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Apolipoprotein status and cognitive functioning in adulthood: role of physical health and social network characteristics

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APOLIPOPROTEIN STATUS AND COGNITIVE FUNCTIONING IN ADULTHOOD: ROLE OF PHYSICAL HEALTH AND SOCIAL NETWORK CHARACTERISTICS

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DEDICATION

This dissertation is dedicated to:

my mother, Cheryl, for teaching me to dream big.

my father, Albert, for showing me that hard work pays tenfold.

my brother, Michael, for being an example of perseverance and strength.

my husband, Anthony, for his never ending love.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

This study examined the relationships among cognitive function, physical health, social network characteristics, and apolipoprotein (APOE) genotype in participants from the Louisiana Healthy Aging Study. Prior literature has shown that the ε4 allele of APOE is associated with cognitive deficits (Wisdom, Callahan, & Hawkins, 2009). This study failed to find any relation between APOE genotype (ε4 carrier vs. non-carrier) and cognitive ability after controlling for age and education level. Tests for physical health mediation and social network moderation did not alter the ε4/cognition null results. This finding conflicts with prior research suggesting that physical activity and health modify the association between the ε4 allele and cognition (Deeny et al., 2008; Haan et al., 1999). Prevalence ratings of the ε4 allele significantly decreased with age, where the oldest-old had approximately 50% fewer ε4 carriers than the younger age groups. Results from the current study indicate that the ε4 allele is predictive of mortality rather than cognitive ability.

INTRODUCTION

Successful Aging

Successful aging has become a growing topic of interest during the past few decades. Individuals over the age of 85 comprise the fastest growing segment of the population, totaling approximately 8.9 million (U.S. Administration on Aging, 2001). Current population estimates predict that one out of every five Americans will be over the age of 65 by the year 2030. With this dramatic growth rate, the promotion of healthy and independent living is key to decreasing the financial strain and caregiver burden that is often associated with an older population. Research aimed towards identifying the determinants of healthy aging is designed to help older adults achieve longer, happier, healthier, and self-sufficient lives while simultaneously reducing the strain commonly placed on family and loved ones. Lastly, this research has strong economic and public policy implications, as healthy aging can lead to less dependence on public assistance and economic programs.

To have a vast majority of the population live into their eighth and ninth decade, while maintaining a healthy and active quality of life, is not an easy and straightforward feat. Many factors are linked with the concept of healthy aging and the interrelations among them are still not fully understood. Rowe and Kahn (1997) report that healthy agers are those persons with low risk and lessened diagnosis of infirmity, have intact cognitive function, and who maintain social engagement. Declines in one or more of these areas may bring about the need for assistance. Lessened physical ability may be the most obvious reason for help during later adulthood. Frozard, Metter, and Brandt (1990) report that 80% of persons over age 65 have at least one chronic disease and many of these persons have multiple conditions, such as arthritis, elevated cholesterol, hypertension, and diabetes. These health declines are frequently associated with decrements in cognitive ability (Cook et al., 1989; Emery, 2000). Declines in cognitive ability

may have a biological origin, such as reduced synaptic processing, deficits in neurotransmitter levels, and/or medication side effects. Consequently, the detachment from friends, relatives, and social settings may result from reduced cognitive and physical health. Hill, Wahlin, Winbald, and Bäckman (1995) found that social activity was positively associated with word recall and the ability to use cognitive support correctly (i.e., cues) in adults aged 75-96 years. Unger, McAvay, Bruce, Berkman, and Seeman (1999) found a relationship between social support and self-reported physical health in 850 persons aged 70-79 years. They reported that the number of social ties was negatively correlated with functional decline. Cherry and colleagues (2009) also found that social network characteristics accurately predicted objective and subjective physical health in older adults. From this body of literature, the main aspects of successful aging appear to be highly predictive of one another.

Healthy cognition may be the critical element of successful aging, as deficiencies have potential to lessen social activity and diminish physical health and well-being. Gradual cognitive declines can lower health through a variety of mechanisms: impaired persons may no longer be capable of providing adequate self-care by monitoring their medications, engaging in physical activities, or attending medical appointments. Cognitive impairments may also lead to withdrawal from society due to feelings of embarrassment, shame, or self-consciousness. Current research into cognitive aging centers around two separate but equally important concepts, the preservation of basic capability and the adaptation to inevitable declines. It is true that no form of memory is resistant to age-related declines (Bäckman, Small, Wahlin, and Larsson, 2000), but some persons exhibit more pronounced trajectory deficits compared to normal population estimates. As a result, a logical first step in healthy aging research is to distinguish persons of higher and lower cognitive ability, as this will help investigators isolate individual difference factors that discriminate these two groups.

Apolipoprotein Background

As mentioned, the other two elements of successful aging, physical health and social engagement, are shown to be accurate predictors of cognitive performance, measured via objective and subjective indices (Bazargan and Barbre, 1994; Christensen, Korten, Jorm, Henderson, Scott, & Mackinnon, 1996; Hultsch, Hammer, & Small, 1993). While these factors may act as general indicators of cognition, they cannot give early detection as they only provide insight into current cognitive status. Other variables could act as true predictors if they provide the early information needed to detect those most vulnerable to non-normative declines in cognition. Genes have been suspected to act as one such true predictor because an individuals' genotype is determined from conception and cannot be altered later in life. One gene linked with cognitive functioning during adulthood is the code for apolipoprotein (APOE; Bartrés-Far, 2002; Bondi, Galasko, Salmon, & Thomas, 1999; Corder, Saunders, Strittmatter et al., 1993; Greenwood, Lambert, Sunderl&, & Parasuraman, 2005; Hollingsworth et al., 2006; Mahley & Huang, 2006; Small, Rosnick, Fratiglioni, & Bäckman, 2004). The function of APOE was not originally linked to cognition, but to the transportation and binding of lipoproteins to receptor sites within the nervous system. APOE has also been implicated in both cellular repair and lipid metabolism in the brain and spinal cord (for a review see Mahley, 1988). Further research has shown that APOE facilitates cholesterol movement during the brain's synaptic reconstruction process (Poirier, Hess, May, & Finch, 1991). From this literature, scientists had concluded that the primary function of APOE was not aimed toward cognition, but to lipid transport and cellular repairs in the central nervous system.

The genetic code for APOE lies on chromosome 19 and has three allele variants, which are coded differentially as ε2, ε3, and ε4. The ε3 variant is most common and is found in roughly 74% to 78% of individuals. The ε4 allele is identified in about 15% to 25% of persons

and is associated with deficits in cognition, while the ε2 allele is in 1% to 7% of persons and is correlated with a reduced risk for mortality (Stritmatter & Roses, 1995; Utermann, Langenbeck, Beisegel, & Weber, 1980). All persons possess two APOE alleles, one maternal and paternal, and will have one of six possible genotype variants: ε2ε2; ε2ε3; ε2ε4; ε3ε3; ε3ε4; and ε4ε4. The prevalence rates for each allele differs with race and these reported estimates are based on a predominantly Caucasian population (Crews, Kamboh, Mancilha et al., 1993; Singh, Singh, & Mastana 2002; Singh, Singh, & Mastana, 2006; Stritmatter & Roses, 1995; Ueki, Kawano, Namba et al., 1993; Utermann, Langenbeck, Beisegel, & Weber, 1980).

Research has indicated that possessing one copy of the ε4 allele is linked with cognitive decline among middle-aged and older adults (Bartrés-Far, 2002; Bondi, Galasko, Salmon, & Thomas, 1999; Feskens, Havekes, Kalmijn, Knijff, Launer, & Kromhout, 1994; Flory, Manuck, Ferrell, Ryan, & Muldoon, 2000; Greenwood, Lambert, Sunderland, & Parasuraman, 2005). The allele is also associated with early onset and familial Alzheimer's disease (Hollingsworth et al., 2006; Mahley & Huang, 2006; Saunders, Strittmatter et al., 1993). The effects of the allele are considered to be dose-dependent, where having two copies of the allele is indicative of larger cognitive declines, compared to those with only one ε4 allele, which have smaller but significant decrements. Poirier and colleagues (1995) identified the mechanisms of APOE. These authors report that the ε4 allele is related to dysfunction within the brain's cholinergic system in a dose-dependent manner. This dysfunction is associated with declines in acetylcholine levels in the synapses of the cortex, which is a prominent feature of patients with Alzheimer's disease and other forms of dementia (for a review see Smith, 2002).

Other investigations have linked the ε4 allele with deficits in global memory performance among community dwelling individuals (Christensen et al., 2008; Ercoli, Siddarth, Dunkin, Bramen, & Small, 2003; Packard et al., 2007). Global cognitive performance tends to exhibit

linear age-related declines during later adulthood (Bäckman et al., 2000). One common index of global functioning is the Mini-Mental State Exam (MMSE; Cockrell & Folstein, 1988; Foreman, Fletcher, Mion, & Simon, 1996; McDowell, Kristjansson, Hill, & Hebert, 1977). Packard and colleagues (2007) examined the relationship between APOE status and scores on the MMSE in 5,804 participants who ranged in age from 70 to 82 years. Results indicated a dose-dependent impact of ε4, where carriers with two copies of the allele exhibited greater deficits on the MMSE compared to those with one or no copies. Results from additional measures including the Stroop task, Letter-Digit coding, and picture/word recall also revealed a dose-dependent association. Packard et al., subsequently reported that declines on the MMSE were greater in ε4 carriers and the conversion to Alzheimer's disease was 2.48 times greater in those with the ε4 allele. This pattern was reproduced when the MMSE performance range was restricted to those participants scoring above the suspected-dementia range (26-30 points). Christensen and colleagues (2008) assessed MMSE performance over a four-year period in 2,021 persons ranging in age from 20-69. They found that performance on the MMSE was significantly worse for ε4 homozygotes (two ε4 alleles) compared to heterozygotes (one ε4 allele) or non-carriers. A cross-sectional analysis determined that the effects of the ε4 allele were only found in persons aged 65-69, after controlling for injury and education history. Christensen et al., concluded that the negative impact of ε4 may not appear until later adulthood, at or around the age of 65. Ercoli, Siddarth, Dunkin, Bramen, and Small (2003) examined the individual subcomponents of the MMSE in 54 individuals (23 carriers and 31 non-carriers), ranging in age from 50-84 years. Results showed that the MMSE total score and the MMSE individual item scores, including visuo-spatial and naming performance, were lower in ε4 carriers. Other studies have also incorporated MMSE score, but have used it as an indicator of dementia, where persons who score in the probable dementia range (less than 25) are not included in analyses (Bartrés-Far, Junque, Moral, Lopez-

Alomar, Sanchez-Aldeguer, & Clemente, 2000; Jorm, Mather, Butterworth, Antsey, Christensen, & Easteal, 2007; Nilsson, Adolfsson, Bäckman, Cruts, Nyberg, Small, & Van Broeckoven, 2006; Swan, Lessov-Schlaggar, Carmelli, Schellenberg, & Rue, 2005).

Specific processes, such as episodic memory and executive functioning performance, have also exhibited ε4-related deficits. Swan, Lessov-Schlaggar, Carmelli, Schellenberg, and Rue (2005) reported deficits in executive functioning in a community-dwelling, older adult sample. All participants were over the age of 60 and were free of cognitive impairment, as all scored above 23 on the MMSE. Results showed that both men and women exhibited ε4-related deficits on two measures of executive function, the Trail Making and Color-Word tasks. The effect was more pronounced in men, who also had greater ε4-related declines in episodic recall, in contrast to females. Swan et al., concluded the possibility of a gender-specific impact of ε4. Nilsson and colleagues (2006) found ε4-related decrements in episodic memory performance in 1,897 individuals over 70 years of age. Episodic memory was indexed through semantic recall. It should be mentioned that these authors eliminated participants who dropped three or more points on the MMSE between Wave 1 and Wave 2 assessments and the link between MMSE and ε4 was not tested. Small et al., (1999) found and increase in self-reported cognitive complaints and lower memory self-appraisal among middle-aged and older adults with the ε4 allele. Flory, Manuck Ferrell, Ryan & Muldoon (2000) found ε4 linked declines in tasks of recall and recognition-based memory assessments in participants aged 24-60 years. Wisdom, Callahan, and Hawkins (2009) replicated theses results via a large meta-analysis testing 77 studies of APOE genotype and cognition.

There is a subset of research that conflicts with these studies just presented and has failed to demonstrate a significant relation between ε4 and cognitive functioning. Small, Rosnick, Fratiglioni, and Bäckman (2004) carried out a large-scale, meta-analysis of current APOE

literature. The authors analyzed a series of 38 studies with 5,230 ε4 carriers and 15,535 non-carriers, and tested the association between the ε4 allele and various measures of cognition. Their results demonstrated that the ε4 allele did not predict performance on measures of verbal ability, processing speed, attention span, and visuo-spatial memory. Small et al., further stated that the connection between ε4 and global cognitive performance, episodic memory, and executive functioning is minuscule. Collie, Maruff, and Currie (2002) found no ε4 prevalence differences between cognitively impaired patients and age-matched controls. Flory, Manuck Ferrell, Ryan & Muldoon (2000) had no connection between ε4 allele status and attention span and processing speed. Jorn, Butterworth, Anstey, Christensen, and Eastel (2007) examined the influence of the ε4 allele in an age-stratified sample of 6,560 participants (aged 20-64 years). They reported no negative impact of the ε4 allele on measures of episodic memory, working memory, mental speed, reaction time, and vocabulary. From these inconsistencies in the current literature, debate still exists as to whether the ε4 allele could negatively influence global and specific memory processes.

The aforementioned studies have all tested the link between ε4 and cognitive ability, but the following have investigated the association with overall physical health, functional ability, and global well-being (Bernstein, Costanza, James, Morris, Cambien, Raoux, and Morabia, 2002; Blazer, Fillenbaum, & Burchett, 2001; Deeny et al., 2008; Elosua, et al., 2004; Haan, Shermanski, Jagust, Manolio, & Kuller, 1999; Kuller et al., 1998; Packard et al., 2007; Podewils, Guallar, Kuller, Fried, Lopez, Carlson, & Lyketsos, 2005; Zhang, et al., 2008). Blazer and colleagues (2001) reported that the ε4 allele was related to functional decline in both African American and Caucasian women. Across both races, ε4 carriers possessed lower scores on physical performance measures and activities of daily living. Next, results from the Framingham Heart Study found that diabetic men with the ε4 allele had lower levels of cardiovascular

function, while diabetic ε2 carriers had higher levels (Elosua et al., 2004). Packard et al., (2007) found deficits in physical functioning and decreased engagement in instrumental activities of daily living among ε4 carriers aged 70-82 years.

Bernstein, Costanza, James, Morris, Cambien, Raoux, and Morabia, (2002) proposed that excellent physical health and continued exercise may reduce lipid transport in ε4 carriers, since these persons are genetically predisposed to increased lipid levels in their cardiovascular system. Therefore, any reduction in lipid transport is suspected to lower risk for cardiovascular disease, and this effect should be limited to ε4 carriers. Haan et al. (1999) were among the first to test possible modifying effects of APOE genotype on measures of cardiovascular disease, diabetes mellitus, and cognitive function (via MMSE and Digit Symbol substitution). Haan and colleagues sampled a total of 5888 individuals that were over 65 years of age. Their sampled population was 57% female and 97% Caucasian. Participants were tested repeatedly over a 7-year time period with various physical and cognitive assessments. Results indicated when linked with decreased cardiovascular function (e.g. arteriosclerosis, peripheral vascular disease, and diabetes mellitus), that the ε4 genotype provided the greatest association with cognitive decline. Those individuals with at least one copy of the ε4 allele and low ankle-arm blood pressure had cognitive declines that were 8.43 times greater than those with neither characteristic. On a similar note, ε4 carriers with elevated carotid artery thickness (e.g. arteriosclerosis) had cognitive declines 3.9 times greater than non-carriers. Participants with a history of diabetes and at least one copy of the ε4 allele demonstrated cognitive declines 1.67 times greater than those without the allele. Haan and colleagues determined that ε4 carriers could be labeled as a high-risk group, as these persons were more likely to exhibit cognitive deficits over time. Furthermore, the authors also conclude that the prevention of arteriosclerosis and other forms of cardiovascular disease may reduce one's risk for dementia.

