2013

Relationship Between Occupational Complexity and Dementia Risk in Late Life: A Population Study

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RELATIONSHIP BETWEEN OCCUPATIONAL

COMPLEXITY AND DEMENTIA RISK IN

LATE-LIFE: A POPULATION STUDY

by

Daylee R. Greene

A dissertation submitted in partial fulfillment
of the requirements for the degree

of

DOCTOR OF PHILOSOPHY

in

Family and Human Development

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UTAH STATE UNIVERSITY
Logan, Utah

2013

ABSTRACT

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In Cox regression models, individuals holding agricultural occupations and occupations high in complexity of interaction with machinery, equipment, tools, and inanimate objects (“things”) had an increased risk for both AD and dementia. Socioeconomic status was found to partially mediate the relationship between high *things* complexity and dementia/AD risk, as well as the relationship between agricultural occupations and dementia/AD risk. While there has been some debate regarding whether results reflect a true effect of occupational complexity or simply an effect of education, results from this study indicate that both occupational complexity and education contribute unique effects to dementia/AD risk. Gender, job duration, and APOE genotype were not found to moderate any of the above associations. An understanding of how occupational complexity impacts cognitive reserve and risk for dementia/AD will enable individuals as well as clinicians to implement activities that enhance cognitive reserve and lead to a greater number of years lived symptom-free from dementia/AD.

(109 pages)

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ACKNOWLEDGMENTS

I would like to thank Dr. Maria Norton for her unwavering commitment, dedication, and encouragement to me throughout the writing of my dissertation. This project would likely never have come to fruition if not for her many hours of editing, question answering, and general support. I will forever be indebted to her for providing me with her amazing set of knowledge, experience, and patience to help me throughout the entire process.

I give special thanks to my family and friends as well for their constant support, encouragement, and understanding as I made my way through this dissertation from a simple idea to my final edits. In particular, I would like to thank my husband, Kurtis, for always supporting my educational pursuits and reminding me why I set out on this journey to begin with, and my best friend, Mandy, for being my number one cheerleader through all of the ups and downs (especially the downs). I would not have made it without you. Thank you.

Daylee R. Greene

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CHAPTER I

INTRODUCTION

Dementia affects nearly 6.4% of people over the age of 65 (van der Flier & Scheltens, 2005), and with the baby boom generation numbering around 75 million (Martini, Garrett, Lindquist, & Isham, 2007), that means almost 5 million new cases of dementia will occur over the next 20 years. Alzheimer's disease (AD) is the most common form of dementia, and symptoms can include forgetfulness, irritability, confusion, aggression, mood swing, and language difficulties. There is no cure for AD, and because it is degenerative, individuals with the disease require assistance from others for many daily tasks (MetLife Mature Market Institute, 2006). Spouses are the most common caregivers for individuals with AD, and it would be hard to say if the financial cost (around $75,000 a year for both paid and unpaid care) or the emotional cost (social, psychological, and physical) is greater (Schneider, Murray, Banerjee, & Mann, 1999; Thompson et al., 2007). This information makes it clear that dementia (particularly AD) is an important public health concern, one that seems likely to get worse before it gets better.

Researching factors that influence the etiologic origins of dementia is an important step in ameliorating the negative effects of dementia. Hallmark indicators of AD include neurofibrillary tangles and neuritic plaques in the cerebral cortex (Gasparini et al., 1998), and impaired blood flow within the brain, along with impaired communication between axons, have also been implicated in AD pathology (Massaad et al., 2010). These abnormalities lead to the clinical symptoms observed in dementia cases. Factors that have been implicated in the development of these etiological causes of dementia include atherosclerosis (Dolan et al., 2010), physical frailty (Boyle, Buchman, Wilson, Leurgans, & Bennett, 2010), exercise (Middleton, Barnes, Lui, & Yaffe, 2010), high cholesterol levels (Reiman et al., 2010), exposure to chemicals (Schmechel, Browndyke, & Ghi, 2006; Weisskopf et al., 2004), and psychological stress, as from experiencing the death of a parent in childhood (Norton, Ostbye, Smith, Munger, & Tschanz, 2009; Persson & Skoog, 1996) or having a spouse who is diagnosed with dementia (Norton et al., 2010). It is not always possible to prevent exposure to these factors that are linked with neuro-degeneration, but it is possible to identify interventions or other factors that buffer their negative effects.

Primary prevention involves taking steps before biological onset of the disease (Gordon, 1983), therefore, preventing the disease (and any negative clinical symptoms) from developing. Primary prevention can be implemented for the general public, as it involves taking steps that are low-risk, such as modifying diet and exercising, with preventative measures potentially having a positive effect on a large number of individuals. In consideration of targets for prevention, it is important to take into account both environmental and genetic factors. While there have been important recent advances regarding the role of genetics in dementia onset, it will likely be a number of years before scientists are able to implement genetic engineering to “correct” genetic factors responsible for disease. However, an individual's genetic profile may indicate that they are at an increased vulnerability to negative environmental exposures, so even if it is not feasible to “repair” an individual’s genetic blueprint, the genetic profile can be of great value in the selection of at-risk subpopulations for appropriate interventions. In terms of actual risk reduction, however, a focus on potential risk factors is a desirable approach for primary dementia prevention.

One such potential risk factor is occupation, which is the focus of this paper. A connection has been established between occupational attainment and dementia; namely that low occupational attainment is associated with an increased risk for dementia (Bickel & Kurz, 2009), while high occupational attainment is associated with a reduced risk of dementia, likely by building a reserve that delays the clinical expression of the disease (Meng & D'Arcy, 2012; Stern et al., 1994). Occupation is an important lifestyle factor that is associated with dementia in late-life and one which plays a large role in human development. Investigating the relationship between occupational complexity and dementia and AD can give important insights into protective and risk factors associated with the diseases.

Theoretical Framework

Lifespan developmental theory is the study of change throughout life, with the ultimate goal of research invoking this theory being to gain knowledge about individual similarities and differences in development, along with the degree and condition of individual plasticity in adulthood (Baltes, Reese, & Nesselroade, 1977). Plasticity is an area of lifespan theory that has particular applicability to the link between occupation and dementia, as it has long been presumed that intelligence declines with old age (Baltes & Schaie, 1976), and that individuals not appearing to follow this trend are the exceptions rather than the norm. The concept of plasticity does not support this assertion; Baltes and Schaie (1974) found that individuals seem to retain their adult level of functioning well into the sixth and seventh decades of life, when tested on measures reflecting educational experience. The key seems to be in the words "educational experience," as this is a factor that would vary greatly among individuals. Variability is a point of focus in lifespan developmental theory, as one implication of the theory is that individual differences in development may be brought about by individual experiences and choices throughout the lifespan. Such choices, in the context of Alzheimer's disease risk, might include educational attainment, diet, and physical and social activities.

One hypothesis that is relevant to the study of cognitive decline and which also is informed by lifespan developmental theory is the cognitive reserve hypothesis. The cognitive reserve hypothesis can exemplify the plasticity of individual's adaptation to a neurodegenerative disease process, such as dementia. The cognitive reserve hypothesis focuses on environmental factors that may delay symptom onset in dementia; specifically, higher IQ, advanced education, high occupational attainment, or participation in leisure activities may reduce the risk of getting Alzheimer's disease (AD) (Stern, 2006). The term "cognitive reserve" refers to functional ability, rather than physiological characteristics of the brain. That is, individuals with more cognitive reserve (as the result of higher advanced education or high occupational attainment, for example) are better able to perform cognitive tasks for a longer period of time after sustaining brain damage than are individuals without similar levels of cognitive reserve (Stern, 2002). In the case of dementia, individuals can have the physiological signs of dementia (brain pathology indicative of AD, diagnosed post-mortem), without expressing clinical symptoms of AD prior to death, due to larger than average brain size (Katzman et al., 1989).

Environmental Factors Influencing Cognitive Reserve

One environmental factor that can influence dementia risk via building cognitive reserve capacity is occupational complexity. The prospect of occupation as a protective or risk factor for dementia has the potential to be very important (Andel et al., 2005), as the majority of American adults are likely to spend a considerable amount of time at their job each week. The duration of time in years that individuals typically spend in the workforce is also substantial. The fact that the typical American will enter the workforce around the age of 20 and exit it nearly 45 years later (accounting for over half of the typical American lifespan) renders occupation a formidable influence on many aspects of Americans' lives, including mental and cognitive health (Andel et al., 2005). There is already some evidence to suggest that one aspect of occupation, higher number of working hours per week, is related to poorer cognitive performance in middle-age (Virtanen et al., 2009). Researching the link between occupation and dementia may provide valuable information about jobs as protective or risk factors for dementia, which would enable clinicians, researchers, and individuals to take proactive steps to increase the likelihood of healthy cognition in late-life.

Having a higher pre-morbid intellectual ability indicates a cognitive reserve that can have an impact on the clinical expression of dementia (Alexander et al., 1997). Formal education is also an important method of building cognitive reserve (Stern, 2006), with studies demonstrating an inverse association between higher educational attainment and dementia risk (Bickel & Kurz, 2009). In many of the existing studies on occupation and dementia, education is controlled for carefully, as it is thought to have a significant influence on dementia incidence and progression (McDowell, Xi, Lindsay, & Tierney, 2007). In general, both higher educational and more complex occupational attainment lead to delayed onset of dementia (Bickel & Kurz, 2009; King, Selden, Todd, Aucone, & Golden, 2001). This relationship is thought to be mediated by the higher level of cognitive reserve experienced by these higher-educated and higher-occupation attaining individuals (King et al., 2001).

In that same vein, it is important to note that education and intellect are sometimes considered to be proxies for occupational experience and intellectually demanding work. Yet, there is a small body of literature suggesting that, independent of the effects of education and intelligence, there is a significant association between intellectually demanding work and cognitive performance in late-life (Potter, Helms, & Plassman, 2008), as well as the clinical expression of AD (Stern et al., 1995). Thus, individual differences in lifestyle (such as in the form of occupational complexity) may impact cognitive reserve by partially mediating the association between degree of neurodegeneration and the clinical expression of AD (Scarmeas et al., 2003).

One way that occupation may assist in both the preservation of existing cognitive abilities, while at the same time building cognitive reserve and reducing dementia risk, is through the complexity of tasks that an individual faces each day at work (Andel et al., 2005). Frequent engagement in intellectually demanding tasks at work may provide mental exercise that supports brain functioning and performance in late-life (Potter et al., 2008). Specifically, high complexity of working with people, such as in teamwork and supervisory capacities, has been found to be associated with higher cognitive functioning and a reduced risk of Alzheimer’s disease and dementia in late-life, independent of age, gender, and level of education (Andel et al., 2005; Kroger et al., 2008; Potter et al., 2008), though Kroger et al. (2008) found this to be true only among participants who held their job for 23 years or longer.

There is some evidence to suggest that individuals may reap cognitive benefits when adult accomplishments (such as holding a complex job) offset deleterious socioeconomic or educational factors early in life, in particular, lower intellectual ability (Potter et al., 2008). The opposite pattern -- late-life cognition suffering after high intellectual ability in early life coupled with low occupational complexity in adulthood -- does not appear to be true (Potter et al., 2008). This could indicate that individuals with higher intellectual aptitude already possess the cognitive skills that individuals with lower aptitude develop while at a complex job. Therefore, it may be the case that the potential gains experienced by individuals with higher intellect are more modest than the gains experienced by people with lower intellect at an intellectually demanding job (Potter et al., 2008). Unfortunately, there have been few studies designed to address how these various patterns of high versus low complexity across both domains of formal education and occupational history may impact late-life cognitive health, including rate of cognitive decline and risk for AD and other dementias.

Study Objective

This study seeks to add to the literature by examining the impact of occupational complexity on cognitive status in late-life while using a population-based sample. Many of the studies previously conducted on occupation and cognitive status include only men (Potter, Helms, Burke, Steffens, & Plassman, 2007; Potter et al., 2008; Potter, Plassman, Helms, Foster, & Edwards, 2006) or utilize a clinical sample (Stern et al., 1995). To address these limitations, data from the Cache County Memory Study (CCMS), a population-based longitudinal epidemiological study of dementia was used. The CCMS included 2,164 males and 2,928 females aged 65 to 105 years at baseline, completing four triennial waves of assessment, implementing a rigorous clinical dementia evaluation protocol.

In order to contribute to the existing foundation of literature on the topic of occupation and dementia, this study will examine the separate and joint effects of formal education and occupational complexity. Additionally, this study will look at the potential offsetting effect of high/low occupational attainment, given the level of educational attainment. Another objective of this study is to investigate the effect of stagnation versus challenge/change in occupation on cognitive status in late-life. The challenge that comes with additional complexities from changing jobs may also buffer against negative cognitive outcomes in late-life.

CHAPTER II

LITERATURE REVIEW

AD, Dementia, and Cognitive Status

Dementia is a late-life health issue, and people are increasingly living to older ages (average life expectancy is currently 78.5 years in the U.S.; National Center for Health Statistics, 2012), which combine to make the issue of dementia a salient one. Also, dementia risk increases with age, doubling every 5 years after the age of 60 (Brookmeyer, Gray, & Kawas, 1998), making dementia a major public health concern. Alzheimer's disease (AD) is the most common type of dementia, with prevalence rates of about 6.4% at age 60 in the United States (Mayeux & Stern, 2012), and 28% at age 90 (Breitner et al., 1999). AD is characterized by incurable cognitive and physical degeneration (Gasparini et al., 1998). Other physiological markers of AD include neuritic plaques and neurofibrillary tangles (Gasparini et al., 1998; Salmon, Heindel, & Lange, 1999), which lead to neuropathological lesions characteristic of AD (Gasparini et al., 1998). These physical changes can lead to a loss of cognitive functioning, including deficits in information retention, memory, learning, executive functioning, and language (Mendez & Cummings, 2003). Eventually, there is a loss of independent functioning associated with these deficits, until the individual can no longer take care of him or herself. Diagnosis of AD is based on a thorough clinical evaluation that includes a neurological examination, MRI brain scans, and neuropsychological assessments, and is based on criteria developed by the National Institute of Neurologic and Communicative Disorders and Stroke, as well as the AD and Related Disorders Association Work Group

(McKhann et al., 1984). In addition to AD, other types of dementia can also lead to a loss of independent functioning.

