. However, precise physiological changes that trigger AD development still remain unidentified (AA, 2012).

Over the past 150 years, advances in the treatment of heart disease and cancer are responsible for postponement of mortality and a marked change in aging biodemographics. In addition, other improvements in public health and medical care

during the 20th century have led to considerable increases in life expectancy (Carrillo et al., 2013). As a result, the principal causes of death have shifted dramatically from chiefly infectious diseases to cardiovascular disease, cancers, and increasingly, progressive neurodegenerative dementias such as AD (Kling, Trojanowski, Wolk, Lee, & Arnold, 2013). If this trend continues, individuals who were born at the beginning of the 21st century can expect to live past the age of 100, nearly double the average life expectancy only one century ago (Carrillo et al., 2013).

Most individuals with AD usually live 4 to 8 years after their diagnosis (AA, 2012). However, there are those who live as long as 20 years after being diagnosed. EOAD patients are diagnosed before the age of 65 and LOAD patients are diagnosed on or after the age of 65. By studying and comparing symptoms of EOAD and LOAD patients, it may be possible to identify the characteristics that can help increase patient survivability in general. These individuals live longer in the severe stage of the disease than any other stage. This slow progression of AD usually means a frightening fate for AD patients, not to mention having to spend the rest of their years in a nursing home. Two-thirds of individuals, who die of dementia, usually do so in nursing homes as compared to 20% of those who die from cancer or 28% of those who die from all other conditions (AA, 2012). AD is the sixth leading cause of death. In addition, slow progression of the disease also has a statistical impact on public health (Okie, 2011).

There is an incomplete understanding of the differences in disease progression between EOAD and LOAD (Panagyres & Chen, 2013; 2014). Disease progression of

EOAD and LOAD will be examined to determine whether or not cognitive/behavioral symptoms have a relation to AD time of onset. EOAD is a rare form of Alzheimer's disease in which individuals are diagnosed with the disease before age 65 (AA, 2014). LOAD is the most common form of Alzheimer's disease, in which individuals are diagnosed with the disease after age 65 (AA, 2014). There are suggestions that the underlying pathology may be different when it comes to cognitive and behavioral symptoms (Eriksson et al., 2014). Eriksson et al. (2014) concluded that there are differences between EOAD and LOAD in demographics, diagnostic work-up and pharmacological treatment. The purpose of this study was to investigate cognitive/behavioral symptoms as related to time of onset, whether that of EOAD and/or LOAD patients.

Research indicates that memory loss, impairment, and distortion are core features of Alzheimer's disease (Sternberg, 2009). Brain structures involved in memory deficits are also linked to behavior functions (Nadel & Peterson, 2013: Yu et al., 2013). In early-onset AD, genetic risk factors include amyloid precursor protein (APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2). In late-onset AD, the apolipoprotein E (ApoE) protein is also an important genetic risk factor, having at least three variations of its kind called E2, E3, and E4 alleles. According to previous studies, mutations in these various genes have been presented on AD timelines according to age (Bagyinszky, Youn, An, & Kim, 2014). The following research questions and hypotheses guided this study.

Research Questions and Hypotheses

RQ1: Are there differences in cognitive symptoms between EOAD patients and LOAD patients?

$H_0$1: EOAD patients have the same cognitive symptoms as LOAD patients.

H_a1: EOAD patients have different cognitive symptoms than LOAD patients.

RQ2: Are there differences in behavioral symptoms between EOAD patients and LOAD patients?

$H_0$2: EOAD patients have the same behavioral symptoms as LOAD patients.

H_a2: EOAD patients have different behavioral symptoms than LOAD patients.

Framework

I used the traditional memory model for this research. This model indicated that memory is the means by which we retain and draw on prior experiences to utilize information for present experience. Atkinson and Shiffrin (1968) posited that memory can be perceived in three memory stores: sensory memory, short-term memory, and long-term memory. When AD is present, memory is lost, specifically episodic memory in the early stage of AD; as the disease progresses, semantic memory is impaired. However, non-declarative memory is still intact until near death (Sternberg, 2009), which will be discussed in further detail in Chapter 2.

Further research is needed to understand specific stages of the disease in comparative groups: EOAD patients versus LOAD patients, as well as behaviors noticed after cognitive decline. As a result, this study was pursued using quantitative informant

instruments, the Behavioral Pathology in Alzheimer's disease (BEHAVE-AD) (Reisberg, Borenstein, Salob, Ferris, Franssen, & Georgotas, 1987) and the Short Form of the Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE) (Jorm, 1994) as well as a qualitative interview conducted with several of the participating caregivers on behalf of their AD patients/family members. The research design was a mixed method approach.

Nature of the Study

I used a mixed methodology in this study, both quantitative and qualitative approaches. Data was obtained from caregivers of individuals who had been diagnosed with AD. The caregivers were given a demographic background questionnaire (Bivin, 2013) to complete on behalf of the individual with AD. The BEHAVE-AD Informant instrument (Reisberg et al., 1987) and the Short IQCODE (Jorm, 1994) were completed by the caregiver on behalf of the AD patient as well. A qualitative interview was given to several participants to obtain personal perspectives and to explore symptoms in more detail. Because the cognitive and behavioral informant instruments, and the demographic questionnaire, were filled out by the caregiver instead of the actual AD patient, information was not as precise. The BEHAVE-AD Informant assessed behavioral symptoms of the AD patient and the Short IQCODE assessed cognitive symptoms. But before these quantitative tools were presented, I conducted a qualitative interview with six of the participant caregivers. Once the caregiver completed each assessment, this information was scored and categorized into EOAD/LOAD. To obtain the present stage

of the AD patient, a definition for each stage was presented on the demographic questionnaire, which I handed out to Alzheimer Association Support groups for caregivers in various locations throughout the state of Texas. Further details were discussed in Chapter 3.

Information was obtained from experts in the fields of psychology and psychiatry, as well as from dissertation committee chair and members, to assist in determining relevant symptoms and stage levels of the AD population. I collected data from the Alzheimer's Association, the National Institute of Aging, as well as various partnerships. In regards to the Alzheimer's Association, the caregivers were the sole source of information on behalf of the sample of the AD patient population. The same method was used to determine the AD stage level; stage levels were defined according to Reisberg's seven-stage framework in Alzheimer Association's website (AA, 2013). Quantitative analysis drawn from the data (information from the caregiver and symptoms endorsed from research instruments) provided statistical inferences of the most salient symptoms. In addition, it was the intent of this study to explore and obtain themes/paradigms that originated from the qualitative aspect of the research.

Definition of Terms

The following are definitions of cognitive and neurological terms used in describing Alzheimer's disease.

Acetylcholine (ACh): a key neurotransmitter that modulates neural processing within the cortex and between the thalamus and cortex (Savage, 2012).

Alzheimer's disease: the major cause of dementia in old age, characterized by neurofibrillary tangles, amyloid plaques, and neuron loss (Pinel, 2009).

Amyloid: a protein that is normally present in small amounts in the human brain but is a major constituent of the numerous plaques in the brains of Alzheimer's patients (Pinel, 2009).

Apolipoprotein E: a gene product that is a significant risk factor for late onset Alzheimer's disease (Bagyinsky et al., 2014).

Atrophy: degeneration or wasting away of an organ, structure, or body part through disease, inadequate nutrition, or disuse (Colman, 2006).

Cerebrospinal fluid (CSF): colorless fluid produced in the brain that fills the subarachnoid space that circulates through the cerebral ventricles before flowing passively into the venous bloodstream (Colman, 2006; Pinel 2009).

Declarative memory: A storage system for declarative knowledge, involving structures in the "temporal lobes, especially the hippocampus. Information contained in it is acquired by a form of learning that requires conscious awareness and that occurs quickly (Coleman, 2006).

Early-onset Alzheimer's disease (EOAD): a rare form of Alzheimer's disease in which individuals are diagnosed with the disease before age 65 (AA, 2014).

Episodic memory: A type of long-term memory for personal experiences and events (Coleman, 2006).

Explicit memory: Memory that is revealed when performance on a task requires conscious recollection of information previously learnt (Coleman, 2006).

Familial AD: early-onset Alzheimer's disease that runs in families, where copies of one or two genes are inherited from an individual's parents (Bagyinsky et al., 2014).

Genetic mutation: a permanent change in the DNA sequence that makes up a gene. Gene mutations occur in two ways: they can be inherited from a parent or acquired during a person's lifetime (NIH, 2014).

Implicit memory: A type of memory that is revealed when learning facilitates performance on a task that does not require conscious or intentional recollection of what was learnt (Coleman, 2006).

Late-onset Alzheimer's disease (LOAD): the most common form of Alzheimer's disease in which individuals are diagnosed with the disease after age 65 (AA, 2014).

Mild Cognitive Impairment: a condition characterized by slight amnesia without dementia or other forms of cognitive impairment, often a precursor of Alzheimer's disease (Colman, 2006).

Mutation: a process that creates genetic variation or a change in the "genes or chromosomes of a cell" (Colman, 2006).

Neurofibrillary tangles: a knotty mass of neurofibrils and insoluble fibers composed chiefly of breakdown products of the tau protein, occurring in the brains of most people over 70 years old and found abundantly in the hippocampi and amygdalae of patients with Alzheimer's disease and other disorders (Colman, 2006).

Neurogenesis: the generation of new neurons to replace damaged ones (Colman, 2006).

Neurons: cells of the nervous system that are specialized for receiving and transmitting electrochemical signals (Pinel, 2009).

Neurotransmitter: a small amine or peptide but also a substance such as the gas nitric oxide, by which a neuron communicates with another neuron or with a muscle or gland via a synapse (Colman, 2006).

Non-declarative memory: Memory for non-declarative knowledge, involving memory systems that do not draw on the individual's general knowledge (Coleman, 2006).

Precursor: a forerunner, or something that precedes or heralds something else; in particular, a chemical substance from which another more important substance is derived or synthesized (Colman, 2006).

Procedural memory: a form of non-declarative memory, which is a storage system for procedural knowledge, information in it being acquired through a form of learning that is relatively slow, requiring repetition over many tasks, and often occurring without conscious awareness (Coleman, 2006).

Semantic memory: A type of long-term memory for factual information about the world, excluding personal episodes in one's life (Coleman, 2006).

Sporadic AD: early-onset Alzheimer's disease without any family history or inheritance pattern of mutated genes, like that of familial AD (Bagyinsky et al., 2014).

Significance

The significance of this study is that it contributed to the current knowledge base regarding AD and illuminated similar/different symptoms and stages related to early versus late onset of the disease. Many researchers have focused attention on the temporal lobe of the brain because amyloid plaques and neurofibrillary fibers play important roles in the spread of AD to brain tissues in this area (Good, Hale, & Staal, 2007). Khachaturian, Mielke, and Khachaturian (2012) brought attention to cognitive dysfunction during various stages of AD, and how it influenced patients' behaviors.

In Chapter 2, I will discuss research that has and is being conducted on memory and behavioral aspects of AD. There maybe evidence-based knowledge revealed from studying symptoms and stages of the disease by focusing on the comparison of EOAD to that of LOAD. This could lead to better and more meaningful ways for caregivers and clinical professionals to detect/identify symptoms of AD patients at specific stages of the disease.

Summary

This study was conducted to contribute to the current knowledge base concerning AD presented by previous researchers. AD is the sixth leading cause of death in the United States, but is the fifth leading cause of death for individuals aged 65 and older (AA, 2016). The financial burden to treat AD is approximately $200 to $600 billion annually. However, when the baby boomer generation reaches the critical age when the onset of AD appears, the financial cost could increase to $1 trillion, annually (Okie,

2011). Considering there is no known cure for AD, this study focused on and compared symptoms and stages of AD in groups who had EOAD versus those who had LOAD. My intent was to offer a better understanding of the progression of AD. These implications could in turn be shared with other researchers, scientists, and clinical professionals to improve future treatment/prevention outcomes. In addition, this research provided information that could contribute to the development of treatments to address the continued increase in the aging population's possibility of inheriting or developing AD.

Chapter 2: Literature Review

Introduction

Alzheimer's disease (AD) is the most common form of dementia (Alzheimer's A, 2009). Dementia is impairment or loss of memory, especially evident in the learning of new information, and of thinking, language, judgment, and other cognitive faculties, without clouding of consciousness (Colman, 2006). AD is a type of dementia or condition that develops when neurons, or nerve cells, in the brain die. Death of these nerve cells causes deficits in an individual's memory, behavior, and ability to think. These impairments caused by AD can prevent an individual from performing basic bodily functions and eventually cause death (Pinel, 2009).

The Alzheimer's Association (AA, 2016) reports that in the United States, Alzheimer's disease is the sixth leading cause of death. In Americans over the age of 65 years (LOAD), it is the fifth leading cause of death. It is estimated that 5.4 million Americans have AD including 200,000 individuals who are considered early onset sufferers (EOAD), diagnosed before the age of 65 (AA, 2016). Over the next decade, 10 million baby boomers are expected to develop AD. By the year 2050, the prevalence of AD will increase to between 11 million and 16 million cases across all racial and ethnic groups (LOAD), specifically those over age 85 (AA, 2012). Other causes of death such as stroke, heart disease, and prostate cancer, have decreased by 20%, 13%, 8%, respectively, in the past several years. However, deaths from AD have increased by 66% (AA, 2012).

In 2012, a total of $200 billion dollars were expended on the care of individuals with AD and other dementias.

Although AD was identified more than 100 years ago, there is no known cure for this degenerative disease (AA, 2012). It was only in the past 30 years that widespread attention has been given to research that involved AD symptoms, risk factors, and treatment (Cummings, Golde, Sano, & Tariot, 2007; Khachaturian, Khachaturian, & Thies, 2012). It has only been a few years since collaborations among private, government, and academic institutions have been formed to create a national research initiative (NAPA, 2011). Following is an explanation of how this literature review was accomplished.

Literature Search

The literature search was conducted by retrieving articles from Walden University library using the PSYCArticles database, peer-reviewed articles retrieved from subscription copies of *Alzheimer's & Dementia: The Journal of the Alzheimer's Association (2012/2013), Archives of General Psychiatry, Clinical Geriatrics: A Clinical Journal of the American Geriatrics Society, Current Psychiatry, Cognitive Science, and the Psychological Review*. I used the Alzheimer's Organization website to review updated information that had been presented by members of Alz.org. I also used several books to compare information and use during the search process. Words or phrases that I used to retrieve peer reviewed articles included: *Alzheimer's disease, mild cognitive impairment, symptoms of Alzheimer's disease, risk factors for Alzheimer's disease,*

memory loss, caregivers and Alzheimer's disease, stages and *progression and Alzheimer's disease*. All sources were evaluated for relevancy of topics concerning Alzheimer's disease.

Amyloid Hypothesis and Memory Theory of Alzheimer's Disease

AD is a syndrome consisting of deficits in memory, reasoning, and judgment, and changes in behavior, communication abilities, and mood (Berwig, Leicht, Hartwig, & Gertz, 2011; Gagnon & Belleville, 2011; Mathias & Burke, 2009). Duara et al. (2013) posited that Alzheimer's disease occurs as a result of protein accumulation in key areas of the brain linked to the creation and maintenance of memories and the accuracy of those memories. Activity in the hippocampus increases in response to this protein accumulation in an effort to protect these memories. Over time this excess activity can cause damage to the hippocampus as AD progresses (Gauthier & Molinuevo, 2013).Although there has been a significant increase in understanding of how the brain changes with AD, researchers do not know the cause of this fatal disorder.

The amyloid hypothesis is the leading theory explaining AD pathogenesis. Braak and Del Tredici (2012) posited that aberrant processing of amyloid precursor protein (APP) leads to the accumulation of insoluble amyloid in the brain. Lelos, Thomas, Kidd, and Good (2011), Lim et al. (2013), and Nekkiksimmons et al. (2013) published literature reaching the same conclusion. Neurotoxic amyloid β (Aβ) peptide Aβ42 is an APP processing product. The gathering or aggregation of Aβ42 into multiple oligomeric forms

and deposition in amyloid plaques is considered an initial event in AD, which is followed by neurofibrillary tangle formation, neuronal loss and dysfunction, and then dementia.

Genetic Varieties of Alzheimer's disease

Neuropathological hallmarks of familial and sporadic AD include extracellular parenchymal and cerebrovascular amyloid deposits, intracellular neurofibrillary tangles, and loss of neurons and synaptic integrity in explicit areas of the brain (Kar, Slowikowski, Westaway, & Howard, 2004; Yu et al., 2013). Genetic and environmental factors can both contribute to AD development.

Early onset AD (EOAD)/Familial and Sporadic AD

Familial AD runs in families (copies of one or two genes inherited from an individual's parents) and sporadic AD or nonfamilial AD has no inheritance pattern of mutated genes like that of familial AD (Alzheimer's Association, 2016). EOAD may be either familial or sporadic and may be caused by mutations in three genes: amyloid precursor protein (APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2), which are located on three chromosomes (Bagyinszky, Youn, An, & Kim, 2014). Mutations in the APP gene will cause an abnormal form of amyloid protein to be produced. Mutations in the PSEN1 gene will cause an abnormal presenilin 1 protein to be produced. Mutations in the PSEN2 gene will case an abnormal presenilin 2 protein to be produced (Bagyinsky et al., 2014).

According to the National Institute of Health, amyloid precursor protein (APP) is found in the brain and is believed to play a role in neuron formation (NIH, 2014).

Presenilin proteins help to process amyloid proteins by cutting them into smaller segments or peptides with the help of other enzymes (Bagyinsky et al., 2014): However when mutations of the presenilin genes occur, this disrupts the processing of the amyloid precursor protein, causing overproduction of amyloid-β peptide (Bagyinsky et al., 2014). This protein fragment can build up in the brain and cause formation of clumps, called amyloid plaques, with the end result likely leading to neuronal death and to progressive signs and symptoms of AD (Bagyinsky et al., 2014; Kar et al., 2004).

Point mutations in the gene for amyloid precursor protein (APP) on chromosome 21 have been associated with early-onset (< 65 years) familial AD cases (Yu et al., 2013). On the other hand, many early onset cases have been linked to alterations in 2 other genes: PSEN1 on chromosome 14, where most AD risk factor mutations have been detected; and PSEN2 on chromosome 1. Mutations of these three genes can account for 30%-50% of all autosomal dominant early onset cases (Kar et al., 2004).

Late onset AD (LOAD)/Apolipoprotein E

Bagyinszky et al. (2014) stated that the apolipoprotein E (APOE) gene is inherited and is an important genetic risk factor for LOAD. Apolipoprotein E is a major cholesterol carrier in the brain and can be involved in the repair and maintenance of neurons (Bagyinsky et al., 2014). There are at least three variations of the APOE gene, which consist of ε2, ε3, and ε4 alleles. The ε4 allele of the APOE gene, on chromosome 19, has been linked with a significant high risk for late-onset of AD (Bagyinsky et al., 2014; Brainerd et al., 2013). Kar et al. (2004) explained that having a single copy of the ε4

allele can increase the chances of inheriting or developing AD 2 to 5 times, but having two ε4 alleles can raise the chances to more than 5 times. Bagyinsky et al. (2014) report that ε3 is the most common APOE gene found in the general population. Both ε2 and ε3 may participate in neuronal repair and maintenance. The ε2 allele, on the other hand, protects against developing AD (Bagyinsky et al., 2014; Kar et al., 2004). Both ε2 and ε4 alleles have been associated with chromosome 19. Nonetheless, Kar et al. (2004) determined that none of the AD cases in their sample were associated with any of these genes.

Recent postmortem research (Yu et al., 2013) was conducted on participants (*N*=581) who came from two longitudinal clinical-pathological studies, the Religious Orders Study (ROS) and the Memory and Aging Project (MAP). The authors' goal was to test the hypothesis of an association of APOE ε4 allele with cognitive decline. Participants underwent cognitive performance evaluations annually for 18 years prior to death. Assessments provided objective evidence suggesting that ε4 is an important determinant of late-life change in cognition (including terminal decline) and may contribute to AD pathology (Yu et al., 2013). There still remains controversy concerning whether ε4 is a risk factor in the transition from mild cognitive impairment to AD (Brainerd et al., 2013).

Neurofibrillary tangles are abundant in the brains of individuals with AD, especially in the entorhinal cortex, hippocampus, amygdala, association cortices of the frontal, temporal, and parietal lobes, and certain subcortical regions projecting to these

regions (Kar, Slowikowski, Westaway, & Howard, 2004). Neurofibrillary tangles are composed of paired helical filaments (PHF) and sometimes single straight filaments containing an abnormal hyperphosphorylated form of the microtubule-associated protein tau. PHF formation reduces the ability of tau to stabilize microtubules which leads to neuronal transport disruption and eventually to the death of affected neurons. The degree of neurofibrillary pathology, and specifically the amount of cortical neurofibrillary tangles, positively correlates with the severity of dementia (Kar et al., 2004).

Yu et al. (2013) stated that neuritic plaques are multicellular lesions containing amyloid peptide deposits surrounded by dystrophic neuritis, reactive astrocytes, and activated microglia. The main amyloid peptides found in the plaques are β-amyloid$_{1-42}$ (Aβ_{1-42}) and Aβ_{1-40p} peptides that are generated by proteolytic cleavage of APP. Aβ_{1-42} is deposited first and is the predominant form in senile plaques, but Aβ_{1-40} is deposited later on during progression of AD. Evidence suggests that Aβ peptide accumulation in the brain, over time, initiates or contributes to AD pathogenesis (Kar et al., 2004; Yu et al., 2013). Overproduction or reduced clearance, or both, of Aβ peptides are likely key to amyloid aggregation. This in turn adds to neurofibrillary tangle development and subsequent neuronal degeneration. Research studies of adult animals and of APP transgenic mice demonstrate that injection of aggregated Aβ induces neuronal loss in selected regions of the brain (Kar et al., 2004; Yu et al., 2013).

Vloeberghs, Van Dam, Coen, Staufenbiel, and De Deyn (2006) conducted in vivo research involving APP23 transgenic mouse models, which are valuable animal models

of AD. These researchers suggested that transgenic mice models mimic memory deficits as well as several devastating behavioral disturbances of demented patients. These transgenic mouse models approximate the clinical situation and are able to provide an instrument to evaluate diverse therapeutic interventions (Vloeberghs et al., 2006). Aβ injection peptide can increase formation of neurofibrillary tangles in tau transgenic mice (Vloeberghs et al., 2006). Evidence of this relation was initially observed in family members with familial AD. Although results suggest that Aβ peptides play a role in the neurodegenerative process, both the role they play in the brain and the means by which they cause neuronal loss and tau abnormalities in AD are poorly understood (Kar, Slowikowski, Westaway, & Howard, 2004).

Who is affected by Alzheimer's disease?