A more recent investigation of APOE genotype and physical function was conducted by Deeny et al., (2008). These authors examined if one's physical activity levels modified the relationship between ε4 and cognitive performance, in particular, working memory ability. Working memory was measured via the Sternberg task, where fast reaction times are indicative of better ability. Physical activity levels were measured using the Yale Physical Activity Survey (YPAS), a self-report measure of everyday activity. Deeny and colleagues used regression analyses to determine if the ε4 allele was predictive of cognitive ability after controlling for age, gender, and education level. Results produced a significant interaction of YPAS score with ε4 genotype, where ε4 carriers who engaged in physical activity and exercise had faster reaction times and better performance on measures of working memory, where non-carriers did not exhibit such a benefit. In sum, these results were similar to those reported by Haan et al. (1999) which suggest that physical health and activity modify the relation between the ε4 allele and specific measures of cognition.

In sum, identifying the determinants of successful aging has become a challenge for current researchers. Rowe and Kahn (1997) stated that the primary components to healthy aging are the maintenance of physical function, preservation of cognitive ability, and continued involvement in social activities. All three of these variables are considered to be predictive of one another (Bazargan & Barbre, 1994; Christensen, Korten, Jorm, Henderson, Scott, & Mackinnon, 1996; Hultsch et al., 1993). Other identifiers, such as genotype, may give earlier insight into prospective declines that may inevitably block healthy aging. A strong subset of literature has implicated the APOE genotype as an indicator of cognitive function, where the ε4 allele is associated with mild cognitive impairment, dementia, and Alzheimer's disease in older adults (Bartrés-Far, 2002; Bondi, Galasko, Salmon, & Thomas, 1999; Feskens, Havekes, Kalmijn, Knijff, Launer, & Kromhout, 1994; Flory, Manuck, Ferrell, Ryan, & Muldoon, 2000;

Greenwood, Lambert, Sunderland, & Parasuraman, 2005; Hollingsworth et al., 2006; Mahley & Huang, 2006; Saunders, Strittmatter et al., 1993 Swan, Lessov-Schlaggar, Carmelli, Schellenberg, & Rue, 2005). This allele is hypothesized to impact cognitive ability by producing deficiencies in acetylcholine levels (Poirier et al., 1995). Specific processes, such as global cognitive performance, executive functioning, and episodic memory have been associated with the ε4 allele (Wisdom, Callahan, & Hawkins, 2009). While other processes, such as verbal memory, attention span, visuo-spatial memory, and speed of processing are suspected to have no relation with ε4 status (Small, Rosnick, Fratiglioni, & Bäckman, 2004). Cross-sectional analysis has shown that the association between ε4 and cognitive function may not be apparent until age 65 or older (Christensen et al., 2008).

Recent literature also suggested that the ε4 allele may produce deficits in physical health and well-being (Deeny et al., 2008; Elosua, et al., 2004; Haan et al., 1999; Kuller et al., 1998; Packard et al., 2007; Podewils, Guallar, Kuller, Fried, Lopez, Carlson, & Lyketsos, 2005; Zhang et al., 2008). ε4 carriers are considered predisposed to elevated lipid levels, which may induce cardiovascular decline through arteriosclerosis and peripheral vascular disease (Bernstein, Costanza, James, Morris, Cambien, Raoux, & Morabia, 2002). Few studies to date have tested the modulating influence of physical health on the relationship between ε4 and cognitive ability. Haan and colleagues (1999) associate lower physical health with deficits in cognitive performance, indexed by the modified MMSE and Digit-Substitution task. Deeny et al., (2008) reported that high levels of physical activity and exercise elevated working memory performance for ε4 individuals, while a benefit was not found in non-carriers. Conflicting research has also shown that the benefits of exercise are reduced in ε4 carriers (Zhang et al., 2008).

From the studies reviewed, there are several major gaps that should be addressed in future research. The most common issue, restriction of age range, has been a large problem with

the majority of prior investigations. For example, Packard and colleagues (2007) only recruited participants who ranged in age from 70-82 years. Jorn, Butterworth, Anstey, Christensen, and Eastel, (2007) and Christensen et al., (2008) recruited persons that were 20-69 years of age, and failed to examine persons over 70. Swan, Lessov-Schlaggar, Carmelli, Schellenberg, and Rue (2005) do not report the age range of their older adult sample. Samples with a broad age range will permit a researcher to clearly understand if and when ε4-related deficits appear. Most cognitive declines do not begin until midlife (Bäckman et al., 2000) and a lifespan approach would allow researchers to identify differences in decline trajectories among ε4 carriers and non-carriers. A second limitation is that a large portion of prior research has only used participants who meet stringent cognitive and physical standards. Therefore, results from these past investigations can only generalize to high functioning persons. It is understood that healthy persons are more likely to volunteer for research programs, however the deliberate elimination of participants based on health criteria defeats the primary goal of healthy aging research: to differentiate lower functioning persons from higher ones in order to isolate variables associated with greater health and well-being. There is a significant group of studies which use the MMSE as a diagnostic tool, where only persons who score above 23, 24, or 25 are included in their study (Bartrés-Far, Junque, Moral, Lopez-Alomar, Sanchez-Aldeguer, & Clemente, 2000; Jorm, Mather, Butterworth, Antsey, Christensen, & Easteal, 2007; Nilsson, Adolfsson, Bäckman, Cruts, Nyberg, Small, & Van Broeckoven, 2006; Swan, Lessov-Schlaggar, Carmelli, Schellenberg, & Rue, 2005). The use of cutoff scores does have a purpose, as participants who score in dementia range may not possess the capacity or stamina required to perform higher-level cognitive tasks. To resolve this issue, future studies should design two distinct analyses to test for ε4-related changes in cognition: the first series should include all participants and test for changes in global cognitive performance, while the second analysis would utilize only those

capable of completing higher-level tasks. Use of this design will allow researchers to draw conclusions that can generalize to a large-scale population. The last significant shortfall is the failure to evaluate other age-related factors that may modify the link between ε4 and cognitive functioning. Individual difference factors, such as physical health and social engagement, are both associated with cognitive performance in older adults. Together, these factors are considered the primary components of successful aging (Rowe & Kahn, 1997) and should be measured across all participants. To date, Haan et al. (1999) and Deeny et al. (2008) are among the few studies that suggest that physical health and exercise may interact with the relationship between ε4 status and cognition. A large-scale investigation into the determinants of healthy aging would be most equipped to further explore this issue, as these studies assess various measures of physical health, cognitive functioning, and social engagement (Poon et al., 2007).

Conceptual Framework and Hypotheses

This investigation provides an examination into the relationships among cognitive function, APOE genotype, physical health, and social involvement in an adult population. The purpose of the present research is to present new evidence confirming the link between the ε4 allele and deficits in cognition, specifically in measures of global functioning, primary, and working memory. These measures of cognition were chosen because they exhibit well-documented age-related declines, which are linked with the ε4 allele (Christensen et al., 2008; Ercoli, Siddarth, Dunkin, Bramen, & Small, 2003; Packard et al., 2007; Wisdom, Callahan, & Hawkins 2009). The MMSE is employed as the measure of global cognitive performance because it has been used in prior studies and will permit cross-study comparisons. Forward and backward digit spans are used as measures of primary and working memory respectively. The Size Judgment Span task is used as an additional measure of working memory, since ε4-related deficits have yet to be examined with this tool. Previous ε4 literature has utilized a variety of

working memory tasks, including the Sternberg (Deeny et al., 2008) and the Digit Symbol Substitution (Haan et al., 1999), and have reported consistent ε4-related deficits. The construct of working memory is complex, consequently the addition of a new working memory measure will help detect task-specific differences. Next, physical health is tested using both objective and self-report measures to ensure an accurate assessment of current health status. Social network characteristics are measured by a series of likert scale questions aimed to assess three distinct elements: social engagement, involvement in everyday social activities, and satisfaction with support received.

This study offers a novel contribution to the existing literature by addressing the aforementioned limitations. First, this investigation utilizes a general adult population of persons aged 21-103 years. Taking a broad lifespan approach is necessary to identify any age-related differences in cognition, health, social networks, and genotype status. Secondly, this study includes individuals who score in the mild cognitive impairment or probable-dementia range on the MMSE. Those who score below 25 on the MMSE are included in the evaluation of global cognitive function, while only those with scores above 25 complete primary and working memory measures. The inclusion of lower functioning persons is vital to conducting ecologically valid research into the determinants of healthy aging. Lastly, this study is among the first to test individual difference factors that may modify the relationship between ε4 and cognitive performance. In total, this study has three main hypotheses:

1. It is hypothesized that ε4 carriers will have lower scores on cognitive measures of global functioning, primary, and working memory compared to non-ε4 carriers.

Justification for this hypothesis is evidenced in the large subset of prior investigations that have reported a significant link between the ε4 allele and declines in cognition (Christensen et al., 2008; Ercoli, Siddarth, Dunkin, Bramen, & Small, 2003; Packard et al., 2007; Wisdom,

Callahan, & Hawkins, 2009). To directly test this hypothesis, a series of regression and correlation analyses are utilized to measure the relationship between the ε4 allele and cognition after controlling for two influential variables, age and education.

2. It is hypothesized that physical health will <u>mediate</u> the link between ε4 status and cognition, as indexed by measures of global performance, primary, and working memory.

Mediation occurs when a variable explains the relationship between a predictor (e.g. ε4 status) and an outcome variable (e.g. cognition). The hypothesized relationship is depicted in Figure 1, where it is predicted that physical health will mediate the relationship between ε4 status and cognition. Justification for this hypothesis is evidenced in the large body of research reporting a strong relationship between the ε4 allele and cognitive ability (Figure 1; Path C). Additionally, recent investigations implicate the ε4 allele with reduced physical health (Deeny et al., 2008; Elosua, et al., 2004; Haan et al., 1999). The ε4 allele is suspected to increase lipid transport, which produces an elevated risk for cardiovascular disorders, such as arteriosclerosis and peripheral vascular disease (Bernstein, Costanza, James, Morris, Cambien, Raoux, & Morabia, 2002). Therefore, it is predicted that there will be a relationship between ε4 status and physical functioning, where ε4 carriers will have lower physical health scores compared to non-carriers (Figure 1, Path A). Lastly, Rowe and Kahn (1997) have reported a positive relationship between physical health and cognitive performance (Figure 1; Path B).

From these reports, a causal chain is predicted. It is hypothesized that the ε4 allele will be associated with reduced physical health (Path A), indexed via subjective and objective measurement tools. It is also hypothesized that the physical decrements associated with the ε4 allele will in turn produce cognitive deficits (Path B). Therefore the relationship between the allele and cognition is mediated (e.g. caused) by physical health. This study tests for potential mediation using statistical regression procedures modeled after Baron and Kenny (1986). While

causality cannot be definitively proven, as this study is a test of genetic relationships, appropriate statistic procedures are applied to test for potential causality.

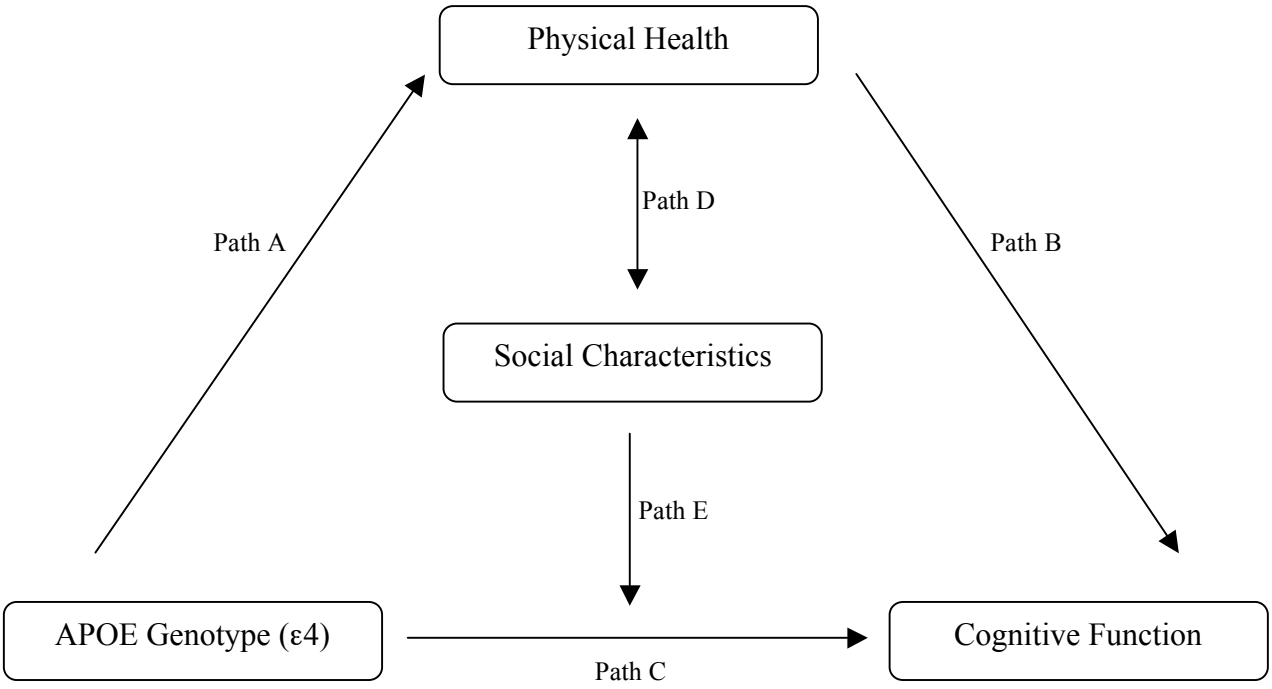

Figure 1. Hypothetical Example of Physical Health Mediation and Social Characteristics Moderation in Relation to Apolipoprotein ε4 Status and Cognitive Function

3. It is hypothesized that social network characteristics <u>moderate</u> the link between ε4 status and cognition, as indexed by measures of global performance, primary, and working memory.

Moderation occurs when a variable alters the strength of the relationship between a predictor (e.g. ε4 status) and an outcome variable (e.g. cognition). It is a test of interaction effects and does not imply causality. Justification for this hypothesis lies in the literature reporting a strong association among social support, health, and cognition (Cherry et al., 2009; Hill et al., 1995; Rowe & Kahn 1997; Unger, McAvay, Bruce, Berkman, & Seeman, 1999). Cherry et al., have shown that social network characteristics are strong predictors of self-report and objective physical health status, where increased social activities are correlated with

increased health. The positive correlation between social networks characteristics and physical health is evidenced in Figure 1, Path D.

Prior research has failed to test the relationship between the ε4 allele and social network characteristics. It is predicted that the ε4 allele will be associated with reduced social network characteristics. Subsequently, the association with the ε4 allele will interact (e.g. change) with cognitive performance (Path E). A significant interaction is predicted if physical health proves to be a strong mediator (*hypothesis ii*), as the two variables (health and social networks) are highly correlated (Path D). The opposite interaction pattern is predicted for non-carriers, who should possess increased social network characteristics and better cognitive performance. This study tests for social network moderation effects using statistical regression procedures modeled after Baron and Kenny (1986).

METHODOLOGY

Participants

A total of 869 participants, who range in age from 21 to 103 years were sampled from the Louisiana Healthy Aging Study (LHAS) and the data from these individuals were used in the current investigation. The LHAS is a multidisciplinary study of the oldest-old individuals. The primary goal of the LHAS is to use physiological and psychological measures to determine the features associated with successful aging in the Louisiana population. This project is carried out in collaboration with behavioral and medical researchers from Louisiana State University (LSU)-Baton Rouge, LSU Health Sciences Center-New Orleans, Pennington Biomedical Research Center (PBRC), the University of Pittsburgh, and the University of Alabama at Birmingham.