Though different in clinical expression and physiological symptomatology, non-AD dementias, such as vascular dementia, frontotemporal dementia, and Lewy Body dementia, can be equally devastating for the individual as well as their families. Non-AD type dementias affect about 4.2% of the U.S. population, which equates to about 1 million affected individuals (Plassman et al., 2007). The progression of dementia can last up to 20 years (Fitzpatrick, Kuller, Lopez, Kawas, & Jagust, 2005; Mendez & Cummings, 2003). Such losses can lead to a large burden on family members who are often the primary caregivers, charged with the responsibility of providing intensive and often arduous care for their ill loved one. Individuals whose spouses have dementia are also at an increased risk to develop dementia themselves (Norton et al., 2010), illustrating the impact that the disease can have on family members.

Preceding an official diagnosis of dementia, individuals will generally experience a period of declining cognitive abilities, known variously as mild cognitive impairment (MCI; Solfrizzi et al., 2004). In most cases, individuals experience at least slight MCI as part of the normative aging process. These individuals may realize that they are not doing quite as well as they used to, but their symptoms are not severe enough that it affects optimal functioning.

There are a number of factors that can influence the progression of cognitive decline in late-life, and there is great variability in the speed of decline among individuals. One such factor that has the potential to influence the rate of cognitive decline among individuals is cognitive reserve, although cognitive reserve appears to delay the clinical onset of AD, while speeding up cognitive decline after the onset (Andel, Vigen, Mack, Clark, & Gatz, 2006; Stern, 2002, 2006). Cognitive reserve refers to the ability to display no outward symptoms of pathology taking place within the brain. The concept of cognitive reserve is discussed more thoroughly later in this chapter.

Theoretical Framework

Lifespan developmental theory focuses on both constancy and change throughout the lifetime (Baltes, 1987). When it comes to aging and cognitive status, lifespan theory focuses on cognitive declines that take place as individuals age, but asserts that aging is an individual rather than universal process (Christensen, 2001; Smith & Baltes, 1999). Thus, while there is a general decline observed in cognitive abilities in late-life, there is great variability in the amount of decline between individuals. Beyond genetic influences, some of these individual differences may be due to different choices made by individuals over the course of their lifetime, such as occupation and education.

Within lifespan developmental theory, there are several concepts that are of particular relevance to the study of cognitive status and reserve. The first of these is *multidirectionality*, which proposes that there is a great deal of diversity in the changes that take place during ontogenesis (Baltes, 1987). Multidirectionality also suggests that some behaviors increase and others decrease, even during the same developmental period. *Development as gain/loss* proposes that development does not always result in growth. Development can also occur in the form of loss/decline, such as decrements in cognitive abilities, both normative age-related declines and more severe cognitive deficits brought on by neurodegenerative diseases such as AD. *Plasticity*, mentioned briefly above, is a term that accounts for individual uniqueness, so to speak. An individual's developmental course can differ greatly, depending on the context in which experiences take place, and the individual's ability to adapt to a changing environment. *Lifespan development* is a concept that suggests that no age period is superior in its contributions to the development of the individual. That is, individuals grow and learn throughout their lives, and all of these experiences have the potential to contribute to the individual's overall development. Therefore, a job held by an individual at any point during the life course has potential to influence their cognitive reserve, status, and development.

Multidirectionality pertains to cognitive status and reserve in a similar way. Individuals who possess a large amount of cognitive reserve are likely to have a steady cognitive status in late-life and for a longer period of time than are individuals who have a small amount of cognitive reserve. Thus, behaviors associated with high cognitive status are likely to increase in individuals with large amounts of cognitive reserve, and decrease among individuals with small amounts of cognitive reserve. Development as gain/loss applies directly to the idea of cognitive status, as many aging individuals will experience at least some decline in their cognitive status in late-life. Declines may have a gradual course such as in development of a neurodegenerative disease such as AD, or may be more sudden as in persons whose cognitive capacity is more abruptly altered by experiences such as cerebrovascular accident or traumatic brain injury. Plasticity is a term very relevant to cognitive status and reserve, as every individual will have unique experiences that have the potential to build their cognitive reserve, an important resource for adaptation to neurodegenerative disease.

Cognitive Reserve

There are two different models of reserve regarding brain damage. Brain reserve refers to a physical quality of the brain, specifically the size or neuronal count within the brain (Stern, 2006). In this model, called "brain reserve capacity," (BRC) there is theorized to be a threshold of BRC, which once surpassed, leads to the clinical expression of dementia. The second model of reserve, and the focus for this project, is cognitive reserve. This model suggests that the brain uses cognitive processing approaches already established, or utilizes a compensatory approach, to actively cope with brain damage (Mortimer, Borenstein, Gosche, & Snowdon, 2005; Stern, 2002). Thus, individuals with higher amounts of cognitive reserve would be more likely to succeed at coping with equal amounts of brain damage (Stern, 2006).

As the name implies, cognitive reserve refers to a reserve of cognitive abilities, rather than a reserve of physical brain mass. Thus, it is possible to experience the physical deterioration of the brain which is the hallmark physiological indicator of Alzheimer's, while not experiencing the debilitating cognitive and/or behavioral symptoms of the disease (Roe et al., 2008; Stern, 2002; Stern et al., 1995). This is a significant distinction, as it is the cognitive and behavioral symptoms of the physical damage to the brain which are at the heart of the problems that the disease creates. The absence of these observable symptoms of AD can present as normal functioning, akin to not having the disease at all. The distinct difference between the physical and symptomatic aspects of the disease means that even with the physiological development of the disease, individuals can still live productive, "normal" lives by building cognitive reserve. Having this reserve enables individuals with the brain pathology indicative of AD to cope with the damage to their brain by either using already existing cognitive processing strategies or compensatory strategies (Stern, 2006) and live symptom-free for a longer period of time than individuals who do not have a cognitive reserve built up. It would be nearly impossible for individuals to avoid all risk factors for AD, however, building a cognitive reserve would help to buffer against the negative effects of those risk factors.

Cognitive reserve hypothesis functions within the broader framework of lifespan developmental theory, with the concept of plasticity being the bridge between the two concepts. Cognitive reserve hypothesis asserts that individuals have the ability to influence their own risk for dementia and AD through the experiences they have within the environment in which they are developing. In fact, plasticity can be thought of as the mechanism through which cognitive reserve is built. Developmental plasticity refers to changes in neural connections and synaptic activity as a result of interactions within the environment, such as learning (Fratiglioni & Wang, 2007). Thus, over the course of the lifetime, individuals can build cognitive reserve by utilizing the brain's ability (plasticity) to create changes in neural connections through choices they make in their environment. In this way, plasticity is very much related to individuality, as individuals choose their environments, and these environments influence adaptation to biological and social challenges. Occupational complexity may encourage better adaptability in individuals who have a higher risk for dementia due to more risk factors in other domains (e.g., genes).

Occupational Classification

Occupation, one category of life experiences that has the potential to build substantial cognitive reserve, has been categorized several different ways for the purposes of studying the relationship between occupation and cognitive status in late-life. Certain aspects of occupation, such as complexity of work and level of intellectual, interpersonal, and physical demand (Stern et al., 1995), as well as high occupational attainment (Stern et al., 1994), may build the reserve, effectively staving off the clinical symptoms of AD. Occupations that are high in complexity give the brain stimulation and cognitive reserve growth opportunities. Studies that have looked at the impact of occupational complexity on risk for AD in late-life have focused on the job of longest duration (Andel et al., 2005; Helmer et al., 2001; Stern et al., 1995), using various methods (survey, interview) to decide upon the complexity of the main occupation.

One approach to classification of occupational complexity is with reference to job duties involving complexity with data, people, and *things*. Complexity with data refers to occupations that involve skills in relation to information, knowledge, or concepts (Information Technology Associates, 2012). Complexity with people refers to occupations that require skills that involve interacting with other human beings. Complexity with *things* refers to occupations that require skills that involve working with inanimate objects such as machinery.

Another method used to categorize occupational complexity is by mathematical, language, and reasoning development needed to perform the job duties (Potter et al., 2007). Aspects of both formal and informal education are incorporated into these variables, and are coded from 1 (most simple) to either 6 (most complex, for math and reasoning), or 5 (for language). Mathematical development ranges from basic math skills to advanced mathematical and statistical problems. Language development ranges from simple reading and writing tasks to creative writing and reading and writing of scientific, technical, or legal reports. Reasoning development ranges from following simple instructions to applying abstract concepts of logical or scientific thinking.

Yet another way to conceptualize and categorize occupational complexity is by using the Specific Vocational Preparation (SVP) variable. The SVP variable refers to the amount of time it generally takes an individual to learn how to complete their job at a level of average performance (United States Employment Service, 1991). The term “time” can include time spent learning necessary skills in high school or college, apprenticeship training, on-the-job training, and knowledge gained in lower grade positions that qualify the candidate for higher grade positions.

There are some methods of classifying occupation that studies have used when looking at the relationship between occupation and cognitive status that do not focus on complexity (such as the Institut National des Statistiques et Ettudes Economiques, or INSEE method). These methods group occupations were put together into categories of related jobs, such as housewives or inactives, blue collar workers, craftsmen and shopkeepers, professionals and managerials and so forth. Occupations are not grouped together according to level of complexity necessary to complete tasks successfully, nor do the groups take into consideration amount of education/time required to learn necessary skills to accomplish tasks within the different occupations. Rather, the INSEE method is a somewhat gross method used to classify jobs into categories that contain occupations which require similar skills. The INSEE method is not commonly used in studies focusing on occupation and cognitive status outcomes, and when it is utilized, it is often in conjunction with another method (such as occupational complexity).

Because of the link between occupational complexity, cognitive reserve, and cognitive status in late-life, occupational complexity based on data, people, and *things* is the most frequently used method in research on the topic. Therefore, it has been chosen as one of the constructs to use for the purposes of this study. Because both the SVP and math/language/reasoning variables use principles similar to the data/people/*things* complexity variable (all three variables use different approaches to measure the same outcome: complexity), they will also be included as constructs used to measure the impact of occupational complexity on cognitive status in late-life.

Findings: Occupational Classifications and Cognitive Status in Late-life

Several of the above-mentioned ways to operationalize the construct of "occupational complexity" have been linked to late-life cognitive outcomes. For example, occupations that are high in complexity with people are related to a reduced risk of AD; some studies report hazard ratios of 0.31 (Kroger et al., 2008), indicating a 69% decrease in the risk for AD while others report an odds ratio of 0.86 (Andel et al., 2005), indicating a reduction in the risk for AD of 14%. High complexity with people is also related to non-AD types of dementia, with effect sizes ranging from .83 (Andel et al., 2005) for all types of dementia (AD included) to .36 (Kroger et al., 2008) for all-cause dementia. These results remain significant even after controlling for variables such as age, gender, and education. There is some variability in these findings, however, as duration of occupation may have an impact on results (Kroger et al., 2008), with no significant findings for individuals who hold their primary occupation for less than 24 years (and significant findings for individuals who hold their primary occupation for 24 years or longer). Operationalization of the term "complexity with people" can differ from study to study and also may lead to inconsistency across studies. For example, Andel et al. (1995) included tasks that required mental demands associated with organizing as well as social demands associated with negotiating and supervising in the "complexity with people" category.

Occupations that have high levels of complexity with data are also related to a reduced risk of all-cause dementia (with a hazard ratio of 1.11, due to coding of complexity, HR > 1.0 indicates a decreased risk for dementia; Potter et al., 2007), after controlling for age, gender, and education. In contrast, Kroger et al., 2008, found that in individuals who held their job for 24 years or more, high complexity of work with data was associated with an increased risk of non-AD and non-vascular dementia (hazard ratio = 1.77) and AD (hazard ratio = 2.83). This is a perplexing finding, as the same study also found that no aspect of occupational complexity was associated with AD or any other types of dementia when individuals held their primary occupation for 23 years or less. This difference may be attributed to either a reduction in statistical power (when dividing the sample into two groups) or the shorter exposure time perhaps being insufficient to generate sufficient cognitive reserve.

In contrast, occupational complexity with "*things*" may decrease the risk of AD (hazard ratio = .48) and non-vascular, non-AD dementia (hazard ratio = .45; Kroger et al., 2008). Again, this finding only holds true for individuals who have held their job for 24 years or longer; those who were at their primary occupation for 23 years or less did not show the same decreased risk.

Explanations for the apparent protective effect of occupations held for 24 years or longer and high in complexity with data, people, or *things* are varied. It is believed that spending an extended amount of time in a complex environment while at work has an impact on intellectual flexibility throughout the life course (Andel et al., 2005). Specifically, cognitive reserve can be established and maintained through stimulating work environments by providing mental "exercise" which build more complex cerebral networks in old age (Churchill et al., 2002). This increase in cognitive reserve may enable these individuals to withstand dementia neuropathology for a longer amount of time as the disease progresses (Stern et al., 1995). Thus, occupations high in complexity do not necessarily prevent disease onset, but delay the clinical expression of the disease such that the individual lives a relatively unaffected life.

Some studies do not use the categories of complexity with data, people, and *things* in isolation, but use those aspects in combination with other factors in order to decide the impact of general intellectual demands on cognitive status. One study found a positive 5.3-point difference (out of a possible 50 points) in participants' modified telephone interview for cognitive status (*TICS*-m) scores in individuals who had higher levels of general intelligence (Potter et al., 2008). Factors included in the "general intelligence" category for this study include job characteristics pertaining to complexity with people and data, reasoning, language, and mathematics aptitude, and more time spent in vocational preparation. Bickel and Kurz (2009) looked at type of training required for participants' occupations, as well as whether or not participants had ever held a position of leadership (average duration of a leadership position in the study was 12 years). Participants in a non-leadership position and those with no occupational training were significantly more likely to have dementia (OR = 3.0 and OR = 9.1, respectively). These results seem to suggest that the challenge of securing and maintaining a leadership position, along with the challenge of occupational training, provide mentally stimulating activities that build cognitive reserve and stave off observable symptoms of dementia.

It is important to note that there is potential confounding between occupational complexity and socioeconomic status (SES). Individuals with higher education frequently have higher levels of wealth, and these higher socioeconomic status individuals report better physical and mental health than their lower status counterparts (Grzywacz, Almeida, Neupert, & Ettner, 2004). Education and family income appear to be strongly related to the number of chronic diseases an individual experiences (Sturm & Gresenz, 2002), pointing to the connection between education, occupation, and SES. While SES appears to be negatively related to AD risk in late-life, this effect disappears when education is introduced into a model, suggesting that the protective effect is actually due to education, rather than SES (Karp et al., 2004). While this does not point to a conclusive relationship between SES and AD, it does suggest that the interplay of SES, education, and AD is a complex one, and that it is important to include indicators of both education and/or SES in analyses, when possible.