Individuals affected by AD experience a variety of symptoms that can ultimately lead to death. The healthcare system, the government, academia, and scientific communities, as well as family members and caregivers are also affected by the effects of this degenerative disorder (Delavande, Hurd, Martovell, & Langa, 2013; Reuben, 2007; Stefanacci, 2008). The baby boomers will comprise about 10 million individuals who will contract the disease over the next decade. With this in mind, the healthcare system as well as the government will need to understand and prepare for the impact this will have on future spending, medical and psychological treatment, outcomes, and prevention measures (Furiak et al., 2012; Mielke et al., 2012; Naylor et al., 2012; Wimo, Jonson, Bond, Prince, & Winblad, 2013). In 2012, the estimated cost of treatment for Alzheimer's

patients was $200 billion (Okie, 2011). There are also roughly 10 million unpaid caregivers who are currently assisting individuals who have been diagnosed with the disease.

Brain Functions and Structures

Postmortem studies on AD have focused on some of the brain structures involved in memory, such as the hippocampus (Nadel & Peterson, 2013; Yu et al., 2013). Examinations of AD patients have also identified some of the microscopic aberrations associated with the disease process (unique tangled fibers and plaques in the brain tissue). Even though lesion techniques provide a basic foundation for understanding the brain's relationship to behavior, these techniques are limited because they cannot be performed on the living human brain (Kar, Slowikowski, Westaway, & Howard, 2004).

If scientists want to understand physiological processes and functions of the brain, they have to use in vivo research, which is performed solely on animals (Vloebergs, Van Dam, Coen, Staufenbiel, & De Deyn, 2006). Early in vivo research consisted of inserting microelectrodes into the brain of an animal (i.e., a cat, mouse, or a monkey) in order to obtain a single-cell recording of a single neuron in the brain. In humans, Langeslag and van Strien (2009) revealed how the brain is being studied by using electrical analyses (e.g., electroencephalograms and event-related potentials), X-ray techniques (e.g., angiograms and computer tomograms) and magnetic field computer analyses within the brain (magnetic resonance imaging). Taylor, Rastle, and Davis (2013) conducted a

similar study showing blood flow and metabolism computer analysis within the brain (positron emission tomography and functional magnetic resonance imaging).

Yerokhim et al. (2012) conducted a pilot study demonstrating the benefits of exercise on memory and cognition using EEG and ERP. Currently, none of these techniques provides definite mappings of exact functions to particular brain structures, regions, or processes (Baxter & Bucci, 2013; Brainerd et al., 2013; Yu et al., 2013). However, some discrete brain structures, regions, or processes have been found to be involved in particular cognitive functions (Nadel & Peterson, 2013). Thus, present understanding of this involvement allows only correlational evidence of some type of relationship. Sophisticated analyses can highlight increasingly precise relationships, but research is not at the point where a specific cause-effect relationship between a given brain structure or process and a particular cognitive function can be determined. Lastly, the above techniques provide the best information only in combination with other experimental techniques for understanding cognitive functioning complexities (Baxter & Bucci, 2013; Brainerd et al., 2013; Yu et al., 2013).

Brain Regions

The brain is part of the nervous system and can be viewed as being divided into three major regions: forebrain, midbrain, and hindbrain (Sternberg, 2009). The forebrain is the region located toward the top and front of the brain and contains the cerebral cortex, the basal ganglia, the limbic system, the thalamus, and the hypothalamus. The limbic system is important to emotion, motivation, memory, and learning. Therefore, the

limbic system is important to Alzheimer's disease, especially if memory is distorted or impaired. MacDuffie et al. (2012) posited that memory distortion in AD is a clinically relevant concern. AD patients and their caregivers frequently report incidents of getting lost, misplacing possessions, and confusing present experiences with past ones. The limbic system allows individuals to better adapt to a changing environment. It comprises three central interconnected cerebral structures, which includes the amygdale, the septum, and the hippocampus (Sternberg, 2009).

Wolk and Dickerson (2011) indicated that the medial temporal lobes (MTL), particularly the hippocampus, play a central role in episodic memory function. The most profound forms of amnesia are associated with damage to these brain structures. Alzheimer's disease is the most common form of acquired amnesia (Wolf & Dickerson, 2011). Given the involvement of neuropathology, specifically neurofibrillary tangles in the medial temporal lobes (MTL) of AD patients, much of the work examining AD memory impairment has focused attention on the hippocampus and other structures of the MTL (Wolk & Dickerson, 2011).

The hippocampus is a structure within the limbic system (Nadel & Peterson, 2013). The hippocampus and nearby cerebral structures are important for explicit memory of experiences and other declarative information. The hippocampus also plays a key role in declarative information encoding. According to Nadel and Peterson (2013), it is involved in the transfer of newly synthesized information into long-term structures supporting declarative knowledge. The basal ganglia are memory structures responsible

for nondeclarative memory forms. These structures are primary in controlling procedural knowledge, one form of nondeclarative memory (Willems, Salmon, & Van der Linden, 2008).

Memory Processes

Memory loss, memory impairment, and memory distortion, as well as impairment in thinking, are core features of AD (MacDuffie et al., 2013). Therefore, a general review of memory processes can be useful in understanding these specific memory symptoms in AD.

Memory is the means by which individuals retain and draw on prior experiences in order to function in the present. It is the ability of the brain to store and access learned experiences (Sternberg, 2009). Memory and learning are two ways of thinking about the same thing. Each of these processes deals with the brain's ability to change in response to experience. Memory allows changes of the brain to be stored and then reactivated (Pinel, 2009).

MacDuffie et al. (2013) conducted a study on memory distortions comparing performance of mild-to-moderate AD patients to that of aged-matched, healthy older adult participants on short-term memory (STM) and long-term memory (LTM) tasks. Participants were tested on the STM version of the Deese-Roediger-McDermott (DRM) task to measure recall memory for four-word lists and were tested on the LTM version of the DRM task to measure recall memory for 12-word lists. AD participants showed

greater impairment on the LTM task than the STM task. Authors concluded that STM impairment with some preserved semantic process is evident in AD.

Memory is the capacity for storing and retrieving information. Encoding, storage, and retrieval are the three processes involved in memory. These three processes contribute to whether information is remembered or forgotten (Sternberg, 2009).

Encoding

Vermeulin, Chang, Mermillow, Pleyers, and Corneille (2013) agreed that processing information into memory is called encoding. There are several ways of encoding information verbally. Structural encoding entails focusing on what words look like; phonemic encoding entails focusing on the sound of words; and semantic encoding entails focusing on the meaning of words. Castle, Balota, and McCabe (2009) focused on encoding, implying that older adults perform poorer on tasks involving executive processes, working memory and frontal lobe functions, leading to difficulties on tasks such as attention and memory. Hence, examination of attention control impairments and behavioral development measures can serve as useful early diagnostic measures of AD.

Storage

After information enters the brain it is stored. Atkinson and Shiffrin (1968) proposed the three-stage model used to describe the storage process. This model indicated that information is stored in three memory systems (sensory memory, short-term memory, and long-term memory) sequentially.

Sensory memory. Winkler and Cowan (2005) explained that sensory memory stores information which is received through sense organs, but only for an instant. The information is unprocessed, but sensory memory capacity is very large. Information is sometimes transferred from sensory memory into short-term memory (STM), which holds information for about 20 seconds. However if this information is rehearsed it can stay within STM between 15 and 30 seconds. Rehearsal of information in STM can be accomplished by repeating items verbally (Winker & Cowan, 2005).

Short-term memory/working memory. Vermeulen, Chang, Mermillod, Pleyers, and Corneille (2013) and other researchers referred to short-term memory as working memory. Instead of referring to it as a temporary information storage system, working memory is an active system used to manipulate information. It holds information individuals are consciously thinking about in the present, i.e., processes like adding and subtracting, problem solving, thinking about the meaning of what is heard or read, or carrying out a sequence of operations. Working memory holds information that is derived from sensory inputs or retrieved from long-term memory (Vermeulen et al., 2013).

The concept of working memory was first introduced by Baddeley and Hitch (1974). The authors proposed that short-term memory be reformulated as a working memory that could perform a number of different functions. Baddeley and Hitch (1974) believed that Atkinson's and Shiffrin's (1968) short-term memory described in the multi-store model was too simple. The model depicted STM as a single system or store without any subsystems. Baddeley and Hitch (1974) indicated that working memory is short-term

memory, but instead of information going into one single system, there exist different systems for different types of information. The authors suggested that working memory consists of a central executive that controls and coordinates operation of the phonological loop and the visuo-spatial sketch pad, which are two subsystems. The central executive directs the memory system and allocates data and resources to the two subsystems. The visuo-spatial sketchpad is used for navigation and stores and processes information in a visual or spatial form. The phonological loop is responsible for manipulation of speech-based information and deals with written and spoken material.

Long-term memory. Winkler and Cowan (2005) indicated that information can be transferred from short-term/working memory to long-term memory (LTM) and vice versa. LTM may store information for a lifetime and it may have an infinite amount of capacity. However, because information stays in an individual's LTM does not mean that the information will be readily or easily retrieved (Winkler & Cowan, 2005). Retrieval is the process of getting information out of long-term memory and into short-term or working memory. The brain organizes information by category in LTM. Another way information is organized in LTM is by connection to other information, relevance, and familiarity. Tulving (1972) proposed subdivisions of long-term memory, e.g., explicit memory, which involves episodic and semantic memory, and implicit memory which involves procedural memory.

Explicit and Implicit Memory

Learning changes the brain and memory refers to the storage and retrieval of information of these changes (Pinel, 2009). Memory includes both explicit and implicit memory, which are two functionally and anatomically separable long-term memory systems in humans (Pinel, 2009). Long-term memory stores a lifetime of information and allows the retention of physical skills and word meanings that have been learned. Experts and research psychologists that gain insight into memory from amnesia victims are able to distinguish between explicit and implicit memories (Eakin & Smith, 2012; Tulving & Schacter, 1990; Willems, Salmon, & Van der Linden, 2008). As a result, amnesia patients have been studied to gain valuable insight into memory functioning in general.

Explicit Memory: Episodic and Semantic

Gold and Budson (2008) posited that explicit memory, also referred to as declarative memory, is the intentional memory or conscious recollections of facts and events gained from past experiences (e.g., cooking, driving to work, and using the computer). Explicit memory is also referred to as declarative memory because it can be remembered and described in words (Tulving & Schacter, 1990). Older individuals often experience problems with explicit memory (Ward, Berry, & Shanks, 2013).

Lah and Smith (2014) reported differential relations between two varieties of explicit long-term memories: episodic and semantic memories. These authors conclude that children with semantic memory impairments who experience medial temporal lobe

epilepsy have problems with reading comprehension, spelling, and reading accuracy. However, children with episodic memory impairments do not experience any problems in reading comprehension, but do have disturbance in spelling and reading accuracy (Lah & Smith, 2014). As in AD, these children do not have the ability to store new information, which would be the case of spelling and reading accuracy that involves new meaning of words and being able to spell new words. Glosser, Friedmand, and Grugan (1999) conducted a study on 21 AD patients and 27 matched controls to understand why AD patients performed slightly below controls on all reading and spelling tasks. The authors concluded that the mild alexia and agraphia in AD reflected semantic deficits and nonlinguistic impairments, which occur in patients with focal lesions in the left hemisphere.

In other words, Glosser et al. (1999) explained that:

> "basic orthographic and phonological knowledge that relies on procedural integrity mediated by the regions within the left, language-dominant cerebral hemisphere remain intact through the middle stages of AD. However, lexical-semantic, episodic, and working memory functions that are subserved by a more distributed cerebral network become impaired in the early stages of AD. This can result in oral and written language disturbance seen in individuals with probable AD," p. 357.

Episodic memory. Gold and Budson (2008) suggested that there are six cognitive domains that are commonly disturbed in individuals suffering from AD. They include

memory, language, executive functioning, visuospatial functioning, affect, and attention. Memory impairment is the central problem of all the disturbances. Memory problems are also one of the main reasons for admission to residential nursing facilities. A longitudinal study reported that annual savings of $4 billion could be achieved by delaying the onset of nursing home care by 1 month for elderly adults with dementia illnesses (Gold & Budson, 2008). Knowledge of the specific memorial processes that are impaired in AD may be important to researchers and scientists developing therapies and assessing the efficacy of those therapies. Gold and Budson (2008) characterized AD as a progressive neurodegenerative disease manifested by cognitive disturbances, the earliest and most prominent being impaired episodic memory.

Episodic memory is a form of explicit memory that is most affected by amnesia (Pinel, 2009; Wolk & Dickerson, 2011).Episodic memory is a part of long-term memory, which involves conscious thought and is declarative. Episodic memory also involves storing information about events or episodes that have occurred throughout an individual's life (McLeod, 2010).

A number of episodic memory measures involving verbal list learning tasks have been used to diagnose and monitor disease progression in AD (Wolk & Dickerson, 2011). Immediate recall, delayed free recall, and recognition memory are memory measures often assessed using verbal list learning tasks. However, there is a major debate in memory literature of whether recollection is differently represented in the MTL relative to familiarity (Wolk & Dickerson, 2011). Serra et al. (2010) explained that recollection

and familiarity are two types of processes involved in episodic memory recognition. Serra et al. (2010) stated that "recollection is the conscious re-experience of a previous event, and familiarity is the feeling of having previously encountered a stimulus with no associated contextual information," p. 316.

Individuals with amnesic mild cognitive impairment (a-MCI) had an increased risk of developing Alzheimer's disease (Serra et al., 2010). Previous studies have established characteristic episodic memory impairment in a-MCI, with early recognition dysfunction. Serra et al. (2010) conducted a study on 19 patients who had been diagnosed with a-MCI and compared them with 23 healthy patients who were matched for sex, age, and education The authors used the process dissociation procedure (PDP) and the remember/know (R/K) procedure to assess whether the patient group recognition deficits were due to recollection selective impairment rather than familiarity. Both procedural results revealed selective preservation of familiarity in a-MCI patients. During the study phase of the R/K procedure, MCI-patients showed significant recollection impairment for words that were anagrammed or read. Serra et al. (2010) hypothesized recollection and familiarity as being independent processes coupled with different anatomical substrates.

Semantic memory. Semantic memory is also a form of explicit memory and it is an accumulation of factual knowledge, but it is not usually affected by amnesia. However, semantic memory is affected by AD (Pinel, 2009; Wolk & Dickerson, 2011). Perri, Zannino, Caltagirone, and Carlesino (2012) further discussed distinctions of long-term memory. Semantic memory is another part of long-term memory that also involves

conscious thought and is declarative. This part of long-term memory includes knowledge about word meaning as well as general knowledge. Semantic memory is also responsible for storing information about the world. In a disease stage of AD, the authors explain that patients may not be able to name objects or describe the semantic characteristics of concepts. However, they may still possess the ability to produce superordinate category names of objects or place them in the correct semantic category (Perri et al., 2012).

Implicit Memory: Procedural Memory

Implicit memory, referred to as nondeclarative memory, is the unintentional memory or unconscious recollections of facts and events gained from past experiences (Tulving & Schacter, 1990). Generally, implicit memory is not affected by age (Ward, Berry, & Shanks, 2013). Facets of implicit memory appear to remain intact in AD victims through final disease stages until death.

Procedural memory. Procedural memory is a form of implicit memory (long-term memory), which involves knowing how to do things such as memory of motor skills; it is not generally affected by AD (Tulving & Schacter, 1990). This nondeclarative act, procedural memory, does not involve consciousness, and it is an automatic response. Knowing how to ride a bike is an example of procedural memory (Willems, Salmon, & Van der Linden, 2008). Distinction between procedural and declarative memory came from research on patients with amnesia (Gobel et al., 2013). Procedural memory and emotional responses are two forms of nondeclarative memory. Procedural memory, associated with some forms of semantic memory, is not affected by amnesia or damage to

the hippocampus (Willems et al., 2008). However, it is affected by damage to the cerebellum or disorders that alter the basal ganglia (Gobel et al., 2013). The cerebellum is most connected to working memory and its adaptive models of working memory processing are fed back to the frontal lobe for control processes. It allows for the mental manipulation of information during memory encoding (Gobel et al., 2013). Emotional responses are intense personal memories that have close association with the amygdala, which manages fear reactions. Both the amygdala and the hippocampus have close association with each other and each plays key roles in traumatic experiences that provoke anxiety (Willems et al., 2008).

Implicit habit learning is not linked to higher level cortical association because AD patients perform normally on implicit habit learning tests, confirming that habit learning does not rely on explicit memory and the MTL brain regions that subserve explicit memory (Eakin & Smith, 2012). This information supported other studies (Gobel et al., 2013; Wilkinson et al., 2011) confirming that the basal ganglia played a key role in implicit habit learning of AD patients. However, there are other researchers who disagreed and believed that working memory mechanisms were the reasons AD patients performed normally on implicit habit learning tests (Nosofsky et al., 2012; Smith, 2008).

Implicit skill learning depends on nondeclarative memory that operates independent of the MTL memory system and, instead, depends on corticostriatal circuits between the basal ganglia and cortical areas supporting motor function and planning (Gobel et al., 2013). Basal ganglia are a collection of nuclei deep to the white matter of

cerebral cortex, which are inhibitory. The function of the basal ganglia is complex and contributes to some of the subconscious aspects of voluntary movement such as inhibiting tremor and accessory movements (Wilkinson, Khan, & Jahanshahi, 2009).

The basal ganglia do not initiate movement, but contribute to complex motor circuit coordination (Wilkinson et al., 2009). This region of the brain is associated with four neurotransmitters: acetylcholine, dopamine, gamma-aminobutyric acid (GABA), and serotonin (Pinel, 2009). Acetylcholine levels are greatly reduced in AD patients. The reduction in acetylcholine is the result of degeneration of the basal forebrain, which is a midline area located above the hypothalamus (Pinel, 2009). Neurotransmitters and modulators such as acetylcholine (ACh), serotonin, noradrenaline and somatostatin were altered in patients with AD. Karr, Slowikowski, Westaway and Mount (2004) indicated that the amount of activity of the ACh-synthesizing enzyme, choline acetyl-transferase (ChAT) in the neocortex was significantly decreased, correlating positively with the severity of dementia. Decreased choline uptake, and ACh release and cholinergic neuronal loss from the region of the basal forebrain further indicated a selective presynaptic cholinergic deficit in the hippocampus and neocortex of the brains of individuals with AD.

Acetylcholine also appeared to enhance neural transmission associated with memory (Hartig et al., 2014; Kar et al., 2004). High concentrations of acetylcholine were found in the hippocampus of normal people and low concentrations of this neurotransmitter were found in individuals with Alzheimer's disease. Moreover, AD

patients showed severe loss of brain tissue that secreted acetylcholine. Croxson et al. (2012) explained that acetylcholine had been implicated in episodic memory, which was damaged in AD. Acetylcholinesterase inhibitors (AChEIs) such as donepezil, galantamine, and rivastigmine work by raising ACh levels and has demonstrated significant symptomatic efficacy in AD (Parsons et al., 2013).

The three AChEI's underlying mechanisms were distinguished by target protein specificity (Parsons et al., 2013). Donepezil independently has interacted with neuronal nicotinic Ach receptors and is a specific reversible inhibitor of AChE. Rivastigmine, in contrast, is a pseudo-irreversible AChE inhibitor. Rivastigmine has a similar affinity level for butyrylcholinesterase (BuChE), which is a non-specific enzyme that hydrolyses ACh and other cholinesters, which are predominantly outside the CNS, with brain levels that have increased to severe AD. Galantamine has a potential link to amyloid-beta clearance. This AChEI is a selective, reversible inhibitor, which enhances intrinsic ACh action on nicotinic receptors (Parsons et al., 2013). AChEIs have proven to slow cognitive decline, although there is lack of memory improvement. Croxson et al. (2012) suggested that this was due to acetylcholine having a possible role in boosting attentional performance or cortical function.

Symptoms and Stages of Alzheimer's Disease

AD is characterized by the onset of impairments in memory and executive function, in addition to cognitive and behavioral problems, such as depression, apathy, and agitation (Wilson, Arnold, Beck, Bienias, & Bennett, 2008). AD patients have been

known to have different symptoms at different stages of the disease. It is also hard to place individuals in any one stage of AD because the stages can sometimes overlap (AA, 2013).

Dr. Barry Reisberg at the New York University School of Medicine's Sillberstein Aging and Dementia Research Center developed a seven-stage framework for AD (see Appendix B). He indicated that not everyone who develops the disease will have the exact symptoms, or the same rate of progression (AA, 2013).

Risk Factors for Alzheimer's disease

Age and sex are consistent risk factors for Alzheimer's disease (Kalaria et al., 2008; Perez et al., 2012). Most individuals who have been diagnosed with AD are 65-years-plus (LOAD) and are women. They often experience low literacy, which is linked to poverty or lower socioeconomic status, leading to poor health, and lower access to healthcare. According to prevalence studies such as the Chicago Health and Aging Project (CHAP) and the Aging Demographics and Memory Study (ADAMS) approximately two-thirds of Americans with AD are women. Of the 5.2 million older than 65 years with AD in America, 3.4 million are women and 1.8 million are men. The ADAMS study revealed that 16% of females over 71 years of age have AD compared to 11% of males (AA, 2013).

Other risk factors include genetic association and risk genes--many times family members of the diagnosed AD patient have more likelihood of inheriting a predisposition or vulnerability to the disease as well. The gene Apolipoprotein E (APOE ε4 allele) and

the gene SORL1 are also risk factors for AD and they are usually linked to older women who have been diagnosed with LOAD (Brainerd, Reyna, Petersen, Smith, & Taub, 2011). For example, the gene APOE ε4 allele is apparently linked to specific decreases in AD patients' functional connectivity, according to EEG coherence studies. Other risk factors that are associated with AD include stroke injuries, vascular diseases, type 2 diabetes, obesity, hypertension, and decreased physical activity (Bassil & Grossberg, 2010; Mathis & Burke, 2009; Solfrizzi, et al., 2013).

Diagnosis of Alzheimer's Disease

Handen et al. (2012) agreed with research that a definitive diagnosis of AD cannot be made until the death of an individual. It depends on the identification of amyloid plaques and neurofibrillary tangles at brain autopsy. Deposition of amyloid usually begins about 10 years prior to clinical symptoms (Handen et al., 2012). This finding is usually accomplished with the help of brain imaging, e.g., positron emission tomography (PET). Brain damage associated with AD also includes many regions of the brain that perform significant memory functions such as the medial temporal lobe and the prefrontal cortex.

The Alzheimer's Association Report (AA, 2013) indicated that a diagnosis of AD is usually made by a primary care physician (PCP). This individual often obtains medical and family history comprising psychiatric history and cognitive and behavioral changes. The PCP will also ask family members or caregivers about the AD patient to gain input. Additionally, the PCP will conduct cognitive, physical, and neurological examinations,

and will often have the patient undergo MRI to help identify brain changes (Mathis & Burke, 2009). The MRI helps to detect such brain changes as strokes or tumors that can explain the individual's symptoms. In 2011, new criteria and guidelines were proposed by the NIA and the Alzheimer's Association for the diagnosis of AD, which are updated diagnostic criteria and guidelines proposed in 1984 by the Alzheimer's Association and the National Institute of Neurological Disorders and Stroke (AA, 2013; NIA, 2013).