Procedure

LHAS participants live within a 40-mile radius of Baton Rouge (surrounding 8 parishes) and were recruited to participate as follows. Participants were randomly sampled from voter registration lists and the Center for Medicare and Medicaid Services files by personnel in the School of Public Health at the LSU Health Sciences Center in New Orleans. Information about the LHAS was mailed out to potential participants with a self-addressed, stamped envelope and postcard to return to indicate their interest in participating. Those who returned their postcards to the PBRC were called and scheduled for a pre-visit where informed consent was obtained. For those over age 70, this initial information was solicited in a home visit. Nurses from the PBRC, as well as faculty and graduate students from the Department of Psychology of LSU-Baton Rouge, collected physiological and psychological measures from each LHAS participant. Following this preliminary assessment, a day-long testing session was held at the PBRC where participants were scheduled to complete multiple measures of physical and cognitive ability (Table 1). Participants were excluded from this subsequent cognitive testing session if they had

signs of neurological impairment or history of a stroke. All participants were paid at least $150 for their voluntary participation.

TABLE 1. Sample LHAS Participant Schedule at the Pennington Biomedical Research Center

TIME	SCHEDULED TEST
7:00am	Electrocardiogram
7:30am	Blood Draws
7:45am	Resting Metabolic Rate
8:00am	Cold Pressor Test
8:15am	Breakfast
8:45am	Bone Density (DEXA) Scan
9:30am	Physical Exam
10:00am	Pulmonary Function Test
11:00am	Cognitive Function Assessment
12:00pm	Lunch
12:30pm	Objective Physical Health Test

Quality Control Assurance

Data collection for the LHAS began in 2002 and was completed in 2008. Currently there is a longitudinal assessment underway. In the midst of the initial data collection process, hurricanes Katrina and Rita (HKR) impacted the Baton Rouge area in the fall of 2005. In response to these major disasters, an investigation was performed to assess the storm's impact on LHAS participants (Cherry, Galea, & Silva, 2008; Cherry et al., 2009). A portion of LHAS participants who completed testing within 6 months prior to HKR landfall were recruited to participate in a post-HKR assessment. Only those individuals recently tested were selected to participate in order to control for any age-related differences that may occur over time. The same cognitive and health measures collected prior to hurricane landfall were re-administered within 6 months post-HKR landfall. The data from post-HKR were compared directly against pre-HKR performance. The direct analysis of pre- and post-HKR data produced minimal to no differences in cognitive (Mini-Mental State Exam) and health measures (SF-36 subscales), which suggest a limited impact of HKR on the larger LHAS population. These results provided quality

control assurance for the LHAS and therefore data from all 869 participants is used in this investigation.

Overview of Measures

Apolipoprotein Genotype. Blood collection and genotyping procedures were modeled after those outlined in the Georgia Centenarian Study (Poon et al., 2007). The LHAS established the cell, blood, and DNA laboratories necessary to carry out DNA immortalization and APOE genotyping procedures. Blood samples required for analysis were collected from participants in their residences or at the PBRC by an LHAS licensed nurse or geriatric phlebotomist. Blood collection was done in a fasting state. LHAS staff used standard collection needles and winged "butterfly" collection sets.

Samples were immediately transported to the PBRC to ensure they were processed in a sufficient period of time. Blood was processed within a 4-hour time period to guarantee there was no blood component deterioration (Johnson, Houston, Fischer, Poon, & Martin, 1995). Samples were stored at -80˚C until further genotype analysis. DNA immortalization procedures were carried out due to the short life expectancies of the oldest-old participants. This procedure permits future analysis of cell structure and DNA without having to redraw blood from a participant. Researchers at the LSU-Health Sciences Center used the blood samples to determine the APOE genotype for all LHAS participants. Each individual was identified as having one of six possible genotypes ε2 /ε2, ε2 /ε3, ε2/ε4, ε3 /ε3, ε3 /ε4, or ε4/ε4. For data analysis purposes, participants were placed into two groups, ε4 carriers and non-carriers. Double and single ε4 carriers were combined due to the fact that there were only 11 ε4/ε4 carriers. This would have created a cell size less than 15% compared to the other comparison groups, single ε4 carriers (N = 167) and non-carriers (N = 686).

Mini Mental State Exam. The Mini Mental State Exam (MMSE) measured the current cognitive status of all LHAS participants (Appendix A; Folstein, Folstein, & McHugh, 1975). The MMSE is the most widely used cognitive screening tool and is effective in the diagnosis of dementia (Cockrell & Folstein, 1988; Foreman, Fletcher, Mion, & Simon, 1996; McDowell, Kristjansson, Hill, & Hebert, 1977). The MMSE has a minimum score of 0 and a maximum of 30. A diagnosis of dementia may be suspected if an individual earns a score lower than 25 (Folstein, Folstein, & McHugh, 1975; Holsinger, Deveau, Boustani, & Williams, 2007*)*.

The psychometric properties of the MMSE have been well-documented in the literature. Reliability measures, such as internal consistency, were found to be excellent (alpha = 0.96) in normal, dementia, and delirium participants (Foreman, 1987). Albert and Cohen (1992) also found excellent internal consistency (alpha = 0.90) in their population of elderly individuals with cognitive impairment. Test-retest reliability has been another strong element of the MMSE. Tombaugh and McIntyre (1992) conducted a psychometric review and reported that 30 of 24 MMSE investigations had excellent test-retest reliability scores ($r > 0.75$). More recent reports have suggested that repeated administration, about 3 months apart, might increase the accuracy of the MMSE in detecting cognitive impairment (Helkala et al., 2002). Concordance correlations measuring inter-rater reliability have ranged from adequate ($r = 0.69$) to excellent ($r > 0.87$) across students, health professionals, and psychologists (Fabrigoule, Lechevallier, Cransborn, Dartigues, & Orgogozo, 2003; Molloy & Standish, 1997; O'Connor, Pollitt, Hyde, Fellows, Miller, Brooke, & Reiss, 1989).

Although the MMSE has commonly been viewed as a unidimensional screening tool, construct validity tests report that the MMSE can accurately assess distinct areas of cognition such as concentration, language, orientation, memory, and attention (Jones & Gallo, 2000). The MMSE is divided into seven separate cognitive domains, orientation to time and place,

registration of words, attention and calculation, recall of words, verbal language and direction comprehension, and visual construction. Each of these provides unique information and in composition form a measure of global cognitive performance. One advantage of using the MMSE is that one can use both domain and composite scores to measure cognitive performance within any population. Recent evidence has shown that individual questions and domains of the MMSE can adequately predict cognitive decline in the oldest-old (Kliegel & Sliwinski, 2004).

Episodic memory, physical health, and ambulatory levels have all been associated with MMSE scores. Cherry, Hawley, Jackson, Volaufova, Su, and Jazwinksi (2008) documented that the MMSE was highly predictive of episodic recall performance in the oldest-old. Wahlin and colleagues (1992) reported similar findings in an episodic memory task in a younger, but still older-adult population. Physical health indices, such as activities of daily living, functional dependence, and cardiovascular function, were all associated with MMSE in elderly patients with and without dementia (Aguero-Torres, Fratiglioni, Guo, Viitanen, von Strauss, & Winblad, 1998; Matsueda & Ishii, 2000; Pettigrew, Thomas, Howard, Veltkamp, & Toole, 2000).

The MMSE will also be employed for replication purposes. A review of the literature illustrates the use of MMSE as a dependent variable during ε4 investigations of current cognitive function (Ercoli, Siddarth, Dunkin, Bramen, & Small, 2003; Christensen et al., 2008; Hestad, Kveberg, & Engedal, 2005; Hollingsworth, Hamshere, Moskvina et al., 2006; Packard et al., 2007; Poirier et al., 1995; Swan, Lessov-Schlagger, Carmelli, Schellenberg, & La Rue, 2005). The continued use of MMSE as a dependent measure will allow for comparisons to these prior investigations. Results from previous reports have suggested that the ε4 allele may exert domain-specific effects, which can be further explored through continued use of MMSE. Flory and colleagues (2002) reported that persons with the ε4 allele had poorer performance on tests of verbal learning and memory, compared to age-matched controls. Small et al., (1995)

documented those with the ε4 allele had worse performance on measures of verbal recall. Utilization of the MMSE will allow the current project to examine overall cognitive performance by analyzing the MMSE's cumulative score. To bridge gaps in the current literature, use of the MMSE will allow analysis of the subcomponents to identify performance differences between ε4 carriers and non-carriers. To date, most prior investigations examining cognition and ε4 have failed to examine domain-specific effects of the MMSE. This project examines the recall domain (MMSE-R) because previous research has found ε4-related deficits in episodic recall (Wisdom, Callahan, & Hawkins, 2009).

In sum, the MMSE is a strong assessment tool that is extensively utilized in older adult populations. The psychometric properties of the MMSE make it an effective measure for cognitive performance. The ability to use cumulative and domain scores allow researchers to obtain both global and specific measures from one instrument. MMSE scores have been reported in previous genotype investigations and continued use will permit the cross-study comparisons needed to bridge gaps in the literature. Lastly, minor limitations of the MMSE will be addressed during statistical procedures. Education status tends to correlate highly with MMSE and therefore education level will be controlled during analysis (Crum, Anthony, Bassett, & Folstein, 1993). Ceiling effects on the MMSE are found in younger populations and as a result, other tests will be administered to provide extra cognitive performance measures.

Vocabulary. All LHAS participants completed a verbal test adapted from the short form of the WAIS-R Vocabulary subtest, (Jastak & Jastak, 1964; Wechsler, 1981) as an indicator of verbal intelligence (Appendix B). Participants were asked to give the definition for 20 words, such as "breakfast", "edifice", and "travesty". Testing for this task is terminated when a participant consecutively fails 10 items. Vocabulary scores are used in this study because most prior reports failed to test for a link between the ε4 allele and this cognitive domain.

Scoring for the vocabulary task is available in Wechsler's WAIS Manual (Wechsler, 1981). The definition provided for each word is given a score of 2, 1, or 0 based on available scoring criteria. Two-point responses are not only correct, but are also stated in appropriate and understandable language. For example, 2-point answers in response to *breakfast* would be, "the first meal of the day", "to dine in the morning", or "meal after waking or rising". One-point answers are considered scorable and somewhat correct, but contain an element of vagueness in their description. Acceptable 1-point answers for breakfast may be, "a meal", "something you eat", or "bacon and eggs". Related nouns, verbs, or adjectives also receive 1 point. Zero-point answers are linked with a complete disconnect from the correct definition. For example, "break something" or "broken" would be marked as incorrect and receive no points. Based on these scoring criteria, the maximum score on the WAIS vocabulary test would be a 40.

Size Judgment Span. A subset of individuals who score above 25 on the MMSE were given the Size Judgment Span task (SJS; Cherry, Elliott, & Reese, 2007), a measure of non-verbal working memory (Appendix C). The SJS was designed for use with persons of varied educational and occupational backgrounds. The psychometric information for the SJS tasks shows excellent test-retest reliability (Cherry & Park, 1993). Participants are provided with the names of everyday objects and animals and must repeat the list items aloud, in order of their physical size from the smallest to the largest item. For example, a participant may hear the list "strawberry, ambulance, tooth" and the correct answer would be "tooth, strawberry, ambulance". The list length for the SJS task begins with two items and increases by one item every three trials, with a maximum list length of 8 items. Participants continued to the next list length if they were correct on 1 of the 3 trials for the current list length. Testing was terminated when a participant failed all three lists at one list length level or reached the maximum list length of 8. The overall span score was determined by counting the number of list lengths for correct recall

on at least 2 of 3 lists, then adding an additional half-point for a list length in which one list was correctly recalled. For instance, if a participant correctly completed all lists at list lengths 2, 3, and 4, and only 1 of the lists at list length 5, they would receive a score of 4.5.

The processing demands of the SJS task allow for a secondary scoring method (Elliott, Cherry, Silva, Smitherman, Jazwinski, Yu, & Voluafova, 2009). These authors propose that during longer list lengths, participants initially encode all items as presented, then engage in a deliberate reordering all of the items before verbal recall. This is in contrast to simultaneous reordering, where one reorders list items as they are presented. Therefore, order effects may provide additional information compared to the overall span score. The presence of order effects can be measured by first generating a serial position score for each participant. To calculate this a serial position score, credit is given to each item recalled in a list, regardless of whether or not the entire list was correctly recalled. This allows for a final SJS proportion (SJS-PROP) score to be determined by dividing the number of correctly recalled items by the total number of items available in that specific list length.

In sum, the use of the SJS task addresses the issue of ceiling effects frequently found with the MMSE. The SJS task requires additional processing demands not required by the MMSE, and consequently performance variability is increased in younger adults. Furthermore, two scoring methods will permit an in depth analysis of SJS performance in relation to ε4 status.

Weschler Digit Span. Measures for the forward and backward digit spans were adapted from the Weschler Digit Span task (Weschler, 1981). These tasks were given to a subset of LHAS participants who scored 25 or higher on the MMSE. For each task, an experimenter presented a series of digits in one-second intervals. The Forward Digit Span (FDS) required the use of only primary memory, thus participants simply had to repeat the digits (Appendix D). For example, a participant may hear the numbers “6, 5, 2”, and the correct answer would be “6, 5, 2”.

The Backward Digit Span (BDS) was used as a measure of working memory, because participants were asked to recall the digits in reverse order (Appendix D). For instance, a participant may hear "9, 3, 7", and the correct answer would be "7, 3, 9". For both tasks, the length of the digit sequence was increased by one until the participant consecutively failed two trials of the same length or reached the maximum 8-digit sequence. A total digit span score was calculating by adding the number of perfect trials at each digit sequence, while one half-point was given to correctly recalling 1 of 2 trials at a specific sequence length.

36-Item Short Form. The 36-Item Short Form (SF-36; Appendix E) has been used in over 2000 publications as a general indicator of overall health and well-being in various adult populations (Ware & Sherbourne, 1992; Ware, Snow, Kosinski, & Gandek, 1993). It was originally developed for use in the Medical Outcomes Study, which required a physical and mental health measure for a large-scale, population-based study. The SF-36 is designed to achieve three primary goals: to make health generalizations about both single cases and large populations; to predict possible health outcomes from an individuals' quality of life; and to use the 8 distinct constructs of the SF-36 to develop interventions to improve health and well-being in adults (Möller, Smit, & Petr, 2005).

The SF-36 is a self-report questionnaire that measures 8 health constructs (Hays, Sherbourne, & Mazel, 1993; Garratt, Ruta, Abdalla, Buckingham, & Russell, 1993). 1) The *physical functioning* construct indicates how a participant's quality of life is influenced by their perception of their physical health. It determines how capable an individual is at doing daily activities, such as running, lifting heavy objects, walking, and stooping/ kneeling. 2) The *physical role limitation* provides an assessment of the limits placed on daily activities by ones current health. These first two indicators provide the most accurate measure of a participants' current physical health. 3) The *emotional role limitation* is responsible for measuring the limits

placed on daily activities by ones current emotional status, such as feeling nervous, depressed, or anxious. 4) *Social functioning* refers to the limits placed on social activities, such as visiting friends or neighbors. 5) The *bodily pain* index provides an indication to what extend pain interferes with their daily activities, such as work, home, or social obligations. 6) The *mental health* measure looks at how often a participant has felt nervous, anxious, tired, or worn out within the past month. 7) A participant's *vitality* is a measure of how often a participant has felt happy, full of pep, tired, full of pep, or worn out within the past month. 8) The *general health* indicator is the participant's perception of how he/she rates her health status at the current time. Each of these individual constructs yields a scoring ranging from 0 (lowest level of functioning) to 100 (highest level of functioning).

Additionally, these 8 constructs contribute to overall mental (MCS) and physical (PCS) health profile scores for each participant. The MCS is calculated from the mental health, emotional role limitation, and social functioning subscales. The PCS is calculated from the physical functioning, physical role limitation: physical health, and bodily pain subscales. The remaining scales, vitality and general health possess correlations with both PSC and MCS components. These two indices are the primary variables used in statistical analysis.

The psychometric properties of the SF-36 have been well documented in publications. Brazier, Harper, Jones, O'Cathain, Thomas, Usherwood, and Westlake (1992) determined the validity and reliability for the SF-36 in almost 2000 participants aged 16-74 years. Excellent reliability for 7 of the 8 domains (all but social functioning) was found, with alpha levels greater than 0.85 and reliability coefficients above 0.75. These authors determined that the SF-36 fulfills their stringent criteria for psychometric analysis. Jenkinson, Wright, and Coulter (1994) evaluated the criterion validity of the SF-36 in 13,046 individuals between the ages of 18 and 64. The internal consistency levels for all 8 domains and PCS/MCS scores were found to be

excellent. Research into use of the SF-36 with special populations has also been conducted. Lyons, Perry, and Littlepage (1994) determined that the instrument was highly suitable for elderly populations. Together, these evaluations suggest that the SF-36 is a well-established and standardized measure of self-reported health and quality of life, and is suitable for use in the LHAS. Both the PCS and MCS scores are used in the current investigation as indices of a participant's current health status.