It is also important to note that issues of selection may play a part in findings of studies in this topic area. Because participants are self-selecting their occupations, researchers cannot randomly assign participants to different occupations, therefore, possibly introducing bias into the study design. Individuals from the same city, neighborhood, or family may be more likely to choose a particular job based on sociocultural influences. Thus, effects seen in individuals who have self-selected their occupations may not be the result of the occupation itself, but may be a reflection of environmental, genetic, or other factors.

It is not unusual for individuals who have jobs that require higher degrees of complexity to also have higher levels of education (Stern et al., 1995), and higher levels of education often lead to higher paying jobs. Thus, the question becomes whether the relationship between occupational complexity and cognitive status is actually an effect of complexity generating cognitive stimulation, or due to the likely higher SES that more complex occupations typically generate (or both). Most studies attempt to control for SES by using education as a covariate (Bickel & Kurz, 2009; Kroger et al., 2008; Potter et al., 2006, 2007), with a few being able to control for SES in a unique way. For example, the sample used in Bickel and Kurz's (2009) study were members of the Congregation of the School of Sisters of Notre Dame, and all experienced essentially the same living conditions, housing situation, environmental influences, and made the same vow of poverty. Because of this, even sisters who had more complex/demanding occupations still had the same SES as sisters who had less demanding occupations. It is not possible for the majority of studies to have a study design such as this, nor is it always the case that researchers have access to income information (one of the most reliable indicators of SES). Often times, researchers acknowledge the difficulty in separating the influence of SES from occupational complexity, and it remains a limitation of previous studies on the topic.

Moderating Factors

The APOE genotype has been identified as affecting risk for Alzheimer's disease (Strittmatter & Roses, 1996); specifically, the Ɛ4 allele has been shown to increase the risk for, as well as lower the age of onset of, AD (Roses & Saunders, 1997). Individuals who carry the APOE Ɛ4 allele and have been exposed to certain psychosocial stressors, such as low childhood SES (Moceri et al., 2001) or a large family size (Borenstein, Copenhaver, & Mortimer, 2006) are at an increased risk for dementia in late-life. This association suggests that APOE may also moderate the relationship between occupational complexity and dementia risk, so it was included in analyses as a moderator.

Stay at Home Women

Most study samples contain women whose primary occupation was either "homemaker," or who did not report an occupation at all. Because the occupational complexity variables are defined only for gainful employment, homemakers are excluded from the sample (Andel et al., 2005, 2006; Kroger et al., 2008), along with other individuals who do not have an occupational history to report.

Limitations to Existing Studies

Among published studies looking at the association between occupational complexity and late-life cognitive health, some studies only used men (Potter et al., 2006, 2007), and many could not control for socioeconomic factors such as income (Andel et al., 2005; Kroger et al., 2008; Potter et al., 2006, 2007). Further, some studies looked at only prevalent dementia cases (Andel et al., 2005), rather than incident cases, which opens the possibility of confounding due to a survivor bias. Moderation by gender has not been investigated in previous studies on the topic, and given that some studies have found that women have a higher risk for AD (Launer et al., 1999) while at the same time having less access to high-complexity occupations than their male counterparts, this was examined in the proposed study, in order to determine whether occupational complexity and dementia associations are universal or vary by gender. Moderation by APOE status was also investigated, as it was important to determine whether effects varied by presence of **ε**4 allele. Finally, moderation by duration of longest held job was examined as another potential moderator, broken down into two groups: less than 24 years in the participant's primary occupation, or 24 years or greater. This 24 year cutoff was chosen based on the precedent set in prior studies (Kroger et al., 2008), as well as 24 years being very close to the median number of years participants held their primary occupations in the current dataset.

Summary of Extant Literature

Dementia and Alzheimer's disease negatively impact the lives of millions of Americans every year. The illness affects not only the individuals who are diagnosed with it, but also family members, friends, and other loved ones. Medical costs associated with dementia and AD are exorbitant, and the anticipated increase in the number of diagnoses over the coming years will have a severe negative impact on society as a whole. While preventing the physiological processes that cause the disease would be an ideal solution, it is unrealistic to think that this would have been an option any time soon, particularly because of medical advances that enable individuals to live much longer lives than in the past. The next best option may have been to focus on factors that delay the expression of the disease. Thus, even when individuals develop the physiological markers of dementia or AD, their lives are not negatively impacted.

Hallmark indicators of dementia and AD include irreversible physical and cognitive degeneration; the cognitive degeneration is caused by changes occurring within the brain. There is evidence to suggest that these physical changes within the brain do not always result in universal symptoms. Some individuals have fewer or no noticeable symptoms of dementia even when they have similar brain pathology indicative of the disease. This is thought to be possible via cognitive reserve. Cognitive reserve enables individuals to use alternative processes to cope with brain damage, essentially eliminating observable symptoms of the disease. In other words, even in the presence of damaged brain matter inherent in dementia and AD cases, individuals with a cognitive reserve can still function at a level that suggests that there is no brain damage present. Cognitive reserve is thought to be built through various activities including education, certain work activities, stimulating environments outside of work, and other mentally challenging situations. Specifically pertaining to work, it has been found that certain work environments, such as those high in complexity, may be related to a lowered risk of dementia and Alzheimer's disease. This reduction in risk is thought to be due to an increased cognitive reserve, made possible by experiencing a challenging work environment through completion of a job that is high in complexity.

Occupations can be broken down into many different classifications in order to investigate their connection to dementia risk. The most common of these classifications (for research purposes related to occupation and dementia/AD) is complexity with data, people, and *things*. It has been found that occupations high in complexity with people and data may be related to a reduced risk for dementia and/or AD; the results for complexity with *things* have been mixed. There is also research on the link between stimulating activities outside of work and a reduced risk of dementia. It has been found that participating in mentally stimulating activities outside of work may also lead to a reduced risk of dementia/AD by stabilizing or even enhancing cognitive function in late-life. Limitations of existing studies on occupation and dementia/AD include gender-biased studies, inability to control for SES, using prevalent dementia cases, and having a small sample size.

Proposed Study Objectives

The ultimate goal of this line of research would be to identify important targets for primary intervention in order to prevent the development of dementia, particularly in persons at greater risk due to other genetic or environmental factors. The primary purpose of the present study is to clarify the extent to which formal education and occupational complexity are predictive of future dementia risk. A secondary purpose is to learn whether such effects are universal or whether they vary by duration of occupation, gender, or genotype on a well-known AD risk gene. Once this is known, future efforts in career planning, job training, and promotion of more cognitively stimulating leisure activities can be emphasized to a much greater degree both by health care practitioners and the popular media. Such efforts work toward the goals of enhancing cognitive reserve capacity of individuals and reducing prevalence and incidence of dementia in our society over time. The proposed study will utilize extant data from a longitudinal, population-based epidemiological study of dementia, the Cache County Study on Memory in Aging with methodological features that address most of the limitations of prior studies.

Research Questions

To address proposed objectives of this study, the following research questions were investigated, using extant data regarding the job of longest duration during all years in the labor force on participants in the Cache County Study on Memory in Aging.

1. Defining occupational complexity in terms of complexity with data, people, and *things*, do higher levels of complexity (each domain considered separately) predict:

   a. Higher risk for all-cause dementia

   b. Higher risk for Alzheimer's disease

2. Defining occupational complexity in terms of mathematics, language, and reasoning development needed to perform the job, do higher levels of complexity (each domain considered separately) predict:

   a. Higher risk for all-cause dementia

   b. Higher risk for Alzheimer's disease

3. Defining occupational complexity in terms of specific vocational preparation (SVP) needed to perform the job, do higher levels of complexity (each domain considered separately) predict:

   a. Higher risk for all-cause dementia

b. Higher risk for Alzheimer's disease

4. Defining occupational complexity in terms of professional categories of professional/managerial, clerical/sales, service, agriculture, and processing/machine /benchwork/structural, do lower levels of complexity predict:

a. Higher risk for all-cause dementia

b. Higher risk for Alzheimer's disease

5. Are observed effects of higher occupational complexity mediated through higher socioeconomic status, or remain robust after adjustment for the latter?

6. What is the relative influence of occupational complexity (*examining only the specific variables found to be significant predictors among the seven operationalizations of complexity: data/people/things complexity, mathematics/language /reasoning development needed for the job, and specific vocational preparation required to complete the job*) and formal education in predicting:

a. Higher risk for all-cause dementia

b. Higher risk for Alzheimer's disease

7. Does duration of longest held job moderate the findings in the above associations?

8. Does gender moderate the findings in the above associations?

9. Does APOE genotype moderate the findings in the above associations?

CHAPTER III

METHODS

Introduction

The proposed study investigated the relationship between occupational complexity and dementia and AD in late-life. It used extant data from a large-scale, longitudinal, population-based epidemiological study of dementia. The present chapter describes the research design, the sample including generalizability considerations, measurement, procedures including human subjects' protections, and data analysis plans.

Research Design

Data used in this study came from the Cache County Memory Study (CCMS), which is an observational, prospective epidemiological study of dementia. CCMS followed participants over a 13-year period, with four waves of dementia ascertainment between 1995 and 2008 (initial baseline interview plus follow-up interviews at 3, 7, and 10 years). The primary outcomes come from dementia diagnoses rendered across all four study waves, with primary exposure variables derived from information about occupational status that was collected at baseline.

Subjects

The Cache County Study on Memory in Aging had a total eligible population of 5,657. Approximately 90%, or 5,092, chose to participate. Of these 5,092 individuals, 359 had prevalent dementia (and were, therefore, excluded from this study), and 188 individuals with unknown dementia status were also excluded due to incomplete dementia screening. Individuals with no work history (*n* = 407) were also excluded from the sample, leaving 4,138 participants who were included in the final sample. Age at baseline ranged from 65 to 105 years. The sample is 99% Caucasian and 90% of the participants are members of The Church of Jesus Christ of Latter-day Saints.

Procedures

Each participant received an in home visit for an initial screening, and if appropriate, also received an in-home visit for a more detailed clinical evaluation for dementia. Participants were eligible for the more detailed dementia evaluation if they screened positively on a short memory screening test. At the baseline screening visit, participants provided self-reported life histories of occupation. A link between the CCMS database and UPDB information allows data to be utilized from subjects' children's birth certificates and subject's death certificate to compute adulthood SES (details in the mediator section). Informed consent was obtained for the original study (CCMS; NIH AG-011380), at the time of each data collection point, for the study that linked the CCMS to the UPDB (Family-Based Cohort Study, NIH AG-18712), and the study that utilized data from the UPDB to derive SES (Lifespan Stressors and Alzheimer's disease; NIH AG-031272).

Measurement

Dementia and Alzheimer's Disease Outcomes

A multistage dementia ascertainment protocol was implemented in CCMS and was used in four triennial waves beginning in 1995 (Breitner et al., 1999). Participants went through a rigorous screening process which began with a researcher giving the Modified Mini Mental State exam. Informants of participants whose scores were below 60/100 were given the Informant Questionnaire on Cognitive Decline in the Elderly. An in-depth clinical assessment awaited those who screened positive for possible dementia, along with a small subsample of designated controls. The clinical assessments were administered by specially trained psychometric technicians and nurses and were very comprehensive in nature, including a physical exam, medical history, and a neurological exam and tests. All available data were reviewed by expert panel comprised of geropsychiatrists, neuropsychologists, a neuroscientist, and a neurologist. Diagnoses of dementia (overall) were assigned by consensus according to criteria in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised [DSM-III-R] (APA, 1987).

Onset age was defined as the age when the subject unambiguously met criteria for dementia per DSM-III-R. Diagnoses of Alzheimer's disease (AD) were made in accordance with criteria set forth by the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984). For the current study, all diagnoses of AD were used, including "pure" AD with no other co-morbid form of AD, as well as when AD is co-morbid with vascular dementia or any other form of dementia (i.e., whenever the diagnosticians evaluated the individual's cognitive impairment to have had an AD contribution).

Occupational Complexity

A common approach to characterizing occupational complexity is by codification of occupations (given information as to job title, job description, industry, etc.) as found in the *Dictionary of Occupational Titles* (DOT; U.S. Department of Labor, 1997). Within the CCMS study, each job held for a period of 5 or more years was coded by an occupational health nurse specialist into the DOT code most closely matching the job title, description, and industry. The job of longest duration was selected from among all jobs held when deriving all occupational complexity variables.

For all occupational variables except the nominal category, variables were investigated using the extreme groups approach. Each variable was broken down into quartiles of high complexity, moderate complexity, and low complexity, with the two middle quartiles being combined into the moderate complexity category. Also, due to the original coding methodology (wherein occupations are assigned a numerical value based on the complexity of the job), it is not clear what a one-point increase in complexity truly means. The ambiguity of the meaning of a one-point increase on these various scales prompted a decision to categorize continuous occupational complexity variables into quartiles. The nominal job category was grouped according to qualitatively different broad categories of occupations as defined in the DOT (U.S. Department of Labor, 1997).

Data, People, Things Complexity

Complexity categories are created based on the notion that every job requires some degree of interaction with “data,” “people,” and/or “*things*” (Information Technology Associates, 2012). These interactions are classified as worker functions, which gives consistent terminology to summarize what a worker does while on the job. The DOT provides a nine-digit code for every occupation listed in the dictionary; the fourth, fifth, and sixth digits of this code refer to an occupation's relationship to data, people, and *things*, respectively. Each category is reverse-coded, such that 0 = the highest complexity occupation; the higher the numbers go, the less complex the occupation is. The category of occupational complexity with data refers to "information, knowledge, and conceptions, related to data, people, or *things*, obtained by observation, investigation, interpretation, visualization, and mental creation. Data are intangible and include numbers, words, symbols, ideas, concepts, and oral verbalization" (Information Technology Associates, 2012). Complexity with people refers to "human beings; also animals dealt with on an individual basis as if they were human" (Information Technology Associates, 2012). Complexity with *things* refers to "inanimate objects as distinguished from human beings, substances, or materials; it includes working with machines, tools, equipment, work aids, and products. A thing is tangible and has shape, form, and other physical characteristics" (Information Technology Associates, 2012). All occupations listed in the DOT receive a code for all three complexity categories, which are then used to determine the magnitude of complexity for each category. Due to the precedent set in previous literature on this topic area, data, people, and *things* will be investigated as separate variables, each run by itself in models looking at the impact of occupational complexity on dementia outcomes.