Thomas and Fenech (2007) conducted a review on genome mutation and AD, which is similar to memory profiling; this is helpful in identifying MCI cases that will eventually progress into AD. These authors proposed that AD patients could be clinically diagnosed with an approximate accuracy between 60 and 70%, based on cognitive impairment and behavioral change criteria. The criteria were based on the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and related Disorders Association (NINCDS-AD & DA), which are still measured by the mini-mental state examination (MMSE). This examination allows a quantitative measure of cognition status to be conducted (AA, 2013; Almkvist & Tallberg, 2009).

Screening for Alzheimer's disease

The Centers for Medicare and Medicaid Service (CMS) recommended assessment tools for the detection of cognitive impairment (Cordell et al., 2013; Dowling, Herman, La Rue, & Sager, 2010; Kawas et al., 2013). The Alzheimer's Association convened to develop an expert group (Alzheimer's Association Medicare Annual Wellness Visit Algorithm for Assessment of Cognition) that would provide recommendations to primary

care physicians in the screening and detection of dementia to reduce the prevalence of delayed or missed diagnosis. The patient or informant to be screened would be observed by the primary care physician. The PCP would then review Health Risk Assessment information, conduct unstructured queries during the annual wellness visit (AWV), and utilize structured cognitive assessment tools. This recommendation was due in part to a number of studies supporting the fact that 27%-81% of patients in primary care who are affected with cognitive impairment go unrecognized/undiagnosed (Cordell et al., 2013).

Although there is growing attention among developed nations concerning medical, emotional, social, and financial burdens of Alzheimer's disease, there is no definite answer of whether or not screening is beneficial compared to its costs (Furiak, 2012). Nonetheless, most agree that if screening is done early on with patients who have the potential or high risk of developing dementia/AD, both patients and caregivers can initiate planning, organize ongoing care, prepare for long-term planning for both social and financial well-being, prepare to have care-giving training, plan for stress management, or rule out dementia early on in order to search for alternative symptom causes. As a result, treatment can begin much sooner, whether it is pharmacological or non-pharmacological (Borson et al., 2013; Furiak et al., 2012).

Treatment/Prolongation of Alzheimer's disease

Non-pharmacological Therapy

Treatment of AD consists of both non-pharmacological and pharmacological therapy models. The non-pharmacological therapy model is usually conducted by trained

professionals (i.e., psychiatrists, psychologists, or master-level clinicians), who follow practice guidelines recommended by the APA, which put emphasis on neuropsychiatric, psychiatric, and behavioral symptoms. Logsdon, McCurry, and Teri (2007) focused on using evidence-based psychological treatments (EBTs) for dementia patients with behavioral disturbances. Kazdin (2011) suggested that EBTs are the interventions carefully evaluated in research. Evidence-based practice is a broader term. It refers to the clinical practice that is informed by evidence about interventions, clinical experience, and patient needs, values, and preferences and their integration to make decisions about individual care.

The American Psychological Association (APA) Task force set criteria for EBTs for psychological disorders, which have specific coding criteria (APA, 2007). The criteria specified that studies have to treat the same symptom, target problem, or diagnosis. Logsdon et al. (2007) used predetermined behavioral disturbance levels as an eligibility requirement. Treatment interventions involved the progressively lowered stress threshold (PLST) theoretical framework for outcomes between treatment and control groups. The protocol was based on a behavioral problem solving theoretical framework.

Logsdon et al. (2007) discussed three studies, which are collectively known as The Seattle Protocol. The first study included patients who were diagnosed with dementia and depression. The goal of the intervention was to decrease depressive behaviors and increase pleasant events. In the second study, the intervention was combined with a home-based program to decrease behavioral disturbances and improve participants'

physical function. For the third study, the intervention goal was to improve patient caregivers' well-being and decrease behavioral disturbances (Logsdon et al., 2007).

Logsdon et al. (2007) pointed out that results using the PLST indicate that all psychological interventions appear most effective when behavioral problem solving is provided by or supervised directly by clinical professionals who have expertise in both behavior therapy and dementia care. Next, psychological interventions that meet EBT criteria work most effectively with patients with anxious or depressive behaviors. More research is required to prove EBT's efficacy with patients who are severely agitated. Lastly, behavioral disturbances appear less often in early stage dementia patients than they do in patients at the late stage or progression of the disease.

Logsdon et al. (2007) also noted that the progressive worsening of cognitive impairment in individuals with dementia has proven to be a challenge when applying EBT criteria to interventions for behavioral disturbances. Continual adjustment of treatment plans, expectations, and approaches is required depending on the patient and the patient's support system, including the caregiver. Proven efficacy and investigation of treatment approaches, such as cognitive behavior therapy, life review, and psychodynamic therapy, commonly used with older adults have not been conducted on dementia patients who experience behavioral disturbances (Logsdon et al., 2007).

Pharmacological Therapy

Drug delivery to the central nervous system (CNS) is a challenging pharmacological therapy in treating Alzheimer's disease. According to Khawli and

Prabhu (2013), the blood-brain barrier (BBB) only allows molecules that have low molecular weight to enter the brain via the bloodstream through the transcellular route. Khawli and Prabhu (2013) indicated that "less than 10% of therapeutic agents for neurological disease enter into clinical trials because of poor brain penetration," p. 1471. Research efforts focused on manipulating drug characteristics or using endogenous transporters or receptors at the BBB. This can only be accomplished through better understanding of the CNS and the physiology and pathophysiology of the CNS (Khawli & Prabhu, 2013).

The Alzheimer's disease Assessment Scale-cognitive subscale (ADAS-cog) is an instrument used to measure cognition in clinical trials. The Food and Drug Administration (FDA) proposed the use of quantitative disease-drug-trial models such as the ADAS-cog in order to improve drug research and product development for individuals with AD (Gomeni et al., 2012). The authors posit that it is better to test modifying drugs at the earliest stage of AD as well as treat symptoms early on to maintain functional capacity of patients.

Acetylcholine (ACh) is a small-molecular neurotransmitter, which is created by adding an acetyl group to a choline molecule (Baxter & Bucci, 2013). Acetylcholine transmits different kinds of messages to different parts of the brain (adjacent cells), which are brief and rapid (Pinel, 2009). Enzymes are used to break apart neurotransmitters. Baxter and Bucci (2013) indicated that the enzyme acetylcholinesterase is used to break down the neurotransmitter acetylcholine. Cholinergic precursors are chemicals used to

produce acetylcholine in neurons. Neurons releasing acetylcholine are said to be cholinergic (Pinel, 2009).

Schatzberg, Cole, and DeBattista (2010) informed that the first drug FDA-approved to treat AD was tetrahydroaminoacridine (THA; tacrine). This drug was used in Australia to reverse drug-induced coma. Tacrine is a central cholinesterase inhibitor that was thought to act by raising brain levels of acetylcholine and increasing cholinergic brain activity. As a result, it was used to treat AD patients who had mild to moderate dementia (Schatzberg, Cole, & DeBattista, 2010). It is rarely used today because it is hepatotoxic, which is damaging or destructive to liver cells.

Today, the cholinesterase inhibitors (ChEIs) donepezil, galantamine, and rivastigmine are used in the treatment of AD from the mild stages. The most common side effects are nausea, diarrhea, insomnia, fatigue, muscle cramps, and anorexia (Schatzberg et al., 2010). For the moderate stage of AD, the N-methyl-D-aspartate (NMDA) receptor antagonist memantine is a well-established mono-therapy (Gauthier & Molinuevo, 2013). Memantine was approved in 2003 to treat the moderate to severe stage of AD. This antagonist is thought to mitigate toxicity resulting from increased calcium flow into neurons by blocking NMDA receptors (Schatzberg et al., 2010). When NMDA receptors are blocked the neurodegenerative effects resulting from lower glutamate levels and increased calcium influx in AD are reduced. This drug has been quickly adopted in clinical practice because it is benign. In clinical trials, memantine's

rate of side effects is no different than the rate with placebos--side effects may include dizziness, confusion, headaches, and hallucinations.

Schatzberg et al. (2010) explained that moderate to severe AD patients, who take memantine, appear to have more improved cognition and activities of daily living (ADLs) than those who take placebos. Importantly, memantine also modestly reduces the time that caregivers must spend with an Alzheimer's patient. In addition, AD patients who are already taking donepezil appear to improve when memantine is added to their regimen (Schatzberg et al., 2010). ChEIs and memantine have demonstrated symptomatic efficacy in several clinical studies. To treat patients at the moderate to severe stage of AD, who have lost their capacity for independent everyday living, a combination therapy of both non-pharmacological and pharmacological therapy is used (Gauthier & Molinuevo, 2013).

Combination Therapy

Gauthier and Molinuevo (2013) explained that AD symptoms become severe over a period of years, which decreases the AD patient's chances to meet physical, mental, and daily needs. The authors suggest that combined therapy including both psychotherapy and psychopharmacological therapy is necessary in the absence of a cure for AD. Due to the fact that the disease may take up to a decade before it manifests itself, it is important to seek and use treatments that may provide both immediate and sustained long-term effects to slow the rate of clinical decline. Therefore, the use of combination therapy will slow the progression of the disease process by treatment mirroring AD-- using

cholinesterase inhibitors (ChEIs) such as donepezil, galantamine, and rivastigmine to treat mild stages of AD and using the N-methyl-D-aspartate (NMDA) receptor antagonist memantine to treat moderate and onward stages of AD (Gauthier & Molinuevo, 2013). However, interventions that substantially affect the course of the disease or the quality of life of Alzheimer's patients appear to be some distance away (Schatzberg et al., 2010).

Summary

Alzheimer's disease (AD) is the sixth leading cause of death in the United States. It is the fifth leading cause of death in Americans over the age of 65 (AA, 2012). The amyloid hypothesis is the leading theory that explains AD pathogenesis. Accumulation of protein in the brain is the initial event in AD--amyloid plaques followed by neurofibrillary tangle formation. AD is the most common form of dementia (AA, 2009). The disease is degenerative, causing individuals to have memory loss, and changes in reasoning, judgment, and behaviors.

AD is a disorder that primarily affects individuals 65 and older, individual's families, caregivers, government, third-party insurance agencies, academia, and the scientific communities. A collaboration of all entities must come together to find a cure or delay the progression of AD (NAPA, 2011). Brain imaging such as MRIs and PETs are also helpful in diagnosing patients with AD. In addition, criteria based on the NINCDS-AD&DA and use of clinical instruments to measure cognition and behavior resulted in an accurate diagnosis for between 60 and 70% of patients having AD (Thomas

& Fenech, 2007). However, presently, the only way to definitively diagnosis AD is through brain autopsy (Handen et al., 2012).

Consistent risk factors for AD are age and sex (Kalaria et al., 2008; Perez et al., 2012). Most individuals diagnosed with AD are over the age of 65 (LOAD) and are women. Prevalence studies such as the Chicago Health and Aging Project (CHAP) and the Aging Demographics and Memory Study (ADAMS) revealed that about two-thirds of Americans with AD are women. Of the 5.2 million Americans older than 65 years with AD, 3.4 million are women and 1.8 million are men. In addition, the ADAMS study indicated that 16% of females over 71 years of age have AD compared to 11% of males. Other risk factors include genetic association and risk genes such as APOE ε4 and SORL1. In addition, stroke injuries, vascular diseases, type 2 diabetes, obesity, hypertension, and decreased physical activity are also risk factors for AD (Bassil & Grossberg, 2010; Mathis & Burke, 2009; Solfrizzi, et al., 2013).

Memory impairments and executive dysfunction are symptoms of AD. Individuals will experience cognitive and behavioral problems such as depression, agitation, and apathy (Wilson, Arnold, Beck, Bienias, & Bennett, 2008). Each stage of the disease can have different symptoms or sometimes the stages will overlap (AA, 2013). Progression of AD does not consider age chronology. AD victims can experience up to seven stages of the disease, starting from Stage 1, involving no impairment to Stage 7, which can include very severe cognitive impairment (AA, 2013).

The CMS and the AA are agencies that recommend assessment and screening tools to medical and clinical professionals for the diagnosis or detection of dementia/AD (Furiak, 2012). Most developed nations agree that early screening conducted on patients with a high risk potential will allow patients, family members, and caregivers to initiate planning and preparation for long-term financial and social well-being to prepare for training, stress management, and on-going care (Furiak, 2012).

Treatment of AD can be delivered via psychotherapy, pharmaceutical therapy, or a combination of both. There is a great deal of collaboration by the government, public, and private sectors to find a cure for AD (Gauthier & Molineuvo, 2013; Khawli & Prabhu, 2013; Logsdon et al., 2007). The NAPA (2011), which is a research initiative implemented by The Obama Administration, spearheaded additional interest and awareness of AD and commitments to find a cure. Continual sharing of information and financial support from the government and private sectors are necessities headed in the right direction to prolong/put an end to the sixth leading cause of death among 65 year olds and beyond. In addition, the increasing population of baby boomers will also be at risk for contracting AD (AA, 2013), which is another critical reason to compare symptoms and stages of EOAD patients to that of LOAD patients.

The above occurrences have led researchers to the facts that AD patients can and do go through various stages and symptoms of this degenerative disorder (AA, 2013; Gauthier & Molinuevo, 2013; Reisberg, 2013; Wilson et al., 2008). There was a gap in literature that did not focus on caregiver perspectives of what they viewed when caring

for AD patients while the AD patients were experiencing various stages and symptoms of the disease. Chapter 3 focused on research questions, methodology, participant protection and rights, instrumentation, and data collection and analysis, which provided a roadmap or foundation to explore and determine possible future progress treatment plans, incentives and psychological interventions for AD.

Chapter 3: Research Method

Methodology

AD is defined as development of multiple cognitive deficits evidenced by memory impairment or cognitive disturbances that may or may not include the following: language disturbance, inability to carry out motor activities, failure to recognize objects, or the loss of executive functioning. In addition, these multiple cognitive deficits may or may not cause significant impairment in social or occupational functioning and represent a significant decline from previous functioning levels (APA, 2013).

AD is the fifth leading cause of death among Americans ages 65 and older (AA, 2012). Although multiple research entities have formed collaborative efforts to prolong life with the disease or provide treatment interventions, there is no known cure for AD (NAPA, 2011).

Over the past 150 years, advances in the treatment of heart disease and cancer have contributed to increased life expectancy and a marked change in aging bio-demographics. In addition, general improvements in public health and medical care during the 20th century, such as advances in laboratory techniques and technology, investments in disease surveillance, regulation of tobacco products, screening of newborns for metabolic and other heritable disorders have added increased life expectancy (Carrillo et al., 2013; CDC, 2011). As a result, the principal causes of death have shifted dramatically from chiefly infectious diseases to cardiovascular disease,

cancers, and increasingly, progressive neurodegenerative dementias, such as AD (Kling, Trojanowski, Wolk, Lee, & Arnold, 2013).

AD is the most common form of dementia (AA, 2009). Those commonly affected by AD are individuals ranging from age 65 years to 85 years. This group will most likely include a significant number of future baby boomers, since they began turning 65 in 2011. It has been estimated that by the year 2050 the rising cost to treat this population will be $1 trillion or more (Okie, 2011). AD patients have also been known to have different symptoms at different stages of the disease. Due to the fact that stages can and do overlap, it is hard to place individuals in any one stage of AD (AA, 2013). Therefore, comparing symptoms between EOAD patients and LOAD patients offers further insight into ways to generate treatment/intervention plans, to slow the progression of the disease, or perhaps find a cure for this disorder.

Research Design and Rationale

Chapter 3 described the methodological approach including the mixed-method research design, setting, and participants. The mixed-method design was a combination of qualitative and quantitative components, including an inductive approach, using personal perspectives together with statistical inferences. Chapter 3 also included and described instruments used to acquire and analyze data. Process descriptions of ethical requirements were presented in this chapter as well. The research questions answered in this study were as follows:

Research Question and Hypotheses

RQ1: Are there differences in cognitive symptoms between EOAD patients and LOAD patients?

$H_0$1: EOAD patients have the same cognitive symptoms as LOAD patients.

H_a1: EOAD patients have different cognitive symptoms than LOAD patients.

RQ2: Are there differences in behavioral symptoms between EOAD patients and LOAD patients?

$H_0$2: EOAD patients have the same behavioral symptoms as LOAD patients.

H_a2: EOAD patients have different behavioral symptoms than LOAD patients.

Mixed Method Approach

A quantitative review was conducted, using a demographic background survey, in order to obtain information from caregivers who provided care to AD patients who had EOAD or LOAD. These caregivers supplied answers to questions that determined the particular stage level of the AD patient. Quantitative instruments, the BEHAVE-AD (Reisberg, et al., 1987) and the Short IQCODE (Jorm, 1994) were used to gain empirical evidence of the AD patient's behavior, which were filled out by the caregiver. A qualitative interview preceded caregivers filling out quantitative measures such as the BEHAVE-AD and the Short IQCODE. As a result, this research design is both quantitative and qualitative in nature, using a sequential mixed method approach.

Creswell (2009) indicated that quantitative research is a means for testing objective theories by examining the relationship among variables. The variables can then

be measured, usually on instruments, so that numerical data can be examined utilizing statistical processes. Creswell (2009) defined qualitative research as a means for understanding and exploring a social or human problem through the perspectives of groups or individuals. The research process involved emerging questions and procedures, collecting and analyzing data, building from specific to general themes, and making interpretations of data meaning.

Storandt, Balota, Aschenbrenner, and Morris (2014) described the clinical, cognitive, and personality characteristics of 249 participants in a multinational longitudinal study of autosomal dominant Alzheimer's disease (ADAD). Participants were from ADAD families with mutations in 1 of 3 genes (APP, PSEN1, or PSEN2). The authors compared cognitively normal mutation carriers, cognitively normal mutation noncarriers, and very mildly impaired mutation carriers using mixed model analyses. Results revealed that global cognitive deficits like those observed in late-life sporadic AD exist in mild ADAD compared with cognitively normal carriers and noncarriers on all but two measures of Storandt et al. (2014) concluded that cognitive and personality deficits, overall, in very mild ADAD are similar to those seen in sporadic AD and cognitive deficits also took place in asymptomatic mutation carriers who were nearer the age of dementia onset.

Participants and Sample Size

My introduction to the Alzheimer's Association was facilitated by the Chief Program Director of the Houston Southeast Chapter via letter of cooperation (see

Appendix C). This individual provided me access to Alzheimer's caregiver group locations throughout the Houston area and surrounding towns. I distributed flyers throughout the Houston Southeast Chapter Alzheimer's Association locations inviting/recruiting caregivers to participate (see Appendix K). I had no relationships with the Chief Program Director or any of the Alzheimer's Association group participants. I recruited participants from various caregiver groups, who were members of the Alzheimer's Association, Houston Southeast Chapter, and provided care to individuals who had been diagnosed with AD according to criteria in the DSM-V (APA, 2013). The study included a qualitative aspect, which consisted of caregivers answering interview questions related to operational constructs such as cognitive/behavioral symptoms of AD.

Grounded theory was the research tool I used to seek out and understand potential social patterns and structures of Alzheimer's disease through the process of constant comparison. Grounded theory generally reflects the participant's own interpretations or coming from their own perspectives, rather than being introduced or imposed by the investigator (Coleman, 2006). In qualitative research, the number to reach action or grounded theory is between 5 and 20 (Patton, 2001). The process of grounded theory involved using multiple stages of data collection and the interrelationship of categorical information. I compared data with emerging categories and sampling of different groups to maximize the similarities and differences of information.

Beard, Sakhtah, Imse, and Galvin (2012) investigated dyads where one spouse had been diagnosed with memory loss. The authors conducted in-depth qualitative

interviews with 10 couples (*N*=20). Beard et al. (2012) used grounded theory approaches to collect, code, and analyze data into data themes. The authors found that community services and care practices were insightful to ways that couples organized and prioritized their relationship prior to diagnosis in order to encourage positive care patterns between them, foster successful adaptation changing needs of the couple, and support in-home arrangements for as long as possible.

During my research study, the caregivers received a background demographic questionnaire from me to complete (See Appendix D) on behalf of the individuals that they cared for with AD *N* = 20. There were two groups for the duration of illness comparison and behavioral/cognitive symptoms/changes. Group I (*n* = 8) consisted of EOAD patients (younger than age 65) and Group II (*n* = 12) consisted of LOAD patients (older than age 65). I used demographic survey screening to obtain each group. Preceding the quantitative portion of the study, six of the total caregivers received from me a qualitative interview to gain their perspectives of what they observed the AD clients experiencing in regards to behavioral and cognitive changes.

Participant Protection and Rights

The caregivers were the sole source of information on behalf of the patient sample in this study. I explained informed consent and confidentiality to caregivers. They were informed that their participation in the research was voluntary, without any compensation; and at any time during the research they could withdraw without any form of penalty. I protected the rights of all participants as per certification of the National

Institute of Health training course (See Appendix J). In addition, I adhered to questions from the standard demographic background questionnaire (See Appendix D), both informant questionnaires (See Appendices E and F), a qualitative interview (Appendix G) to gain caregiver perspectives of the cognition and behavior of AD clients, and caregivers/participants were not coerced in any way through use of personal biases. Materials such as questionnaires and statistical instruments were coded with numbers and kept in a secured area inside a locked file cabinet. I used email addresses and phone numbers to communicate with participants. Once the research study was completed I locked all materials and secured them in a locked file cabinet to be kept for 5 years. After the 5 years I will destroy the material by shredding it. Upon completion of my study, all participants were debriefed via telephone/email. I also provided participants with summary results of the study and how it would benefit others living with or caring for those with AD in the future.

Instrumentation

Participants were given sufficient information about the study. Once caregivers acknowledged that they understood it well enough to make an intelligent decision concerning whether or not they wanted to participate, I administered the structured demographic questionnaire (see Appendix D) via telephone. If the caregiver had care recipients who met criteria as reflected in the demographic questionnaire, then I asked them to participate in completing the BEHAVE-AD informant form (see Appendix E) and the Short IQCODE (see Appendix F). I administered the BEHAVE-AD and the

Short IQCODE informant instruments via telephone to the caregiver to obtain information regarding the individual they were providing care for. I used these instruments to assess cognitive, behavioral and general clinical symptoms of the AD patient. I used the BEHAVE-AD and the Short IQCODE assess behavioral and cognitive symptoms separately so as not to result in a so-called *halo effect*, meaning that the rating of one area, e.g.: behavioral, can influence rating of another area, e.g.: cognition. It is usually advantageous that assessment of behavioral symptoms and cognitive evaluation be separately measured or performed with different instruments in research (Auer, Monteiro, & Reisberg, 1996). Prior to the caregivers completing the behavioral and cognitive informant form on behalf of AD patients (N= 20), the qualitative interview (see Appendix G) was conducted. I chose six of the participating caregivers to take part in the qualitative interview process. I scored the informant questionnaires using the SPSS Software, and the qualitative interview (see Appendix G) was organized and evaluated by hand. I provided definitions of the stages of AD to each respondent via the background demographic questionnaire (see Appendix D) to help them categorize their care recipient's status.