Objective Health. A measure of objective health was incorporated given that subjective measures, such as the SF-36, may not provide an ample evaluation of health status. Self-report measures usually evaluate a participant's perception of their current health and are often based on complaints and views about dysfunction or decline (König, Jagsch, Kryspin-Exner, & Koriska, 2006). Conversely, objective health indices may tap into the diagnosis of disease, actual functional ability, and/or number of days in the hospital. Data from these variables can help interpret the impact of health on one's daily life and are not influenced by perception. This comparison is not to suggest that subjective measures are unacceptable, but is meant to describe the differences between the two indices and how the use of both subjective and objective measures will provide a better appraisal of health status.

Evidence from the Berlin Aging Study (Baltes & Mayer, 1997), suggests that the relationship between subjective and objective health reports changes during late life (over 70 years). A negative correlation exists between age and objective health reports in later life, where as age decline, so does ones' physical health Subjective reports are commonly considered "age-invariant" and do not have age-related declines (Baltes & Mayer, 1997; Brandtstäder & Greve, 1994; Heckhausen & Schulz, 1995). The current investigation utilizes persons ranging in age from young adulthood to centenarians, thus a subjective measure may not be an ideal tool for

measuring current health status. Consequently, an objective health measure was used in conjunction with scores from the SF-36.

Objective health status for the current study was based on a cumulative index measuring the presence of five chronic conditions: high cholesterol, hypertension, diabetes, arthritis, and heart problems. An LHAS nurse documented these conditions in each participant's medical history. These five conditions were selected in order to provide a broad assessment of health in an adult population. These conditions range in severity from mild/moderate (e.g., high cholesterol and arthritis) to more severe (e.g., heart problems and hypertension). Prior research has shown that the number of chronic conditions systematically increases with age (U.S. Administration on Aging, 2001) and consequently this is seen as an adequate index of health. For each participant, scores of 0 (absence) and 1 (presence) were assigned for each health condition. The individual condition scores were added to create a cumulative, composite index of health, ranging from 0 to 5 points.

Cherry et al., (2009) used a near identical measure of objective health in their previous investigations. These authors created a chronic health index derived from the presence of six chronic conditions, those listed above with the addition of cancer. Data from 364 LHAS participants was used to assess the relationship between current health status and social network characteristics in older adults. Results indicated that aspects of social networks (described below) were predictive of both subjective and objective health status, as measured by the SF-36 and cumulative chronic condition index. Similar results in both predictive models suggest that the objective health measure comparably with SF-36 results.

Social Network Characteristics. All LHAS participants completed a series of four questions (SS-4) regarding their current social networks status. These were administered on the demographic questionnaire that assessed current health and education status (Appendix F). Each

question of the SS-4 is intended to measure the social support dimensions of (1) social engagement, (2) everyday social activities, (3) satisfaction with social support, and (4) availability of social support. The first three items have 4-point likert response options. The fourth item has a dichotomous response format (yes/no). The SS-4 was initially developed by LHAS researchers and has been used to evaluate the social network characteristics of their research population (Cherry et al., 2009).

Social Support Validation Experiment

Rationale. Items from the SS-4 have not been compared to well-validated measures of social support, and consequently the construct validity for each SS-4 dimension has remained relatively unclear. The current investigation did not want to incorporate the SS-4 items without a pilot analysis to determine if the individual domains correlated with other validated measures of social support and social networks. Secondly, this pilot work was conducted to determine if all SS-4 items measured the same unique construct, which would permit one to create a composite SS-4 score. Overall, to rationalize the use of SS-4 in the current study, a scale analysis was performed directly comparing items to other indices of *social engagement* (SS-4/CLUBS*), everyday social activities* (SS-4/HOURS), *satisfaction with social support* (SS-4/SUPPORT), and *availability of social support* (SS-4/CONFIDANT). The primary goal of this pilot study was to pair each SS-4 dimension with a well-validated comparison measure to assess the overall effectiveness of the SS-4 and to create a composite SS-4 index, if deemed necessary.

Participants. This pilot investigation was conducted with 172 students at Louisiana State University during the fall semester of 2008. Recruited participants were enrolled in *Introduction to Psychology* and *Adult Development and Aging* courses. All potential participants were provided with informed consent and asked to voluntarily complete the SS-4 and four additional social support indices (Appendix G). Their responses remained confidential and participants

were given course credit for their participation. The appropriate Institutional Review Board at Louisiana State University approved this project.

Methodology. The *social engagement* dimension (SS-4/CLUBS) was compared against the Personal Engagement Assessment Scale (PEAS; Morgan, Dallosso, & Ebrahim, 1985). This 10-item scale indicated the level of involvement of elderly individuals in a variety of activities, such as using the telephone, going to the library, and engaging in social networks. Higher scores on the PEAS indicate greater levels of social engagement. Morgan and colleagues have reported good psychometric properties for the PEAS (alpha = 0.67). Next, responses on the *everyday social activities* dimension (SS-4/HOURS) were compared against the Frenchay Activities Index (FIA; Holbrook & Skillbeck, 1983). The FIA is a 13-item scale that examines activities done in and outside of one's residence, including shopping, gardening, household maintenance, and daily household chores. Higher levels on the FIA correspond to more social activities. Holbrook and Skillbeck report that the FIA has excellent psychometric properties and has been consistent with other measures of social activities, like the Barthel Activities of Daily Living ($r = 0.66$). The third dimension, *social support satisfaction* (SS-4/SUPPORT), was compared with the Social Support Scale (SSS; Bernal, Maldonado-Molina, & del Rio, 2003). This 7-item scale measures the presence of emotion, instrumental, and interpersonal support. This study utilized the 2-item SSS subscale, which measures ones' overall satisfaction with support received. These two items have likert response options with higher scores indicating increased levels of satisfaction. Bernal and colleagues report high reliability for the subscale items (alpha = 0.89) along with the overall measure (alpha = 0.68). Lastly, *availability of social support* (SS-4/CONFIDANT) was compared with the Duke Social Support Inventory (DSSI; Goodger, Byles, Higgenbotham, & Mishra, 1999). The 11 items on the DSSI were designed to measure the frequency of social

support received within the previous week. Higher summed scores indicate greater availability of social support. Goodger et al., had sound psychometric properties on the DSSI (alpha = 0.80).

Results. Prior to statistical analysis, an undergraduate student coded and recorded the data for each of the 172 participants. The data entry procedure was double-checked to ensure accuracy. The first analyses consisted of a series of correlations to determine the relationship between each SS-4 item and their respective comparison measures (Table 2). The *social engagement* dimension correlated significantly with the PEAS ($r = 0.61$). The *social support satisfaction* item did show a strong relationship with the SSS subscale ($r = 0.46$). In contrast, a relationship was not observed for the *everyday social activities* and the FIA ($r = 0.09$). A marked ceiling effect was observed for this question, as most college students engage in outside activities more than 20 hours per week. It is plausible that older adults, who are out of school and workforce, may provide the response variability needed to find a significant correlation. No analyses were conducted for the final comparison pair (*availability of social support* and DSSI). This was due to the dramatic ceiling effect observed for the *availability of social support*. Only three participants out of 172 reported they did not have a confidant or someone they could talk to about issues of concern. Upon more investigation, this response pattern was replicated in the sampled LHAS population, and therefore this last item is not incorporated in the current study.

A factor analysis was conducted on the first three items of the SS-4 to determine if they loaded on a single factor. If the individual items load on the same factor, SS-4 scores for each LHAS participants will be summed to form one composite score. Principal axis factoring was performed followed by varimax rotation. One factor with an eigenvalue greater than 1 was produced. A factor loading cutoff score of 0.35 was chosen based on Tabachnick and Fidell's (2007) criteria. The factor scores for each SS-4 item are presented in Table 3. *Social engagement* was the only item loading above the cutoff (0.40). *Everyday social activities* and

social support satisfaction produced lower scores of 0.15 and 0.27 respectively. From these results, it was unclear as to if the items from the SS-4 measure a solitary construct.

TABLE 2. Correlation Analysis of SS-4 Items and Comparison Measures (N = 172)
Note: ** represents $p < 0.01$, * represents $p < 0.05$.

SS-4 Item	Comparison Measure	Correlation Coefficient
Social Engagement (Clubs/Organizations)	Personal Engagement Scale	Spearman $r = .613$**
Everyday Social Activities (Hours)	Frenchay Activities Index	Spearman $r = .097$
Social Support Satisfaction (Support Received)	Social Support Scale	Spearman $r = .461$**
Availability of Social Support (Confidant)	Duke Social Support Index	No correlation conducted

An identical factor analysis was performed with the larger LHAS population to determine if this pattern of factor loadings would be replicated. The LHAS has a greater age range (21 to 103 years), and therefore the population is distinctly different from the sampled college students. The LHAS factor analysis produced two factors with eigenvalues greater than 1. Factor loading scores are also available in Table 3. For the first factor, *social engagement* and *social support satisfaction* both loaded above the cutoff score (0.41 and 0.42 respectively). *Everyday social activities* had a factor score of 0.00, however this item did produce a score above the cutoff for the 2nd factor (0.36).

Conclusion. The results from the correlational analyses advocate the use of the SS-4 as a preliminary measure of social network characteristics for the current investigation. These two of the three items (SS-4/CLUBS and SS-4/SUPPORT) significantly correlated to their well-validated comparison measures. These results suggest that these SS-4 items adequately measure constructs related to social support and social networks. In contrast, the SS-4/HOURS item did

not correlate with its selected counterpart measure, and this might have been due to the marked ceiling effects observed in the sampled student population. It is predicted that a general adult population sample would provide a different pattern of results, which would reveal a strong correlation. The remaining item, SS-4/CONFIDANT, is eliminated from subsequent analyses due to the marked ceiling effects in both the student and LHAS samples.

TABLE 3. Summary of Exploratory Factor Analyses Results of Social Network Characteristic Items Using Principle Axis Factoring with Varimax Rotation.

	Factor Loadings (Pilot Study; N = 172)	
SS-4 Item	Factor 1	Factor 2
Social Engagement (Clubs/Organizations)	**.40**	n/a
Everyday Social Activities (Hours)	.15	n/a
Social Support Satisfaction (Support Received)	.27	n/a
	Factor Loadings (LHAS; N = 869)	
SS-4 Item	Factor 1	Factor 2
Social Engagement (Clubs/Organizations)	**.41**	.18
Everyday Social Activities (Hours)	.00	**.36**
Social Support Satisfaction (Support Received)	**.42**	-.16

Secondly, the factor analysis results do not advocate the use of a composite SS-4 measure. From these findings, the SS-4 items must undergo statistical analysis independent of one another. Overall, these items did not load on a single factor and therefore may not measure an individual social support construct. However separately, each item can successfully tap into a respective aspect of social support.

RESULTS

Statistical Procedure

The statistical procedures were separated into two distinct phases, identified as Phase 1 (P_1) and Phase 2 (P_2). All LHAS participants were included in P_1 (n = 869), while P_2 consisted of a subset of participants (n = 369). P_1 individuals completed the MMSE, vocabulary index, SF-36 health measure, chronic cumulative index, and the SS-4. There were no exclusionary criteria in place for the first phase of analysis. The P_2 population includes a subset of those who scored 25 or higher on the MMSE, were free of neurological impairment or stroke, and over the age of 45. These persons completed the FDS, BDS, and SJS (SJS-PROP) measures, in addition to those from P_1. The SJS-PROP scores were only available for 220 participants, out of the 369 sampled.

Statistical analyses for P_1 and P_2 were nearly identical. All dependent measures underwent a series of parametric analyses. First, a series of analyses of variance were conducted to determine age-related differences in memory, health status, and social networks. Secondly, stepwise regressions were used to examine the impact of APOE genotype on memory, health, and social networks after adjusting for age and education status. A series of regression equations were produced to test for physical health mediator effects on memory performance. Moderation effects from social network characteristics were tested using hierarchical multivariate regressions. To manage any missing data, pairwise deletion was selected for all statistical procedures. A significance level of 0.05 was chosen for individual analyses. Tukey post-hoc analyses were used when appropriate. Data was processed using SPSS 16.0 statistical software.

Phase 1 Data Analyses

P_1 Population Characteristics and Age-Related Effects. Differences in age, education, cognitive function, health status, and social networks appear in Table 4. To test for age related differences, participants were systematically placed into one of four age groups: younger (21-44

years; $M = 34.80$), middle (45-64 years; $M = 52.74$), older (65-84 years; $M = 74.47$) and oldest-old (85+ years; $M = 91.82$). To examine these variables, ANOVAs were conducted with age group as a between group factor. Means for all dependent variables are presented by age group and also separated by ε4 genotype (carriers and non-carriers). During descriptive analyses, data were collapsed across genotype because the test of ε4 influence was conducted in subsequent analyses. Education status for the sample was measured using a likert scale response format (1 = less than 7th grade; 2 = 7th - 9th grade; 3 = 10th - 11th grade; 4 = high school diploma or GED equivalent; 5 = partial college or specialized training; 6 = college degree; 7 = graduate degree). A main effect of education status was significant, $F(3, 843) = 25.45$, $p < 0.001$. Post-hoc analysis confirmed that the oldest-old had significantly lower education levels compared to the remaining age groups, which did not differ from one another ($p < 0.001$ for all comparisons).

Given that education level varied across age groups, an ANCOVA was chosen to test for age differences on the MMSE, MMSE-R, and VOCAB scores. Education level was treated as a covariate in the following analyses. A main effect of MMSE was revealed, $F(3, 832) = 93.36$, $p < 0.001$. Pairwise comparisons confirmed that the oldest-old had significantly lower MMSE scores than the other age groups, which did not differ from one another ($p < 0.001$ for all comparisons). Ceiling effects were observed for the MMSE, as most participants' performance was near perfect (Figure 3). Variability in MMSE performance was not observed until age 85.

A main effect of MMSE-R was found, $F(3, 830) = 86.21$, $p < 0.001$. Group comparisons demonstrated a systematic decline of MMSE-R with age, where all four groups differ from one another ($p < 0.05$ for all comparisons). Scores on the vocabulary index demonstrated a main effect, $F(3, 818) = 10.09$, $p < 0.001$. Pairwise comparisons show that the youngest and oldest-old adults' mean VOCAB scores were lower than the other two age groups (middle and older) who did not differ from each other ($p < 0.001$). Full and partial are available in Table 5.

TABLE 4: Phase 1 Population Characteristics. Standard deviations are reported in parentheses.