Mathematical, Language, and Reasoning Development

An alternative way which was used to characterize each subject's job of longest duration is by the mathematical, language and reasoning development needed to perform the job duties, following the example set by Potter and colleagues (2007). In this classification scheme, both formal and informal educational requirements are reflected. These requirements are ones that are necessary for individuals to perform at a satisfactory level in their given occupation. The different categories are coded so that lower scores (scores start at a value of one) indicate basic skills and higher scores (e.g., five for language, and a maximum of six for reasoning and mathematical) indicate more complex skills necessary for an individual to complete their job in a satisfactory manner.

Specific Vocational Preparation

The final way occupational complexity was defined is the "specific vocational preparation" (SVP) needed for the given occupation (Oswald, Campbell, McCoy, Rivkin, & Lewis, 1999). The SVP variable was created to measure the amount of specific occupational training and experience required to perform a job at an average level of performance. In this case, "amount of specific occupational training and experience" refers specifically to an amount of lapsed time. This training can be obtained in a variety of settings, including but not limited to school, work, training, and previous employment (Foreign Labor Certification Data Center, 2012). Examples of vocational training include vocational education, apprenticeship training, on the job training, and necessary experience from other jobs.

Nominal Job Category

The first variable derived from the DOT code is a nominal variable denoting a broad category of occupation. Job of longest duration was coded into one of nine categories (U.S. Department of Labor, 1997). These occupations include: (1) professional, technical, and managerial; (2) clerical and sales; (3) service; (4) agricultural, fishery, forestry, and related; (5) processing; (6) machine trades; (7) benchwork; (8) structural occupations; and (9) miscellaneous. Examples of occupations in category 1 include jobs in architecture, engineering, surveying, mathematics, physical sciences, education, medicine and health, law and religion, and writing, art, and entertainment. Category 2 examples include typing and filing, computing, stock clerks, clerical occupations, and sales and services. Examples of category 3 jobs include: food service, cosmetology, apparel and furnishings services, and protective service. Examples of category 4 jobs include farming, fishery, and hunting and trapping. Category 5 job examples include making goods and products (such as metal, food, paper, petroleum, gas, and chemicals). Examples of category 6 jobs include machining of any type. Examples of category 7 jobs include painting, fabrication of materials such as plastics, wood products, metal products, and related products. Category 8 job examples include welding, cutting, assembling, installing, cementing, excavating, and paving. Category 9 job examples include radio and television, motor freight, transportation, extraction of minerals, and distribution of utilities.

Education

Formal educational attainment was collected via self-report at baseline interview (while subjects were still dementia-free) and was coded in years.

Mediators, Moderators, and Covariates

Mediator: Adulth ood socioeconomic status. Because socioeconomic status (SES) and occupation are closely related, the potential for occupational complexity to affect dementia risk through the mechanism of enhanced SES was addressed by an independently-acquired measure of adulthood SES via objective records. The Utah Population Database (UPDB) is a very unique resource, as it contains a vast amount of information on Utah residents, including demographic, genetic, and epidemiological information (Utah Population Database, 2011). Over 14 million records are contained within the database, representing almost 7 million individuals. The CCMS database and UPDB records are already connected, with 5,091 out of 5,092 CCMS participants appearing in the UPDB. Data to be utilized from the UPDB included offspring birth records and subject death certificates.

Each subject’s SES was derived primarily from their offspring birth records whereon father's occupation is listed. In this sample, born from 1895-1930, women derived their SES primarily from the husband’s occupation, therefore, the occupation listed on each one of a woman’s children’s birth certificates under “father’s occupation” was used to capture SES for each woman in this study (likewise for men in this study, “father’s occupation” was used). SES was derived using a methodology developed by Nam and Powers, to rate socioeconomic status (NP-SES; Nam & Powers, 1983). This method used census-wide information about the association between education and income, as they relate to individual occupations. Higher NP-SES has been found to be negatively associated with mortality risks for both men and women (Smith, Mineau, Garibotti, & Kerber, 2009). NP-SES was aggregated across all children and, regardless of the number of children on whom SES was based (ranging from 1 to 11 children) or the amount of variability in occupations across the adult lifespan, the maximum SES score across all offspring birth records was used to define SES. This method was used for 3,391 participants with eligible offspring birth record data. SES was derived on an additional 711 participants via subject's death certificate, which included "usual occupation" and was also coded into a NP-SES score. Occupations that fall into the highest NP-SES categories included dentists, physicians, and surgeons, while the lowest categories included occupations such as attendants in cafeterias and coffee shops, and dishwashers (Nam & Powers, 1983).

Moderators. Duration of longest-held job was dichotomized, following the example of Kroger et al. (2008) into 0-23 years versus 24 or more years. Gender was coded as either male (1) or female (2), and APOE genotype was obtained from buccal DNA using the polymerase chain reaction (PCR) amplification method (Saunders et al., 1993) and was coded as (0) no **ε**4 alleles or (1) at least one **ε**4 allele. Finally, age (coded in years as of baseline interview) was included as a covariate.

Data Analysis

Initial, exploratory analyses was conducted to assess distributional properties of all variables, amount of missing data, and simple bivariate relationships between occupational complexity and SES measures and whether ever diagnosed with dementia (all-cause) or AD specifically. Attrition bias was analyzed by comparing occupational complexity and basic demographic variables such as age and gender between those subjects who were right-censored prior to the last study wave in the CCMS (i.e., who never received a dementia diagnosis but dropped out of the study before wave 4) and those who remained in the study through wave 4 or received an earlier diagnosis of dementia (i.e., did not drop out). Basic statistical analyses were also conducted to describe the various samples used in various analyses as to distribution by age, gender, and APOE status.

Cox regression analysis was conducted to determine the relationship between occupational complexity (each measure analyzed separately) and the development of incident dementia, and incident AD. Initial models included only the complexity variable, then covariates of baseline age and gender were added. Models testing for relative effects of occupational complexity and education were conducted by computing separate models for education only, complexity only, then both included in the same model.

Models testing moderation by gender also included interaction term(s) between complexity and gender. Models testing moderation by APOE also included APOE status (0 vs. 1 or more **ε**4 alleles) and interaction term(s) between complexity and APOE status. Models testing moderation by job duration (0 to 23 years vs. 24 or more years) included interaction term(s) between complexity and job duration. Models testing mediation by adulthood socioeconomic status (SES) were tested by examining the impact on the effect size for each complexity measure after addition of SES to the model. In these models assessing potential mediation through SES, because subjects' SES comes from different data sources (see details above in Measures section), an indicator variable to denote data source was included in the model and retained if significant, or removed if non-significant (to control for effects of data source).

Due to the different statistical analyses being run, sample size varied somewhat, depending on the specific analysis being run. Research questions 1-4 utilized the full sample of 4,138 CCMS participants, or subset thereof, who gave self-reported occupational history at baseline interview. Research question 5 contained 3,672 participants who had SES data in the UPDB and had non-missing values for other essential datapoints. This number is smaller than the full sample of 4,138 because only 4,102 individuals in the original sample of 5,092 had SES data, and some of these individuals did not appear in the final sample of 4,138, due to a lack of one or more variables. Research questions 6-9 revert back to the full sample of 4,138 participants.

In order to avoid confusion, the occupational complexity measures are identified as follows throughout the rest of this dissertation: *data*, *people*, things, mathematics, language, and reasoning. The Specific Vocational Preparation variable was referred to as "SVP." The nominal occupational category was referred to as "nominal occupational category."

CHAPTER IV

RESULTS

The primary objective of this study was to clarify the extent to which formal education and occupational complexity are predictive of future dementia risk. A secondary objective of this study was to investigate whether these effects are universal, or whether they differ based on duration of occupation, gender, or genes (presence of the APOE ε4 genotype). This was achieved by using extant data from the Cache County Study on Memory in Aging, a large population-based sample of older adults whose dementia status was determined through in-depth clinical evaluation and occupational histories were collected via self-report. This section will begin with descriptive statistics of the study sample, including demographic information and sample characteristics. Exploratory analyses and regression models will then be presented separately for each research question.

Sample Characteristics

Out of the 4,138 individuals included in the final sample, 528 went on to develop incident dementia, 357 of which were Alzheimer's type dementia. The remaining 3,610 were never diagnosed with dementia during the course of the study, and were considered right censored as of their last visit.

Demographics

The final sample had a mean age of 74.84 (*SD* =6.82, range 65-100) years. It contained 52.4% female participants, and at least one APOE epsilon 4 allele was present in 29.8% of participants (see Table 1). Mean educational level was 13.32 (*SD* = 2.95) years, and men reported significantly more years of education (*M* = 13.84, *SD* = 3.41) than women (*M* = 12.85, *SD* = 2.35; $p < .001$). The sample was 99% Caucasian.

Socioeconomic Status

The theoretical range for participant scores on the NP-SES measure is from 0-100, and scores in the current sample ranged from 2-99. Participants had a normally distributed, diverse range of SES scores, with a skewness statistic of -0.01 and a mean score of 59.79 (*SD* = 22.72).

Table 1

Demographics of Study Sample and Bivariate Tests of Association with Incident Dementia and Incident Alzheimer's Disease

		p-value[a]	
Demographical characteristic	Overall sample	Dementia	AD
Baseline age, years (*M, SD*)	74.84, 6.82	< .001	< .001
Gender: female (*N*, %)	2168, 52.4	< .001	< .001
APOE ε4 carrier (*N*, %)	1233, 29.8	< .001	< .001
Education, years (*M, SD*)	13.32, 2.95	< .001	< .001

[a]*p*-values are from independent groups *t* tests for comparison of age and education; *p*-values are from chi-squared tests for comparisons of gender and *APOE* status.

Occupational Characteristics

Within the final sample, 4,138 participants held at least one job over their lifetime. Job duration was normally distributed, with a mean score of 27.61 years (*SD* = 16.95); the skewness statistic for this variable was 0.45, indicating that it was not significantly positively or negatively skewed. The distribution of job duration varied within each occupation ($p < .001$ for all occupational variables). Data complexity had mean job durations of 36.09 (*SD* = 17.69), 23.74 (*SD* = 14.30), and 21.32 (*SD* = 15.16) years for high, medium, and low complexity jobs, respectively. People complexity had mean job durations of 26.03 (*SD* = 13.40), 30.29 (*SD* = 18.30), and 23.19 (*SD* = 15.32) years for high, medium, and low complexity jobs, respectively. Things complexity had mean job durations of 37.66 (*SD* = 18.44), 22.34 (*SD* = 14.70), and 23.78 (*SD* = 13.65) years for high, medium, and low complexity jobs, respectively. Math complexity had mean job durations of 32.23 (*SD* = 11.55), 30.18 (*SD* = 17.98), and 21.13 (*SD* = 14.57) years for high, medium, and low complexity jobs, respectively. Language complexity had mean job durations of 27.13 (*SD* = 13.20), 30.76 (*SD* = 18.29), and 20.27 (*SD* = 14.51) years for high, medium, and low complexity jobs, respectively. Reasoning complexity had mean job durations of 27.36 (*SD* = 13.48), 32.67 (*SD* = 18.77), and 21.24 (*SD* = 14.75) years for high, medium, and low complexity jobs, respectively. The SVP complexity variable had mean job durations of 31.59 (*SD* = 12.80), 29.60 (*SD* = 17.95), and 19.98 (*SD* = 14.16) years for high, medium, and low complexity jobs, respectively. The nominal occupational variable had mean job durations of 27.32 (*SD* = 13.78) years for the professional/managerial category, 19.40 (*SD* = 12.59) years for the sales/clerical category, 18.77 (*SD* = 13.50) years for the service category, 46.21 (*SD* = 18.31) years for the agriculture category, and 28.45 (*SD* = 15.29) years for the processing/machine /benchwork/structural category.

Exploratory analyses were conducted to determine whether age, gender, and APOE were potential confounding variables, as summarized below. Tests were computed including: chi-square tests of independence, Pearson correlations, and *t* tests to determine whether relationships existed between any of the occupational attainment variables and these potential confounders.

Baseline Age

One-way analyses of variance were conducted to determine whether mean subject age differed significantly between the low, moderate, and high levels of complexity. Consistently, younger age was associated with greater complexity. Results revealed that math complexity had a lower mean age of participants in the least complex category (*M* = 75.40, *SD* = 7.04) compared to the most complex category (*M* =73.72, *SD* = 6.00; $p < .001$). Language complexity showed a mean age of 75.66 (*SD* = 7.00) years for participants in the least complex category and a mean age of 74.26 (*SD* = 6.66) years for those in the most complex category ($p < .001$). Participants in the least complex reasoning category had a mean age of 75.49 (*SD* = 7.03) years, while participants in the most complex reasoning category had a mean age of 74.14 (*SD* = 6.61; $p < .001$) years. There was a 1.5-year mean age difference between participants in the least complex category (*M* =75.34; *SD* = 6.95) and participants in the most complex category (*M* = 73.76; *SD* = 6.25) for the SVP variable ($p < .001$). Finally, participants in the nominal occupational group also differed significantly in regards to baseline age: the service group had a mean age of 76.30 (*SD* = 7.01) years, the agriculture group had a mean age of 75.98 (*SD* = 6.91) years, the miscellaneous group's mean age was 75.03 (*SD* = 6.82) years, the clerical/sales group had a mean age of 74.25 (*SD* = 6.58) years, and the professional, technical, managerial group had a mean age of 74.17 (*SD* = 6.57) years. A correlation was run to determine the association between baseline age and duration in longest held job, and this test revealed that there was not a significant relationship between duration in longest held job and baseline age ($p = 0.30$).