Demographic Questionnaire

The background demographic questionnaire (see Appendix D), which is a standard survey questionnaire, was used to gain the necessary background information/criteria (Bivin, 2013). It consisted of a 13-item self-report questionnaire. It

provided age, gender, age at which AD patient was diagnosed, socioeconomic status, education level, and stage of the disease.

Behavioral Pathology in Alzheimer's Disease Rating Scale

The Behavior Pathology in Alzheimer's disease Rating Scale (BEHAVE-AD) is composed of 25 symptomatic items describing behavioral disturbances (Reisberg, et al., 1987). This instrument covers symptoms in seven categories: paranoid and delusional ideation, hallucinations, activity disturbances, diurnal rhythm disturbances, aggressiveness, affective disorders and anxieties, and phobias (Robert, 2010; Auer, Monteiro, & Reisberg, 1996). The BEHAVE-AD scale takes approximately 20 minutes to administer (Robert, 2010). The behavior is rated as mild, moderate, or severe. The instrument evaluates the importance of each of the 25 symptoms in the seven categories using a 4-point severity scale with a score of "0" indicating that the item is not present; a score of "1" indicating present of the symptom; a score of "2" indicating the symptom is present, generally including an emotional component; and a score of "3" indicating the symptom is present, generally with an emotional and physical component. The total BEHAVE-AD scores range from 0 to a maximum score of 75. A global scale rating is obtained of the degree to which these symptoms are troubling to the caregiver/informant and/or dangerous to the patient (Reisberg et al., 2014; Robert et al., 2010; Auer, Monteiro, & Reisberg, 1996).

I received permission to use the BEHAVE-AD Informant Scale via email from Barry Reisberg, MD, at NYU Alzheimer's Disease Center, New York University

Langone Medical Center, New York on March 11, 2015 (see Appendix H). Dr. Reisberg's condition for the scale utility was that it be properly referenced and the copyright noted in all reproductions. The BEHAVE-AD Informant was chosen because it is an informant-based rating scale and was developed to elicit information obtained from caregiver reports (Auer, Monteiro, & Reisberg, 1996). It assesses behavioral symptoms in AD patients, independent of comparatively difficult to treat cognitive symptoms (Robert et. al, 2010). This instrument had limitations because it was used to evaluate AD patients based solely on information from their caregivers (i.e., spouses, children, parents). Nonetheless, the instrument had good reliability in discriminating and good validation in AD cases, whether non-pharmacological or pharmacological (Reisberg et al., 2014).

Short Informant Questionnaire on Cognitive Decline in the Elderly

The Short Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is a subjective rating scale that measures cognitive decline from a pre-morbid level using informant reports (Jorm, 1994). The instrument was developed by Professor Anthony Jorm in 1994 as a brief version of the IQCODE developed by Jorm and Jacomb in 1989. I sent Dr. Jorm's an email to inform him that I would be using this tool (see Appendix I). The Short IQCODE is used to assess cognitive decline and dementia in the elderly. The informant or caregiver is required to have known the elderly individual for ten years or longer in order to provide information that compares his/her present performance with 10 years ago. The questionnaire takes about 15 minutes. The score for each question is summed and then divided by the number of questions, which are 16 for

the Short IQCODE (Jorm, 1994). The range of scores is from 1 to 5 compared with 10 years ago how is his/her performance. A "1" indicates much improved, "2" a bit improved, "3" not much change, "4" a bit worse, and "5" much worse. The Short IQCODE (Jorm, 1994) was chosen because it has been proven to be useful for individuals who are unable to undergo direct-cognitive testing due to acute illness, lack of cooperation or death. Furthermore, this tool is also valuable in screening populations with low education and literacy levels. Although the Short IQCODE (Jorm, 1994) was developed for self-completion by informants, it has been and can be used as a face-to-face or telephone interview. Another variation involves the 10-year time frame. A number of users have found difficulty in finding informants/caregivers who possess the required contact with the subject for over 10 years. As a result, this has led to the modification of a 5-year time frame, which was the time frame for this study.

The Short IQCODE (Jorm, 1994) has high reliability. It measures a single general factor of cognitive decline and validly reflects past cognitive decline, performs at least as well as conventional cognitive screening test for dementia. Studies have also compared the IQCODE to neuropathological diagnosis (Rockwood et al., 1998; Thomas et al., 1994). This instrument was significantly correlated with 130 kDa amyloid precursor protein in AD patients' blood (Thomas, 1996).

Qualitative Interview

The qualitative interview (see Appendix G) consisted of two questions. The first question allowed caregivers to give their perspectives of what memory/behavioral

changes they had observed in their AD care recipients over the past 2 to 5 years. The first question had eight subcategories that were semi-structured. The second question allowed the caregiver participants to be more general and explain more in detail what they viewed as memory/behavioral changes. These qualitative interview questions were chosen to explore more detail of what the caregivers observed in their shared experiences with the AD population.

Data Collection and Analysis

As mentioned prior, I presented a background demographic questionnaire to caregivers from various Alzheimer's Association caregiver group locations throughout Houston and surrounding areas. This particular questionnaire included demographic questions about AD care recipients' age, gender, socioeconomics, meeting DSM-V criteria for AD, age at which AD diagnosis was made, stage of the disease, as well as the age, length of time caregiver had known care recipient, and the relationship of caregiver to AD care recipient (i.e., spouse, adult child, parent, other). Once, this stage of the process had been completed, caregiver participants were asked to complete the BEHAVE-AD and Short IQCODE Informant Report Forms, as well as provide narratives on the cognitive/behavioral changes they had viewed in the AD care recipients through use of a structured qualitative interview. Both instruments took approximately 45 minutes to administer.

Quantitative Analysis

I used the analysis of variance (ANOVA) for statistical analysis. ANOVA is a hypothesis-testing procedure to estimate mean differences between two or more populations (Gravetter & Wallnau, 2009). Onset of diagnosis (EOAD or LOAD) was analyzed as a between subject variable. Scores on the BEHAVE-AD and Short IQCODE were treated as dependent variables. Alpha was set at 0.05. Statistical analysis drawn from the sample data (survey answers supplied from the caregiver and symptoms endorsed from research instruments) revealed the most salient memory/behavioral symptoms, whether patients were of EOAD or LOAD. The prediction after the BEHAVE-AD and the Short IQCODE were scored—summing up totals of caregiver answers—yield quantitative measures of memory/behavioral symptoms that were compared to onset of AD and determined appropriate stage levels, and used with caution to generalize to other AD victims. Symptoms on the BEHAVE-AD and the Short IQCODE were scored using version 21 of the SPSS program.

Qualitative Analysis

Grounded theory has been described as "the most influential paradigm for qualitative research in the social science arena today" (Patton, 2002). Grounded theory originated out of the collaboration of Glaser and Strauss (1967), who developed a methodological approach based on the theory of symbolic interactionism between 1920 and 1950. This sociological approach posited fluid and dynamic interpersonal processes in which meaning was created within and derived from social interactions (Kendall,

1999). Grounded theorists cross-examined the meanings created in these social relationships by trying to discover how these groups of individuals defined their realities based on their understanding of interpersonal interactions (Cutcliffe, 2000), which is why I am using this theory.

I conducted face-to-face/phone interviews in participants' homes, business/facility conference rooms, and public libraries, using grounded theory to gain information that gave each caregiver's perspective. Two open-ended questions were given to 6 of the 20 participating caregivers by me after I had built and established rapport (see Appendix G). I analyzed qualitative data using Braun and Clark's (2006) six-phase thematic analysis: 1) data was gathered/collected from observational data, questionnaire and interview statements, and audio recording; 2) data were coded by hand, every two to three lines of text was coded with handles identifying key words, concepts, and reflections; 3) codes were validated by reading and re-reading the data to integrate codes in order for themes to emerge; 4) themes were reviewed, defined, and refined; subthemes were formed; and eventually this step allowed patterns to emerge from the data; 5) themes were named and descriptions written in order to help communicate meaning to readers; and 6) a data-driven report was written, making an argument in relation to the research question(s), hopefully, convincing the reader of its merit and validity of the analysis. I also included these steps in an inductive approach.

For example, when each caregiver had: (a) provided me their interpretation, answers, and understanding of the two interview questions; (b) provided me

clarification/elaboration of the two interview questions, tape/audio recordings, notes and memos; then (c) I evaluated and compared each caregiver statements and answers my final quantitative results. This was done to obtain trustworthiness, which involved credibility, transferability, dependability, and confirmability (Lincoln & Guba, 1985).

Lincoln and Guba (1985) suggested that trustworthiness is the standard by which a qualitative study can be judged. The authors explained that the central organizing principle, trustworthiness, was linked to standards applied to quantitative studies such as validity, reliability, generalizability, and objectivity. There was a series of techniques that Lincoln and Guba (1985) mentioned that I used to evaluate qualitative data analysis such as establishing credibility, transferability, dependability, and confirmability.

Furthermore, the additional narrative themes that became salient from qualitative interviews, I received from caregivers, can and will shed light on present and future treatment plans and/or preventive measures for AD.

Summary

Over the past 150 years, advances in the treatment of heart disease and cancer are responsible for postponement of mortality and a marked change in aging bio-demographics. In addition, improvements in public health and medical care during the 20th century led to considerable increases in life expectancy (Carrillo et al., 2013). As a result, the principal causes of death have shifted dramatically from chiefly infectious diseases to cardiovascular disease, cancers, and increasingly, progressive

neurodegenerative dementias, in this case, Alzheimer's disease (Kling, Trojanowski, Wolk, Lee, & Arnold, 2013).

AD is the fifth leading cause of death among Americans age 65 and older (AA, 2012). In order to conduct research on human subjects (caregivers), I considered ethical issues such as informed consent, privacy, confidentiality, and authorization to disclose PHI. I presented these forms to caregivers on behalf of the AD care recipients. In addition, to keep participants safe from harm, I addressed this through participant protection and rights.

The methodological approach I used to examine symptoms and stages of AD among participants (EOAD and LOAD patients) was a mixed method design (Creswell, 2009). I recruited participants from Alzheimer's Association caregiver groups across the Houston Metropolitan and surrounding areas. I used the following instruments to study and obtain new information and details about AD: (a) the BEHAVE-AD Informant Report form (Appendix E); (b) the Short IQCODE (Appendix F); (c) the qualitative interview (Appendix G); and (d) the demographic background questionnaire (Appendix D). Once I scored the quantitative instruments through the SPSS program; reached saturation for themes and subthemes from qualitative interview questions; and integrated both approaches, I obtained detailed results and analyses that are provided in Chapter 4.

Chapter 4: Results

Introduction

The purpose of this mixed-method study was to determine whether or not individuals with EOAD or LOAD experience different behavioral and cognitive symptoms, using caregivers as informants. For the qualitative analysis, a qualitative, semi-structured interview was used to understand the experiences of caregivers, who gave personal perspectives of what they observed while caring for an individual who had been diagnosed with EOAD or LOAD. Each interview was audio-taped and then transcribed verbatim and coded and categorized in order to create successful, thematic outcomes.

For the quantitative analysis, behavioral symptoms were measured by having caregivers fill out the BEHAVE-AD informant questionnaire and the Short IQCODE informant questionnaire for memory symptoms. The independent variable was type of diagnosis (EOAD vs. LOAD). The dependent variables were behavioral and memory symptoms. I conducted a one-way ANOVA analysis to determine if differences existed in behavioral and memory symptoms between early- versus late-onset AD individuals. This chapter will restate the purpose of the study as well as research questions and hypothesis. It will discuss the setting, demographics, data collection process, as well as report data analysis and results describing the qualitative components followed by the quantitative components.

Research Questions and Hypotheses

RQ1*:* Are there differences in cognitive symptoms between EOAD patients and LOAD patients?

$H_0$1: EOAD patients have the same cognitive symptoms as LOAD patients.

H_a1: EOAD patients have different cognitive symptoms than LOAD patients.

RQ2: Are there differences in behavioral symptoms between EOAD patients and LOAD patients?

H_o2: EOAD patients have the same behavioral symptoms as LOAD patients.

H_a2: EOAD patients have different behavioral symptoms than LOAD patients.

Demographic Samples and Data Collection

I used the Alzheimer's Association's Houston Southeast Chapter to recruit participants from various caregiver support groups. Criteria included that caregivers were age 18 and older, and cared for someone who had been diagnosed with AD before the age of 65 (EOAD) or after the age of 65 (LOAD). The diagnosis of AD had to be according to criteria in the DSM-V (APA, 2013). Flyers were either posted or hand-delivered by me to various caregiver support facilities throughout the Houston metropolitan area and other surrounding cities and towns (League City, Clear Lake, Pasadena, Texas City, Pearland, Missouri City, Sugar Land, Bellaire, Memorial, Lake Jackson, and Conroe). Caregivers acted as informants on behalf of the individuals who had been diagnosed as EOAD or LOAD.

Between October 12, 2015 and March 16, 2016, I presented caregiver participants with research packets after they had agreed to participate in the study. Caregiver participants contacted me by cell phone or in person after support group meetings. Research packets for the qualitative component of the study took 30 to 45 minutes to complete, and consisted of informed consent forms, demographic questionnaires and qualitative, semi-structured, open-ended interview questions.

Research packets for the quantitative component of the study took about 45 minutes to an hour to complete and consisted of informed consent forms, demographic questionnaires and two quantitative measures: a) the BEHAVE-AD informant survey, used to measure behavioral symptoms, and b) the Short-IQCODE survey, used to measure cognitive/memory symptoms. Due to the mixed method nature of this study, I used a sequential design (qualitative component followed by the quantitative component).

Originally, 31 packets were passed out and sent to caregiver support group facilities. Twenty (65%) of the 31 packets were returned. Study sample participants (N =20) consisted of two groups: EOAD (n=8) and LOAD (n=12). This was a slight deviation from the data collection plan I had hoped to pursue, which indicated counts (N= 26, which were (Group 1, n =13 participants and Group 2, n =13). Each participant in the two groups was given a quantitative packet. Consent forms were explained in detail and in person to participants. Before they signed and agreed to the study, they were asked if they understood the details that were explained to them. After they indicated understanding, consent forms were presented for their signatures. Six of the 20

individuals also participated in the qualitative component of the study. They were divided into two groups: Group 1: EOAD (*n*=3) and Group 2: LOAD (*n* = 3). Group 1 consisted of two men and one woman; Group 2 consisted of two women and one man.

The qualitative data collection process consisted of a face-to-face qualitative interview, which consisted of two, open-ended questions with question one including eight (8) short sub-questions. Each participant was audio recorded with a mini tape recorder. Each interview was transcribed verbatim. The quantitative data collection process consisted of participants either filling out packets in person, over the telephone, or via the internet. Both qualitative and quantitative interviews were conducted in library conference rooms, private offices, and in participant homes. Overall demographics for this study are presented in Table 1.

Table 1

Subject Demographics of Research Sample (*N* = 20)

Variable	%	*N*
English Speaking		
Yes	100.0	20
AD Patient Age		
59-69	35.0	7
70-79	30.0	6
80-94	35.0	7
Gender		
Male	35.0	7
Female	65.0	13
Race/Ethnicity		
Black/African American	40.0	8
Hispanic/Latino	5.0	1
White/Caucasian	55.0	11
Marital Status		
Single	10.0	2
Married	55.0	11
Divorced	5.0	1
Widowed	30.0	6
Highest Level of Education		
High school	15.0	3
Some college	35.0	7
College graduate	30.0	6
Post graduate degree	15.0	3
No school/college	5.0	1
Economic ($) Status of AD patient		
1 to 4,999	5.0	1
5,000 to 19,999	15.0	3
20,000 to 49,000	35.0	7
50,000 to 69,000	20.0	4
100,000 and above	10.0	2
Declined to state	15.0	3
Primary Caregiver		
Yes	85.0	17
No	15.0	3

(continued)

Table 1. Subject Demographics (continued)

Variable	%	*N*
Relationship to care recipient		
Spouse	35.0	7
Adult/Child/Grandchild	40.0	8
Other	25.0	5
Age at AD diagnosis		
< 65 years	35.0	7
> 65 years	65.0	13
Patient's Stage of AD		
Stage 2	5.0	1
Stage 3	5.0	1
Stage 4	30.0	6
Stage 5	15.0	3
Stage 6	35.0	7
Stage 7	10.0	2

Note: *N* = 20; < = less than; > = greater than

Data Analysis

Qualitative Component

I conducted the qualitative component before the quantitative component. This sequence was done purposefully, in order not to taint caregiver informant answers to the semi-structured, qualitative interview questions, which asked about behavioral and cognitive changes in the care recipients. The questions were similar to those found on the BEHAVE-AD and Short-IQCODE questionnaires, which were used in the quantitative component of this study. Each caregiver participant told his/her personal perspective of what behaviors/cognitive symptoms they observed in their loved ones or patients who had EOAD/LOAD.

The six-phase thematic analysis (Braun & Clark, 2006) was the process used to analyze the data. First, the six qualitative interviews were audio-taped and transcribed verbatim. Second, each interview was read and coded by hand (identifying key words and phrases). Third, interviews were read and re-read; comparisons were made to integrate codes and to develop themes. Fourth, themes were labeled as well as subthemes leading to various patterns. Fifth, themes were finalized upon reaching saturation. Sixth, themes were analyzed to determine alignment with interview questions in order to produce the analytical report. Once the data was coded by hand, the Maxqda program was not necessary (as indicated in Chapter 3). However, by not using the Maxqda program, the process took much longer.

Participants' narrative answers to the qualitative interviews questions resulted in various codes such as: (a) short-term memory loss; (b) aphasia; (c) patterns of emotions (i.e., from happiness to sadness, from jovial to withdrawn to openness, from scared to crying to jovial); (d) spending and giving away money; (e) selling personal belongings and property; (f) problem eating; (g) problem bathing: (g) problem putting on clothes; (h) anxiety; (i) irritation; (j) frustration; (k) depression; (l) paranoia; (m) hallucinations; (n) drug abuse; (o) alcohol abuse; (p) fighting; (q) biting; (r) cursing; (s) and screaming. The primary themes were: (a) cognitive impairment; (b) mood swings; (c) impulsiveness; (d) struggling with activities of daily living; (e) psychological behaviors; and (f) maladaptive (adverse) behaviors. Further analysis is included in the results section of qualitative component analysis (Table 2).

Quantitative Component

Table 1 indicated the demographic background of the quantitative component of this study. The following research questions were answered after conducting quantitative analysis through use of the SPSS software version 21.0 (IBM Corp. Released 2012).

RQ1*:* Are there differences in cognitive symptoms between EOAD patients and LOAD patients?

$H_0$1: EOAD patients have the same cognitive symptoms as LOAD patients.

H_a1: EOAD patients have different cognitive symptoms than LOAD patients.

RQ2: Are there differences in behavioral symptoms between EOAD patients and LOAD patients?

H_o2: EOAD patients have the same behavioral symptoms as LOAD patients.

H_a2: EOAD patients have different behavioral symptoms than LOAD patients.

To answer RQ1, I gave caregiver participants the Short-IQCODE, which is a subjective rating scale that measures cognitive decline from a pre-morbid level using informant reports. Informants were required to have known the individual with EOAD/LOAD for at least 5 years. The questionnaire took about 15 minutes to complete with a total of 16 questions. The range of scores were from 1 to 5, with "1" indicating much improved, "2" a bit improved, "3" not much change, "4" a bit worse, and "5" much worse. The independent variable was type of diagnosis (EOAD vs. LOAD) and the dependent variables were the outcomes of the 16 questions completed by participants on the Short-IQCODE questionnaire. See (Table 3).

To answer RQ2, I gave each participant (caregiver) the BEHAVE-AD to fill out on behalf of the AD patient (EOAD/LOAD). This tool measures 25 symptoms describing behavioral disturbances in seven categories (Paranoid and Delusional; Hallucinations; Activity Disturbances; Aggressiveness; Diurnal Rhythm Disturbance; Affective Disturbances; and Anxieties and Phobias). The instrument evaluates the importance of each of the 25 symptoms in the seven categories using a 4-point severity scale with a score of "0" indicating symptom is not present; "1" indicating present of symptom; "2" symptom is present with an emotional component; and "3" symptom is present with an emotional and physical component. In addition, this instrument allows a global scale rating to be obtained which describes the degree to which the behavioral symptoms are

troubling to the caregiver and/or dangerous to the patient. It took 20 to 25 minutes to administer the BEHAVE-AD questionnaire.

Results of Qualitative Component (Qualitative Interview Q1 and Q2)

Demographics of caregiver recipients: early-onset AD (EOAD) patients were 3 (2 men and 1 woman) and late-onset AD (LOAD) patients were 3 (1 man and 2 women). The average age of caregiver recipients was 74 years. Half of the AD patients who were being cared for by caregivers were Black/African American and the other half were White/Caucasian. The primary and sub-themes that emerged out of the data are as follows and also listed in Table 2. Caregiver informants were asked to elaborate on Q1: Over the past 2 – 5 years, what are some of the things you observed about this person's change in memory/behavior and Q2: What are some of the most favorable/unfavorable moments you have observed about this individual's memory/behavioral changes? Following are the primary themes that emerged from the interviews.

Primary theme 1: cognitive impairment: All of the caregiver informants described both early- and late-onset AD patients as having short-term memory loss as well as aphasia. One of the three EOAD patients was described as having long-term memory loss.

Primary theme 2: mood swings: All of the caregiver informants discussed emotional patterns that they observed in each of the AD patients. One EOAD patient was described as being frightened then began crying and then appeared to be jovial. Three (2 EOAD patients and 1 LOAD patient) were described as being in a happy mood, then going from sadness to jovial. Two LOAD patients were described as being jovial, then becoming

withdrawn, and later appearing very open to teenagers or individuals they were socializing/visiting with.

Primary theme 3: impulsiveness: All of the EOAD patients fell into this theme (category). The sub-themes told of how each of the three went though a phase where they did a lot of frivolous spending where they began spending money, giving away money, and selling off personal belongings. By assessing the present stage of the disease (according to Reisberg's seven stages of Alzheimer's) the caregiver informants reported the majority of the EOAD group to be in stage 4. However, impulsive behaviors were reported to have taken place even before the AD patients had been diagnosed.