	Young adults (N = 210)	Middle adults (N = 215)	Older adults (N = 144)	Oldest-old adults (N = 300)
AGE	34.80 (6.4)	52.74 (4.9)	74.47 (5.3)	91.82 (2.8)
EDUCATION	5.30 (1.0)[a]	5.26 (1.1)[a]	5.01 (1.3)[a]	4.39 (1.7)[b]
ε4 STATUS				
ε4	28%[a]	30%[a]	24%[a]	15%[b]
No-ε4	72%[a]	70%[a]	76%[a]	85%[b]
MMSE	*29.43 (1.0)*[a]	*29.10 (1.4)*[a]	*28.58 (1.5)*[a]	*25.30 (4.3)*[b]
ε4	29.42 (.83)	29.31 (.86)	28.44 (1.8)	25.29 (4.8)
No-ε4	29.43 (1.1)	29.02 (1.6)	28.62 (1.5)	25.27 (4.2)
MMSE-R	*2.78 (.50)*[a]	*2.61 (.75)*[b]	*2.29 (.87)*[c]	*1.50 (1.2)*[d]
ε4	2.76 (.47)	2.66 (.66)	2.18 (.90)	1.49 (1.2)
no-ε4	2.79 (.51)	2.59 (.78)	2.33 (.86)	1.52 (1.2)
VOCAB	*22.50 (7.5)*[a]	*24.69 (7.9)*[b]	*24.68 (7.4)*[b]	*19.83 (8.4)*[c]
ε4	22.15 (7.2)	25.44 (7.5)	24.18 (7.7)	21.18 (7.8)
no-ε4	22.67 (7.6)	24.26 (8.0)	24.84 (7.3)	19.68 (8.5)
SF-36 MCS	*50.96 (9.7)*[a]	*51.95 (10.0)*[a]	*56.48 (.69)*[b]	*56.54 (7.5)*[b]
ε4	52.41 (8.6)	54.41 (7.1)	55.07 (6.5)	55.40 (7.8)
no-ε4	50.56 (10.0)	51.05 (10.0)	57.12 (6.9)	56.75 (7.5)
SF-36 PCS	*51.37 (8.1)*[a]	*48.95 (9.6)*[a]	*43.85 (10.0)*[b]	*39.01 (11.0)*[c]
ε4	52.75 (6.7)	50.30 (9.6)	46.93 (9.0)	41.33 (11.0)
no-ε4	50.88 (8.5)	48.46 (9.6)	43.06 (10.0)	38.64 (11.2)
CHRONIC 5	0.21 (.71)[a]	1.23 (1.2)[a]	2.35 (1.3)[b]	2.21 (1.2)[b]
ε4	0.42 (.72)	1.11 (1.1)	2.41 (1.5)	2.56 (1.2)
no-ε4	0.43 (.70)	1.26 (1.2)	2.30 (1.2)	2.18 (1.2)
SS-4: CLUBS	1.82 (.50)[a]	1.97 (.63)[a]	2.21 (.60)[b]	2.09 (.62)[b]
ε4	1.89 (.53)	2.06 (.66)	2.29 (.63)	2.24 (.79)
no-ε4	1.79 (.50)	1.92 (.62)	2.19 (.59)	2.07 (.58)
SS-4: HOURS	4.40 (1.0)[a]	4.31 (1.0)[a]	3.62 (1.2)[b]	2.92 (1.3)[c]
ε4	4.62 (.76)	4.36 (1.0)	3.59 (1.4)	2.95 (1.3)
no-ε4	4.32 (1.0)	4.29 (1.1)	3.63 (1.1)	2.91 (1.2)
SS-4: SUPPORT	3.34 (.78)[a]	3.34 (.77)[a]	3.73 (.53)[b]	3.79 (.49)[b]
ε4	3.36 (.78)	3.47 (.70)	3.76 (.43)	3.71 (.68)
no-ε4	3.33 (.78)	3.29 (.80)	3.72 (.56)	3.80 (.45)

One-way ANOVAs tested for age-related declines in SF-36 scores (PCS and MCS) and objective (chronic) health. MCS scores had a main effect of age group, F (3, 816) = 22.78, $p <$ 0.001. The two oldest groups had significantly higher MCS scores than the two younger groups. PCS scores demonstrated a main effect of age group, F (3, 816) = 72.95, $p < 0.001$. Pairwise comparisons show a PCS decline across age group, with the oldest and oldest-old having lower PCS scores than the two youngest groups, which did not differ ($p < 0.001$ for all comparisons). Chronic cumulative index scores measured objective health and were significant, F (3, 865) = 136.83, $p < 0.001$. Age group contrasts show that the two younger groups had significantly lower levels of chronic conditions than the two oldest groups, who did not differ from one another. Full and partial correlations among PCS, MCS and CHRONIC are presented in Table 5.

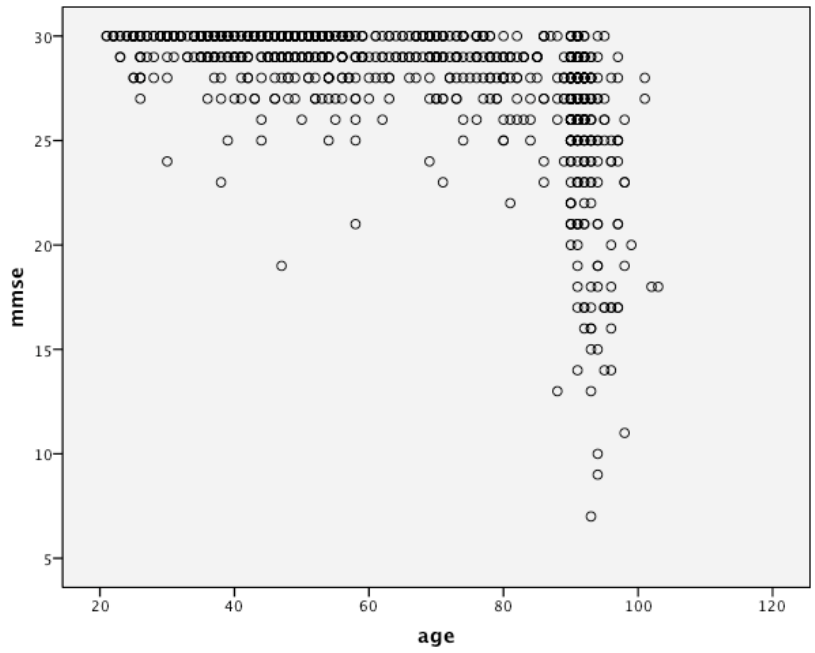

Figure 2. Scatterplot of MMSE and Age.

A series of one-way ANOVAs were used to examine age-related differences in social network characteristics (SS-4) and results are shown in Table 4. SS-4/CLUBS (*social engagement*) scores had a main effect of age group, F (3, 840) = 14.48, $p < 0.001$. Age-group

TABLE 5: Phase 1 Correlations of APOE, Memory Health, and SS-4 Items with Age, and Age Accounted.
Note: ** represents $p < 0.01$, * represents $p < 0.05$.

	1	2	3	4	5	6	7	8	9	10	11
AGE (1)											
ε4 STATUS (2); N	.137** 868		**.017 842**	**-.010 840**	**.034 823**	**.044 817**	**.093** 817**	**.044 865**	**.100** 844**	**.046 838**	**.029 834**
MMSE (3) N	.527** 846	.087* 845		**.609** 841**	**.474** 826**	**.085** 807**	**.073* 807**	**.042 843**	**.092** 831**	**.215** 829**	**.034 827**
MMSE-R (4); N	.522** 844	.063* 843	.716** 844		**.288** 821**	**.065 805**	**.020 805**	**.009 841**	**.033 829**	**.094** 827**	**.016 825**
VOCAB (5) N	.150** 830	.054 829	.478** 826	.321** 824		**.094** 795**	**.140** 795**	**-.085** 827**	**.171** 817**	**.271** 816**	**.042 812**
SF36 MCS (6); N	.272** 820	.005 820	-.074** 810	-.088* 808	.049 798		**.091** 817**	**-.020 817**	**.124** 806**	**.148** 804**	**.129** 801**
SF36 PCS (7); N	.466** 820	.146** 820	.300** 810	.258** 808	.193** 798	-.049 820		**-.321** 817**	**.065 806**	**.245** 804**	**.129** 801**
CHRONIC (8); N	.550** 869	-.039 868	-.259 846	-.281 844	-.153 830	.133** 820	-.493** 820		**.033 841**	**-.058 839**	**.028 835**
CLUBS (9); N	.191** 844	.071* 843	-.024 834	-.072* 832	.137 820	.169** 809	-.032 809	.132** 844		**.188** 839**	**.091** 835**
HOURS (10); N	-.493* 842	.107* 841	-.419** 832	.327** 832	.307** 819	-.011 807	.419** 807	-313** 842	.066 842		**.110** 833**
SUPPORT (11); N	.303** 838	-.014** 837	-.132** 830	-.145** 828	-.006 815	.378** 804	-.033 804	.144** 838	.143** 838	-.059 836	

comparisons show that the two oldest groups had higher levels of social engagement compared to younger individuals ($p < 0.05$). SS-4/HOURS (*everyday social activity*) also had a main effect of age, F (3, 838) = 93.97, $p < 0.001$. Post-hoc analysis found that the two youngest groups (younger and middle) spent significantly more hours outside of the home compared to the two older groups, who differed respectively ($p < 0.001$). SS-4/SUPPORT (*support satisfaction*) had an age-effect, F (3, 834) = 31.22, $p < 0.001$. Comparisons show that the two oldest groups were more satisfied with support received compared to their younger counterparts ($p < 0.001$), who did not differ. Full and partial correlations of SS-4 items are available in Table 5.

Lastly, a two-way chi-square test of independence was used to examine the relationship between APOE genotype and age group. The relation between these variables was significant, χ^2 (3, N = 868) = 18.71, $p < 0.01$. The ε4-allele prevalence rates for each age group are presented in Table 3. The oldest-old had a lower ε4-allele incidence rate compared to the other age groups. Correlations between APOE-ε4 presence and cognitive, health, and social network indices are also available in Tables 2. When age is controlled in the equation, the significant correlations between genotype and most remaining measures become non-significant. The partial correlation between ε4 status and PCS and SS-4 CLUBS (*social engagement*) scores remained significant, where having at least one copy of the ε4-allele is associated with better physical health ($r = .09$, $p < 0.01$) and increased social engagement with clubs and organizations ($r = .10$, $p < 0.01$).

P_1 APOE-ε4 Allele Effects. A series of regression analyses were carried out to determine if presence of the ε4-allele was predictive of cognitive performance, (MMSE; MMSE-R), scores on vocabulary (VOCAB), current physical health status (PCS, MCS, and CHRONIC), and social network characteristics (SS-4 items). Step-wise entry was identical for each regression with age (as a continuous variable) and education level being entered on the first step

of the equation. APOE genotype (ε4 carrier vs. non-carrier) was entered on the second step of the regression. This step-wise entry method was chosen to verify if possession of the ε4-allele was a significant predictor after controlling for these influential demographics.

Regression results are available in Table 6. Regression analysis revealed that age and education were highly significant predictors of MMSE (β = -.45; β =*.28*, $p < .001$), MMSE-R (β = -.49; β =*.10*, $p < .003$), PCS (β = -.43; β =*.15*, $p < .001$), MCS (β = .31; β =*.13*, $p < .001$), SS-4/CLUBS (β = .26; β =*.26*, $p < .001$), and SS-4/HOURS (β = -.45; β =*.17*, $p < .001$). Age was not a predictor of VOCAB scores (β = .01, p = .95), and education did not predict CHRONIC scores (β = -.05, p = .12) or SS-4/SUPPORT (β = .04, p = .26). The ε4-genotype did not significantly predict MMSE (β = -.01, p = .86), MMSE-R (β = -.02, p = .62), VOCAB (β = -.01, p = .87), MCS (β = .03, p = .31), CHRONIC (β = .04, p = .16), SS-4/HOURS (β = .03, p = .32) and SS-4/SUPPORT (β = .03, p = .40) scores. In contrast, ε4-genotype was a significant predictor of physical health as indexed by the PCS component of the SF-36 (β = .07, p = .02). The ε4-genotype was also a significant predictor of social engagement as indicated by the CLUBS item of the SS-4 index (β = .09, p = .01).

P_1 Testing Physical Health Status as a Mediator. Four individual mediation analyses were conducted given that there were two indices of physical health (PCS and CHRONIC) and two indices of cognitive performance (MMSE and MMSE-R). A series of three step-wise regression equations provided the test for each mediation analysis. This statistical procedure was directly adapted from Baron and Kenny (1986). For each regression equation, age and education level were entered on the first step, while respective predictor variables were entered on the second step. The first series of regressions tested PCS mediation of ε4 genotype on memory performance (MMSE). First, PCS was regressed on ε4 genotype; second, MMSE score was regressed on ε4 genotype; and third, MMSE was regressed on the combination of PCS and ε4

genotype. Table 7 presents findings from this regression series. Results showed that ε4 genotype was a significant factor on the mediator (PCS; $\beta = .08$, $p < .001$), but not for the MMSE ($\beta = -.01$, $p = .76$). Compared to the isolated effect, the effect of ε4 genotype on MMSE did not change with the inclusion of PCS ($\beta = .01$, $p = .93$). From these results, the combination of PCS and ε4 genotype accounted for the same amount of the variance in MMSE scores (35%) compared to ε4 genotype alone (35%). It should be noted that ε4 genotype was entered on the second step of the regression equation; therefore the 35% of variance is attributed to age and education status, rather than genotype (as evidenced in Table 6).

TABLE 6. A Series of Regression Analyses Predicting Memory, Health, and Social Network Characteristics from Genotype Status. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

		Variable	*ß*	R^2	*F*	ΔR^2
	Step 1	*Age*	-.45**			
		Education	.28**	.35**	224.8**	
1. MMSE	*Step 2*	*ε4 Status*	-.01	.35**	149.4**	.00
	Step 1	*Age*	-.49**			
2. MMSE-R		*Education*	.10 **	.28**	159.9**	
	Step 2	*ε4 Status*	-.01	.28**	106.6**	.00
	Step 1	*Age*	-.01			
		Education	.57**	.31**	185.4**	
3. VOCAB	*Step 2*	*ε4 Status*	-.02	.31**	123.6**	.00
	Step 1	*Age*	.31**			
4. SF-36		*Education*	.13**	.09**	40.8**	
MCS	*Step 2*	*ε4 Status*	.03	.09**	27.5**	.00
	Step 1	*Age*	-.43**			
5. SF-36		*Education*	.15**	.23**	125.5**	
PCS	*Step 2*	*ε4 Status*	-.08	.24**	86.4**	.01**
	Step 1	*Age*	.55**			
6.		*Education*	-.04	.31**	193.4**	
CHRONIC	*Step 2*	*ε4 Status*	-.04	.31**	129.8**	.00
	Step 1	*Age*	.26**			
7. SS-4;		*Education*	.26**	.10**	45.6**	
CLUBS	*Step 2*	*ε4 Status*	.09**	.11**	32.9**	.01**
	Step 1	*Age*	-.45**			
8. SS-4;		*Education*	.17**	.27**	153.5**	
HOURS	*Step 2*	*ε4 Status*	.03	.27**	102.7**	.00
	Step 1	*Age*	.31**			
9. SS-4;		*Education*	.04	.09**	42.6**	
SUPPORT	*Step 2*	*ε4 Status*	-.03	.09**	28.6**	.00

TABLE 7: Testing SF-36 Health Mediator Effects Using Hierarchical Multiple Regression.
Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	*B*	R^2	*F*
Equation 1: Effect on mediator (SF-36 PCS)			
ε4 Status	.08**	.24	86.40**
Equation 2: Effect on outcome (MMSE Score)			
ε4 Status	-.01	.35	149.49**
Equation 3: Effect on outcome (MMSE Score)			
SF-36 PCS	.03		
ε4 Status	.01	.35	105.93**

The second series of mediation analyses tested for physical health mediation (via PCS) of ε4 genotype on MMSE-R. First, PCS was regressed on ε4 genotype; second, MMSE-R score was regressed on ε4 genotype; and third, MMSE-R was regressed on the combination of PCS and ε4 genotype. Table 8 presents findings from this regression series. Results showed that ε4 genotype was a significant factor on the mediator (PCS; $\beta = .08$, $p < .01$), but not for the MMSE-R ($\beta = -.01$, $p = .71$). Compared to the isolated effect, the effect of ε4 genotype on MMSE-R did not change with the inclusion of PCS ($\beta = -.01$, $p = .71$). From these results, the combination of PCS and ε4 genotype accounted for a similar amount of the variance in MMSE-R scores (27%) compared to ε4 genotype alone (28%). It should be noted that ε4 genotype was entered on the second step of the regression equation; therefore the 27% of variance is attributed to age and education status, rather than genotype (as evidenced in Table 6).

TABLE 8: Testing SF-36 Health Mediator Effects Using Hierarchical Multiple Regression.
Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	*B*	R^2	*F*
Equation 1: Effect on mediator (SF-36 PCS)			
e4 Status	.08**	.24	86.40**
Equation 2: Effect on outcome (MMSE-R Score)			
ε4 Status	-.01	.28	106.12**
Equation 3: Effect on outcome (MMSE-R Score)			
SF-36 PCS	.01		
ε4 Status	-.01	.27	73.91**

The third series of mediation analyses tested for physical health mediation (via CHRONIC) of ε4 genotype on MMSE. First, CHRONIC was regressed on ε4 genotype; second, MMSE score was regressed on ε4 genotype; and third, MMSE was regressed on the combination of CHRONIC and ε4 genotype. Table 9 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (CHRONIC; $\beta = .04$, $p = .15$) and for the MMSE ($\beta = -.01$, $p = .76$). Compared to the isolated effect, the effect of ε4 genotype on MMSE did not change with the inclusion of CHRONIC ($\beta = -.01$, $p = .69$). From these results, the combination of CHRONIC and ε4 genotype accounted for the same amount of the variance in MMSE scores (35%) compared to ε4 genotype alone (35%). It should be noted that ε4 genotype was entered on the second step of the regression equation; therefore the 35% of variance is attributed to age and education status, rather than genotype (as evidenced in Table 6).