Gender

Consistently, men reported significantly more complex jobs than women (Table 2). The *t* tests revealed that there were significant differences between the genders in occupational characteristics; average duration of longest job held was normally distributed and had a mean value of 36.96 (*SD* = 15.50) years for men and 16.10 (*SD* = 14.09) years for women ($p = .015$). According to χ^2 tests of independence, gender was significantly associated with job duration, with 81.6% of men holding their primary occupation for 24 years or longer, compared to 32.2% of women ($p < .001$). A significant association was also found between gender and occupational complexity, with men reporting jobs of consistently higher complexity, relative to women ($p < .001$ for all tests). Specifically, the proportion of men in occupations high in complexity of work with data was 52.3% versus 19.6% for women; proportion of men in occupations high in complexity of work with people was 20.8% versus 19.6% for women; proportion of men in occupations high in complexity of work with *things* was 46.6% versus 16.1% for

Table 2

Occupational Characteristics by Gender

	Male		Female		Sample	
Occupational variable	*N*	%	*N*	%	*N*	%
Longest job duration in years [a]						
(*M, SD*)	36.96	15.50*	16.10	14.09*	2761	16.95
24 + years [b] (N, %)	1608	81.6%**	699	32.2%**	2307	55.8%
Data complexity [c] (high)	1030	52.3%**	425	19.6%**	1455	35.2%
People complexity [c] (high)	409	20.8%**	426	19.6%**	835	20.2%
Things complexity [c] (high)	918	46.6%**	350	16.1%**	1268	30.6%
Mathematics complexity [c] (high)	370	18.8%**	87	4.0%**	457	11.0%
Language complexity [c] (high)	498	25.3%**	465	21.4%**	963	23.3%
Reasoning complexity [c] (high)	593	30.1%**	514	23.7%**	1107	26.8%
Vocational preparation [d] (high)	514	26.1%**	128	5.9%**	642	15.5%
Nominal categorical occupation						
Professional, technical, managerial	759	38.5%**	678	31.3%**		
Clerical, sales	161	8.2%**	768	35.4%**		
Service	84	4.3%**	383	17.7%**		
Agriculture	489	24.8%**	134	6.2%**		
Misc [e]	477	24.2%**	205	9.5%**		

[a] duration of longest held job; [b] represents individuals whose longest job held was 24 years or longer (rather than 23 years or less); [c] represents individuals who fall into the "high complexity" category (rather than medium or low complexity); [d] represents individuals who fall into occupations requiring the most preparation; [e] includes processing, machine work, bench work, structural work, and a miscellaneous category
*p <.05; **p <.001

women.

Occupational skill level also differed significantly by gender, with a higher proportion of men than women reporting occupations with the highest general education development (GED) math (18.8% versus 4.0% for women), language (25.3% versus 21.4% for women), and reasoning (30.1% versus 23.7% for women; $p < .001$ for all three variables). Vocational preparation showed a similar trend for participants in the "most complex category," with 26.1% of men and 5.9% of women in that category ($p < .001$).

Level of occupational attainment was also significantly associated with gender ($p < .001$); 38.5% of men held professional/managerial jobs compared to 31.3% of women; 8.2% of men held clerical/sales jobs compared to 35.4% of women; 4.3% of men held service-related jobs compared to 17.7% of women; 24.8% of men held agricultural jobs compared to 6.2% of women; and 24.2% of men held miscellaneous jobs (including processing, machine, benchwork, and structural jobs) compared to 9.5% of women.

APOE Ɛ4 Allele

Analyses revealed that the APOE Ɛ4 allele was not significantly related to any occupational attainment variable. Significance levels for χ^2 tests of independence between APOE status (presence vs. absence of at least one Ɛ4 allele) and complexity levels of low, moderate, and high were as follows: complexity with data ($p = 0.45$), complexity with people ($p = 0.50$), complexity *things* ($p = 0.35$), math complexity ($p = 0.22$), language complexity ($p = 0.20$), reasoning complexity ($p = 0.72$), vocational preparation ($p = 0.99$), and the nominal occupational category ($p = 0.67$).

According to these exploratory analyses, gender and age are significantly associated with occupational complexity. Therefore, Cox regression models are reported in simple bivariate form, then after adjustment for these covariates, in order to determine robustness of observed effects, net of the effect of these potential confounders. For each research question a parallel set of tables of results is provided for all-cause dementia and Alzheimer's disease as outcomes. Unless otherwise noted, the following comments pertain to models *after* covariate adjustment, although models *before* covariate adjustment are also available in the corresponding tables of results.

Research Questions

Research Question 1

Defining occupational complexity in terms of complexity with *data*, *people*, and *things*, do higher levels of complexity (each domain considered separately) predict (a) Higher risk for all-cause dementia, and (b) Higher risk for Alzheimer's disease.

Cox regression models revealed that complexity of work with data was not a significant predictor of all-cause dementia for either high compared to low complexity or high compared to moderate complexity (Table 3). The same was true for complexity of work with data and AD (Table 4). Complexity of work with people was also not significant for both low and moderate comparisons for all-cause dementia as well as AD. Complexity of work with *things*, however, was a significant predictor of both all-cause dementia and AD. Jobs of low and moderate complexity of work with *things* showed a 25% and 29% reduced risk for all-cause dementia and a 23% and 36% decreased risk for AD, compared to jobs of high complexity of work with *things* (i.e., jobs focused heavily on working with machinery and other inanimate objects).

Post-hoc analyses were run on models containing various combinations of *data*, *people*, and *things* complexity (*data* and *things*, *data* and *people*, *people* and *things*, and *data*, *people*, and *things*) to determine the unique effect of each of the different dimensions of complexity (i.e., the "net effect" of each domain, controlling for first one other, then both of the other two domains). Tables 5 and 6 show that, as with models

Table 3

Cox Regression Main Effects of Occupational Complexity Variables on Incident All-Cause Dementia Risk Outcomes for Occupational Variables Before and After Addition of Covariates[f]

	Before covariates		After covariates	
Occupational variable	HR	CI [a]	HR	CI
Data complexity [b]				
Low	0.94	0.73-1.21	0.85	0.65-1.11
Moderate	0.99	0.82-1.20	0.96	0.65-1.11
People complexity [b]				
Low	1.09	0.85-1.40	1.05	0.82-1.34
Moderate	0.92	0.74-1.14	0.96	0.77-1.19
Things complexity [b]				
Low	0.76	0.62-0.92	0.75	0.61-0.93
Moderate	0.67	0.54-0.84	0.71	0.55-0.90
Mathematics complexity [b]				
Low	1.19	0.89-1.59	0.95	0.70-1.30
Moderate	1.06	0.81-1.39	0.89	0.67-1.17
Language complexity [b]				
Low	1.13	0.87-1.45	0.97	0.75-1.26
Moderate	1.06	0.86-1.30	0.99	0.81-1.22
Reasoning complexity [b]				
Low	1.21	0.97-1.52	1.08	0.86-1.36
Moderate	1.15	0.93-1.41	1.07	0.86-1.32
Vocational complexity [c]				
Low	1.08	0.80-1.46	0.94	0.68-1.29
Moderate	1.35	1.06-1.73	1.14	0.88-1.48
Nominal categorical occupation [d]				
Clerical, sales	0.89	0.70-1.14	0.88	0.68-1.13
Service	1.69	1.29-2.21	1.30	0.98-1.72
Agriculture	1.50	1.17-1.92	1.34	1.04-1.73
Misc. [e]	1.25	0.93-1.69	0.88	0.67-1.17

[a] 95% confidence interval; [b] reference category: most complex; [c] reference category: highest preparation required; [d] reference category: professional, technical, managerial occupations; [e] includes processing, machine work, benchwork, structural work, and a miscellaneous category
[f] Covariates included age, gender, and presence of APOE ε4 allele; each variable in the above model (with the exception of the nominal categorical occupation variable) was analyzed in a separate Cox regression model, with individual single-degree-of-freedom contrasts, as indicated beneath each occupational complexity variable

Table 4

Cox Regression Main Effects of Occupational Complexity Variables on Incident Alzheimer's Disease Risk Before and After Addition of Covariates [f]

	Before covariates		After covariates	
Occupational variable	HR	CI [a]	HR	CI
Data complexity [b]				
Low	1.05	0.77-1.43	0.90	0.65-1.24
Moderate	1.06	0.84-1.34	0.99	0.77-1.28
People complexity [b]				
Low	1.03	0.77-1.38	0.97	0.72-1.30
Moderate	0.79	0.61-1.02	0.84	0.65-1.09
Things complexity [b]				
Low	0.81	0.64-1.03	0.77	0.60-0.99
Moderate	0.65	0.49-0.86	0.64	0.47-0.86
Mathematics complexity [b]				
Low	1.30	0.91-1.85	0.93	0.63-1.36
Moderate	1.08	0.77-1.51	0.83	0.59-1.18
Language complexity [b]				
Low	1.11	0.82-1.50	0.92	0.67-1.25
Moderate	0.96	0.75-1.23	0.90	0.70-1.15
Reasoning complexity [b]				
Low	1.20	0.92-1.57	1.03	0.78-1.36
Moderate	1.03	0.80-1.33	0.96	0.74-1.24
Vocational complexity [c]				
Low	1.14	0.80-1.63	0.87	0.59-1.28
Moderate	1.32	0.98-1.79	1.02	0.74-1.40
Nominal categorical occupation [d]				
Clerical, sales	0.86	0.64-1.16	0.81	0.59-1.09
Service	1.64	1.18-2.29	1.16	0.82-1.63
Agriculture	1.49	1.11-2.02	1.42	1.03-1.95
Misc. [e]	1.13	0.82-1.56	0.98	0.71-1.36

[a] 95% confidence interval; [b] reference category: most complex; [c] reference category: highest preparation required; [d] reference category: professional, technical, managerial occupations; [e] includes processing, machine work, benchwork, structural work, and a miscellaneous category

[f] Covariates included age, gender, and presence of APOE ε4 allele; each variable in the above model (with the exception of the nominal categorical occupation variable) was analyzed in a separate Cox regression model, with individual single-degree-of-freedom contrasts, as indicated beneath each occupational complexity variable

Table 5

Cox Regression Post-Hoc Analysis of Data, People, and Things Complexity Variables on Incident All-Cause Dementia Risk Outcomes After Addition of Covariates [a]

	Model 1		Model 2		Model 3		Model 4	
Complexity	HR	CI [b]	HR	CI	HR	CI	HR	CI
Data complexity [c]								
Low complexity	0.99	0.73-1.25			0.72	0.51-1.00	0.90	0.61-1.33
Moderate complexity	1.03	0.83-1.27			0.91	0.74-1.13	0.99	0.70-1.24
People complexity [c]								
Low complexity			1.01	0.76-1.33	1.23	0.92-1.65	1.06	0.76-1.47
Moderate complexity			0.92	0.72-1.16	0.97	0.78-1.21	0.93	0.73-1.17
Things complexity [c]								
Low complexity	0.75	0.61-0.93	0.74	0.60-0.93			0.76	0.60-0.97
Moderate complexity	0.71	0.54-0.93	0.71	0.55-0.90			0.74	0.55-0.98

[a] Covariates included age, gender, and presence of APOE ε4 allele; [b] 95% confidence interval; [c] reference category: most complex

Table 6

Cox Regression Post-Hoc Analysis of Data, People, and Things Complexity Variables on Incident Alzheimer's Disease Risk Outcomes [a]

	Model 1		Model 2		Model 3		Model 4	
Complexity	HR	CI [b]	HR	CI	HR	CI	HR	CI
Data complexity [c]								
Low complexity	1.14	0.79-1.65			0.76	0.51-1.15	1.06	0.66-1.71
Moderate complexity	1.10	0.85-1.42			0.94	0.73-1.23	1.07	0.81-1.40
People complexity [c]								
Low complexity			0.98	0.71-1.35	1.11	0.78-1.59	0.95	0.64-1.42
Moderate complexity			0.83	0.63-1.10	0.85	0.66-1.11	0.83	0.62-1.10
Things complexity [c]								
Low complexity	0.75	0.58-0.97	0.74	0.57-0.97			0.73	0.54-0.98
Moderate complexity	0.60	0.43-0.85	0.64	0.47-0.87			0.63	0.44-0.89

[a] Covariates included age, gender, and presence of APOE ε4 allele; [b] 95% confidence interval; [c] reference category: most complex

analyzing occupations separately, *things* complexity is the only complexity variable that remains significant after addition of covariates. This finding indicates that *things* complexity contributes uniquely to predicting dementia risk, beyond *data* and *people* complexity.

Research Question 2

Defining occupational complexity in terms of mathematics, language, and reasoning development needed to perform the job, do higher levels of complexity (each domain considered separately) predict (a) higher risk for all-cause dementia, and (b) higher risk for Alzheimer's disease. Cox regressions showed that mathematics, language, and reasoning development requirements did not predict all-cause dementia (Table 3) or AD (Table 4).

Research Question 3

Defining occupational complexity in terms of specific vocational preparation (SVP) needed to perform the job, do higher levels of complexity (each domain considered separately) predict: (a) higher risk for all-cause dementia, and (b) higher risk for Alzheimer's disease. Cox regressions showed that the amount of vocational preparation needed to perform participants' job of longest duration was not significantly related to all-cause dementia (Table 3) or AD (Table 4).

Research Question 4

Defining occupational complexity in terms of professional categories of professional /managerial, clerical/sales, service, agriculture, and processing/machine/benchwork/structural, do lower levels of complexity predict: (a) higher risk for all-cause dementia, and (b) higher risk for Alzheimer's disease. Cox regressions indicate that individuals whose primary occupations fall into the "agriculture" category have an increased risk for both all-cause dementia and AD in late-life (Tables 3 and 4). Risk for all-cause dementia is 34% higher and risk for AD is 42% higher for these individuals, compared to individuals in the professional/ technical/managerial category.

To further explore this association, a cross-tabulation of *data*, *people*, and *things* complexity by nominal occupation category was conducted which revealed a significant association, with an overwhelming majority of participants (83.8%) with "agriculture" as their primary profession ranked within the top quartile on *data* complexity (χ^2 = 2452.976, df = 8, p < .001. The distribution of job categories within the top quartile on *data* complexity variable is as follows: professional (56.4%), clerical/sales (1.6%), service (3.2%), agriculture (35.9%), miscellaneous (3.0%). The top quartile for *people* complexity had 1.4% of participants with agriculture as their primary profession ranked within the top quartile (χ^2 = 2957.788, df = 8, p < .001). The nominal job distribution within the top quartile on *people* complexity variable is as follows: professional (86.3%), clerical/sales (2.2%), service (5.3%), agriculture (1.1%), and miscellaneous (5.1%). Finally, *things* complexity showed a very high percent (83.9%) of individuals with agricultural occupations falling into the top quartile (χ^2 = 2162.837, df = 8, p <.001). The nominal job distribution within the top quartile on *things* complexity variable is as follows: professional (20.3%), clerical/sales (0.0%), service (13.2%), agriculture (41.2%), and miscellaneous (25.2%).