*Primary theme 4: struggles with activities of daily living***:** Caregiver informants stated that 5 out of the 6 AD patients struggled with or needed help with eating, bathing/showering, putting on clothes, brushing his/her teeth, and going to or using the bathroom.

Primary theme 5: psychological behaviors: All of the caregiver informants indicated that they observed their care recipients to have periods where they often went through anxiousness, agitation, irritability, frustration, depression, paranoia, and sometimes hallucinations, depending on the present state of the disease.

Primary theme 6: maladaptive (adverse) behaviors: One of the EOAD patients was reported to have a history of drinking alcohol and using drugs. Many of the other individuals in this qualitative study were observed by their caregivers to be aggressive at times when they would fight, bite, kick, curse, or scream. These actions were reported to

take place prior to the AD patient taking a bath/shower, staff members entering AD patient's room to help them with ADLs; or watching a television program.

As indicated in Table 2 the primary themes were: cognitive impairment, mood swings, impulsivity, struggles with ADLs, psychological behaviors, and maladaptive behaviors. Both EOAD participants #5, #6, #7 (EP5, EP6, EP7) and LOAD participants #1, #2, #3 (LP1, LP2, LP3) were reported to have experienced cognitive deficits, especially short-term memory.

Caregiver participants indicated that care recipients' cognitive symptoms seemed to get worse as the disease progressed. Caregiver informants used criteria for caregiver recipient stage levels according to Reiberg's seven stages of AD: LP1, LP2, and EP6 were in stage 6 and LP3, EP5, and EP7 were in stage 4 of the disease. In regards to aphasia, the majority (2 out of 3) of LOAD caregiver recipients showed common characteristics. Wandering seemed to play a role in the majority (2 out of 3) of EOAD caregiver recipients. There was an equal number of EOAD and LOAD caregiver recipients who experienced mood swings and half (2 out of 4) were in stage 4 and the other half (2 out of 4) were in stage 6. The same held true for impulsivity (LP2 and EP6 were in stage 6; and EP5 and EP7 were in stage 4). The majority (3 out of 5) of caregiver recipients who struggled with ADLs were in stage 6 of the disease. As far as psychological behaviors, it appeared that both EOAD and LOAD caregiver recipients experienced these behaviors at different stages of the disease, which was unlike the cognitive deficits that got worse as progression of AD occurred. Maladaptive behaviors

were experienced evenly among both EOAD (EP5 – stage 4) and LOAD (LP2 – stage 6) care recipients. After comparison of data and emerging themes, the EOAD and the LOAD group were both utilized to maximize similarities and differences, as outcomes are presented in Table 2.

Table 2

Primary and Sub-themes for Qualitative Analysis (Early- and Late-onset Participant)

Primary themes	Subthemes	Caregiver/participant extracted response (s)
Cog. Impairment	*S-term Memory loss*	LP1"She has almost virtually no s-term memory" LP2 "Her s-term memory was basically non-existent" LP3 "His s-term memory is pretty much non-existent" EP5 "The next 5 or 10 minutes she don't remember" EP6 "No he don't remember any of the birthdays" EP7 "He would tell stories that were the same stories"
	Aphasia	LP1 "She can't remember names or anything." LP3 "He doesn't make full sentences" EP7 "He will struggle with words and names"
	Wandering	LP3 "He drove to the store and ended up walking back EP5 "She was roaming trying to leave" EP7 "He got lost in Dallas going to meet his brother"
Mood Swings	*Emotional Patterns*	LP1 "She goes from sadness to euphoria" LP2 "It's odd, like on a dime she's from happy to mean" EP5 "…5/10 minutes, pass she cries, she's angry, scared" EP7 "His mood is better, he is more jovial"
Impulsivity	*Frivolous Spending*	LP2 "Several times/week she paid him $100 for the yard" EP5 "It's got to be high dollar, nothing cheap" EP6 "He was selling off all equipment, spending freely"
	Decision-making	EP7 "Gave daughter permission to visit w/o recollection"
Struggles with ADLs		LP1 "They feed her and put her in wheel chair" LP2 "It's harder for her to keep up with eating, bathing" LP3 "He needs help as far as grooming, bathing, eating" EP6 "He don't (eating, dressing) I take care of all of that" EP7 "He has lack of understanding of the shower"

(continued)

Table 2. Primary and Sub-themes for Qualitative Analysis (continued)

Primary themes	Subthemes	Caregiver/participant extracted response (s)
Psychological Behaviors		LP1 "Yea, she gets irritated" LP2 "Starting to get more agitated and more frustrated LP3 "He gets frustrated a lot. The look on his face" EP5 "The voice, the behavior, she is very agitated" EP6 "They have him on medicine for his depression" EP7 "He started actively hallucinating the last 3 months"
Maladaptive Behaviors Aggression		LP2 "Started getting more combative with staff" EP5 "She was whipping their behinds up there (staff)"

Notes: S-term = short-term; EP5, EP6, EP7 = EOAD participant #; LP1, LP2, LP3 = LOAD participant #; ADLs = activities of daily living

Results of Quantitative Component (Research Questions 1 & 2)

Results of the quantitative-component analysis in this study are summarized in Tables 3-11. RQ1 asked if there are differences in cognitive symptoms between EOAD patients and LOAD patients. Table 3 describes mean differences for EOAD and LOAD patients when it comes to cognitive symptom scores using a one-way ANOVA. In regards to EOAD and LOAD patients when it came to separate cognitive symptoms alpha was set at .05. There were no statistically significant differences in cognitive symptom between EOAD (n = 8) and LOAD (n = 12) groups.

Table 4 describes Total Cognitive Symptom Scores. Results indicate that there were no statistically significant differences in total cognitive symptom scores between EOAD and LOAD groups, F (1, 18) = 1.019, p = .326, η^2 = 0.05.

Table 5 describes the assumption of variances using Levene's test of equality of variances. This test was used to determine whether variances between EOAD and LOAD groups for cognitive symptoms are equal. Six of the 16 separate cognitive symptoms were statistically significant (which indicates violation of the assumption of homogeneity). This included the following: Remembering things that happened recently, $p = .005$; Recalling conversation a few days later, $p = .005$; Remembering his/her address and phone number, $p = .005$; Knowing how to work familiar machines, $p = .028$; Handling money for shopping, $p = .017$; and using his/her intelligence to understand, $p = .028$. The assumption of homogeneity of variances was violated, as assessed by Levene's test for variances. However, looking at the bottom of Table 5, when overall (total) cognitive scores were analyzed for EOAD ($n = 8$) and LOAD ($n = 12$), the Levene's test is not statistically significant or the group samples were drawn from populations with the same variance. Therefore, there was homogeneity of variances, as assessed by Levene's test for equality of variances ($p = .184$).

Table 6 provides descriptive statistics for cognitive symptom scores between EOAD and LOAD care recipients. Mean score for EOAD was 78.3750 ($SD = 2.77$) and mean score for LOAD was 75.75 ($SD = 6.94$). Total cognitive scores for EOAD had a range from 72-90 and cognitive scores for LOAD had a range from 56-80, indicating lower cognitive scores than the counterpart. According to the Short IQCODE questionnaire, caregiver participants reported EOAD caregiver recipients as having higher cognitive scores than LOAD caregiver recipients.

Table 7 provides descriptive statistics for behavioral symptom scores of the BEHAVE-AD tool. The mean score for EOAD was 19.25 (*SD* = 21.37) and the mean score for LOAD was 11.08 (*SD* = 11.86). Total behavioral scores for EOAD care recipients ranged from 0-69; whereas, the Total behavioral symptom scores for LOAD caregiver recipients ranged from 2-45; again LOAD caregiver recipients indicate lower behavioral symptom scores.

Table 8 summarizes the one-way ANOVA comparing means between EOAD and LOAD patients with behavioral disturbances. Simply looking at p-values, there is only one indication of behavioral significance between groups (Activity Disturbances), F (1, 18) = 5.858, p = .026, η^2 = 0.25 indicating LOAD caregiver recipients scored higher on Activity Disturbances.

Although Table 8 showed at least one mean difference among the group, Table 9 summarized specific behavioral differences in groups using the Test of homogeneity of variances. The Levene's test was statistically significant and showed that at least two of behavioral disturbances violated the assumptions of homogeneity and showed that two of the dependent variables (Aggressiveness: p = .044; and Anxieties and Phobias: p = .032) between groups were not equal. However, Table 10 indicates that overall results for total behavioral symptom scores using the one-way ANOVA reveal that the symptom scores or the differences between the symptoms for AD caregiver recipients were not statistically significant. Therefore, there was no evidence to reject the null hypothesis. There are no differences between EOAD and LOAD behavioral symptoms. This is also

indicated in Table 11 where the Levene's test showed overall behavioral symptom scores were not statistically significant indicating that the assumption of homogeneity of variances is met. The Levene's test of equality of variances tests the null hypothesis that the population variances are equal. In other words, the group samples are drawn from populations with the same variance. Finally, there were no statistically significant differences in behavioral symptom scores between EOAD and LOAD groups, F (1, 18), 1.215, p = .285.

Table 3
Analysis of Variance (Cognitive Symptoms)

		SS	*df*	*MS*	*F*	*Sig.*
Remembering things about family	Between Groups	.208	1	.208	.677	.421
	Within Groups	5.542	18	.308		
	Total	5.750	19			
Remembering recent things	Between Groups	.300	1	.300	2.400	.139
	Within Groups	2.250	18	.125		
	Total	2.550	19			
Recalling conversations days later	Between Groups	.300	1	.300	2.400	.139
	Within Groups	2.250	18	.125		
	Total	2.550	19			
Remembering his/her address	Between Groups	1.200	1	1.200	4.320	.052
	Within Groups	5.000	18	278		
	Total	6.200	19			
Remembering what day it is	Between Groups	.000	1	.000	.000	1.000
	Within Groups	3.750	18	.208		
	Total	3.750	19			

(continued)

Table 3. Analysis of Variance (continued)

		SS	*df*	*MS*	*F*	*Sig.*
Remembering where things are kept	Between Groups	.075	1	.075	.220	.644
	Within Groups	6.125	18	.340		
	Total	6.200	19			
Remembering where to find things	Between Groups	.075	1	.075	.432	.519
	Within Groups	3.125	18	.174		
	Total	3.200	19			
Knowing how to work fam. machines	Between Groups	.408	1	.408	1.269	.275
	Within Groups	5.792	18	.322		
	Total	6.200	19			
Learning to use a new gadget/machine	Between Groups	.133	1	.133	.655	.429
	Within Groups	3.667	18	.204		
	Total	3.800	19			
Learning new things in general	Between Groups	.033	1	.033	.655	.429
	Within Groups	.917	18	.051		
	Total	.950	19			
Following a story in a book or on TV	Between Groups	.000	1	.000	.000	1.000
	Within Groups	5.750	18	.319		
	Total	5.750	19			
Making decisions on everyday matters	Between Groups	.133	1	.133	.655	.429
	Within Groups	3.667	18	.204		
	Total	3.800	19			
Handling money for shopping	Between Groups	.300	1	.300	1.271	.274
	Within Groups	4.250	18	.236		
	Total	4.550	19			
Handling financial matters	Between Groups	.133	1	.133	.655	.429
	Within Groups	3.667	18	.204		
	Total	3.800	19			
Handling other arithmetic problems	Between Groups	.033	1	.033	.084	.776
	Within Groups	7.167	18	.398		
	Total	7.200	19			

(continued)

Table 3. Analysis of Variance (continued)

		SS	*df*	*MS*	*F*	*Sig.*
Using intelligence to understand reason	Between Groups	.408	1	.408	1.269	.275
	Within Groups	5.792	18	.322		
	Total	6.200	19			

Note: SS = sum of square; df = degrees of freedom; MS = mean squared; F = F-ratio; Sig. = p-value

Table 4

Total Cognitive Symptom Scores

	SS	*df*	*MS*	*F*	*Sig.*
Between Groups	33.075	1	33.075	1.019	.326
Within Groups	584.125	18	32.451		
Total	617.200	19			

Note: SS = sum of squares; df = degrees of freedom; MS = mean squared; F = F-ratio
Sig. = p-value.

Table 5

Test of Homogeneity of Variances

	Levene Statistic	*df1*	*df2*	*Sig.*
Remembering things about family, friends, e.g., work, birthdays, address	3.166	1	18	.092
Remembering things that have happened recently	21.600	1	18	.000
Recalling conversations a few days later	21.600	1	18	.000
Remembering his/her address and phone number	32.073	1	18	.000

(continued)

Table 5. Test of Homogeneity of Variances (continued)

	Levene Statistic	*df1*	*df2*	*Sig.*
Remembering what day and month it is	.000	1	18	1.000
Remembering where things are usually kept	1.593	1	18	.223
Remembering where to find things when placed differently	2.000	1	18	.174
Knowing how to work familiar machines	5.748	1	18	.028
Learning to use a new gadget or machine	3.168	1	18	.092
Learning new things in general	3.168	1	18	.092
Following a story in a book or on TV	.059	1	18	.811
Making decisions on everyday matters	3.168	1	18	.092
Handling money for shopping	6.923	1	18	.017
Handling financial matters e.g. the pension, dealing with the bank	3.168	1	18	.092
Handling other everyday arithmetic problems (how much food to buy).	.333	1	18	.571
Using his/her intelligence to understand and to reason things through	5.748	1	18	.028
Total Cognitive Symptoms	1.911	1	18	.184

Notes: df1 = Degrees of freedom # 1; Sig. = significance or p-value

Table 6

Descriptive for Total Cognitive Scores

	N	*M*	*SD*	*SE*	*95% CI for M* *LL*	*UL*	*Min*	*Max*
Early onset	8	78.3750	2.77424	.98084	76.0557	80.6943	72.00	80.00
Late onset	12	75.7500	6.94295	2.00426	71.3387	80.1613	56.00	80.00
Total	20	76.8000	5.69949	1.27445	74.1326	79.4674	56.00	80.00

Notes: N = Number in population; M = Mean; SD = standard deviation; SE = standard error; CI = confidence interval; LL = lower limit; UL = upper limit; Min = minimum; Max = maximum

Table 7

Statistics for Total Behavioral Symptom Scores

	N	*M*	*SD*	*SE*	*95% CI for M* *LL*	*UL*	*Min*	*Max*
Early onset	8	19.2500	21.36586	7.55397	1.3877	37.1123	.00	69.00
Late onset	12	11.0833	11.85870	3.42331	3.5487	18.6180	2.00	45.00
Total	20	14.3500	16.32330	3.65000	6.7105	21.9895	.00	69.00

Notes: N = Number in population; M = Mean; SD = standard deviation; SE = standard error; CI = confidence interval; LL = lower limit; UL = upper limit; Min = minimum; Max = maximum

Table 8

Analysis of Variance (Behavioral Symptoms)

		SS	*df*	*MS*	*F*	*Sig.*
Paranoid and Delusional	Between Groups	32.033	1	32.033	1.226	.283
	Within Groups	470.167	18	26.120		
	Total	502.200	19			
Hallucinations	Between Groups	2.133	1	2.133	.114	.739
	Within Groups	336.417	18	18.690		
	Total	338.550	19			
Activity Disturbances	Between Groups	19.200	1	19.200	5.858	.026
	Within Groups	59.000	18	3.278		
	Total	78.200	19			
Aggressiveness	Between Groups	10.800	1	10.800	2.113	.163
	Within Groups	92.000	18	5.111		
	Total	102.800	19			
Diurnal Rhythm Disturbance	Between Groups	.008	1	.008	.014	.907
	Within Groups	10.792	18	.600		
	Total	10.800	19			
Affective Disturbances	Between Groups	.033	1	.033	.013	.909
	Within Groups	44.917	18	2.495		
	Total	44.950	19			
Anxieties and Phobias	Between Groups	8.008	18	.008	.958	.341
	Within Groups	150.542	18	8.363		
	Total	158.550	19			

Note: SS = sum of squares; df = degrees of freedom; MS = mean squared; F = F-ratio Sig. = p-value.

Table 9

Test of Homogeneity of Variances for Behavioral Symptoms

	Levene Statistic	*df1*	*df2*	*Sig.*
Paranoid and Delusional	1.189	1	18	.290
Hallucinations	.628	1	18	.438
Activity Disturbances	2.775	1	18	.113
Aggressiveness	4.684	1	18	.044
Diurnal Rhythm Disturbance	2.449	1	18	.135
Affective Disturbances	.430	1	18	.520
Anxieties and Phobias	5.405	1	18	.032

Notes: df1 = Degrees of freedom # 1; Sig. = significance or p-value

Table 10

Total Behavioral Symptom Scores

	SS	*df*	*MS*	*F*	*Sig.*
Between Groups	320.133	1	320.133	1.215	.285
Within Groups	4742.417	18	263.468		
Total	5062.550	19			

Note: SS = sum of squares; df = degrees of freedom; MS = mean squared;
F = F-ratio; Sig. = p-value.

Table 11

Test of Homogeneity of Variances of
Total Behavioral Symptom Scores

Levene Statistic	*df1*	*df2*	*Sig.*
.635	1	18	.436

Notes: df1 = degrees of freedom #1; Sig. = p-value

Evidence of Trustworthiness

The qualitative component of this research study utilized and followed proven procedures, the six-phase thematic analysis (Braun & Clarke, 2006) and grounded theory (Patton, 2002). This researcher reported a step-by-step approach in the previous qualitative component section. This section explained all codes and phrases that emerged from re-reading audio-taped, qualitative interviews. Finally, primary and sub-themes were presented including examples and extracts as supporting evidence. Reliability of themes was checked against each caregiver participant's Microsoft Word-typed written, audio-taped report for accuracy and confirmation. Validity was obtained by comparing codes and themes against the quantitative database used in SPSS that arose out of questionnaire responses from caregiver participants.

The quantitative component of this research study used the BEHAVE-AD informant survey that has been successfully used by various researchers. It has good reliability in discriminating and good validation in AD cases (Reisberg et al., 2014; Robert et al, 2010). The BEHAVE-AD questionnaire is an informant-based rating scale that assesses behavioral symptoms in AD patients, independent of comparatively difficult to treat cognitive symptoms. It was chosen because it is an informant-based rating scale and was developed to elicit information obtained from caregiver reports. In addition to the BEHAVE-AD instrument used to measure behavioral symptoms, the Short-IQCODE questionnaire was chosen because it has been proven to be useful for individuals who are unable to undergo direct-cognitive testing due to acute illness, lack of cooperation, or

death. This instrument measures a single general factor of cognitive decline and validly reflects past cognitive decline. Researchers have compared the Short-IQCODE to neuro-pathological diagnosis (Rockwood et al., 1998; Thomas et al., 1994) and it has been significantly correlated with amyloid precursor protein in AD patient's blood (Thomas, 1996). Both the BEHAVE-AD and Short-IQCODE overall scores (dependent variables) reported by caregiver participants were inputted into the SPSS program, using the one-way ANOVA to analyze groups (EOAD and LOAD). This revealed synthesis of evidence that was similar to both qualitative and quantitative outcomes.

Summary

The purpose of this mixed-method study was to determine whether or not individuals with EOAD vs. LOAD experience different behavioral and cognitive (memory) symptoms. Caregiver participants were used as informants on behalf of AD patients. Research questions included RQ1(Are there differences in cognitive symptoms between EOAD patients and LOAD patients?) and RQ2 (Are there behavioral between EOAD patients and LOAD patients?).

Participants/informants were recruited from various caregiver support group facilities throughout the Houston metropolitan and surrounding areas. Most of the participants were members of the Alzheimer's Association's Houston Southeast Chapter. The specific criteria requirements included: Must be 18 years of age or older; caring for an individual who had been diagnosed with early-onset AD (EOAD)/late-onset AD

(LOAD); diagnosis had to be in accordance with criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition – DSM-V (APA, 2013).

Demographic samples and data collection were between October 12, 2015 and March 16, 2016. Caregiver participants were divided into two groups (EOAD and LOAD) and were given instruments to measure both cognitive and behavioral symptoms. Consent forms were provided and discussed and signatures were not obtained until understanding of the study was indicated by all participants. Six participants were included in the qualitative data collection process of the study. Twenty participants were included in the quantitative component of the study. Qualitative caregiver participants were given demographic background surveys to fill out; and they were audio-taped in person, with the researcher using two open-ended, semi-structured interview questions. These interview questions were transcribed in Microsoft word verbatim. The quantitative data collection process of the study consisted of participants filling out packets face-to-face, over the phone, or via the internet. All face-to-face interviews (qualitative and quantitative) were conducted in library conference rooms, private offices, and in participants' homes.

Results of the qualitative component of the study were presented in Table 2 with several primary themes: 1) cognitive impairment; 2) mood swings; 3) impulsiveness; 4) struggles with activities of daily living (ADLs); 5) psychological behaviors; and 6) maladaptive (adverse) behaviors. According to caregiver participants, 100% of caregiver recipients experienced cognitive impairment, specifically short-term memory loss. This

was also true for psychological behaviors. It was reported that 6 out of 6 of the caregiver recipients went through periods when they experienced anxiousness, agitation, irritability, frustration, depression, paranoia, and hallucinations, depending on the present state of the disease.

Results of the quantitative component indicated that (RQ1) there were no statistically significant differences in total cognitive symptom scores between EOAD and LOAD groups, F (1, 18) = 1.019, p = .326, η^2 = 0.05. Results for RQ2 indicated that there were no statistically significant differences in behavioral symptom scores between EOAD and LOAD groups, F (1, 18) = 1.215, p = .285, η^2= 0.06. Findings, limitations, and recommendations will be discussed in Chapter 5.

Chapter 5: Findings, Limitations, and Recommendations

Introduction

The purpose of this study was to explore Alzheimer's disease, specifically early-onset AD (EOAD) versus late-onset AD (LOAD) in individuals, and determine whether there are differences or similarities among behavioral and cognitive symptoms between these two groups. I used a mixed-method approach and caregiver participants were used as informants on behalf of EOAD and LOAD patients to answer research questions. In this chapter, I provided discussions and findings presented in Chapter 4. In addition, I will discuss the limitations of the current study and recommendations for future research. Finally, I will offer implications for social change.

Interpretation of the Findings

Qualitative Findings

Two themes that emerged from qualitative data analysis using grounded theory and thematic analysis were cognitive impairment and psychological behaviors. When it came to cognition, the majority of caregiver participants indicated that care recipients suffered from lack of short-term memory. When it came to behavioral observations, the majority of caregiver participants indicated that care recipients suffered from psychological disturbances that included anxiety, agitation, irritability, frustration, depression, paranoia, and hallucinations. This was supported by the narratives they provided to the qualitative interview question: Over the past 2 – 5 years, what are some of the things you observed about this person's change in memory/behavior?

Activities of daily living and maladaptive behaviors were two themes that the majority of caregiver participants found to be the most challenging to witness or experience the care recipient going through. This was supported by the narratives they provided to the qualitative interview question: What are some of the most favorable/unfavorable moments you have observed about this individual's memory/behavioral changes?