TABLE 9: Testing Chronic 5 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (Chronic 5)			
ε4 Status	.04	.32	129.76**
Equation 2: Effect on outcome (MMSE Score)			
ε4 Status	-.01	.35	149.49**
Equation 3: Effect on outcome (MMSE Score)			
Chronic 5	.06		
ε4 Status	-.01	.35	113.59**

The final series of mediation analyses tested for physical health mediation (via CHRONIC) of ε4 genotype on MMSE-R. First, CHRONIC was regressed on ε4 genotype; second, MMSE-R score was regressed on ε4 genotype; and third, MMSE-R was regressed on the combination of CHRONIC and ε4 genotype. Table 10 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (CHRONIC; $\beta = .04$, $p = .15$) and for the MMSE-R ($\beta = -.01$, $p = .71$). Compared to the isolated effect, the

effect of ε4 genotype on MMSE-R did not change with the inclusion of CHRONIC (β = -.01, p = .69). From these results, the combination of CHRONIC and ε4 genotype accounted for the same amount of the variance in MMSE scores (28%) compared to ε4 genotype alone (28%). It should be noted that ε4 genotype was entered on the second step of the equation; therefore the 28% of variance is attributed to age and education status, rather than genotype (as in Table 6).

TABLE 10: Testing Chronic 5 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (Chronic 5)			
ε4 Status	.04	.32	129.76**
Equation 2: Effect on outcome (MMSE-R Score)			
ε4 Status	-.01	.28	106.12**
Equation 3: Effect on outcome (MMSE-R Score)			
Chronic 5	.02		
ε4 Status	-.01	.28	79.57**

P_1 Testing Social Network Characteristics as a Moderator: A series of hierarchical multiple regression equations tested the hypothesis that the social network characteristics may moderate the relationship between ε4 genotype and cognitive performance. This statistical procedure was directly adapted from Baron and Kenny (1986). A set of six analyses were conducted given that there were three items on the SS-4 (CLUBS, HOURS, and SUPPORT) and two cognitive performance measures (MMSE and MMSE-R). Results from the moderation analyses are presented in Tables 11 and 12. For all regression equations, age and education were entered on the first step, followed by ε4 genotype and one of the SS-4 items (CLUBS, HOURS or SUPPORT) on the second step, and the interaction between ε4 genotype and SS-4 item (CLUBS, HOURS or SUPPORT) was entered on the third and final step of the equation. Analyses 1-3 test for moderation on the MMSE and, analyses 4-6 test the MMSE-R.

For analyses 1-3, SS-4 variables were regressed on the MMSE memory measure. Results are presented in Table 11. Regression analyses show that age (β = -.45; β = -.44, $p < .001$) and

education (β = .30, p < .001) account for a significant proportion the variance for all three SS-4 items. This variance percentage does not significantly change with the inclusion of ε4 genotype (β = .00, p < .99), CLUBS (β = .01, p = .76), or SUPPORT (β = .02, p = .46). The inclusion of HOURS into the equation does significantly change the variance (β = .15, p < .001). However, the interaction between ε4 genotype and CLUBS, HOURS, and SUPPORT items does not alter the isolated effect of ε4 genotype and SS-4 on MMSE. Moderation does not appear evident in these three models.

TABLE 11: Testing Social Network Moderator Effects on MMSE via a Series of Hierarchical Multiple Regressions. Note: ** represents p < 0.01, * represents p < 0.05.

Step and variable	*B*	R^2	*F*	ΔR^2
Step 1				
Age	-.45**			
Education	.30**	.36	277.66**	
Step 2				
ε4 Status	.00			
Clubs/Organizations	.01	.36	113.60**	.00
Step 3				
ε4 Status X Clubs/Organizations	-.03	.36	90.80**	.00
Step 1				
Age	-.45**			
Education	.30**	.36	231.65**	
Step 2				
ε4 Status	-.01			
Hours	.15**	.37	124.23**	.01*
Step *3*				
ε4 Status X Hours	-.15	.37	100.01**	.00
Step 1				
Age	-.44**			
Education	.30**	.35	225.82**	
Step 2				
ε4 Status	.00			
Support Received	.02	.35	112.85**	.00
Step 3				
ε4 Status X Support Received	-.09	.35	90.28**	.00

For analyses 4-6, items from the SS-4 were regressed on the MMSE-R delayed recall memory measure. Results are presented in Table 12. Regression analyses show that age (β = -.49, p < .001) and education (β = .10; β = .13 p < .001) account for a significant proportion the variance for all three SS-4 items. This overall variance percentage does not significantly change with the inclusion of ε4 genotype (β = -.01, p < .74), CLUBS (β = .00, p = .95), HOURS (β = .08, p = .03), or SUPPORT (β = .01, p = .74). The interaction between ε4 genotype and CLUBS, HOURS, and SUPPORT items does not alter the isolated effect of ε4 genotype and SS-4 on MMSE-R. Moderation was not shown in these three models.

TABLE 12: Testing Social Network Moderator Effects on MMSE-R via a Series of Hierarchical Multiple Regressions. Note: ** represents p < 0.01, * represents p < 0.05.

Step and variable	*B*	R^2	*F*	ΔR^2
Step 1				
Age	-.49**			
Education	.10**	.27	157.42**	
Step 2				
ε4 Status	-.01			
Clubs/Organizations	.00	.27	78.55**	.00
Step 3				
ε4 Status X Clubs/Organizations	-.01	.27	62.77**	.00
Step 1				
Age	-.49**			
Education	.10**	.27	156.13**	
Step 2				
ε4 Status	-.01			
Hours	.08	.27	79.60**	.00
Step *3*				
ε4 Status X Hours	.05	.27	63.66**	.00
Step 1				
Age	-.49**			
Education	.10**	.27	155.73**	
Step 2				
ε4 Status	-.01			
Support Received	.01	.27	77.76**	.00
Step 3				
ε4 Status X Support Received	.02	.27	62.14**	.00

Phase 2 Data Analyses

P_2 Population Characteristics and Age-Related Effects. Population descriptives for P_2 are presented in Table 13. These participants were a subset of those individuals from P_1. Means for all dependent variables are presented by age group and also separated by ε4 genotype (carriers and non-carriers). Following descriptive analyses participants were collapsed across genotype, because impact of genotype was tested in the next series of analyses. A main effect of education status was significant, F (2, 366) = 3.74, $p < 0.03$. Post-hoc analysis confirmed that the oldest-old had significantly lower education levels (M = 4.86; $p < 0.02$) compared to the two younger age groups, which did not differ from one another (M = 5.30 and 5.06).

TABLE 13: Phase 2 Population Characteristics. Standard deviations in parentheses.

	Middle adults (N = 106)	Older adults (N = 116)	Oldest-old adults (N = 147)
AGE	53.36 (5.4)	74.27 (5.4)	90.90 (2.3)
EDUCATION	5.30 (1.1) [a]	5.06 (1.2) [a]	4.86 (1.4) [b]
ε4 STATUS			
ε4	27% [a]	25% [a]	16% [b]
no-ε4	73% [a]	75% [a]	84% [b]
FDS	*6.08 (1.0)* [a]	*5.53 (.97)*	*5.54 (.96)*
ε4	6.31 (1.1)	5.64 (.99)	5.75 (.78)
no-ε4	5.98 (.96)	5.50 (.97)	5.50 (1.0)
BDS	*4.39 (1.1)* [a]	*4.22 (.89)* [a]	*3.92 (.94)* [b]
ε4	4.33 (1.1)	4.43 (.82)	3.92 (.79)
no-ε4	4.41 (1.1)	4.16 (1.1)	3.92 (.97)
SJS	*4.59 (.86)* [a]	*4.10 (.70)* [b]	*3.59 (.70)* [c]
ε4	4.75 (.98)	4.16 (.70)	3.50 (.72)
no-ε4	4.51 (.80)	4.09 (.70)	3.60 (.53)
SJS-PROP	*.77 (.13)* [a]	*.66 (.11)* [b]	*.57 (.14)* [c]
ε4	.78 (.13)	.64 (.14)	.56 (.13)
no-ε4	.76 (.13)	.67 (.11)	.58 (.14)

Given that education statuses differ across age groups, analyses of covariance (ANCOVAs) were used to test for age-related differences in memory performance (FDS, BDS, SJS, and SJS-PROP). Education level was treated as a covariate. Means and standard deviations are presented in Table 13. A main effect of FDS score was significant, F (2, 364) = 6.05, $p <$ 0.001. Planned pairwise comparisons show that the middle-age group performed significantly better on the FDS compared to the two oldest groups, who did not differ from another ($p < .001$ for all comparisons). BDS scores also demonstrated a main effect of age group, F (2, 365) = 4.79, $p < 0.005$. Planned pairwise comparisons show that the oldest-old group had performed significantly worse on the BDS compared to the two younger groups, who did not differ from another ($p < .03$ for all comparisons). SJS scores had a significant decline with age, F (2, 365) = 50.82, $p < 0.001$. Direct comparisons show that all three groups significantly differed from one another, with middle adults performing best, older groups performing slightly worse, and the oldest-old performing worst overall ($p < 0.001$ for all comparisons). A main effect of age group was shown for SJS-PROP scores, F (2, 215) = 38.92, $p < 0.001$. Group comparisons are similar to SJS results, which produce a systematic decline with age, with all three groups significantly differing from one another ($p < 0.001$ for all comparisons). Full and partial correlations are in Table 14.

P_2 APOE-ε4 Allele Effects. As conducted in P_1, a series of regression analyses were carried out to determine if presence of the ε4-allele was predictive of memory performance as indexed by the FDS, BDS, SJS, and SJS-PROP. Step-wise entry was identical for each regression with age (as a continuous variable) and education level being entered on the first step of the equation. APOE genotype (ε4 carrier vs. non-carrier) was entered on the second step of the regression. This step-wise entry method was chosen to verify if possession of the ε4-allele

was a significant predictor after controlling for these influential demographics. Results for these regressions are presented in Table 15.

TABLE 14: Correlations Among APOE and Memory Performance with Age, and Age Accounted For. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

	1	2	3	4	5	6
AGE (1)						
ε4 STATUS (2); N	-.137** 868		**.088** **367**	**0.16** **367**	**.025** **367**	**-.024** **216**
FDS (3) N	-.249** 370	.118* 370		**.426**** **367**	**.383**** **367**	**.336**** **216**
BDS (4) N	-.247** 370	.049 370	.416** 370		**.374**** **367**	**.356**** **216**
SJS (5) N	-.513** 370	.091 370	.446** 370	.438** 370		**.796**** **216**
SJS-PROP (6) N	-.567** 219	.047 219	.400** 219	.409** 219	.858** 219	

TABLE 15: A Series of Multiple Regression Analyses Predicting Memory Performance from Genotype Status. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

		Variable	*ß*	R^2	*F*	ΔR^2
	Step 1	*Age*	-.21**			
		Education	.25**	.11**	23.19**	
FDS	*Step 2*	*ε4 Status*	.07	.12**	17.63**	.01
	Step 1	*Age*	-.21**			
		Education	.27**	.12**	23.06**	
BDS	*Step 2*	*ε4 Status*	-.01	.12**	15.38**	.00
	Step 1	*Age*	-.49**			
		Education	.15**	.28**	72.68**	
SJS	*Step 2*	*ε4 Status*	.01	.28**	48.35**	.00
	Step 1	*Age*	-.55**			
SJS – PROP		*Education*	.15**	.34**	56.69**	
	Step 2	*ε4 Status*	-.03	.34**	37.90**	.00

Regression analysis revealed that age and education were highly significant predictors of FDS ($ß$ = -.21; $ß$ =.25, $p < .001$), BDS ($ß$ = -.21; $ß$ =.27, $p < .003$), SJS ($ß$ = -.49; $ß$ =.15, $p <$ .001), and SJS-PROP ($ß$ = -.55; $ß$ =.15, $p < .001$). The ε4-genotype did not significantly predict

scores on the FDS (β = .07, p = .19), BDS (β = -.01, p = .95), SJS (β = .01, p = .80), and SJS-PROP (β = .03, p = .55). Full and partial correlations between APOE-ε4 presence and all P_2 cognitive measures available in Table 14. When age is controlled in the equation, the significant correlations between ε4 genotype and all dependent measures become non-significant.

P_2 Testing Physical Health as a Mediator. Eight individual mediation analyses were conducted given that there were two measures of physical health (PCS and CHRONIC) and four indices of memory performance (FDS, BDS, SJS, and SJS-PROP). A series of three step-wise regression equations provided the test for each mediation analysis. This statistical procedure was directly adapted from Baron and Kenny (1986). For each regression equation, age and education level were entered on the first step, while respective predictor variables were entered on the second step. Mediation analyses 1-4 test for PCS mediation of memory measures, while analyses 5-8 test for CHRONIC mediation of memory measures. Results for all analyses are presented in Tables 16 through 23.

The first series of regressions tested PCS mediation of ε4 genotype on FDS. First, PCS was regressed on ε4 genotype; second, FDS score was regressed on ε4 genotype; and third, FDS was regressed on the combination of PCS and ε4 genotype. Table 16 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (PCS; β = .08, p =.10), and FDS (β = .07, p = .19). Compared to the isolated effect, the effect of ε4 genotype on FDS did not change with the inclusion of PCS (β = .06, p = .97). From these results, the combination of PCS and ε4 genotype accounted for the same amount of the variance in FDS scores (12%) compared to ε4 genotype alone (12%). Given that ε4 genotype was entered on the second step of the regression equation, the 12% of variance can be attributed to age and education status rather than genotype (as shown in Table 15).

TABLE 16: Testing SF-36 Health Mediator Effects Using Hierarchical Multiple Regression.
Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	*β*	R^2	*F*
Equation 1: Effect on mediator (SF-36 PCS)			
ε4 Status	.08	.16	23.40**
Equation 2: Effect on outcome (FDS Score)			
ε4 Status	.07	.12	17.63**
Equation 3: Effect on outcome (FDS Score)			
SF-36 PCS	.00		
ε4 Status	.06	.12	12.81**

The second series of regressions tested PCS mediation of ε4 genotype BDS. First, PCS was regressed on ε4 genotype; second, BDS score was regressed on ε4 genotype; and third, BDS was regressed on the combination of PCS and ε4 genotype. Table 17 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (PCS; $\beta = .08$, $p = .10$), and BDS ($\beta = -.01$, $p = .95$). Compared to the isolated effect, the effect of ε4 genotype on BDS did not change with the inclusion of PCS ($\beta = .01$, $p = .92$). From these results, the combination of PCS and ε4 genotype accounted for the same amount of the variance in BDS scores (12%) compared to ε4 genotype alone (12%). Given that ε4 genotype was entered on the second step of the regression equation, the 12% of variance can be attributed to age and education status rather than genotype (as shown in Table 15).

TABLE 17: Testing SF-36 Health Mediator Effects Using Hierarchical Multiple Regression.
Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	*β*	R^2	*F*
Equation 1: Effect on mediator (SF-36 PCS)			
ε4 Status	.08	.16	23.40**
Equation 2: Effect on outcome (BDS Score)			
ε4 Status	-.01	.12	15.38**
Equation 3: Effect on outcome (BDS Score)			
SF-36 PCS	-.08		
ε4 Status	.01	.12	13.61**

The third series of regressions tested PCS mediation of ε4 genotype SJS. First, PCS was

regressed on ε4 genotype; second, SJS score was regressed on ε4 genotype; and third, SJS was regressed on the combination of PCS and ε4 genotype. Table 18 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (PCS; β = .08, p =.10), and SJS (β = .01, p = .80). Compared to the isolated effect, the effect of ε4 genotype on SJS did not change with the inclusion of PCS (β = .02, p = .74). From these results, the combination of PCS and ε4 genotype accounted for the same amount of the variance in SJS scores (28%) compared to ε4 genotype alone (28%). Given that ε4 genotype was entered on the second step of the regression equation, the 28% of variance can be attributed to age and education status rather than genotype (as shown in Table 15).