Research Question 5

Are observed effects of higher occupational complexity mediated through higher socioeconomic status, or remain robust after adjustment for the latter? (*examining only the specific variables found to be significant predictors among the eight operationalizations of complexity).* Cox regressions indicated that SES does at least partially mediate the association between certain types of occupational complexity and both all-cause dementia and AD (see Tables 7 and 8). When SES is added to the model, the significant effect seen in complexity of work with *things* is generally robust for both all-cause dementia and AD, (i.e., SES does not mediate the association between complexity of work with *things* and AD/dementia risk for individuals in the moderate vs. high *things* complexity category, but it does partially mediate the relationship between low vs. high *things* complexity and both dementia outcomes). Before SES is added to the model, moderate vs. high *things* complexity shows a significant effect on both all-cause dementia and AD risk; this model retains significance after the addition of SES, indicating that the observed effect is not simply due to differences in SES between moderate and high levels of *things* complexity. The significance of the low versus high *things* complexity effect becomes non-significant after addition of SES, however, the 95% confidence interval just barely overlaps 1.0. So, it can be concluded that SES only partially mediates the overall effect of *things* complexity and dementia risk.

In models testing potential SES mediation on the effect of nominal occupation category, results suggest partial mediation for both all-cause dementia and AD. The higher risk associated with service jobs was robust to adjustment for SES, meaning that the effect was not mediated by the addition of SES. However, the higher risk associated

Table 7

Cox Regression Models to Test Mediating Effect of Socioeconomic Status on Association between Occupational Complexity and Incident All-Cause Dementia Risk

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
Variable	HR	CI [a]	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI
SES	1.00	0.99-1.00			1.00	0.99-1.00	1.00	1.00-1.01			1.00	0.99-1.00	1.00	1.00-1.01
Age (years)							1.14	1.12-1.15					1.14	1.12-1.15
Gender: female [b]							1.09	0.89-1.33					0.98	0.79-1.22
APOE: ε4 carrier [c]							0.51	0.42-0.61					0.51	0.42-0.62
Things complexity [d]														
Low complexity			0.76	0.62-0.92	0.82	0.66-1.02	0.88	0.68-1.14						
Moderate complexity			0.67	0.52-0.84	0.67	0.52-0.85	0.62	0.46-0.84						
Nominal occupational category [e]														
Clerical, sales									0.89	0.70-1.14	0.82	0.63-1.07	0.93	0.70-1.22
Service									1.69	1.29-2.21	1.50	1.10-2.05	1.41	1.02-1.94
Agricultural									1.50	1.17-1.92	1.28	0.97-1.70	1.23	0.92-1.65
Misc [f]									1.03	0.78-1.25	0.88	0.65-1.19	0.91	0.66-1.24

[a] 95% confidence interval; [b] reference category: female; [c] reference category: presence of one or more ε4 alleles; [d] reference category: most complex; [e] reference category: professional, technical, managerial occupations; [f] includes processing, machine work, bench work, structural work, and a miscellaneous category

Table 8

Cox Regression Models to Test Mediating Effect of Socioeconomic Status on Association between Occupational Complexity and Incident Alzheimer's Disease Risk

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
Variable	HR	CI [a]	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI
SES	1.00	0.99-1.00			1.00	0.99-1.00	1.00	1.00-1.01			1.00	0.99-1.00	1.01	1.00-1.01
Age (years)							1.15	1.13-1.17					1.15	1.14-1.17
Gender: female [b]							1.34	1.05-1.72					1.29	0.99-1.68
APOE: ε4 carrier [c]							0.44	0.35-0.56					0.43	0.34-0.54
Things complexity [d]														
Low complexity			0.81	0.64-1.03	0.88	0.68-1.14	0.81	0.62-1.07						
Moderate complexity			0.65	0.49-0.86	0.62	0.46-0.84	0.64	0.46-0.89						
Nominal occupational category [e]														
Clerical, sales									0.86	0.64-1.16	0.81	0.59-1.12	0.88	0.62-1.23
Service									1.63	1.17-2.28	1.58	1.09-2.30	1.39	0.95-2.04
Agricultural									1.49	1.10-2.01	1.34	0.96-1.89	1.48	1.03-2.14
Misc [f]									1.30	0.91-1.87	1.00	0.70-1.44	1.14	0.79-1.65

[a] 95% confidence interval; [b] reference category: female; [c] reference category: presence of one or more ε4 alleles; [d] reference category: most complex; [e] reference category: professional, technical, managerial occupations; [f] includes processing, machine work, bench work, structural work, and a miscellaneous category

with jobs in agriculture became non-significant after accounting for SES.

Research Question 6

What is the relative influence of occupational complexity and formal education (*examining only the specific variables found to be significant predictors among the eight operationalizations of complexity)* in predicting: (a) higher risk for all-cause dementia, and (b) higher risk for Alzheimer's disease? When education is added to models examining the association between occupational complexity of *things* and all-cause dementia and AD, the significant effect persists (Tables 9 and 10). This suggests that each variable provides a *unique* contribution to prediction of risk for both all-cause dementia and AD. In models of the nominal occupational category, when education is added to the model, the significance of the service job category remains robust, while the significance of the agriculture job category becomes non-significant (though interestingly, returns to significance after inclusion of the remaining covariates). Thus, job category and education appear to hold unique predictive information regarding dementia risk, but this is strongest among persons in the service professions.

Research Question 7

Does duration of longest held job moderate the findings in the above associations? Duration of longest job held was operationalized from 0-23 years (n = 2238) versus 24+ years (n = 2307), consistent with how this variable has been conceptualized and found to be a significant moderator in other studies (Kroger et al., 2008). However, in the present study, in Cox regression, this dichotomous duration variable did not moderate any of the significant associations discussed in previous research questions, as evidenced by non-

Table 9

Cox Regression Models to Test Relative Effect of Occupational Complexity Versus Education on Incident All-cause Dementia Risk

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
Variable	HR	CI [a]	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI
Education	0.96	0.93-0.99			0.96	0.94-0.99	1.02	0.98-1.05			0.97	0.94-1.01	1.02	0.98-1.06
Age							1.14	1.12-1.15					1.14	1.12-1.15
Gender: female [b]							1.19	0.98-1.44					1.10	0.90-1.34
APOE: ε4 carrier [c]							0.51	0.43-0.61					0.51	0.42-0.60
Things complexity [d]														
Low complexity			0.76	0.62-0.92	0.79	0.65-0.97	0.73	0.59-0.91						
Moderate complexity			0.67	0.54-0.84	0.96	0.94-0.99	0.70	0.55-0.89						
Nominal occupational category [e]														
Clerical, sales									0.89	0.70-1.14	0.79	0.58-1.08	0.92	0.70-1.20
Service									1.69	1.29-2.21	1.45	1.00-2.09	1.38	1.02-1.88
Agricultural									1.50	1.17-1.92	1.36	0.98-1.88	1.41	1.06-1.88
Misc [f]									1.03	0.78-1.35	1.00	0.70-1.42	1.00	0.70-1.42

[a] 95% confidence interval; [b] reference category: female; [c] reference category: presence of one or more ε4 alleles; [d] reference category: most complex; [e] reference category: professional, technical, managerial occupations; [f] includes processing, machine work, bench work, structural work, and a miscellaneous category

Table 10

Cox Regression Models to Test Relative Effect of Occupational Complexity Versus Education on Incident Alzheimer's Disease Risk

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
Variable	HR	CI [a]	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI	HR	CI
Education	0.96	0.93-0.99			0.96	0.92-0.99	1.02	0.98-1.06			0.97	0.93-1.01	1.03	0.98-1.08
Age							1.15	1.13-1.17					1.15	1.13-1.17
Gender: female [b]							1.43	1.13-1.82					1.39	1.09-1.78
APOE: ε4 carrier [c]							0.45	0.37-0.56					0.44	0.36-0.55
Things complexity [d]														
Low complexity			0.81	0.64-1.03	0.85	0.67-0.97	0.74	0.57-0.97						
Moderate complexity			0.65	0.49-0.86	0.96	0.94-1.09	0.64	0.47-0.86						
Nominal occupational category [e]														
Clerical, sales									0.86	0.64-1.16	0.79	0.58-1.08	0.86	0.62-1.20
Service									1.63	1.17-2.28	1.45	1.01-2.09	1.28	0.88-1.86
Agricultural									1.49	1.10-2.01	1.36	0.98-1.88	1.56	1.10-2.22
Misc [f]									1.30	0.91-1.87	1.00	0.70-1.42	1.09	0.75-1.86

[a] 95% confidence interval; [b] reference category: female; [c] reference category: presence of one or more ε4 alleles; [d] reference category: most complex; [e] reference category: professional, technical, managerial occupations; [f] includes processing, machine work, bench work, structural work, and a miscellaneous category

Table 11

*Cox Regression Models to Test Moderating Effect of Job Duration on Association Between Occupational Complexity and Incident All-Cause Dementia Risk**

Variable	Model 1 omnibus	Model 2 omnibus	Model 3 omnibus	Model 4 omnibus	Model 5 omnibus	Model 6 omnibus
Age				< .001		.001
Gender: female [a]				.09		0.41
APOE: ε4 carrier [b]				< .001		0.50
Things [c]	.008					
Duration [d]		0.29				
Things* duration			0.42	0.23		
Nominal occupational category [e] high duration (omnibus)					0.57	0.73

[a] reference category: male; [b] reference category: presence of one or more ε4 alleles; [c] reference category: most complex; [d] duration of job defined as 0-23 and 24+ years; [e] reference category: professional, technical, managerial occupations
**p*-values in table represent omnibus Wald tests for each effect

Table 12

*Cox Regression Models to Test Moderating Effect of Job Duration on Association Between Occupational Complexity and Incident Alzheimer's Disease Risk**

Variable	Model 1 omnibus	Model 2 omnibus	Model 3 omnibus	Model 4 omnibus	Model 5 omnibus	Model 6 omnibus
Age				< .001		< .001
Gender: female [a]				< .001		0.03
APOE: ε4 carrier [b]				< .001		< .001
Things [c]	.01					
Duration [d]		0.53				
Things* duration			0.76	0.74		
Nominal occupational category [e] high duration (omnibus)					0.42	0.87

[a] reference category: male; [b] reference category: presence of one or more ε4 alleles; [c] reference category: most complex; [d] duration of job defined as 0-23 and 24+ years; [e] reference category: professional, technical, managerial occupations
**p*-values in table represent omnibus Wald tests for each effect

significant interaction effects between duration and complexity (Tables 11 and 12).

Due to findings in the exploratory analyses, which indicated a large gender difference in duration of longest job held among male participants (36.96 years, *SD* = 15.50) versus female participants (16.10 years, 14.09 years), a post-hoc analysis was run which used a continuous variable for duration of longest job held. Results were nearly identical, however, indicating that this sample did not experience a difference in dementia risk based on the duration of their longest held occupation.

Research Question 8

Does gender moderate the findings in the above associations? Cox regressions indicated that gender did not moderate the association between complexity of work with *things* and dementia outcomes (all-cause dementia and AD), given the non-significant interaction effect between gender and complexity. Gender also did not moderate the association between the nominal occupation variable and dementia outcomes (Tables 13 and 14).

Research Question 9

Does APOE genotype moderate the findings in the above associations? Cox regressions showed that APOE did not moderate the association between any of the occupational complexity variables and dementia or AD risk, given that interaction effects between APOE and each complexity variable were consistently non-significant (Tables 15 and 16).

Table 13

*Cox Regression Models to Test Moderating Effect of Gender on Association between Occupational Complexity and Incident All-Cause Dementia Risk**

Variable	Model 1 omnibus	Model 2 omnibus	Model 3 omnibus	Model 4 omnibus	Model 5 omnibus	Model 6 omnibus
Age				< .001		< .001
Gender: female [a]		0.07		0.90		0.82
APOE: ε4 carrier [b]				< .001		< .001
Things [c]	0.008					
Things* gender			0.34	0.29		
Nominal occupational category [d] gender					0.74	0.80

[a] reference category: male; [b] reference category: presence of one or more ε4 alleles; [c] reference category: most complex; [d] reference category: professional, technical, managerial occupations
**p*-values in table represent omnibus Wald tests for each effect

Table 14

*Cox Regression Models to Test Moderating Effect of Gender on Association between Occupational Complexity and Incident Alzheimer's Disease Risk**

Variable	Model 1 omnibus	Model 2 omnibus	Model 3 omnibus	Model 4 omnibus	Model 5 omnibus	Model 6 omnibus
Age				< .001		< .001
Gender: female [a]		0.76		0.11		0.11
APOE: ε4 carrier [b]				< .001		< .001
Things [c]	0.01					
Things* gender			0.55	0.72		
Nominal occupational category [d] gender					0.99	0.99

[a] reference category: male; [b] reference category: presence of one or more ε4 alleles; [c] reference category: most complex; [d] reference category: professional, technical, managerial occupations
*p-values in table represent omnibus Wald tests for each effect

Table 15

*Cox Regression Models to Test Moderating Effect of APOE Genotype on Association Between Occupational Complexity and Incident All-Cause Dementia Risk**

Variable	Model 1 omnibus	Model 2 omnibus	Model 3 omnibus	Model 4 omnibus	Model 5 omnibus	Model 6 omnibus
Age				< .001		< .001
Gender: female [a]				0.14		0.51
APOE: ε4 carrier [b]		<.001		< .001		< .001
Things [c]	0.008					
Things* APOE			0.23	0.36		
Nominal occupational category [d] APOE					0.43	0.83

[a] reference category: male; [b] reference category: presence of one or more ε4 alleles; [c] reference category: most complex; [d] reference category: professional, technical, managerial occupations
**p*-values in table represent omnibus Wald tests for each effect

Table 16

*Cox Regression Models to Test Moderating Effect of APOE Genotype on Association Between Occupational Complexity and Incident Alzheimer's Disease Risk**

Variable	Model 1 omnibus	Model 2 omnibus	Model 3 omnibus	Model 4 omnibus	Model 5 omnibus	Model 6 omnibus
Age				< .001		< .001
Gender: female [a]				0.005		0.02
APOE: ε4 carrier [b]		< .001		.001		< .001
Things [c]	0.01					
Things* APOE			0.15	0.21		
Nominal occupational category [d] APOE					0.18	0.23

[a] reference category: male; [b] reference category: presence of one or more ε4 alleles; [c] reference category: most complex; [d] reference category: professional, technical, managerial occupations
**p*-values in table represent omnibus Wald tests for each effect

CHAPTER V

DISCUSSION

This study investigated the relationship between occupational complexity of longest held job over the lifespan, and risk for dementia in late-life, in a population-based epidemiologic study of dementia. Occupational history is important to study within the context of dementia development, as they are modifiable lifestyle factors that can influence dementia risk (Bickel & Kurz, 2009; Meng & D'Arcy, 2012; Stern et al., 1994).