Quantitative Findings

Research Question 1 was used to assess if EOAD patients have different cognitive symptoms than LOAD patients. There was insufficient evidence to reject the null hypothesis. EOAD patients have the same cognitive symptoms as LOAD patients. Total caregiver recipients (N = 20) were divided into two groups: EOAD caregiver recipients (n = 8) and LOAD caregiver recipients (n = 12). Mean score for EOAD was 78.3750 (SD = 2.77) and mean score for LOAD was 75.75 (SD = 6.94). Total cognitive scores for EOAD had a range from 72 – 90 and cognitive scores for LOAD had a range from 56 – 80, indicating lower cognitive scores than the counterpart. This was supported by questionnaire responses to the Short-IQCODE by caregiver participants.

Research question 2 was used to determine if EOAD patients have different behavioral symptoms than LOAD patients. There was insufficient evidence to reject the null hypothesis. EOAD patients have the same behavioral symptoms as LOAD patients. Total caregiver recipients (N = 20) were divided into two groups: EOAD caregiver recipients (n = 8) and LOAD caregiver recipients (n = 12). Mean score for EOAD was

19.25 (*SD* = 21.37) and mean score for LOAD was 11.08 (*SD* = 11.86). Total behavioral scores for EOAD had a range from 0 – 69 and behavioral scores for LOAD had a range from 2 – 45. The maximum EOAD total behavioral score was 69 and the maximum LOAD total behavioral score was 45, indicating lower behavioral scores for LOAD caregiver recipients. This was supported by questionnaire responses to the BEHAVE-AD informant instrument provided by caregiver participants.

Summary of Findings

Research studies indicate that AD is characterized by the onset of impairments in memory and executive function, in addition to cognitive and behavioral problems such as depression, apathy, and agitation (Wilson, Arnold, Beck, Bienias, & Bennett, 2008). Previous studies also indicated that not everyone who develops the disease will have the exact same symptoms, or the same rate of progression (AA, 2013).

In this study, both groups of caregiver participants, whether they cared for an individual who had been diagnosed before the age of 65 (EOAD) or after the age of 65 (LOAD), all agreed that when it came to cognitive symptoms, care recipients showed a decline in memory as the disease progressed. However, when it came to behavioral symptoms, care recipients exhibited different behavioral symptoms at different stages of the disease. In other words, progression of behavioral symptoms did not happen in a linear pattern/sequence. Each stage of the disease can have different symptoms or sometimes the stages will overlap (AA, 2013).

The demographic background and characteristics of the study included 35% of men and 65% of women, with 74.5 years being the mean age of participants. Consistent risk factors for AD are age and sex (Kalaria et al., 2008; Perez et al., 2012). Prevalence studies such as the Chicago Health and Aging Project (CHAP) and the aging Demographics and Memory Study (ADAMS) revealed that about two-thirds of Americans with AD are women. Of the 5.2 million Americans older than 65 years with AD, 3.4 million are women and 1.8 million are men.

Limitations

Limitations of the study included recruitment of participants, location of Alzheimer's caregiver support groups, and race/ethnic backgrounds. The participants in the study were recruited from various support groups that included members from the Alzheimer's Association. Due to time and cost constraints, the quantitative sample size (N=20) of the study was small. The locations of the support groups were throughout the Houston metropolitan area and surrounding cities and towns. Participants were recruited from the Houston Southeast Chapter of the Alzheimer's Association. As a result, it is not possible to generalize the findings of this study to other Alzheimer's caregiver support groups outside of the Houston and surrounding areas or chapters of the Alzheimer's Association outside of Houston or the United States.

This study consisted of 40% Black/African American; 5% Hispanic/Latino; and 55% White/Caucasian participants. Therefore, generalizing this study to other races/ethnicities should be carefully considered.

Recommendations

In future studies it would perhaps be more beneficial to interview a larger number of caregiver participants, which would bring about a higher number of care recipients in regards to races/ethnicities, socioeconomic backgrounds, as well as to include different areas in the United States and other countries. Collaboration with previous, present, and future researchers could perhaps build on this study. Consistency of successful outcomes could result in better protocols and better planning and treatment for AD clients and/or patients. Then, perhaps, such a study could be generalized to larger populations in regard to culture, race, socio-economic, states, and countries.

Stage was also a factor in both cognitive and behavioral symptoms. It would be beneficial to have care recipients evaluated regularly with the BEHAVE-AD and the Short-IQCODE. These instruments could be used by psychiatrists, psychologists and other clinicians to assess cognitive and behavioral symptoms at each stage of Alzheimer's disease. Whether or not the client or patient has been diagnosed with EOAD or LOAD, the fact still remains that these symptoms are present and are indications that there is a need for better treatment planning and prevention.

Implications for Social Change

Continual use of caregiver participants for future studies can ensure that care recipients, whether they have been diagnosed at EO AD or LOAD, have a voice. Many care recipients in this study were affected by cognitive impairment, i.e., short-term memory loss and aphasia, which appeared to get worse as the disease progressed. Quality

of life for these individuals could be improved through use of cognitive and behavioral measures instituted regularly before and after disease progression.

Behavioral and cognitive charts can be created by various facilities and given to caregivers to be used from one month to the next. On a monthly basis, on behalf of their care recipients, caregivers could then pass these charts on to treating private-care physicians, psychiatrists, psychologists, and/or clinicians. This process would give the treating staff an idea of what cognitive decline or behavioral disturbances care recipient have experienced over the past month. This protocol or particular instrument could be used as standard of care procedures for all patients with AD. This extra information would be provided by care recipients/caregivers along with personal backgrounds, bio-psychosocial history, and medical records when visiting their treating clinicians in private practices, hospitals, community emergency centers, nursing homes, or residential homes/facilities. This standard of care procedure could ensure a more accurate assessment of the patient, resulting in better diagnosis, treatment, preventative measures and successful outcomes.

Conclusion

This mixed-method study was conducted in order to fill a gap in research by using sequential use of a qualitative component and materials, followed by a quantitative component and materials. Caregiver participants were used as informants and gave their responses/perspectives on cognitive and behavioral symptoms that they observed in EOAD and LOAD care recipients. Once the data collection phase of the study was complete, I

called each participant via phone and went over interviews, questionnaires, and demographic surveys to ensure the accuracy of the information. I determined that there were no significant variable differences between EOAD and LOAD caregiver recipients.

Caregiver participants (N = 6) were interviewed and asked to give personal perspectives of what they observed in the EOAD (n = 3) and LOAD (n = 3) care recipients they had cared for in the last 2 – 5 years. Two themes that emerged from the qualitative portion of the study were: cognitive impairment and psychological behaviors. Caregiver participants indicated that care recipients suffered from lack of short-term memory and psychological disturbances such as anxiety, agitation, irritability, frustration, depression, paranoia, and hallucinations.

Caregiver participants (N = 20) were asked to fill out survey questions (BEHAVE – AD and Short IQCODE). Through the quantitative portion of the study, I determined that there were no significant variable differences (cognitive/behavioral symptoms) between EOAD (n = 8) and LOAD (n = 12) caregiver recipients. In other words, results revealed that individuals with AD have the same cognitive and behavioral symptoms whether they have an early onset or a late onset of the disease (Wilson, Arnold, Beck, Bienias, & Bennett, 2008). However, previous studies have indicated that not everyone who develops the disease will have the exact symptoms, or the same rate of progression (AA, 2013).

When both qualitative and quantitative results were combined, it was determined that there were no differences in cognitive symptoms (cognitive impairment, mood swings,

impulsivity, struggles with ADLs), or behavioral symptoms (psychological behaviors, maladaptive behaviors), whether experienced by EOAD or LOAD care recipients. The cognitive/behavioral symptoms may have been experienced at different stages of the disease; however, the same symptoms were present.

During the collection phase of this study, many of the participants discussed their loved one's cognitive impairments and psychological behaviors. It did not matter whether the individual was in their early 50's and 60's or in their later 70's or 80's. Race, gender, socioeconomic status, education, religion, or sexual orientation did not impact these impairments or behaviors. Reisberg et al. (2014) suggested that cognition-based symptoms of AD occur universally and progressively with the advance of AD and that behavioral symptoms of AD are not progressive, but peak at some stage prior to the final stage of the disease.

Age and gender continue to be risk factors for AD (Kalaria et al, 2008; Perez et al., 2012). The Chicago Health and Aging project (CHAP) and the Aging Demographics and Memory Study (ADAMS) are prevalence studies that revealed that about two-thirds of Americans with AD are women. Of the 5.2 million Americans older than 65 years of age with AD, 3.4 million are women and 1.8 million are men. Baby-boomers continue to age and the majority will be women according to various studies on Alzheimer's disease (AA, 2013; Kalaria et al., 2008; Perez et al., 2012). This disease is still one of the top ten causes of death in the United States and the fifth leading cause of death among Americans over the age of 65 (AA, 2015). This fatal disease is a neurodegenerative brain disorder of

unknown cause with neuropathological and neurochemical features. It is usually insidious in onset and increases slowly, but steadily. After diagnosis, individuals with the disease can live as long as 8 to 20 years (AA, 2013). Unfortunately, there still remains no known cure for AD.

This study has certain strengths as well as limitations. In order to reduce selection bias, participants recruited were from member facilities that belong to the Alzheimer Association. In addition, inclusion criterion for diagnosis for AD was used according to the DSM-V (APA, 2013). Caregiver roles were that of informants for caregiver recipients who had AD—given the fact that some individuals with AD are not always cognitively capable, as a result, informants were a positive alternative. Behavioral and cognitive instruments (BEHAVE-AD and Short IQCODE) were tools utilized by all participants and scored by a statistical software program (SPSS). However, these tools are subjective, as well as the perspective of caregivers when it comes to being sensitive enough to answer the question or differences in cognitive or behavioral symptoms. Therefore, a future study is warranted to possibly assess AD clients more objectively.

References

Almkvist, O., & Tallberg, I-M. (2009). Cognitive decline from estimated premorbid statuses predicts neurodegeneration in Alzheimer's disease. *Neuropsychology, 23*(1), 117-124.

Alzheimer's Association. (2016). Alzheimer's Association Report: 2016 Alzheimer's disease facts and figures. Retrieved from http://www.alz.org.

Alzheimer's Association. (2012). Alzheimer's Association Report: 2012 Alzheimer's disease facts and figures. Retrieved from http://www.alz.org.

Alzheimer's Association. (2009). Alzheimer's disease and the brain. Retrieved from http://www.alz.org/brain/01.asp.

Alzheimer's Association. (2012). 2012 Alzheimer's disease facts and figures. *Alzheimer's & Dementia, 8*(2), 131-168.

Alzheimer's Association. (2013). Alz.org. Alzheimer's Association. Retrieved May 26, 2013, from http://www.alz.org.

Alzheimer's Association. (2013). 2013Alzheimer's disease facts and figures. *Alzheimer's & Dementia, 9*(1), 208-245.

American Cancer Society. (2013). Cancer facts and figures 2013. Retrieved from http://www.cancer.org/acs/groups.

American Heart Association. (2014). Heart Disease and Stroke Statistics--2014 Update: A report from the American Heart Association. Retrieved from http://www.circ.ahajournals.org.

American Psychiatric Association. (2007). Practice Guideline for the Treatment of Patients with Alzheimer's disease and other dementias, *The American Journal of Psychiatry, 164*(12), 5-56. APA: Author.

APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders*. *Fifth Edition*. (DSM-V). Washington, DC: American Psychiatric Association.

Atkinson, R. C., & Shiffrin, R. M. (1968). The control of short-term memory. *Scientific American*, 225, 82-90.

Atkinson, R. C., & Shiffrin, R. M. (1968). Human memory: A proposed system and its control processes. In K. W. Spence & J. T. Spence (Eds.), *The psychology of learning and motivation* (pp. 89-195). New York, NY: Academic Press.

Backman, L., Forsell, Y., Vitanen, M., & Hassng, L. (1996). Episodic remembering in a population-based sample of nonagenarians: Does major depression exacerbate the memory deficits seen in Alzheimer's disease? *Psychology and Aging, 11(*4), 649-657.

Baddeley, A. D., & Hitch, G. (1974). Working memory. An integrative model: Working memory. In R. J. Sternberg (2009). *Cognitive psychology* (pp. 191-196). Belmont, CA: Wadsworth.

Bagyinszky, E., Youn, Y. C., An, S. S., & Kim, S. (2014). The genetics of Alzheimer's disease. *Clinical Interventions in Aging, 9*(1), 535-551.

Bassil, N., & Grossberg, G. T. (2010). Lowering risk of Alzheimer's disease. *Current Psychiatry, 9*(6), 22-35.

Baxter, M. G., & Bucci, D. J. (2013). Selective immunotoxic of basal forebrain cholinergic neurons: Twenty years of research and new directions. *Behavioral Neuroscience, 127*(5), 611-618.

Beard, R. L., Sakhtah, S., Imse, V., & Galvin, J. E. (2012). Negotiating the Joint Career: Couples adapting to Alzheimer's and aging in place. *Journal of Aging Research, 2012*(1), 1-12.

Belanger, S., & Belleville, S. (2009). Semantic inhibition impairment in mild cognitive impairment: A distinctive feature of upcoming cognitive decline? *Neuropsychology,* 23(5), 592-606.

Bennow, K., & Hampel, H. (2003). CSF markers for incipient Alzheimer's disease. *Lancet Neurology, 2*(1), 605-613.

Berwig, M., Leicht, H., Hartwig, K., & Gertz, H. J. (2011). Self-rated quality of life in mild cognitive impairment and Alzheimer's disease. *GeroPsych, 24(*1), 45-41.

Bivin, M. I. (2013). Influence of gender on caregiving for early and moderate stage Alzheimer's disease patients. (order No. 3590438, Walden University). *Proquest Dissertations and Theses,* 97. Retrieved http://search.proquest.com/docview/143198147?accountid=14872.

Borson, S., Frank, L., Bayley, P. J., Boustani, M., Dean, M., Lin, P-J. et al. (2013). Improving dementia care: The role of screening and detection of cognitive impairment. *Alzheimer's& Dementia: The Journal of the Alzheimer's Association, 9*(2), 151-159.

Braak, H., & Del Tredici. (2012). Alzheimer's disease: Pathogenesis and prevention. *Alzheimers & Dementia. The Journal of the Alzheimer's Association, 8(*3), 227-233.

Brainerd, C. J., Reyna, V. F., Petersen, R. C., Smith, G. E., Kenney, A. E., Gross, … Plassman, B. L. (2013). The Alipoprotein E genotype predicts longitudinal transitions to mild cognitive impairment but not to Alzheimer's dementia: Findings from a nationally representative study. *Neuropsychology, 27*(1), 86-94.

Brainerd, C. J., Reyna, V. F., Petersen, R. C., Smith, G. E., & Taub, E. S. (2011). Is the apolipoprotein E genotype a biomarker for mild cognitive impairment? Findings from a nationally representative study. *Neuropsychology, 25*(6), 679-689.

Brousseau, G., Burke, B., Rourke, B. P. (2007). Acetylchlinesterase inhibitors, neuropsychiatric symptoms, and Alzheimer's disease subtypes: An alternate hypothesis to global cognitive enhancement. *Experimental and Clinical Psychopharmacology, 15*(6), 546-554. doi: 10.1037/1064-1297.15.6.546.

Browning, P. G. F., Gaffan, D., Croxson, P. L., & Baxter, M. G. (2010). Severe scene learning impairment, but intact recognition memory, after cholinergic depletion of inferotemporal cortex followed by fornix transaction. *Cerebral Cortex, 20*(1), 281-293.

CDC. (2011). Ten great public health achievements: United States 2001 - 2010. *Morbidity and Mortality Weekly Report, 60*(19), 619-623.

Carrillo, M. C., et al. (2013). Can we prevent Alzheimer's disease? Secondary "prevention" trials in Alzheimer's disease. *Alzheimer's & Dementia, 9*(2), 123-131.

Castle, A. D., Balota, D. A., & McCabe, D. P. (2009). Memory efficiency and the strategic control of attention at encoding: Impairments of value-directed remembering in Alzheimer's disease. *Neuropsychology, 23*(3), 297-306.

Cheung, Z. H., & Ip, N. Y. (2011). Autophagy deregulation in neurodegenerative diseases - recent advances and future perspectives. *Journal of Neurochemistry, 118*(3), 317-325.

Colman, A. W. (2006). *Dictionary of psychology*. (2nd ed.). New York, NY: Oxford University Press, Inc.

Cordell, C. B., Borson, S., Boustani, M., Chodosh, J., Reuben, D., Verghese, J., Thies, & W., Fried, L. B. (2013). Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 9*(2), 141-150.

Coubard, O. A., Boura, M., Gripon, A., Ferrufino, L., Renaud, M., & Bherer, L. (2011). Attentional control in normal aging and Alzheimer's disease. *Neuropsychology, 25*(3), 353-367. doi: 10.1037/a0022058.

Creswell, J. W. (2009). *Research design: Qualitative, quantitative, and mixed methods approaches*. (3rd ed.). Thousand Oaks, CA: SAGE Publications, Inc.

Croxson, P. L., Browning, P. G. F., Gaffin, D., & Baxter, M. G. (2012). Acetylcholine facilitates recovery of episodic memory after brain damage. *The Journal of Neuroscience, 32*(40), 13787-13795.

Cummings, J. L., Golde, T. E., Sano, M., & Tariot, P. N. (2007). Looking to the future of Alzheimer's disease treatments: Anti-amyloid disease-modifying therapies, *CNS News, Special Edition,* CME, 91-100.

Cutcliffe, J. R. (2000). Methodological issues in grounded theory. *Journal of Advanced Nursing, 31*(6), 1476-1485.

Dean, A C., Victor, T. L., Boone, Philpott, L. M., & Hess, R. H. (2009). Dementia and effort test performance. *The Clinical Neuropsychologist, 23*(4), 133-152. doi: 10.1080/13854040701819050.

Dowling, N. M., Hermann, B., La Rue, A., & Sager, M. A. (2010). Latent structure and factorial invariance of a neuropsychological test battery for the study of preclinical Alzheimer's Disease, *Neuropsychology, 24(*6), 742-756.

Duara, R., Loewenstein, D.A., Shen, S., Barker, W., Potter, E., Varon, D., Heurlin, K., & Buckley, C. (2013). Amyloid positron emission tomography with ^{18}F-flutemetamol and structural magnetic resonance imaging in the classification of mild cognitive impairment and Alzheimer's disease, *Alzheimer's & Dementia: The Journal of Alzheimer's Association, 9*(3), 295-301.

Duberstein, P. R., Chapman, B. P., Sink, K. M., Robbins, J., Jerant, A. F., Franks, P., Tindle, H. A., & Bamonti, P. (2011). Personality and risk for Alzheimer's disease

in adults 72 years of age and older: A 6-year follow-up. *Psychology and Aging, 26(*2), 351-362. doi: 10.1037/a0021377.

Duchek, J. M., Balota, D. A., Thomas, J. B., Snyder, A. Z., Rich, P., Benzinger, T. L., … Ances, B. M. (2013). Relationship between Stroop performing and resting state functional connectivity in cognitively normal older adults. *Neuropsychology, 27*(5), 516-528.

Duke University Medical Center (2002, February 26). Duke Researchers Identify Age At Onset Genes for Alzheimer's and Parkinson's disease. *Science Daily*. Retrieved October 9, 2011, from http://www.sciencedaily.com/releases/2002/02/020226074118.htm.

Eakin, D. K, & Smith, R. (2012). Retroactive interference effects in implicit memory. *Journal of Experimental Psychology: Learning, Memory, & Cognition, 38*(5), 1419-1424.

Eaton, N. R., Krueger, R. F., Skodol, A. E., Grant, B. F., Keyes, K. M., Balsis, S., …Hasin, D. S. (2012). An invariant dimensional liability model of gender differences in mental disorder prevalence: Evidence from a national sample. *Journal of Abnormal Psychology, 121*(1), 282-288.

Engelborghs, S., De Vreese, K., Van de Casteele, T., Vanderstichele, H., Van Everbroeck, B., Cras, P., …De Deyn, P. P. (2008). Diagnostic performance of a CSF biomarker panel in autopsy-confirmed dementia. *Neurobiology Aging, 29* (8), 1143-1159.

Erikson, H., Fereshtehnejad, S. M., Falahati, F., Farahmand, B., Religa, D., & Eriksdotter, M. (2014).Differences in routine clinical practice between early and late onset Alzheimer's disease: data from the Swedish Dementia Registry (SveDem). *Journal of Alzheimer's disease, 41*(2), 411-419. doi:10.3233/JAD-132273.

Fagan, A. M., Mintun, M. A., Shah, A. R., Alsea, P., Roe, C. M., Mach, R. H., …Holtzman, D. M. (2009). Cerebrospinal fluid tau and p-tau (18) increase with cortical amyloid deposition in cognitively normal individuals: implications for future clinical trials of Alzheimer's disease. *EMBO Molecular Medicine, 1*, 371-380.

Feng, Z., & Gao, F. (2011). Stem cell challenges in the treatment of neurodegenerative disease. *CNS Neurosciences & Therapeutics, 18*(2), 142-148

Fisher Center for Alzheimer's Research Foundation. (2014). Genetic risk factors. Retrieved April 17, 2014 from http://www.Alzinfo.org.

Forstmeier, S., Maercker, A., Maier, W., van den Bussche, H., Riedel-Heller, S., Kaduszkiewicz, H., …AgeCoDe Study Group. (2012). Motivational reserve: Motivation-related occupational abilities and risk of mild cognitive impairment and Alzheimer disease. *Psychology and Aging, 27*(2), 353-36. doi:10.1037/a0025117.

Furiak, N. M., Kahle-Wrobleski, K., Callahan, C., Klein, T. M., Klein, R. W., & Siemers, R. R. (2012). Screening and treatment for Alzheimer's disease: Predicting

population-level outcomes. *Alzheimer's & Dementia: The Journal of The Alzheimer's Association, 8*(1), 31-38.

Gagnon, L. G., & Belleville, S. (2011). Working memory in mild cognitive impairment and Alzheimer's disease: Contribution of forgetting and predictive value of complex span tasks. *Neuropsychology, 25*(2), 226-236.

Gauthier, S., & Molinuevo, J. L. (2013). Benefits of combined cholinesterase inhibitor and memantine treatment in moderate-severe Alzheimer's disease. *Alzheimer's & Dementia:The Journal of the Alzheimer's Association, 9*(3), 326-331.

Glaser, B. G., & Strauss, A. L. (1967). *The discovery of grounded theory: Strategies for qualitative research*. Chicago: Aldine.

Glosser, G., Friedman, R. B., & Grugan, P. (1999). Comparison of reading and spelling in patients with probable Alzheimer's disease. *Neuropsychology, 13*(3), 350-358.