TABLE 18: Testing SF-36 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents p < 0.01, * represents p < 0.05.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (SF-36 PCS)			
ε4 Status	.08	.16	23.40**
Equation 2: Effect on outcome (SJS Score)			
ε4 Status	.01	.28	48.35**
Equation 3: Effect on outcome (SJS Score)			
SF-36 PCS	.02		
ε4 Status	.02	.28	35.10**

The fourth series of regressions tested PCS mediation of ε4 genotype on SJS-PROP scores. First, PCS was regressed on ε4 genotype; second, SJS-PROP score was regressed on ε4 genotype; and third, SJS-PROP was regressed on the combination of PCS and ε4 genotype. Table 19 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (PCS; β = .08, p =.10), and SJS-PROP (β = -.03, p = .55). Compared to the isolated effect, the effect of ε4 genotype on SJS-PROP did not change with the inclusion of PCS (β = -.05, p = .42). From these results, the combination of PCS and ε4 genotype accounted for the same amount of the variance in SJS-PROP scores (34%) compared to

ε4 genotype alone (34%). Given that ε4 genotype was entered on the second step of the regression equation, the 34% of variance can be attributed to age and education status rather than genotype (as shown in Table 15).

TABLE 19: Testing SF-36 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	*β*	R^2	*F*
Equation 1: Effect on mediator (SF-36 PCS)			
ε4 Status	.08	.16	23.40**
Equation 2: Effect on outcome (SJS-PROP)			
ε4 Status	-.03	.34	37.34**
Equation 3: Effect on outcome (SJS-PROP)			
SF-36 PCS	.00		
ε4 Status	-.05	.34	28.14**

The fifth series of regressions tested CHRONIC mediation of ε4 genotype on FDS. First, CHRONIC was regressed on ε4 genotype; second, FDS score was regressed on ε4 genotype; and third, FDS was regressed on the combination of CHRONIC and ε4 genotype. Table 20 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (CHRONIC; $\beta = .06$, $p = .20$), and FDS ($\beta = .07$, $p = .19$). Compared to the isolated effect, the effect of ε4 genotype on FDS did not change with the inclusion of CHRONIC ($\beta = .07$, $p = .17$). From these results, the combination of CHRONIC and ε4 genotype accounted for the same amount of the variance in FDS scores (12%) compared to ε4 genotype alone (12%). Given that ε4 genotype was entered on the second step of the regression equation, the 12% of variance can be attributed to age and education status rather than genotype (as in Table 15).

The sixth series of regressions tested CHRONIC mediation of ε4 genotype on BDS. First, CHRONIC was regressed on ε4 genotype; second, BDS score was regressed on ε4 genotype; and third, BDS was regressed on the combination of CHRONIC and ε4 genotype. Table 21 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor

on the mediator (CHRONIC; β = .06, p =.20), and BDS (β = -.01, p = .95). Compared to the isolated effect, the effect of ε4 genotype on BDS did not change with the inclusion of CHRONIC (β = .00, p = .99). From these results, the combination of CHRONIC and ε4 genotype accounted for a similar amount of the variance in BDS scores (12%) compared to ε4 genotype alone (13%). Given that ε4 genotype was entered on the second step of the regression equation, the 12% of variance can be attributed to age and education status rather than genotype (as in Table 15).

TABLE 20: Testing Chronic 5 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (Chronic 5)			
ε4 Status	.06	.16	23.45**
Equation 2: Effect on outcome (FDS Score)			
ε4 Status	.07	.12	17.63**
Equation 3: Effect on outcome (FDS Score)			
Chronic 5	-.04		
ε4 Status	.07	.12	13.37**

TABLE 21: Testing Chronic 5 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (Chronic 5)			
ε4 Status	.06	.16	23.45**
Equation 2: Effect on outcome (BDS Score)			
ε4 Status	-.01	.12	15.38**
Equation 3: Effect on outcome (BDS Score)			
Chronic 5	-.06		
ε4 Status	.00	.13	13.63**

The seventh series of regressions tested CHRONIC mediation of ε4 genotype SJS. First, PCS was regressed on ε4 genotype; second, SJS score was regressed on ε4 genotype; and third, SJS was regressed on the combination of CHRONIC and ε4 genotype. Table 22 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (CHRONIC; β = .06, p =.20), and SJS (β = .01, p = .80). Compared to the

isolated effect, the effect of ε4 genotype on SJS did not change with the inclusion of CHRONIC (β = -.01, p = .78). The combination of CHRONIC and ε4 genotype accounted for a similar amount of the variance in SJS scores (28%) compared to ε4 genotype alone (29%). Given that ε4 genotype was entered on the second step of the regression equation, the 28% of variance can be attributed to age and education status rather than genotype (as shown in Table 15).

TABLE 22: Testing Chronic 5 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (Chronic 5)			
ε4 Status	.06	.16	23.45**
Equation 2: Effect on outcome (SJS Score)			
ε4 Status	.01	.28	48.35**
Equation 3: Effect on outcome (SJS Score)			
Chronic 5	-.01		
ε4 Status	-.01	.29	36.19**

The final series of regressions tested CHRONIC mediation of ε4 genotype on SJS-PROP scores. First, CHRONIC was regressed on ε4 genotype; second, SJS-PROP score was regressed on ε4 genotype; and third, SJS-PROP was regressed on the combination of CHRONIC and ε4 genotype. Table 23 presents findings from this regression series. Results showed that ε4 genotype was not a significant factor on the mediator (CHRONIC; β = .06, p =.20), and SJS-PROP (β = -.03, p = .55). Compared to the isolated effect, the effect of ε4 genotype on SJS-PROP did not change with the inclusion of CHRONIC (β = -.04, p = .49). From these results, the combination of CHRONIC and ε4 genotype accounted for a similar amount of the variance in SJS-PROP scores (34%) compared to ε4 genotype alone (35%). Given that ε4 genotype was entered on the second step of the regression equation, the 34% of variance can be attributed to age and education status rather than genotype (as shown in Table 15).

TABLE 23: Testing Chronic 5 Health Mediator Effects Using Hierarchical Multiple Regression. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Regression equation, Independent Variable	β	R^2	F
Equation 1: Effect on mediator (Chronic 5)			
ε4 Status	.06	.16	23.45**
Equation 2: Effect on outcome (SJS-PROP)			
ε4 Status	-.03	.34	37.34**
Equation 3: Effect on outcome (SJS-PROP)			
Chronic 5	.07		
ε4 Status	-.04	.35	28.42**

P_2 Testing Social Network Characteristics as a Moderator. A set of hierarchical multiple regression equations tested the hypothesis that the social network characteristics may moderate the relationship between ε4 genotype and memory performance. This statistical procedure was directly adapted from Baron and Kenny (1986). A series of twelve analyses were conducted given that there were three items on the SS-4 (CLUBS, HOURS, and SUPPORT) and four memory performance measures (FDS, BDS, SJS and SJS-PROP). Results from the moderation analyses are presented in Tables 24 through 27. For all regression equations, age and education were entered on the first step, followed by ε4 genotype and one of the SS-4 items (CLUBS, HOURS or SUPPORT) on the second step, and the interaction between ε4 genotype and SS-4 item (CLUBS, HOURS or SUPPORT) was entered on the third and final step of the equation. Analyses 1-3 test for moderation on the FDS, analyses 4-6 test the BDS, analyses 7-9 test SJS, and analyses 10-12 test the SJS-PROP scores.

For analyses 1-3, SS-4 variables were regressed on the FDS memory measure. Results are presented in Table 24. Regression analyses show that age (β = -.21; β = -.22 $p < .001$) and education (β = .25; β = .24 $p < .001$) account for a significant proportion the variance for all three SS-4 items. This variance percentage does not significantly change with the inclusion of ε4 genotype (β = .07; β = .06, $p < .22$), CLUBS (β = -.03, p = .53), HOURS, (β = .11, p = .06), or SUPPORT (β = .07, p = .22). The interaction between genotype and CLUBS (β = -.10, p = .54),

HOURS, (β = -.01, p = .98) or SUPPORT (β = -.23, p = .39) does not alter the isolated effect of ε4 genotype and SS-4 on FDS scores. Moderation was not shown in these three models.

TABLE 24: Testing Social Network Moderator Effects on FDS via a Series of Hierarchical Multiple Regressions. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Step and variable	β	R^2	F	ΔR^2
Step 1				
Age	-.21**			
Education	.25**	.12**	25.51**	
Step 2				
ε4 Status	.07			
Clubs/Organizations	-.03	.12**	13.29**	.00
Step 3				
ε4 Status X Clubs/Organizations	-.10	.12**	10.69**	.00
Step 1				
Age	-.22**			
Education	.24**	.12**	25.12**	
Step 2				
ε4 Status	.07			
Hours	.11	.12**	14.02**	.00
Step *3*				
ε4 Status X Hours	.01	.12**	11.19**	.00
Step 1				
Age	-.21**			
Education	.25**	.12**	24.90**	
Step 2				
ε4 Status	.06			
Support Received	-.01	.12**	12.83**	.00
Step 3				
ε4 Status X Support Received	-.23	.12**	10.41**	.00

For analyses 4-6, SS-4 variables were regressed on the BDS memory measure. Results are presented in Table 25. Regression analyses show that age (β = -.20, $p < .001$) and education (β = .27; β = .26 $p < .001$) account for a significant proportion the variance for all three SS-4 items. This variance percentage does not significantly change with the inclusion of ε4 genotype (β = -.01; β = .01, p = .96), CLUBS (β = -.04, p = .45), HOURS, (β = .06, p = .25), or SUPPORT (β = -.01, p = .87). The interaction between genotype and CLUBS (β = -.10, p = .56), HOURS,

(β = .01, p = .96) or SUPPORT (β = .20, p = .47) does not alter the isolated effect of ε4 genotype and SS-4 on BDS scores. Moderation was not shown in these three models.

TABLE 25: Testing Social Network Moderator Effects on BDS via a Series of Hierarchical Multiple Regressions. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Step and variable	β	R^2	F	ΔR^2
Step 1				
Age	-.20**			
Education	.27**	.12**	26.74**	
Step 2				
ε4 Status	-.01			
Clubs/Organizations	-.04	.12**	13.49**	.00
Step 3				
ε4 Status X Clubs/Organizations	-.10	.12**	10.82**	.00
Step 1				
Age	-.20**			
Education	.26**	.12**	26.46**	
Step 2				
ε4 Status	.01			
Hours	.06	.12**	13.54**	.00
Step *3*				
ε4 Status X Hours	.01	.12**	10.80**	.00
Step 1				
Age	-.20**			
Education	.27**	.12**	26.61**	
Step 2				
ε4 Status	-.01			
Support Received	-.01	.12**	13.24**	.00
Step 3				
ε4 Status X Support Received	.20	.12**	10.68*	.00

For analyses 7-9, SS-4 variables were regressed on the SJS memory measure. Results are presented in Table 26. Regression analyses show that age (β = -.50, $p < .001$) and education (β = .14, $p < .001$) account for a significant proportion the variance for all three SS-4 items. This variance percentage does not significantly change with the inclusion of ε4 genotype (β = .01, $p <$ .75), CLUBS (β = .01, p = .18), HOURS, (β = .05, p = .36), or SUPPORT (β = .01, p = .86). The interaction between genotype and CLUBS (β = .16, p = .28) and SUPPORT (β = .01, p = .95),

items do not alter the isolated effect of ε4 genotype on SJS. Moderation was not evident in these two models. The interaction between ε4 genotype and HOURS did significantly change the isolated effect of ε4 genotype and SS-4 (β = .28, p < .05), as it produced a 1% change in variance compared to the isolated effect of the ε4 allele. These results imply that moderation is evident in this last model, however a 1% change in variance is usually not seen as a substantial indicator of moderation (Baron & Kenny, 1986).

TABLE 26: Testing Social Network Moderator Effects on SJS via a Series of Hierarchical Multiple Regressions. Note: ** represents $p < 0.01$, * represents $p < 0.05$.

Step and variable	β	R^2	F	ΔR^2
Step 1				
Age	-.50**			
Education	.14**	.29	74.56**	
Step 2				
ε4 Status	.01			
Clubs/Organizations	.06	.29	57.77**	.00
Step 3				
ε4 Status X Clubs/Organizations	.16	.29	30.45**	.00
Step 1				
Age	-.50**			
Education	.14**	.28	74.44**	
Step 2				
ε4 Status	.02			
Hours	.05	.28	37.35**	.00
Step *3*				
ε4 Status X Hours	.28*	.29	30.83**	.01*
Step 1				
Age	-.50**	.		
Education	.14**	28	73.53**	
Step 2				
ε4 Status	.01			
Support Received	.01	.28	36.60**	.00
Step 3				
ε4 Status X Support Received	-.02	.28	29.20**	.00

For analyses 10-12, SS-4 variables were regressed on the SJS-PROP memory measure. Results are presented in Table 27. Regression analyses show that age (β = -.50, p < .001) and

education (β = .14; β = .13 p < .001) account for a significant proportion the variance for all three SS-4 items. This variance percentage does not significantly change with the inclusion of ε4 genotype (β = .03; β = .04, p < .55), CLUBS (β = .00, p = .92), HOURS, (β = -.01, p = .95), or SUPPORT (β = .07, p = .25). The interaction between genotype and CLUBS (β = -.08, p = .70), HOURS, (β = -.07, p = .70) or SUPPORT (β = -.27, p = .32) does not alter the isolated effect of ε4 genotype and SS-4 on SJS-PROP. Moderation was not shown in these three models.

TABLE 27: Testing Social Network Moderator Effects on SJS-PROP via a Series of Hierarchical Multiple Regressions

Step and variable	*B*	R^2	*F*	ΔR^2
Step 1				
Age	-.55**			
Education	.14**	.33	56.00**	
Step 2				
e4 Status	-.03			
Clubs/Organizations	.00	.33	27.88**	.00
Step 3				
e4 Status X Clubs/Organizations	.08	.33	22.24**	.00
Step 1				
Age	-.55**			
Education	.13**	.33	56.09**	
Step 2				
e4 Status	-.03			
Hours	-.01	.33	27.93**	.00
Step *3*				
e4 Status X Hours	.07	.33	22.28**	.00
Step 1				
Age	-.54**			
Education	.14**	.33	54.60**	
Step 2				
e4 Status	-.04			
Support Received	.07	.33	27.70**	.00
Step 3				
e4 Status X Support Received	-.27	.33	22.36**	.00

DISCUSSION

The primary purpose of this study was to test the link between the ε4 allele and cognitive function in relation to individual difference variables, including current health status, and social networks. To date, it is believed that this is the first investigation to assess ε4 status in relation to all of these variables in a general adult population. While the original intention of this study did not center on determining differences in health and cognition, the current data provides invaluable information about successful aging. Initial analyses revealed age-related differences in memory and physical health measures. In particular, global cognitive performance, as indexed by the MMSE and MMSE-R, demonstrated a decline in very late age. Age-related deficits were also observed in the FDS, BDS, and SJS tasks. These results are consistent with prior literature suggesting that the majority of cognitive deficits emerge during midlife and possess linear declines across each decade (Bäckman et al., 2000; Craik, 2000; Craik & Jennings, 1992). Physical heath, measured with both subjective (PCS) and objective (CHRONIC) indices, exhibited age-related declines. The oldest-old had lower levels of self-reported health and increased numbers of chronic conditions compared to their younger counterparts. Furthermore, responses to the social network characteristic items (SS-4) also changed with age. The two youngest age cohorts were likely to spend more hours outside of their home doing activities (HOURS). The two older groups were more highly involved with clubs/organizations (CLUBS) and exhibited greater satisfaction with support received from others (SUPPORT).

From these data, one might assume that aging is only associated with declines in a variety of areas, such as cognition, health, and social networks. It also may appear that aging is a period of continual decline, and this might be daunting to those individuals who are approaching middle to later adulthood. However, it is important to mention that the mental health of the sampled participants was greatest in the oldest-old cohort. Mental health component scores did not show

age-related declines, but rather age-related increases. The oldest-old participants had greater levels of self-reported mental health (MCS) in comparison to the middle-aged groups. This paradoxical finding is noteworthy, as older adulthood is consistently regarded as a period of declines. This research has shown that despite the cognitive and physical declines, the oldest-old feel good, maintain happiness, and possess a high level of mental health as indexed by the SF-36 MCS scores.