Data, People, Things Complexity

The primary finding was that persons who held jobs that were highly concentrated in work with machinery, tools and inanimate *things* were at higher risk for AD and dementia, with persons in occupations that were low or moderate in *things* complexity having approximately one third lower risk than persons high in *things* complexity. This result was robust to adjustment of covariates including age, APOE ε4 allele, and gender.

Moderate *things* complexity was not mediated by SES, as the significant effect between moderate *things* complexity and both dementia outcomes remained significant after addition of the SES variable. Low *things* complexity, on the other hand, was mediated by SES, as it just surpasses the threshold for non-significance at 1.0 when SES is added to the model. This is a somewhat counterintuitive finding, as one would expect individuals with the least complex jobs to also make the least money, therefore, not providing these individuals with the protective effect commonly associated with higher levels of wealth. Because SES does mediate the relationship, it may be that there is a great deal of variability in SES level among those in the low t*hings* complexity group.

Also, there may be something unique going on with the sample that has influenced this result. For example, it may be that there happens to be a certain type of job available falls into “low *things* complexity” happens to be higher-paying than most jobs of similar *things* complexity. This may impact the SES mediation of this category, leading to a mediation effect when SES is added to the model. *Things* complexity also predicted dementia risk independent of education suggesting that occupations with heavy focus on work with machinery are at greater risk, and this is not confounded with these types of professions being typically held by persons with lower education, but both having achieved a lower level of education, and having held a profession that is heavily focused on machinery, are *independently* associated with higher risk.

Things complexity was not moderated by duration of longest job held, which is in contrast to what one other study found (the only other study examining this moderator in the literature). The explanation may be because in the current study’s sample, a large portion of individuals with agricultural occupations (83.9%) fell into this category (high *things* complexity). Because agricultural occupations accounted for such a small percentage of high *things* complexity occupations in the Kroger et al. (2008) study (4.6% vs. 41.2% for the current study), it is likely that the nature of work compared in the current study and the nature of work compared in Kroger’s study is dissimilar enough to produce disparate results when investigating the *things* complexity variable.

Things complexity was also not moderated by gender, even though gender was identified as being confounded with occupational complexity, and some studies have found women to be at higher risk for both dementia and AD (Fratiglioni et al., 1997). There is also evidence to suggest that women are at higher risk for certain types of Alzheimer's, such as the late-onset familial type, when they also carry the APOE ε4 allele (Payami et al., 1996). Occupational complexity appears to have similar benefits for women as for men. For the fortunate minority of women who were able to attain higher occupational levels with more complexity, their dementia risk was lower than that of women in jobs with lower levels of complexity (e.g., high *things* complexity), in much the same way that more complex occupations afforded protection for men.

Things complexity was also not moderated by the APOE ε4 allele, which means that AD risk among individuals with a copy of the allele was influenced by occupational complexity at a level equivalent to that of individuals without the allele. Other studies have found that APOE genotype moderated associations between various "life stressors" and AD risk (e.g., large family size, Borenstein et al., 2006; low childhood SES, Moceri et al., 2001), with the finding that it was only those at higher genetic risk for AD who were put at further risk from stressful exposures. However, in the present study, the absence of APOE moderation implies that lower occupational complexity is not a sufficient "stressor" to influence one's risk for dementia in late-life any differently for those at higher genetic risk and those at lower genetic risk. Likewise, having the APOE ε4 allele does not appear to negate the benefits of greater occupational complexity.

The findings relative to *things* complexity are in line with some of the previous research in this area, which also found that lower complexity of work with *things* was associated with reduced risk for dementia, but not AD (Andel et al., 2006). However, this finding is in contrast to what Kroger et al. (2008) found when investigating the link between occupational complexity of *things* and dementia risk. Kroger's study found that higher occupational complexity with *things* decreased the risk for dementia, with the highest complexity category showing the most protection. The reason for the difference in effect between the different degrees of complexity may have to do with the nature of work individuals experience within the different complexity categories. The sample in Cache County consisted of individuals from a primarily agriculture-based economy. In fact, agriculture was the single most frequent occupation reported in this cohort (623 individuals or 14% of the entire cohort), with a high level of *things* complexity found in nearly 90% of persons in these occupations.

The results of the current study also seem to suggest that it's most beneficial to work in an occupation that is *moderate* in complexity with *things*, though not *low* in complexity with *things*. It appears that occupations falling in the middle of the continuum of complexity have the ideal mix of circumstances that result in protection against dementia outcomes. It may be that jobs that are high in *things* complexity emphasize use of machines and equipment to the exclusion of other types of activities that offer cognitive challenges, while jobs that are moderate in *things* complexity offer a mix of activities that together provide enough mental stimulation to build sufficient cognitive reserve (Churchill et al., 2002). Additionally, individuals whose primary occupation falls into the high complexity with *things* category may experience the high levels of stress normally associated with these more physically demanding occupations, particularly the afore-mentioned agricultural individuals which, therefore, increases their risk (through a number of different mechanisms described above, along with excess secretions of cortisol) for dementia (Lupien et al., 1998) and negates any possible positive outcomes associated with the complexity found at their jobs.

As regards to *data* complexity, in the present study this was unrelated to dementia risk, a finding that falls somewhere between the findings of Kroger and colleagues (2008) where it was associated with higher dementia risk, and the work of Potter and colleagues (2007) who found a decrease in dementia risk for persons high in *data* complexity. A similar trend was discovered for individuals holding an agricultural occupation and high *data* complexity, as nearly 90% of individuals who worked in agricultural occupations also held a job high in *data* complexity. The same was not true for *people* complexity, however, with not quite 2% of individuals who worked in agricultural occupations also holding a job high in *people* complexity.

The conflicting findings of studies in this topic area may be because the true story behind occupational complexity as an AD risk factor is in aggregate exposure across all three domains. In considering only one exposure variable at a time, researchers are unable to control for the influence of the other two complexity domains, or to identify the optimal mixture of levels of complexity across domains. Different patterns of aggregate exposure may exist between different geographical regions of the U.S., such as in primarily agricultural vs. primarily industrial areas. For example, it may be the case that *data* complexity is protective (as found by Potter et al., 2007), but if in the current sample, the individuals who are high in *data* complexity have a diverse mix of low versus high *things* complexity, making it so that *data* complexity effects would be undetectable.

Perhaps participants in Potter's study were homogeneously low in *things* complexity, having made it much easier to see the effects of the high *data* complexity. It may be that the only way to test the "pure" effect of occupational complexity in each domain is to look at all three domains simultaneously, examining for example, the group that is "high" in only one domain but "low" in other domains.

Nominal Occupation Category

Service Occupations

A second finding of the study was that when occupations were grouped into nominal categories and compared with the highest complexity group of professional/technical/managerial ("professional"), both the agricultural and service categories were associated with higher dementia risk in unadjusted models. In a simple bivariate model, individuals whose primary occupation fell into the service category were at an increased risk for both all-cause dementia and AD. This finding may be related to age rather than the exposure variable, however, as the mean age for individuals in the service category was 76.3, which was the highest average age of all 5 nominal occupation categories. When age is added to the model, the effect disappears. Age is a well-known risk factor for dementia, so it is likely that the initial effect observed is an indication of confounding with age, rather than holding a service-related occupation per se.

Agriculture Occupations

Individuals whose primary occupation was in agriculture also showed an increased risk for both all-cause dementia and AD, but this effect was *robust* to adjustment for age, gender, and APOE ε4. Jobs based in the agriculture industry bring about unique physical and mental challenges, which may influence the *things* category in this particular sample to be a risk factor for, rather than protective against, dementia outcomes. Agriculture is a high-stress occupation, with a very high mortality risk, long working hours under potentially poor conditions, and can be very physically demanding (McCurdy & Carroll, 2000). Workers in the agricultural field also risk being exposed to pesticides and other dangerous chemicals (Gerrard, 1998). Further, there are significant negative mental health outcomes associated with agricultural jobs, such as high levels of stress (Booth & Lloyd, 2000), anxiety and depression (Eisner, Neal, & Scaife, 1998), and increased risk of suicide (Booth & Lloyd, 2000). There is also some evidence to suggest that exposure to pesticides increases one's risk for dementia and AD in late-life (Hayden et al., 2010), though caution should be used when applying the results of Hayden's article to this study, as both studies use the same sample (data for both were from the Cache County Memory Study).

Effect of Gender

In addition to low educational and occupational attainment, female gender, a well-known risk factor for AD (Fratiglioni et al., 1997), was also demonstrated to increase dementia risk in this cohort. While gender did not moderate any occupational or dementia associations, females were at significantly higher dementia risk when gender was considered alone, becoming non-significant when the nominal occupational category was added to the model. Even after education was added to the model, the effect of gender was much less significant than it had been in the simple bivariate association. This confounding between gender and occupational complexity may help to explain women's higher dementia risk via less opportunity for cognitive stimulation in the workplace compared to men. Thus, while some of the higher dementia risk seen for women may come from sex-linked traits, some of the observed higher dementia risk in women seen throughout the literature appears to be due to the lower average occupational attainment of women.

Mechanisms/Mediation

When SES is added to a model including the nominal occupational variable, the previously-seen significant effect for service-related occupations remains for both all-cause dementia and AD, indicating that SES does not play a role in the relationship between service-related occupations and dementia risk. This finding suggests that the mechanism involved is not simply an economic one, but rather it is likely due to a relative dearth of cognitive stimulation in service jobs, lessening the cognitive reserve benefits. In models containing agricultural occupations, however, results become non-significant after addition of SES, indicating that SES does mediate the relationship between this type of occupation and risk for dementia. In other words, although persons in agricultural jobs are at higher risk from job strains and other stressors mentioned above, they also tend to have lower SES than persons in other job categories. Thus, the mechanism of lower SES being associated with poorer health outcomes (Grzywacz et al., 2004; Sturm & Gresenz, 2002), generally may largely be responsible for higher dementia risk in this job category.

When analyses were run to determine independent effect of education, results show that high *things* complexity increases the risk for all-cause dementia and AD, independent from education (the significant effect remains in place after addition of the education covariate). The nominal occupational category showed an opposite trend, with results becoming non-significant after addition of education for agricultural and service-related occupations for both all-cause dementia and AD, with one exception. The significant effect seen with service-related occupations and AD risk remains significant after addition of education, suggesting that there is additional risk conferred by being in a service occupation beyond the fact that it is typically associated with lower education levels. How much of this derives from the absence of cognitive stimulation versus work-related stress in service-related occupations needs further study. It may be that the *things* complexity findings remain significant after the addition of education because the job-related tasks that individuals are exposed to while working in these occupations result in more cognitive disadvantages than any reserve associated with education can account for. Thus, individuals in the high *things* complexity category are impacted by unique experiences within their occupations, which are unrelated to education level. Because the service and agricultural categories had the two highest mean ages of all the nominal occupational categories, it is likely that a large portion of these individuals also had fewer opportunities for educational attainment, as age and education are highly confounded. Also, it may be that education is related to choice of occupation as well as level of occupational attainment, influencing individuals' eventual occupational complexity. It is important to point out that education and occupational complexity have independent effects on dementia risk, however, there is likely to still be residual effect of formal education that is protective against dementia (Bickel & Kurz, 2009; Stern, 2002, 2006).

In addition to these circumstances and outcomes, there may be other more subtle mechanisms through which dementia risk is impacted for individuals who work in agricultural occupations. Because it is theorized that higher educational and occupational attainment can lead to a delay in the clinical expression of dementia (Bickel & Kurz, 2009; King et al., 2001) through a buildup of cognitive reserve (King et al., 2001), it is very likely that individuals in this sample who worked in the agriculture industry were at a double disadvantage when compared to individuals in the professional category. Individuals in the agricultural category had significantly (three years) less education than those in the professional category. This educational deficit would put them at a disadvantage before even beginning work at their occupations.

Second, as cited above, individuals in agriculture jobs tend to have to work longer hours, with more stress and more physically demanding work activities, thus putting them at higher risk. It is important to point out a potential weakness in this study which is directly related to the above conclusions regarding agricultural occupations and SES. The information available for analysis on agricultural jobs in this study is somewhat unrefined; someone in the agricultural category could have had a job with as little complexity as a farm laborer, or they could be responsible for running an entire farm-based business. Farm laborers are going to encounter considerably fewer cognitive challenges and mental stimulation than farm owners, illustrating the point that there is likely to be a great deal of variance in levels of complexity among the agricultural occupation group. While there are sure to be some similarities among all agriculturally-based occupations, it is equally likely that there are considerable differences between the different agricultural occupations, making the current study's method of measuring the complexity of these occupations less than perfect.

Future Directions

Future research can expand on several aspects of this study, to capture additional aspects of cumulative exposure to occupational complexity. One approach would be to compute "pack-years," an approach traditionally used to quantify the amount of cigarettes an individual has smoked by measuring in pack-years, wherein one pack-year represents one pack of cigarettes smoked each day for one year (Clemons, Milton, Klein, Seddon, & Ferris, 2005). Each occupational complexity variable in its original scale (the higher the number, the higher the number of "packs," or complexity) would be multiplied by its duration in years, adding this score up across all jobs. The resulting number would give the pack-year, or "complexity-year" score, representing the cumulative complexity of individuals' occupations over all years in the labor force. This would give researchers a more accurate representation of the cumulative occupational complexity (within each complexity domain) that individuals experienced across the entire time in the labor force.

Another way to capture occupation-related complexity is through exposure to multiple cognitive challenges, which are experienced when individuals change jobs and must learn new skills associated with their new position. In order to measure this aspect of occupational complexity, researchers would look at the total number of unique jobs an individual held across their working life time. Or degree of change experienced within each domain could be computed by subtracting, for example, the "minimum *data* complexity" from the "maximum *data* complexity," which would be a measure of the magnitude of complexity change (and by inference, the amount of cognitive challenge) experienced in the *data* domain across the lifespan. The same would be done for *people* and *things* complexity, then each score could be analyzed separately or combined into one measure by summing the scores. Similarly, the difference between the highest versus lowest nominal occupation category across the working years would give another indicator for the number of "job steps" or changes one experienced.