Gobel, E. W., Blomeke, K., Zadikoff, C., Simani, T., Weintraub, S. & Reber, P. J. (2013). Implicit perceptual-motor skill learning in mild cognitive impairment and Parkinson's disease. *Neuropsychology, 22*(3), 314-321.

Gold, C. A., & Budson, A. E. (2008). Memory loss in Alzheimer's disease: Implications for development of therapeutics. *Expert Reviews Neurotherapeutics, 8*(12), 1879-1891.

Good, M. A., Hale, G., & Staal, V. (2007). Impaired "Episodic-Like" object memory in adult APPswe transgenic mice. *Behavioral Neuroscience, 121*(2), 442-448.

Gravetter, F. J., & Wallnau, L. B. (2009). *Statistics for the Behavioral Sciences*. (8th ed).

Belmont, CA: Wadsworth Cengage Learning.

Handen, B. J., Cohen, A. D., Channamalappa, U., Bulova, P., Cannon, S. A., Cohen, W. I., … Klunk, W. E. (2012). Imaging brain amyloid in nondemented young adults with Down syndrome using Pittsburgh compound B. *Alzheimer's & Dementia, 8*(6), 496-501.

Hartig, W., Saul, A., Kacza, J., Grosche, J., Goldhammer, S., Michalski, D., & Wirths, O. (2014). Immunolesion-induced loss of cholinergic projection neurons promotes β-amyloidosis and tau hyperphosphyorylation in the hippocampus of triple-transgenic mice. *Neuropathology and Applied Neurobiology, 40*(1), 106-120.

HHS. (2011). *National Plan to Address Alzheimer's Disease*. Washington, D.C: U.S.Department of Health and Human Services.

Hampel, H., Lista, S., & Khachaturian, Z. S. (2012). Development of biomarkers to chart all Alzheimer's disease stages: The royal road to cutting the therapeutic Gordian knot. *Alzheimer's & Dementia. The Journal of the Alzheimer's Association, 8*(4), 312-336.

Hyman, B. T., Phelps, C. H., Beach, T. G., Bigio, E. H., Cairns, N. J., Carrillo, M. C., Montine, T. J. (2012). National Institute on Aging--Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. *Alzheimer's & Dementia. The Journal of the Alzheimer's Association, 8*(1), 1-13.

Jongbloed, W., Kester, M. I., van der Flier, W. M., Veerhuis, R., Scheltens, P., Blankenstein, M. A., & Teunissen, C. E. (2013). Discriminatory and predictive

capabilities of enzyme-linked immunosorbent assay and multiplex platforms in a longitudinal Alzheimer's disease study. *Alzheimer's & Dementia. The Journal of the Alzheimer's Association, 9*(3), 276-283.

Jorm, A. F. (1994). A short form of the informant questionnaire on cognitive decline in the elderly (IQCODE): Development and cross-validation. *Psychology Medicine, 24*(1), 145-153.

Kalaria, R. N., Maestre, G. E., Arizaga, R., Friedland, R. P., Galasko, D., Hall, K., …Antuono, P. (2008). Alzheimer's disease and vascular dementia in development countries: Prevalence, management, and risk factors. *Lancet Neurology, 7*(9), 812-826.

Kar, S., Slowikowski, S. P. M., Westaway, D., & Mount, H. T. J. (2004). Interactions between β-Amyloid and central cholinergic neurons; implications for Alzheimer's disease. *Journal of Psychiatry Neuroscience, 29*(6), 427-441.

Kawas, C. H., Greenia, D. E., Bullain, S. S., Clark, C. M., Pontecorvo, M. J., Joshi, A. D., & Corrada, M. M. (2013). Amyloid imaging and cognitive decline in nondemented oldest-old: The 90+ Study. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 9*(2), 199-203.

Kazdin, A. E. (2011). Evidence-based treatment research: Advances, limitations, and next steps. *American Psychologist, 11*(1-2), 685-698.

Kendell, J. (1999). Axial coding and the grounded theory controversy. *Western Journal of Nursing Research, 21*(6), 743-757.

Khachaturian, Z. S., Khachaturian, A. S., & Thies, W. (2012). The draft "National Plan" to address Alzheimer's disease - National Alzheimer's Project Act (NAPA). *Alzheimer's & Dementia, 8*(3), 234-236.

Khawli, L.A., & Prabhu, S. (2013). Drug delivery across the Blood-Brain Barrier. *Molecular Pharmaceutics, 10*(5), 1471-1472.

Kling, M. A., Trojanowski, J. Q., Wolk, D. A., Lee, M. Y., & Arnold, S. E. (2013). Vascular disease and dementias: Paradigm shifts to drive research in new directions. *Alzheimer's & Dementia, 9*(1), 76-92.

Lah, S., & Smith, M. L. (2014). Semantic and episodic memory in children with temporal lobe epilepsy: Do they relate to literacy skills. *Neuropsychology, 28*(1), 113-122.

Langeslag, S. J. E., & van Strien, J. W. (2009). Aging and emotional memory: The co-occurrence of neurophysiological and behavioral positivity effects. *Emotion*, 9(3), 369-377.

Lehman, M., & Malmberg, K. J. (2012). A buffer model of memory encoding and temporal correlations in retrieval. *Psychological Review, 120*(1), 155-189.

Lim, Y. Y., Harrington, K., Kamer, A., Bush, A. I., Darby, D., Masters, C. L., …The AIBL Research Group. (2013). Cognitive consequences of high Aβ amyloid in mild cognitive impairment and healthy older adults: Implications for early detection of Alzheimer's disease. *Neuropsychology, 27*(3), 322-332.

Lincoln, Y., & Guba, E. (1985). *Naturalistic inquiry*. Beverly Hills, CA: Sage.

Logsdon, R. G., McCurry, S. M., & Teri, L. (2007). Evidence-based psychological treatment for disruptive behaviors in individuals with dementia. *Psychology and Aging*, *22*(1), 28-36.

MacDuffie, K. E., Atkins, A. S., Flegal, K. E., Clark, C. M., & Reuter-Lorenz, P. A. (2012). Memory distortion in Alzheimer's disease: Deficient monitoring of short- and long-term memory. *Neuropsychology*, *26*(4), 509-516.

Mathias, J. L., & Burke, J. (2009). Cognitive functioning in Alzheimer's and Vascular Dementia: A meta-analysis. *Neuropsychology, 23(*4), 411-423.

McLeod. S. A. (2010). Long-term memory. Retrieved from http://www.simplypsychology.org/long-term-memory.html.

Mungas, D., Farias, S. T., DeCarli, C., & Reed, B. R. (2009). Age and education effects on relationships of cognitive test scores with brain structure in demographically diverse older persons. *Psychology and Aging, 24*(1), 116-128. doi: 10.1037/a0013421.

Nadel, L., & Peterson, M. A. (2013). The hippocampus: Part of an interactive posterior representational system spanning perceptual and memorial systems. *Journal of Experimental Psychology: General, 142*(4), 1242-1254.

NAPA. (2011). National Plan to Address Alzheimer's Disease. *U.S. Department of Health and Human Resources*, 1-63.

National Institute of Health. (2013). Aging changes organ, tissues, and cells. Retrieved from http://www.nlm.nih.gov/medlineplus/ency/article/0004012.htm.

Nekkisimmon, J., Beckett, L., Schwartz, C., Carmichael, O., Fletcher, E., & DeCarlie, C. (2013). Subgoup ADNI normal controls characterized by atrophy and cognitive decline associated with vascular damage. *Psychology and Aging, 28*(1), 191-201.

Nosofsky, R. M., Denton, S. E., Mrphy-Knudsen, A. F., Unvirsagt, F. W., & Zak, S. R. (2012). Studies of implicit prototype extracton in patients with mild cognitive impairment and early Alzheimer's disease. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 38*(4), 860-880.

Okie, S. (2011). Confronting Alzheimer's disease. *The New England Journal of Medicine,365*(12), 1069-1072.

Panegyres, P. K., & Chen, H. Y. (2013). Differences between early and late onset Alzheimer's disease. *American Journal of Neurodegenerative Disease, 2*(4), 300-306.

Panegyres, P. K., & Chen, H. Y. (2014). Early-onset Alzheimer's disease: A global cross-sectional analysis. *European Journal of Neurology, 21*(9), 1149-1154. doi: 10.1111/ene.12453.

Parsons, C. G., Danysz, W., Dekunjdy, A., & Pulte, I. (2013). Memantine and cholinesterase inhibitors: Complementary mechanisms in the treatment of Alzheimer's disease. *Neurotox Research, 24*, 358-369.

Patton, M. Q. (2002). *Qualitative research & evaluation methods* (3rd ed.). Thousand Oaks, CA: Sage.

Perez, F., Helmer, C., Foubert-Samier, A., Auriacombe, S., Dartigues, J-F., & Tison, F. (2012). Risk of dementia in an elderly population of Parkinson's disease patients: A 13-year population-based study. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 8*(6), 463-469.

Perri, R., Zannino, G., Caltagirone, C., & Carlesino, A. (2012). Alzheimer's disease and semantic deficits: A feature-listing study. *Neuropsychology, 26*(5), 652-663.

Phillips, L. H., Scott, C., Mowat, D., Bell, J. S., & Henry, J. D. (2010). Emotion perception in Alzheimer's disease and mood disorder in old age. *Psychology and Aging, 25(*1), 38-47. doi: 10.1037/a0017369.

Pinel, J. P. J. (2009). *Biopsychology*. (7th ed.). Boston, MA: Pearson Allyn Bacon.

Reisberg, B., Monteiro, I., Torossian, C., Auer, S., Shulman, M. B., Ghimire, S. et al. (2014). The BEHAVE-AD Assessment System: A perspective, a commentary on New findings, and a historical review. *Dementia and Geriatric Cognitive Disorders, 39*(1), 89-146. doi: 10.1159/000357839.

Reisberg, B., Borenstein, J., Salob, S. P., Ferris, S. H., Franssen, E., & Georgotas, A. (1987). Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment. *Journal of Clinical Psychiatry, 48*(5, suppl.), 9-15.

Reuben, D. B. (2007). Better care for older people with chronic diseases: An emerging vision. *JAMA, 298*(27), 2673-2674.

Rueda, A. D., & Schmitter-Edgecombe, M. (2009). Time estimation abilities in mild cognitive impairment and Alzheimer's disease. *Neuropsychology, 23*(2), 178-188.

Savage, L. M. (2012). Sustaining high acetylcholine levels in the frontal cortex, but not retrosplenial cortex, recovers spatial memory performance in a rodent model of diencephalic amnesia. *Behavioral Neuroscience, 126* (2), 226-236.

Schatzberg, A. F., Cole, J. O., & DeBattista, C. (2010). *Manual of clinical psychopharmacology*. (7th ed.). Washington, DC: American Psychiatric Publishing, Inc.

Serra, L., Bozzali, M., Cercignani,M., Perri, R., Fadda, L., Caltagirone, C., & Carlesimo, G. A. (2010). Recollection and familiarity in amnestic mild cognitive impairment. *Neuropsychology, 24*(3), 316-326.

Shoji, M., Kanai, M., Matsubara, E., Ikeda, M., Harigaya, Y., Okamoto, K., & Hirai, S. (2000). Taps to Alzheimer's patients: a continuous Japanese study of cerebrospinal fluid biomarkers. *Annals of Neurology, 48*(1), 402.

Sjogren, M., Andreasen, N., & Blennow, K. (2003). Advances in the detection of Alzheimer's disease-use of cerebrospinal fluid biomarkers. *Clinical Chim. Acta, 332*(1), 1-10.

Slotnick, S. D. (2012). The cognitive neuroscience of memory. *Cognitive Neuroscience, 3*(3-4), 139-141.

Smith, T. E. (2008). The case for implicit category learning. *Cognitive, Affective & Behavioral Neuroscience, 8*(1), 3-16.

Solfrizzi, V., Scafato, E., Frisardi, V., Seripa, D., Logroscino, G., Giancarlo, L., …Italian Longitudinal Study on Aging Working Group.(2013). Frailty syndrome and the

risk of vascular dementia: The Italian Longitudinal Study on aging. *Alzheimer's & Dementia. The Journal of the Alzheimer's Association, 9*(2), 113-122.

Stefanacci, R. G. (2008). Evidence-based treatment of behavioral problems in patients with dementia. *Clinical Geriatrics, 16*(2), 16-18.

Sternberg, R. J. (2009). *Cognitive Psychology*. (5th ed.). Belmont, CA: Wadsworth, Cengage Learning.

Storandt, M., Balota, D. A., Aschenbrenner, A. J., & Morris, J. C. (2014). Clinical and psychological characteristics of the initial cohort of the Dominantly Inherited Alzheimer Network (DIAN). *Neuropsychology, 28*(1), 19-29.

Sunderland, T. et al. (2003). Decreased beta-amyloid 1-42 and increased tau levels in cerebrospinal fluid of patients with Alzheimer's disease. *JAMA, 289* (1), 2094-2103.

Taylor, J. S. H., Rastle, K., & Davis, M. H. (2013). Can cognitive models explain brain activation during word and pseudoword reading? A meta-analysis of 36 neuroimaging studies. *Psychological Bulletin, 139*(4), 766-791.

Thomas, P., & Fenech, M. (2007). A review of genome mutation and Alzheimer's disease. *Mutagenesis, 22*(1), 15-33.

Tulving, E., & Schacter, D. L. (1990). Priming and human memory systems. *Science, 247*, 301-306.

Van Damme, I., & d'Ydewalle, G. (2009). Implicit false memory in the DRM paradigm: Effects of amnesia, encoding instructions, and encoding duration. *Neuropsychology, 23*(5) 635- 648.

Vanderstichele, H., Bibl, M., Engelborghs, S., Le Bastard, N., Lewczuk, P., Molinuevo, J. L., …Blennow, K. (2012). Standardization of pre-analytical aspects of cerebrospinal fluid biomarker testing for Alzheimer's disease diagnosis: A consensus paper from the Alzheimer's Biomarkers Standardization Initiative. *Alzheimer's & Dementia, 8*(1), 65-73.

Vermeulen, N., Chang, B., Mermillod, M., Pleyers, G., & Corneille, O. (2013). Memory for words representing modal concepts: Resource sharing with same-modality percepts is spontaneously required. *Experimental Psychology, 60*(4), 293-301.

Vloeberghs, E., Van Dam, D., Coen, K., Staufenbiel, M., & De Deyn, P. P. (2006). Aggressive male APP23 mice modeling behavior alterations in dementia. *Behavioral Neuroscience, 120*(6), 1380-1383.

Voss, J. L., Lucas, H. D., & Paller, K. A. (2012). More than a feeling: Pervasive influences of memory without awareness of retrieval. *Cognitive Neuroscience, 3*(3-4), 193-226.

Ward, A., Arrighi, H. M., Michels, S., & Cedarbaum, J. M. (2012). Mild cognitive impairment: Disparity of incidence and prevalence estimates. *Alzheimer's & Dementia, 8*(1), 14-21.

Ward, E.V., Berry, C. J., & Shanks, D. R. (2013). An effect of age on implicit memory that is not due to explicit contamination: Implications for single and multiple-systems theories. *Psychology and Aging, 28*(2), 429-442.

Weih, M., Degimenci, U., Kreil, S., & Kornhuber, J. (2010). Physical activity and Alzheimer's disease. A meta-analysis of cohort studies. *GeroPsych, 23(*1), 17-20. doi:10.1024/1662-9647/a000005.

Wilkinson, L., Beigi, M., Lagnado, D. A., & Jahanshahi, M. (2011). Deep brain stimulation of the subthalamic nucleus selectively improves learning of weakly associated cue combinations during probabilistic classification learning in Parkinson's disease. *Neuropsychology, 23*(3), 286-294.

Wilkinson, L., Khan, Z., & Jahanshahi, M. (2009). The role of the basal ganglia and its cortical connections in sequence learning: Evidence from implicit and explicit sequence learning in Parkinson's disease. *Neuropsychologia, 47*, 2564-2573.

Willems, S., Salmon, E., & Van der Lnden, M. (2008). Implicit/explicit memory dissociation in Alzheimer's disease: The consequence of inappropriate processing? *Neuropsychology*, *22*(6), 710-717.

Wilson, R. S., Arnold, S. E., Beck, T. L., Bienias, J. L., & Bennett, D. A. (2008). Change in depressive symptoms during the prodromal phase of Alzheimer disease. *Archives of General Psychiatry, 65*(4), 439-446.

Wimo, A., Jonsson, L. Bond, J., Prince, M., & Winblad, B. (2013). The worldwide economic impact of dementia 2010. *Alzheimer's & Dementia, 9*(1), 1-11.

Winkler, I., & Cowan, N. (2005). From sensory to long-term memory: Evidence from auditory memory reactivation studies. *Experimental Psychology, 52*(1), 3-20.

Wolk, D. A., & Dickerson, B. C. (2011). Fractionating verbal episodic memory in Alzheimer's disease. *NeuroImage, 54*, 1530-1539.

Woolley, S. R., Butler, M. H., & Wampler, K. S. (2000). Unraveling change in theory: Three different process research methodologies. *The American Journal of Family and Therapy, 28*(1), 311-327.

Yerokhin, V., Anderson-Hanley, C., Hogan, M. J., Dunnam, D. H., Osborne, S., & Shulan, M. (2012). Neuropsychological and neurophysiological effects of strengthening exercise for early dementia: A pilot study. *Aging, Neuropsychology, and Cognition: A Journal on Normal and Dysfunctional Development, 193*(3), 380-401.

Yu, L., Boyle, P., Schneider, J. A., Segawa, E., Wilson, R. S., Leurgans, S., & Bennett, D. A. (2013). APOE ε4 Alzheimer's disease pathology, cerebrovascular disease, and cognitive change over the years prior to death. *Psychology and Aging, 28*(4), 1015-1023.

Appendix A: DSM-V Criteria for Major or Mild Neurocognitive Disorder due to Alzheimer's disease

A. The criteria are met for major or mild neurocognitive disorder.

B. There is insidious onset and gradual progression of impairment in one or more cognitive domains (for major neurocognitive disorder, at least two domains must be impaired).

C. Criteria are met for either probable or possible Alzheimer's disease as follows:

For major neurocognitive disorder:

Probable Alzheimer's disease is diagnosed if either of the following is present; otherwise, possible Alzheimer's disease should be diagnosed.

1. Evidence of a causative AD genetic mutation from family history or genetic testing.

2. All three of the following are present:

a. Clear evidence of decline in memory and learning and at least one other cognitive domain (based on detailed history or serial neuropsychological testing).

b. Steadily progressive, gradual decline in cognition, without extended plateaus.

c. No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline).

For mild neurocognitive disorder:

Probable Alzheimer's disease is diagnosed if there is evidence of a causative Alzheimer's disease genetic mutation from either genetic testing or family history.

Possible Alzheimer's disease is diagnosed if there is no evidence of a causative Alzheimer's disease genetic mutation from either genetic testing or family history, and all three of the following are present:

1. Clear evidence of decline in memory and learning
2. Steadily progressive, gradual decline in cognition, without extended plateaus.
3. No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological or systemic disease or condition likely contributing to cognitive decline).

D. The disturbance is not better explained by cerebrovascular disease, another neurodegenerative disease, the effects of a substance, or another mental, neurological, or systemic disorder.

Appendix B: Stages and Symptoms of AD

Stage 1: The No Impairment stage of AD is also known as normal functioning, which is associated with having no memory problems. An individual visiting his or her medical professional would not show any evidence of dementia (Dowling, Hermann, La Rue, & Sager, 2010).

Stage 2: The Very Mild Cognitive Decline stage of AD is also known as normal age-related changes in an individual. This individual will have memory lapses, i.e., forgetting certain words, or where they have put daily objects. But, when interviewed by medical professionals, family members or friends, they will not show any dementia symptoms (Wilson et al., 2008).

Stage 3: Mild Cognitive Decline stage of AD is also referred to as the early-stage AD--some can be diagnosed with symptoms, but not all. At this stage of the disease, individuals may have problems with memory and concentration. Family members, friends, or medical professionals will start to notice the individual having difficulty remembering names, performing tasks at work or at home, misplacing valuables, or having increased difficulty planning and organizing events or materials (Wilson et al., 2008).

Encoding, storage, and retrieval are three stages of memory operations (Sternberg, 2009). Therefore, studying memory impairment can give significant insight to cognitive dysfunction, which limits autonomy in complex activities performed by those in the early dementia stages. Mild cognitive decline, also mild cognitive impairment (MCI) is

abnormal cognitive functioning in older adults without the presence of dementia (Rueda & Schmitter-Edgecombe, 2009; Van Damme, Belanger, & Belleville, 2009; Ward et al., 2013; Wilson et al, 2008). MCI is associated with an increased possibility of suffering from AD. However, 40 percent of those who suffer from MCI will not necessarily develop AD--but examining profiles of MCI cases can often determine which ones will develop AD and which ones will not (Pike, Moss, Rowe, & Savage, 2008; Schmitter-Edgecombe, Greeley, & Woo, 2009).

Stage 4: Very Moderate Decline stage of AD is also known as the mild or early-stage of AD. A medical interview can detect individual symptoms in the areas of forgetfulness, impairment in counting numbers or arithmetic, difficulty in paying bills or keeping up with finances, and becoming withdrawn or moody in social situations (AA, 2013).

Stage 5: The Moderate Severe Cognitive Decline stage is also known as the moderate or mid-stage of AD. At this stage of AD, individuals can still feed themselves and go to the bathroom alone. They also remember family members and friends. The daily activities that may become difficult include recalling addresses, remembering dates, and choosing the proper clothing for the proper seasons or occasions (Gauthier & Molinuevo, 2013).

Stage 6: Severe Cognitive Decline is also known as the moderately severe or mid-stage of AD. Patients/individuals at this stage have significant memory loss with considerable personality change. Clients/individuals become unaware of their

surroundings, may have problems remembering spouse or caregivers' names, or need assistance with putting on their clothes, e.g., may put pajamas over their daytime clothes or put their shoes on the wrong feet. In addition, at this stage of AD, the client can become suspicious of his caregiver or spouse motives, due to the client's personality or behavioral changes. It is also common for individuals at this stage of AD to experience change in sleep patterns and they are subject to wander if they are not supervised properly (AA, 2013).

Stage 7: Very Severe Cognitive Decline can also be known as the Severe or late-stage of AD. Reisberg (2013) explains that patients at this stage of the disease will become totally dependent on others to help with daily activities of living. They are unable to hold their heads up, to use the bathroom or eat without the assistance of a caregiver. In addition, these patients cannot respond to their environment. They are no longer able to carry on a normal conversation with others. They may say a few words or phrases. They can no longer swallow, their reflexes become abnormal, and they can no longer smile or move certain body muscles (Gauthier & Molinuevo, 2013).

Appendix C: Cooperation Email

Email of Cooperation from Alzheimer's Association (Houston Southeast Chapter)

Mon, Oct 14, 2013 10:19 am

Re: Prospectus on Alzheimer's Disease

We at the Alzheimer's Association know the value that research can bring to expanding our understanding of Alzheimer's disease and the caregiver experience. For that reason, we are happy to assist you with accessing care partners through our chapter's programs and services.

What we can offer is this... We serve persons with early stage Alzheimer's disease and their care partners through our Early Stage programs. Of particular interest to you may be our Learning Together and Discovering Connections groups. These groups serve persons with dementia and their care partners by providing education and/or engaging programming, followed by separate support groups for PWD and care partners.

Through those early stage programs you could have access to approximately 15 - 20 care partners. In addition, we offer a wide variety of community-based early stage programs for which we have a mailing list of about 100 couples. You could have access to interested parties from that list, as well.

In addition, we sponsor about 50 caregiver support groups throughout our 37-county region. Those groups meet monthly and we could help you gain access to those

caregivers/groups via email/snail mail introduction. Typically about 250 - 350 persons participate in support groups each month.

Here's a link to the various support groups we run, just to give you an idea of their locations. http://www.alz.org/documents/tex/support_groupsseptember2013.pdf

Let me know what you think about the type of access and the types of folks you could speak with through our chapter's services.

Best,

It was nice speaking with you over the phone yesterday. Attached is my prospectus on Alzheimer's disease. I have completed the prospectus and Chapter 2: Literature Review of my dissertation. I am now working on the Introduction, which is Chapter 1 of the dissertation.

It is policy that I finish Chapter 3: Methodology section in addition to Chapters 1 and 2 of the dissertation in order to get IRB approval from my school. This is why I am contacting you at this point because, I would like you to be able to determine what information you have available that could benefit my research on the subject of caregivers and what information they can provide on the symptoms and stages of the AD patients that they care for and observe on a daily or routine basis. Of course, I would not be able to collect data until Chapters 1, 2, & 3 of my dissertation has been approved by the IRB. However, I am trying to plan ahead by contacting you to give you the attached prospectus in order for you to decide if we could be of service to each other. If you agree, I would need to

receive a letter of intent from you/your organization indicating such--I have form letters that I can send you as well.

I hope this will be the start of a long relationship, especially working on ways to slow the progression or cease the disease, AD, all together.

Note: I am a doctoral student of clinical psychology at Walden University. I am also doing my internship at a private practice in Missouri City/Sugar Land, Texas--my pre-doctoral year ends on December 9, 2013 and I plan to continue my dissertation course through February 2013. I conduct psychotherapy with individuals from age 5 years old to 78 years old. In addition, I conduct psychological evaluations on adults and child and adolescents throughout the week except Thursdays at Ashar Counseling and Psychological Services. On Friday mornings from 9:30 AM to 11:30 AM, I attend training at Charis Psychological Services in the Gessner/Beechnut Area.

Regards,

Appendix D: Demographic Questionnaire

1. Do you (caregiver) speak English? _____yes _____ no

2. What is AD patient age? _____

3. What is AD patient gender? Male___ Female____ Other____

4. What is AD patient race/ethnicity?

a. Asian American
b. Black/African American
c. Hispanic/Latino
d. Native American
e. White/Caucasian
f. Other _____

5. AD patient Marital Status:
a. Single
b. Married
c. Separated
d. Divorced
e. Widowed

6. AD patient highest level of education:
a. GED
b. High school
c. Some college
d. College graduate
e. Post graduate studies
f. Post graduate degree

7. Economic ($) Status of AD Patient:
a. 1 to 19,999
b. 20,000 to 49,999
c. 50,000 to 69,999
d. 70,000 to 99,999
e. 100,000 and above

8. Are you the primary caregiver (provide day to day care)? Yes_____ No_____

9. What is your relationship to the care recipient?
a. Spouse
b. Adult Child/Grandchild
c. Other _____

10. How long have you been a caregiver to AD patient? Year(s)____ Month(s)____.

11. Approximate hours/day provided to AD patient? _____

12. What age was patient when he/she was diagnosed with AD: Less than 65 years old?____ or More than 65 years old?____

13. Patient's stage of AD (AA, 2013). Choose from the following by circling the correct letter:

a. Stage 1 (No Impairment/Normal functioning).
b. Stage 2 (Very Mild Cognitive Decline -- Normal age related changes--forgetting certain words, forget where they put things, no dementia problems).
c. Stage 3 (Early stage of AD/Mild Cognitive Decline -- memory problems, loss of concentration, difficulty remembering names, cannot perform tasks at home or at work, problems planning and organizing events or materials).
d. Stage 4 (Very Moderate Decline/Mild or Early Stage -- forgetfulness, impairment in counting or arithmetic, difficulty in paying bills or keeping up with finances, becomes moody or withdrawn in social situations).
e. Stage 5 (Moderate Severe Cognitive Decline/Moderate or Mid-Stage of Ad -- can feed themselves, go to the bathroom alone, remember family and friends, problems with recalling addresses, dates, choosing right clothing for the proper seasons or occasions).
f. Stage 6 (Severe Cognitive Decline/Moderately Severe or Mid-Stage of AD -- significant memory loss, personality/behavioral change, is unaware of environment, problems remembering caregiver or spouse's name, need assistance putting on clothes--may put shoes on wrong feet or may put pajamas on over their clothes, becomes paranoid/suspicious of caregiver motives, change in sleep pattern, patient may wander off if not supervised properly).
g. Stage 7 (Very Severe Cognitive Decline/Severe or Late-Stage of AD -- patient is totally dependent on caregiver to help with activities of daily living, need assistance with holding their heads up, eating, and using the bathroom; cannot respond to their environment, can only say a few words, can no longer hold a conversation with others, can no longer swallow, they do not have the use of their muscles, reflexes are abnormal, and possibly death occurs).

Appendix E: Behavioral Pathology in Alzheimer's Disease

(BEHAVE-AD)

NAME: _____ ID#: _____ DATE: ___/___/___ PERIOD: _____

BEHAVIORAL PATHOLOGY IN ALZHEIMER'S DISEASE (BEHAVE-AD)[1, 2]

[BASED UPON INFORMATION OBTAINED FROM CAREGIVER AND OTHER INFORMANTS]

INFORMANT: _____ RELATIONSHIP TO PATIENT: _____

PART 1: Symptomatology

(In preceding 2 weeks unless otherwise specified below)

Assessment Interval: _____ weeks

Circle the highest applicable severity rating [0 to 3] for each item. Each category of symptomatology [A to G] is scored independently.

A. Paranoid and Delusional Ideation
(a delusion is a false conviction, not a misidentification)

1. "People are stealing things" delusion.

(0) Not present.
(1) Delusion that people are hiding objects.
(2) Delusion that people are coming into the home and hiding or stealing objects.
(3) Talking and listening to people coming into the home.

2. "One's house is not one's home" delusion.

(0) Not present.
(1) Conviction that the place in which one is residing is not one's home (e.g., packing to go home, complaints while at home of "take me home").
(2) Attempt to leave domiciliary to go home.
(3) Violence in response to attempts to forcibly restrict exit.

3. "Spouse (or other caregiver) is an imposter" delusion.

(0) Not present.
(1) Conviction that spouse (or other caregiver) is an imposter.
(2) Anger towards spouse (or other caregiver) for being an imposter.
(3) Violence towards spouse (or other caregiver) for being an imposter.

4. Delusion of abandonment (e.g.: to an institution).

(0) Not present.
(1) Suspicion of caregiver plotting abandonment or institutionalization (e.g., on the telephone).
(2) Accusation of a conspiracy to abandon or institutionalize.
(3) Accusation of impending or immediate desertion or institutionalization.

[1] Adapted from Reisberg et al., "Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment," J. Clin. Psychiatry, 1987; 48:5 (Suppl.), 9-15.
[2] © 1986 by Barry Reisberg, M.D. (all rights reserved).

5. Delusion of infidelity (social and/or sexual unfaithfulness).

(0) Not present.
(1) Conviction that spouse, children, and/or other caregivers are unfaithful.
(2) Anger towards spouse, relative, or other caregiver for their infidelity.
(3) Violence toward spouse, relative, or other caregiver for their infidelity.

6. Suspiciousness/Paranoia other than above.

(0) Not present.
(1) Suspiciousness (e.g., hiding objects which they may later be unable to locate or a statement such as "I don't trust you").
(2) Paranoid (i.e., fixed conviction with respect to suspicions and/or anger as a result of suspicions).
(3) Violence as a result of suspicions.

Unspecified?_____

Describe:_____

_____

_____

_____

_____

7. Delusions (non-paranoid) other than above.

(0) Not present.
(1) Delusional.
(2) Verbal or emotional manifestations as a result of delusions.
(3) Physical actions or violence as a result of delusions.

Unspecified?_____

Describe:_____

_____

_____

_____

_____

B. Hallucinations

8. Visual hallucinations.

(0) Not present.
(1) Vague, not clearly defined.
(2) Clearly defined hallucinations of objects and persons (e.g., sees other people at the table).
(3) Verbal or physical actions or emotional responses to the hallucinations.

9. Auditory hallucinations.

(0) Not present.
(1) Vague, not clearly defined.
(2) Clearly defined hallucinations of words and phrases.
(3) Verbal or physical actions or emotional responses to the hallucinations.

10. Olfactory hallucinations.

(0) Not present.
(1) Vague, not clearly defined.
(2) Clearly defined hallucinations (e.g., smells a fire or "something burning").
(3) Verbal or physical actions or emotional responses to the hallucinations.

11. Haptic (sense of touch) hallucinations.

(0) Not present.
(1) Vague, not clearly defined.
(2) Clearly defined hallucinations (e.g., "something is crawling on my body").
(3) Verbal or physical actions or emotional responses to the hallucinations.

12. Other hallucinations.

(0) Not present.
(1) Vague, not clearly defined.
(2) Clearly defined hallucinations.
(3) Verbal or physical actions or emotional responses to the hallucinations.

Unspecified?_____

Describe:_____

_____

_____

_____

_____

BEH-04

C. Activity Disturbances.

13. Wandering (e.g., away from home or caregiver).

(0) Not present.
(1) Somewhat, but not sufficient as to require restraint.
(2) Sufficient as to require restraint.
(3) Verbal or physical actions or emotional responses to attempts to prevent wandering.

14. Purposeless activity (cognitive abulia).

(0) Not present.
(1) Repetitive, purposeless activity (e.g., opening and closing pocketbook, packing and unpacking clothing, repeatedly putting on and removing clothing, insistent repeating of demands or questions).
(2) Pacing or other purposeless activity sufficient to require restraint.
(3) Abrasions or physical harm resulting from purposeless activity.

15. Inappropriate activity.

(0) Not present.
(1) Inappropriate activities (e.g., storing and hiding objects in inappropriate places, such as throwing clothing in wastebasket or putting empty plates in the oven, inappropriate sexual behavior such as inappropriate exposure).
(2) Present and sufficient to require restraint.
(3) Present and sufficient to require restraint, and accompanied by anger or violence when restraint is used.

Unspecified?_____

Describe:_____

_____

_____

_____

_____

D. Aggressiveness.

16. Verbal Outbursts.

(0) Not present.
(1) Present (including unaccustomed use of foul or abusive language).
(2) Present and accompanied by anger.
(3) Present, accompanied by anger, and clearly directed at other persons.

17. Physical threats and/or violence.

(0) Not present.
(1) Threatening behavior.
(2) Physical violence.
(3) Physical violence accompanied by vehemence.

18. Agitation (other than above).
(e.g. non-verbal anger; negativity including refusal to bathe, dress, continue walking, take medications, etc. ; hyperventilation).

(0) Not present.
(1) Present.
(2) Present with emotional component.
(3) Present with emotional and physical component.

E. Diurnal Rhythm Disturbances

19. Day/Night disturbance.

(0) Not present.
(1) Repetitive wakening during night (except for purpose of toileting).
(2) 50% to 75% of former sleep cycle at night.
(3) Complete disturbance of diurnal rhythm (less than 50% of former sleep cycle at night).

F. Affective Disturbance

20. Tearfulness (or whimpering or other "crying sounds").

(0) Not present.
(1) Present.
(2) Present accompanied by a clear affective component.
(3) Present and accompanied by affective and physical component (e.g., wringing of hands or other gestures).

21. Depressed mood, other.

(0) Not present.
(1) Present (e.g., occasional statement "I wish I were dead," or "I'm going to kill myself," or "I feel like nothing," without clear affective concomitants).
(2) Present with clear concomitants (e.g., thoughts of death).
(3) Present with emotional and physical concomitants (e.g., suicidal gestures).

Unspecified?_____

Describe:_____

_____

_____

_____

_____

G. Anxieties and Phobias

22. Anxiety regarding upcoming events (Godot syndrome).

(0) Not present.
(1) Present with repeated queries and/or other activities regarding upcoming appointments and/or events (e.g., when are we going?).
(2) Present and disturbing to caregivers.
(3) Present and intolerable to caregivers.

23. Other anxieties.
(e.g., regarding money, the future, being away from home, health, memory, etc. ; or generalized anxiety such as thinking everything is "terribly wrong").

(0) Not present.
(1) Present.
(2) Present and disturbing to caregivers.
(3) Present and intolerable to caregivers.

Unspecified?_____

Describe:_____

_____

_____

_____

_____

24. Fear of being left alone.

(0) Not present.
(1) Present with vocalized fear of being alone.
(2) Vocalized and sufficient to require specific action on the part of caregiver.
(3) Vocalized and sufficient to require patient to be accompanied at all times (e.g., patient must see the caregiver at all times).

25. Other phobias.
(e.g. fear of crowds, travel, darkness, people/strangers, bathing, etc.)

(0) Not present.
(1) Present
(2) Present and of sufficient magnitude to require specific action by caregiver.
(3) Present and sufficient to prevent patient activities.

Unspecified?_____

Describe:_____

_____

_____

_____

_____

TOTAL **SEVERITY** SCORE: _____

BEH - 08

PART 2: Global Rating

Circle one choice. Are the symptoms which have been noted of sufficient magnitude as to be:

(0) Not at all troubling to the caregiver or dangerous to the patient.
(1) Mildly troubling to the caregiver or dangerous to the patient.
(2) Moderately troubling to the caregiver or dangerous to the patient.
(3) Severely troubling to the caregiver or dangerous to the patient.

Symptom most troubling to caregiver

"With respect to the symptoms which have been noted, which is the biggest problem for you and/or other caregivers?" (More than one symptom can be listed, but please give numerical order.)

_____

_____

_____

_____

_____

_____

Clinician: _____ Date: _____/_____/_____

Comments: _____

_____

_____

8

Copyright © 1986 by Barry Risberg, M.D. (all rights reserved).

The BEHAVE-AD has been "reproduced with permission."

Appendix F: Short IQCODE

Short Form of the Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE)

by A. F. Jorm

Centre for Mental Health Research
The Australian National University
Canberra, Australia

There is no copyright on the Short IQCODE. However, the author appreciates being kept informed of research projects which make use of it.

Note: As used in published studies, the IQCODE was preceded by questions to the informant on the subject's sociodemographic characteristics and physical health.

Now we want you to remember what your friend or relative was like 10 years ago and to compare it with what he/she is like now. 10 years ago was in 19__. Below are situations where this person has to use his/her memory or intelligence and we want you to indicate whether this has improved, stayed the same or got worse in that situation over the past 10 years. Note the importance of comparing his/her present performance with 10 years ago. So if 10 years ago this person always forgot where he/she had left things, and he/she still does, then this would be considered "Hasn't changed much". Please indicate the changes you have observed by circling the appropriate answer.

Compared with 10 years ago how is this person at:

	1	2	3	4	5
1. Remembering things about family and friends e.g. occupations, birthdays, addresses	Much improved	A bit improved	Not much change	A bit worse	Much worse
2. Remembering things that have happened recently	Much improved	A bit improved	Not much change	A bit worse	Much worse
3. Recalling conversations a few days later	Much improved	A bit improved	Not much change	A bit worse	Much worse
4. Remembering his/her address and telephone number	Much improved	A bit improved	Not much change	A bit worse	Much worse
5. Remembering what day and month it is	Much improved	A bit improved	Not much change	A bit worse	Much worse
6. Remembering where things are usually kept	Much improved	A bit improved	Not much change	A bit worse	Much worse
7. Remembering where to find things which have been put in a different place from usual	Much improved	A bit improved	Not much change	A bit worse	Much worse
8. Knowing how to work familiar machines around the house	Much improved	A bit improved	Not much change	A bit worse	Much worse

9. Learning to use a new gadget or machine around the house	Much improved	A bit improved	Not much change	A bit worse	Much worse
10. Learning new things in general	Much improved	A bit improved	Not much change	A bit worse	Much worse
11. Following a story in a book or on TV	Much improved	A bit improved	Not much change	A bit worse	Much worse
12. Making decisions on everyday matters	Much improved	A bit improved	Not much change	A bit worse	Much worse
13. Handling money for shopping	Much improved	A bit improved	Not much change	A bit worse	Much worse
14. Handling financial matters e.g. the pension, dealing with the bank	Much improved	A bit improved	Not much change	A bit worse	Much worse
15. Handling other everyday arithmetic problems e.g. knowing how much food to buy, knowing how long between visits from family or friends	Much improved	A bit improved	Not much change	A bit worse	Much worse
16. Using his/her intelligence to understand what's going on and to reason things through	Much improved	A bit improved	Not much change	A bit worse	Much worse

Appendix G: Qualitative Interview

1. Over the past 2 – 5 years, what are some of the things you observed about this person's change in memory/behavior?
    a. Can you elaborate on his/her memory when it comes to their spouse, significant other, family, friends? How does he/she react to them?
    b. Can you elaborate on his/her memory when it comes to family and friends' addresses, birthdays, occupations, etc.? What are her actions?
    c. What are some of the things that he/she does that make you know that she remembers or forgets the time, date, and place? How does he/she behave if they can or can't remember?
    d. What about when it comes to remembering how to work a particular machine/gadget around the house? How does he/she react if they can or can't remember?
    e. How does he/she react to handling money or financial situations?
    f. What about making normal day-to-day decisions (what to eat, what to wear, when to use bathroom, when to brush teeth)? What are some of the ways she reacts to these activities?
    g. Learning new things in general? How does he/she react?
    h. Remembering events that happened the day before? If they can remember, how do they react/if they can't remember, how do they react?

2. What are some of the most favorable moments you have observed about this individuals memory/behavioral changes? What are some of the most unfavorable?

Appendix H: Permission to use BEHAVE-AD Instrument

I would be pleased to provide you with permission to use the BEHAVE-AD in your research in the Clinical Psychology Program at Walden University in association with your dissertation and with the publication of the dissertation provided that you agree to the following conditions:

My conditions are that the scale is properly referenced and that the copyright is noted in all reproductions.

The complete reference for the BEHAVE-AD is:

Reisberg, B., Borenstein, J., Salob, S.P., Ferris, S.H., Franssen, E., Georgotas, A. Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment.*Journal of Clinical Psychiatry*, 1987, 48 (5, suppl.): 9-15.

The copyright notice for the BEHAVE-AD is as follows:

Copyright ©1986 by Barry Reisberg, M.D., all rights reserved.

You should also note that the scale has been "reproduced with permission."

This permission will extend for a period of 8 years after you reply agreeing to the above conditions.

Sent: Tuesday, March 10, 2015 7:11 PM

Subject: Permission Request

Thank you for returning my call on Tuesday, March 10, 2015 in regards to my request to have written permission to include your BEHAVE-AD tool in my dissertation.

I am a doctoral student in the clinical psychology program at Walden University. My dissertation is on Alzheimer's disease and I am comparing early-onset AD patient symptoms to late-onset AD patient symptoms using caregivers as informants. Your Behavioral pathology in Alzheimer's Disease (BEHAVE-AD) tool will be used to measure behavioral symptoms and I will be using the Short Form of the Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE) to measure cognitive symptoms. My research question is: Are there differences in symptomology between EOAD patients and LOAD patients?

In addition to using the BEHAVE-AD as a measuring tool, once my research is complete, Walden University will be publishing it as an appendix at the end of my dissertation.

I hope to hear from you soon.

Thanking you in advance,

Appendix I: Email to/Acknowledgment (Use of Short IQCODE)

Subject: RE: Short IQCODE use in dissertation study

Date: Tue, Aug 18, 2015 8:00 pm

Thanks for letting me know about your project. Best wishes for it.

Regards

Sent: Wednesday, 19 August 2015 10:51 AM

Subject: Short IQCODE use in dissertation study

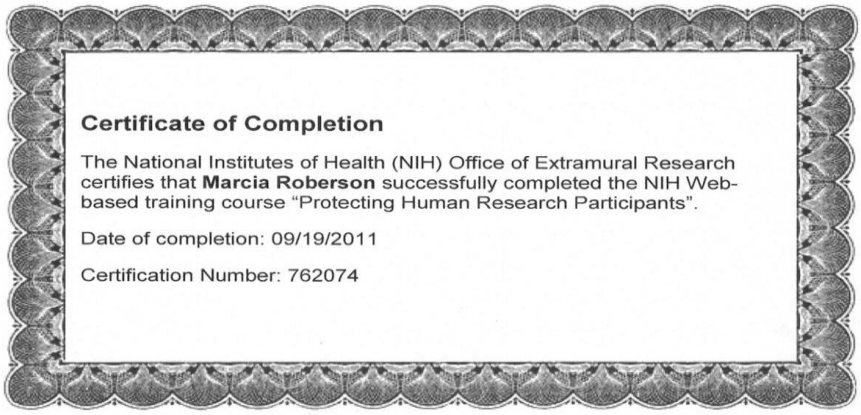
I am a graduate student at Walden University in the Doctoral Clinical Psychology Program (United States). My dissertation topic is "Comparative memory/behavioral symptoms of Alzheimer's disease: EOAD vs LOAD."

This email is to inform you of my plan to use your instrument the Short Form of the Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE) as a tool to obtain information from potential participants (caregivers to Alzheimer patients/victims) for my dissertation research.

I would like to thank you for creating the Short IQCODE, it is an asset greatly appreciated that will enable me to conduct my research study. If you have any questions or concerns, please do not hesitate to contact me at the email or telephone number below.

Regards,

Appendix J: Protecting Human Research Participants



Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that **Marcia Roberson** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 09/19/2011

Certification Number: 762074

Appendix K: Flyer

ALZHEIMER'S DISEASE

Opportunity to be a participant in a dissertation study if

YOU are over 18 and a CAREGIVER to SOMEONE who is one of the following:

√ Diagnosed with Alzheimer's disease before 65 years old (Early onset AD) or

√ Diagnosed with Alzheimer's disease after 65 years old or later (Late onset AD)

♦♦♦♦♦♦♦♦♦