Because the current study (as well as previous studies in this topic area) run models that examine each complexity measure in isolation, it may be beneficial to build a model that examines the effect of occupational complexity on dementia risk that takes into account different combinations of complexity. This could be accomplished by creating a composite complexity variable that aggregates across the existing occupational complexity variables (*data*, *people*, *things*). After dichotomizing each into high versus low, the composite variable would have eight possible categories (e.g., HHH, HHL, HLH, LHH, etc). This approach (or alternatively, including the three dichotomous variables in a model with all possible interaction terms) would allow the researcher to investigate multidimensional effects.

Another area for future study would be to consider a third source of cognitive stimulation. Leisure activities can build cognitive reserve and have been demonstrated to lower the risk of dementia (Verghese et al., 2003; Wang, Karp, Winblad, & Fratiglioni, 2002) and AD (Scarmeas, Levy, Tang, Manly, & Stern, 2001; Wilson et al., 2002). Similar to the way occupational complexity can build cognitive reserve by presenting individuals with mentally challenging and stimulating experiences, so too, can leisure activities. No studies have been conducted on the relative influence of education, occupation, and leisure on late-life cognitive health. While there are studies that have looked at one or two of these variables, examining all three simultaneously would give investigators a better understanding of unique versus shared effects.

Owing to the large number of right-censored individuals at the end of the study, it may be beneficial to investigate the association between occupational complexity and rate of cognitive decline, in addition to studying risk for dementia. This strategy would allow researchers to capture individuals who are experiencing a decline in their cognitive abilities, even if they did not end up developing all-cause dementia or AD before the study ended. Second, because exposure to cognitive complexity varied according to baseline age (birth year), it may be useful to stratify the sample into birth cohorts and investigate the role of occupational complexity within more narrow birth cohorts. Birth cohorts defined by 5-10 year intervals may have experienced different opportunities for cognitively challenging activities on the job, depending on the maturation level of the American industrial economy during the majority of their working years. Controlling for age in this way would result in a more sensitive method to detect an association between occupational complexity and dementia risk in late-life.

Strengths and Limitations

A number of strengths and limitations of this dissertation project should be noted. The CCMS dataset incorporated a longitudinal design, containing information gathered over a period of 13 years, a major strength. The original CCMS study was a large, epidemiological, population-based investigation of dementia, with a strict clinical procedure and diagnostic criteria for diagnosing the disease. The CCMS cohort had a longer life expectancy, higher educational attainment, and lower incidence of chronic disease than other similar populations. The study also benefited from very high participation rates, which dramatically reduce non-responder bias (Norton, Breitner, Welsh, & Wyse, 1994).

Also, because of the ethnic and cultural homogeneity of the sample (99% of participants were Caucasian and 90% identified as belonging to The Church of Jesus Christ of Latter-day Saints), there is likely to be a reduced number of cultural confounds having an influence on the inferences made from the results of this study. The study also contained a wealth of information on variables related to genetic and environmental influences on dementia and AD. Another strength is that participants' reports of their various occupations included: job title, industry of employment, and detailed job duties, which were then reviewed by an occupational health nurse to assign 9-digit detailed occupation codes, following Department of Labor Force standards. Such an approach provides much richer detail than a method lacking such professional expertise in coding (e.g., presenting participants with a finite list of job categories from which to select). In addition to these strengths, several limitations should be mentioned. The cultural homogeneity described above, while an advantage in terms of likely implying fewer confounding variables and thereby increasing internal validity of the study, also has the result of restricting external validity or generalizability to other similar populations. All occupational complexity variables except for the nominal occupation category were collapsed into quartiles (easier interpretation; see also Kroger et al., 2008). A 1-unit increase in each of the raw occupational complexity variables has less practical meaning than lower 25%, middle 50%, upper 25% categories of low, moderate, and high complexity, prompting the decision to categorize complexity in the present study.

However, there is weakness in an approach that uses percentile cut-offs, because these are empirically defined within the present sample, and other geographic regions may have different absolute levels of complexity for these same percentile cut-offs. Additionally, the nominal occupational category variable used the 9-digit occupation code and grouped individuals into broad employment categories. While informative to make comparisons between such groups, it should be noted that there is potentially great heterogeneity in complexity within each such group (e.g., "agriculture" would include farm laborers along with persons who owned and operated large farms and were responsible for marketing, accounting, business planning, etc).

Another limitation which was also related to data analyses pertained to the Cox Regressions that were conducted. One of the statistical assumptions inherent with using a Cox Regression analysis is non-independence of the sample. Because the dataset contained approximately 1,200 married couples, non-independence cannot be assumed. Although it is common practice to model large epidemiological samples as reported herein, the use of a sample with non-independence between all participants may result in smaller standard errors, possibly inflating significance of results.

Also important to note is that the null findings in this study may not indicate a true lack of relationship between occupational complexity and dementia outcomes in late-life. Homogeneity in the demographics of the sample limited the amount of variability, and thus the present study may have been unable to detect an association which does exist in the larger population (e.g., all older adults in the U.S.). In addition, stress is likely to play a large part in the role of occupation and its relationship with dementia outcomes, and this study was not able to capture stress level of participants as part of the analyses.

Last, as was noted in the introduction to this project, due to the self-selecting nature of occupational selection, there is likely to be at least some selection bias present in the findings of this study. Participants chose their own "treatment category" so to speak; this may lead to findings being a result of outside influences.

Clinical Implications

The findings of this study have the potential to influence the realm of dementia and AD in a number of ways and on several different levels. First, there are implications from this study that have an impact at the individual level. It is unlikely that the results of this study will influence people to choose a profession (or switch to a new profession) which is correlated with low dementia risk. However, it is not unreasonable to think that the basic mechanisms behind the associations discussed in this project (i.e., being in an environment that challenges one's thinking and learning instead of one which consists primarily of repetitive use of machines) may be operating in a multitude of ways outside of the employment arena. Individuals may not choose to change their careers, but may see these results as suggesting that there would be benefit in seeking cognitive stimulation in non-work settings such as leisure activities. Additionally, individuals in jobs that offer little in the way of cognitive challenges may wish to make choices in other aspects of their lives that may combat the lack of cognitive reserve generating activities. These lifestyle choices might include such behaviors as eating a healthy, well balanced diet, getting plenty of rest and exercise, and pursuing rich socially engaging experiences.

The findings in this study, in conjunction with findings from other similar studies, indicate that certain individuals are prime candidates for efforts aimed at prevention and/or interventions related to dementia risk. While the results from this study are likely not strong enough to influence society on their own, as research builds in this area, the results of these studies may inform interventions and preventative measures targeting those at an increased risk for dementia and/or AD. For example, individuals in occupations high in complexity with *things* may want to engage in activities that are known to reduce risk for dementia, such as regular exercise and mentally stimulating cognitive activities such as word puzzles, reading, and so forth. Because this study investigated how type of complexity was associated with dementia risk and *not* specific job-related tasks that were responsible for observed associations, conclusions cannot be made regarding which occupational activities to seek to engage in in everyday life to mirror the benefits of various types of occupational complexity. Rather, individuals in these "at-risk" occupations may be well served to engage in protective activities outside of work that may buffer any negative effect of their occupations such as those mentioned above.

At the societal level, findings from this study may influence prevention/intervention efforts of medical professionals, insurance companies, educators, and so forth. For example, a consistent finding in the current study pertained to agricultural occupations and increased risk for dementia. Knowing this information may encourage doctors to evaluate and treat individuals in this at-risk category differently from individuals who are not in this high risk category. Physicians, educators, and insurance companies could offer appropriate activities or interventions to individuals in high-risk groups, with the intention of reducing any predisposition (e.g., genetic or positive family history) to higher dementia risk in such individuals.

At a policy level, changes may be made in existing policies related to dementia, or new policies may be created based on the findings of this study as well as the consistent findings of other studies in this area. It is unlikely that any one study in the social studies/epidemiological arena be sufficient all on its own to change policy, but it is not unreasonable to think that this study may be a small step in the direction of policy change, as pertains to cognitive health in late-life. Perhaps policymakers will initiate a campaign to educate individuals about risk factors for dementia and ways to avoid or counteract these factors. Long-term care insurance companies may offer discounts to individuals who agree to attend a workshop related to occupational influences on dementia risk, and how to reduce these risks. Similarly, groups that specialize in informing the public and providing information about dementia and AD may use the results of this and similar studies to inform their outreach and intervention efforts. These efforts have the potential to influence policy through their public outreach and informational efforts.

Conclusions

This study builds upon previous research on the association between various occupational complexity measures and dementia risk in late-life. Several occupational complexity variables were found to be significantly related to risk for dementia and/or AD in late-life. Individuals who held occupations which were moderate in complexity with *things* (use of machinery) were at a decreased risk for both dementia and AD. This is in agreement with some previous research, but not with others. The discrepancy is likely due to a difference in the job distribution of the different research samples, as the sample for the current study is heavily agriculture-based. Education and occupational complexity (as defined by *things* complexity) are independent and significant predictors of dementia risk. Age and occupational complexity were highly confounded in this cohort, making it hard to isolate the effect of occupational complexity alone. Future research would benefit from focusing on isolating more precise measures of occupational complexity. Findings from this study may guide interventions, prevention efforts, and perhaps even policy change.

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CURRICULUM VITAE

Daylee R. Greene
(May 2013)

ACADEMIC BACKGROUND

8/09-5/13 **Utah State University, Logan, UT**

- PhD: Family and Human Development.
  - Emphasis: Adult development and aging.
- Dissertation Project: Relationship Between Occupational Complexity and Dementia in Late-life.

8/07-5/09 **The University of Alabama, Tuscaloosa, AL**

- MS: Marriage and Family Therapy

8/04-12/06 **The University of Alabama, Tuscaloosa, AL**

- BS: Human Development
- Minor: Psychology

WORK EXPERIENCE

3/13-Present **Admissions/Marketing Director-Raintree Manor, McMinnville, Tennessee**

- Focus on building and maintaining rapport with residents, family members, employees, vendors, and all other individuals or companies that come in contact with the 140-bed nursing home, fostering a sense of compassion and trust in the community
- Responsible for making excellent first impression as the initial point of contact between the facility and community organizations, referral sources, family members and potential residents
- Maintain active relationships with referral sources in Warren County, Tennessee
- Participate in community events to raise community awareness of facility and services; events include local health fairs, Warren County Fair, local fund raising events, etc.
- Make regular visits to referral sources (acute care hospitals, geriatric psychiatry hospitals, assisted living facilities, and boarding homes) in Warren and neighboring counties

1/13;
2/13-3/13 **Interim Admissions/Marketing Director-Raintree Manor, McMinnville, Tennessee**

- Acted as department head for admissions and marketing department (see job duties listed above), while also being responsible for social services department

9/12-3/13 **Social Services Director-Raintree Manor, McMinnville, Tennessee**

- Acted as resident advocate and contact person for family members
- Responsible for social services department (including supervision of one assistant) for 140-bed facility
- Entered data for minimum data set (MDS) requirements, attended care plan meetings and created/updated care plans as necessary, coordinated discharges for all residents leaving the facility, arranged transportation for all resident physician appointments, participated in psychotropic medication reduction meetings, performed intake, discharge, cognitive, behavioral, and depression assessments
- Filled in for marketing/admissions as necessary: market to local agencies approximately once a week, follow referrals through from screening process to admission, assist family members with admission paperwork, help administrator as needed in all aspects of admissions and marketing

8/10-Present **Online Instructor-University of Alabama, Tuscaloosa, Alabama**

- Teaching an introductory course in human development, exclusively online
- Prepare lecture material, tests, and assignments
- Average class size: 40 students

8/09-5/12 **Graduate Teaching and Research Assistant-Utah State University, Logan, Utah**

- Taught upper division undergraduate broadcast class on family and social gerontology, including topics such as retirement, Medicare, caregiving, cultural diversity in the aging process, and death, dying, and grieving (class size: 9 students)
- Taught lower division undergraduate class on introduction to human development through the lifespan; topics included childhood, middle age, and old age (class size: 183 students)
- Assisted with research projects for Cache County Memory Study on dementia and Alzheimer’s. Organized literature reviews, wrote scholarly papers, conducted interviews, collected and analyzed data

8/08-5/09 **Clinic Manager-Marriage and Family Therapy Clinic at the University of Alabama, Tuscaloosa, Alabama**

- Manage day to day activities at clinic including scheduling, expenditures, and seeing clients
- Maintain community relationships, perform intake interviews, schedule and attend weekly meetings

RESEARCH EXPERIENCE

8/11-11/11 **Program Evaluation Internship-Apple Tree Assisted Living, Kaysville, Utah**

- Completed a program evaluation internship for doctoral program at a local assisted living facility
- Designed a survey to determine resident satisfaction with overall experience at Apple Tree; distributing and collecting data while respecting resident dignity and observing facility protocols

1/10-9/11 **Project Manager-Journal Pilot Study, Utah State University, Logan, Utah**

- Managed a pilot study within the Cache County Memory Study (CCMS)
- Contacted participants, conducted interviews, and collected data from CCMS participants
- Managed up to three volunteers as needed for help with data collection, administrative tasks, and literature collection and review
- Wrote evaluations and letters of recommendation for volunteers

VOLUNTEER EXPERIENCE

- Meals on Wheels weekly meal delivery, McMinnville Tennessee (2/2013-Present)
- Alacare Homehealth & Hospice, Northport Alabama (2007-2008)
- Big Brothers Big Sisters, Tuscaloosa Alabama (2006)
- Shelton State GED program, Tuscaloosa Alabama (2006)
- Cornelius Bennett Annual Celebrity Golf Tournament Charity for Ronald McDonald House, Point Clear Alabama (2005)

ACADEMIC HONORS, SCHOLARSHIPS, & AWARDS

8/09-5/12	Graduate Research Assistantship (20 hours/week)
8/08-5/09	Graduate Administrative Assistantship (20 hours/week)
8/07-5/08	Graduate Teaching Assistantship (20 hours/week)
12/06	Graduated Magna Cum Laude from the University of Alabama

1/05-12/06	Dean's List, University of Alabama
8/05-12/06	Jacqueline Vincent Davis Scholarship
8/04-12/04	President's List, University of Alabama

SPECIAL SKILLS

- Well versed in Microsoft Word™; Microsoft Office™ Applications; Microsoft Windows Professional/XP™; Microsoft Internet Explorer™; Mozilla Firefox™; IBM SPSS Statistics™ 21.