Returning to the three main hypotheses of the current study, it was first predicted that carriers of the ε4 allele would show lower cognitive function compared to non-carriers. Early correlation analysis did reveal a significant relationship of the ε4 allele with cognitive function, including the MMSE, MMSE-R, and FDS (Table 5). However, these significant associations were not replicated after controlling for age. Regression analyses did not find a link between the ε4 allele and cognition after controlling for both the education level and age of participants. These two individual difference variables accounted for the largest amount of variance among MMSE, MMSE-R, VOCAB, FDS, BDS, SJS, and SJS-PROP scores. Overall, this study reliably found that age and education are the two strongest indicators of performance on cognitive tasks. This is consistent with Jones and Gallo (2002) who reported a significant association of education status with MMSE performance. While this study did not replicate ε4-related declines in cognition, it was determined that age and education should always be accounted for when conducting investigations examining the relation of ε4 and cognition.

The second tested hypothesis was that physical heath would mediate the relationship between ε4 and cognition. In particular, it was expected that ε4 carriers would have lessened physical health and this in turn would produce cognitive decrements. Prior work has shown that possession of at least one copy of the ε4 allele may increase the risk for cardiovascular disease, (Bernstein, Costanza, James, Morris, Cambien, Raoux, & Morabia, 2002), and this may produce

memory deficits. Preliminary regression and correlation analyses revealed that the ε4 allele was not associated with lower, but rather higher levels of physical health. Tests for causal mediation using Baron and Kenny (1986) statistical procedures found that physical health (PCS or CHRONIC) did not mediate the link between ε4 and cognition. The lack of mediation effects directly conflicts with the work of Haan et al. (1999) and Deeny et al. (2008) who both report that physical health and exercise modify the link between APOE genotype and memory. The last hypothesis was contingent on the former, as it was predicted that social network characteristics (SS-4 items) would interact with the association between ε4 and cognition. This prediction was developed as social support tends to correlates highly with health in adults (Hultsch et al., 1993). Results from this study found no reliable signs of an interaction (i.e. moderation) with any SS-4 item. The inclusion of SS-4 items or an ε4 by SS-4 interaction did not influence the amount of variance attributed to the ε4 allele when predicting cognitive performance. In sum, results from this study did not support the three hypotheses.

There are several reasons that may explain the non-existent relations among the ε4 allele, cognition, health, and social network characteristics in the current study. The first limitation is that the LHAS population can generally be described as a high-functioning sample. The younger LHAS participants (85 years and under) may be considered representative of the larger Louisiana population. In contrast, many of the LHAS oldest-old participants (85+) live independently and continue to maintain a good quality of life. It is plausible that the health and cognitive ability of the sampled oldest-old are far above the norm when compared to the general population. The LHAS oldest-old can be seen as survivors because they are not victims of mortality. Bernstein and colleagues (2002) related the presence of the ε4 allele with increased risk for cardiovascular disease, which is a frequent cause of mortality in adulthood (American Heart Association, 2006). In the current study, a chi-square analysis revealed that the oldest-old (85 and older) had a

significantly lower incidence rate of the ε4 allele (15%) compared to the three younger groups (28%, 30%, and 24% respectively). It could be concluded that ε4 carriers are less likely to live past the seventh decade and become members of the oldest-old cohort, which supports the notion that the ε4 allele is linked with mortality in adulthood. These results are consistent with the mortality rates reported by Rosvall, Rizzuto, Wang, Winbald, Graff, and Fratiglioni (2008). These authors recruited adults over the age of 75 and followed them for approximately 18 years. Rosvall and colleagues reported that ε4 carriers had a 49% elevated risk level for death compared to non-carriers. While this study cannot definitely prove that the ε4 allele is related to mortality, these results when combined with those of Rosvall et al., are suggestive that the allele may act as a substantial risk factor.

Secondly, this study may have chosen cognitive measures that were not sensitive enough to detect ε4-related deficits. While the MMSE is considered a common screening tool, prior studies have shown performance deficits in ε4 carriers compared to non-carriers (Christensen et al., 2008; Ercoli, Siddarth, Dunkin, Bramen, & Small, 2003; Packard et al. 2007). The current study did exhibit a large ceiling effect on the MMSE until around age 85, where only the oldest-old participants produced MMSE variability when compared to younger groups. A follow-up pairwise (*t-test*) analysis did not reveal any difference between ε4 carriers and non-carriers on the total MMSE score in the oldest-old age cohort ($t = -.03$; $p = .98$). Next, scores on the working memory measures were not associated with presence of the ε4 allele. These tasks did produce performance variability and none produced marked ceiling effects. These measures have sound psychometric properties in adult populations. This study selected various measures of working memory, as this construct has demonstrated ε4-related declines in prior literature (Widsom, Callahan, and Hawkins, 2009). This study failed to find a link between ε4 and working memory performance. One plausible explanation centers on the notion that working memory tasks are

highly variable and may not utilize similar cognitive processes. For example, both the Sternberg and the SJS tasks have been considered to be working memory measures, however the goals and task rules differ greatly. Therefore, there is a continual debate as to whether or not these tasks actually measure one's working memory performance. The ε4-related declines reported in prior investigations might be task dependent, rather than indicative of performance on all working memory assessments.

While results from this study did not support the proposed hypotheses, useful information about successful aging was obtained. First, although later adulthood may commonly be associated with cognitive and physical declines, older adults remain satisfied with their lives and maintain high levels of mental health. The mental health scores of the LHAS oldest-old adults were significantly higher than the three younger age groups. Secondly, this study found that age and education were the two most influential predictors of cognition, health, and social networks. Next, the ε4 allele was associated with cognition in the current population, however this finding was not replicated after controlling for age and education of the participants. Physical health did not mediate this relation, and social network characteristics did not moderate this same relationship. It is plausible that the lack of sensitivity in the selected cognitive measures, the discrepancies about working memory tasks, and/or the high-functioning distinctiveness of the LHAS sample, could explain the non-significant results. To provide adequate resolution, subsequent studies should examine a variety of working memory measures to determine if ε4-related deficits are task-specific. Researchers should broaden their sample by recruiting lower functioning individuals to make their results more generalizable to a larger population. Lastly, a novel finding may shed light on a key aspect of healthy aging. The prevalence rates of the ε4 allele significantly declined with age, where the oldest-old had a 50% lower incidence of ε4 compared to younger age groups. These prevalence ratings support the notion that the ε4 allele is

associated with mortality in adulthood. Individuals who possess at least one copy of the ε4 allele are more likely to have higher lipid levels, suffer decreased cardiovascular fitness, and consequently die. Overall findings from the current study indicate that the ε4 allele may be predictive of mortality rather than cognitive functionality in later adulthood.

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APPENDIX A: MINI-MENTAL STATE EXAM

INSTRUCTIONS: Place a check above correct answers, as appropriate. Record score for each item in the margin. Total scores will be calculated later.

Assess level of consciousness along a continuum: Alert Drowsy Stupor Coma

ORIENTATION

1. Ask Ss for the date. Then specifically ask for the parts omitted.
(SCORE: 1 point for each) (5) _____

"What is the (year) (season) (date) (month) (day)?"

2. "Can you tell me the name of the: (state) (parish) (5) _____
(town) (hospital/or where we are today) (floor/or room we're in today)?"

(Note: you may use the term, "facility" or "building" instead of hospital
If testing Ss at home, say "where we are today/room we're in today)

REGISTRATION

Tell the Ss that you have a memory task for him/her. Then say the following, clearly and slowly (i.e., 1 second to say each):

3. "Remember these 3 words: cup, pencil, airplane." (3) _____

After you have said all 3, ask Ss to repeat them. Give 1 point for each correct answer. Then repeat them until the Ss learns all 3. Count trials and record. (SCORE: number of words correct on first attempt (0-3). Allow up to 6 trials)

Number of repetitions _____

ATTENTION AND CALCULATION

4. "I want you to count backwards from 100 by 7's." Stop after 5 subtractions (93, 86, 79, 72, 65) (SCORE: 1 point for each correct subtraction of 7 from the previous number).

"Now spell "world" backwards." (SCORE: number of letters in correct order, i.e., DLROW=5; DLORW=3).

Score both tasks, but only count the best one toward the total score (5) _____

RECALL

5. "Do you remember the words I gave you earlier? What were they?"
(the 3 objects repeated above. 1 point for each correct) (3) _____

LANGUAGE

6. NAMING. Point to a wristwatch and ask the Ss what it is.
Repeat this for pencil (2) _____

REPETITION

7. As the Ss to repeat the following:
"No ifs, ands or buts." (1) _____

COMPREHENSION

8. (Follow a 3-stage command). Place a piece of paper in front of the Ss and say:
"Take a paper in your right hand,
fold it in half, and put it on the floor." (3) _____

Read and the following and do what it says:
(Have Ss read "close your eyes" on attached sheet. They also need to make up their own sentence. Credit is given for copy a design only if they get all of the angles right).

CLOSE YOUR EYES (1 point)
Write a sentence (1 point)
Copy a design (1 point) (3) _____

TOTAL SCORE: _____

C L O S E Y O U R E Y E S

APPENDIX B: VOCABULARY MEASURE

Write the meaning of each word in the space provided:

1. Breakfast _____

_____

2. Slice _____

_____

3. Fabric _____

_____

4. Regulate _____

_____

5. Enormous _____

_____

6. Conceal _____

_____

7. Hasten _____

_____

8. Designate _____

_____

9. Commence _____

_____

10. Obstruct _____

_____

11. Ponder _____

_____

12. Calamity _____

_____

13. Tangible _____

_____

14. Fortitude _____

_____

15. Audacious _____

_____

16. Edifice _____

_____

17. Ominous _____

_____

18. Tirade _____

_____

19. Impale _____

_____

20. Travesty _____

_____

APPENDIX C: SIZE JUDGMENT SPAN TASK

Size Judgement Span Exp _____ Rp _____

3 Sets of 2					
WASTEBASKET, SCORPION		FIREPLACE, TOAST		BRICK, UMBRELLA	
Correct:	Rp Response:	Correct:	Rp Response:	Correct:	Rp Response:
scorpion	_____	toast	_____	brick	_____
wastebasket	_____	fireplace	_____	umbrella	_____
Check one:	_____ Pass _____ Fail		_____ Pass _____ Fail		_____ Pass _____ Fail
3 Sets of 3					
BUTTERFLY, ELEPHANT, NEWSPAPER		FROG, PIANO, HAIRPIN		AMBULANCE, STRAWBERRY, TOOTH	
Correct:	Rp Response:	Correct:	Rp Response:	Correct:	Rp Response:
butterfly	_____	hairpin	_____	tooth	_____
newspaper	_____	frog	_____	strawberry	_____
elephant	_____	piano	_____	ambulance	_____
Check one:	_____ Pass _____ Fail		_____ Pass _____ Fail		_____ Pass _____ Fail

3 Sets of 4					
HOOF, GARAGE, TOASTER, BARREL		DOVE, SPLINTER, ALLIGATOR, COTTON BALL		REVOLVER, TRUMPET, SUITCASE, NAIL	
Correct:	Rp Response:	Correct:	Rp Response:	Correct:	Rp Response:
hoof	_____	splinter	_____	nail	_____
toaster	_____	cotton ball	_____	revolver	_____
barrel	_____	dove	_____	trumpet	_____
garage	_____	alligator	_____	suitcase	_____
Check one:	_____ Pass _____ Fail		_____ Pass _____ Fail		_____ Pass _____ Fail
3 Sets of 5					
FOX, MOOSE, BULLET, LOBSTER, BUCKET		BEAVER, PENCIL, CATERPILLAR, STEAMBOAT, SKILLET		OVEN, BANDAID, RIVER, SLIPPER, LEMON	
Correct:	Rp Response:	Correct:	Rp Response:	Correct:	Rp Response:
bullet	_____	caterpillar	_____	bandaid	_____
lobster	_____	pencil	_____	lemon	_____
bucket	_____	skillet	_____	slipper	_____
fox	_____	beaver	_____	oven	_____
moose	_____	steamboat	_____	river	_____
Check one:	_____ Pass _____ Fail		_____ Pass _____ Fail		_____ Pass _____ Fail

3 Sets of 6

DONKEY, CATHEDRAL, TACK SHOE, CHECKBOOK, SHOTGUN	RACCOON, GIRAFFE, MOUNTAIN, PEACH, BOOK, NEEDLE	CRACKER, FIRE ENGINE, POTATO MAILBOX, PEA, SAWHORSE
Correct: Rp Response:	Correct: Rp Response:	Correct: Rp Response:
tack _____	needle _____	pea _____
checkbook _____	peach _____	cracker _____
shoe _____	book _____	potato _____
shotgun _____	raccoon _____	mailbox _____
donkey _____	giraffe _____	sawhorse _____
cathedral _____	mountain _____	fire engine _____
Check one: _____ Pass _____ Fail	_____ Pass _____ Fail	_____ Pass _____ Fail

3 Sets of 7

SOFA, CIGARETTE, ROSE, HELICOPTER, CANYON, INFANT, PAPERCLIP	HOUSE, WALNUT, MOSQUITO, STOPSIGN, LADDER, VOLCANO, CAMERA	COAT HANGER, HINGE, PUMPKIN, RAKE, CANOE, BICYCLE, JELLYBEAN
Correct: Rp Response:	Correct: Rp Response:	Correct: Rp Response:
paperclip _____	mosquito _____	jellybean _____
cigarette _____	walnut _____	hinge _____
rose _____	camera _____	coat hanger _____
infant _____	stopsign _____	pumpkin _____
sofa _____	ladder _____	rake _____
helicopter _____	house _____	bicycle _____
canyon _____	volcano _____	canoe _____
Check one: _____ Pass _____ Fail	_____ Pass _____ Fail	_____ Pass _____ Fail

3 Sets of 8

BATHTOWEL, DUSTPAN, MOUSETRAP, TRAIN, BUTTON, GLACIER, LAWNMOWER, KEY		TOOTHPICK, ICE CUBE, SUBMARINE, DOORKNOB, GOLF COURSE, HARP, TELEPHONE, PILLOW		BASKETBALL, WASP, LICENSE PLATE, ROCKET, SCISSORS, WATERMELON, CLOTHESPIN, OCEAN	
Correct:	Rp Response:	Correct:	Rp Response:	Correct:	Rp Response:
button	_____	toothpick	_____	wasp	_____
key	_____	ice cube	_____	clothespin	_____
mousetrap	_____	doorknob	_____	scissors	_____
dustpan	_____	telephone	_____	license plate	_____
bathtowel	_____	pillow	_____	basketball	_____
lawnmower	_____	harp	_____	watermelon	_____
train	_____	submarine	_____	rocket	_____
glacier	_____	golf course	_____	ocean	_____
Check one:	_____ Pass _____ Fail		_____ Pass _____ Fail		_____ Pass _____ Fail

APPENDIX D: FORWARD AND BACKWARD DIGIT SPANS

FORWARD BACKWARD DIGIT SPAN		Pass/Fail
1.	5 - 8 - 2	
	6 - 9 - 4	
2.	6 - 4 - 3 - 9	
	7 - 2 - 8 - 6	
3.	4 - 2 - 7 - 3 - 1	
	7 - 5 - 8 - 3 - 6	
4.	6 - 1 - 9 - 4 - 7 - 3	
	3 - 9 - 2 - 4 - 8 - 7	
5.	5 - 9 - 1 - 7 - 4 - 2 - 8	
	4 - 1 - 7 - 9 - 3 - 8 - 6	
6.	5 - 8 - 1 - 9 - 2 - 6 - 4 - 7	
	3 - 8 - 2 - 9 - 5 - 1 - 7 - 4	
7.	2 - 7 - 5 - 8 - 6 - 2 - 5 – 8 - 4	
	7 - 1 - 3 - 9 - 4 - 2 - 5 – 6 - 8	

BACKWARD DIGIT SPAN		Pass/Fail
1.	2 - 4	
	5 - 8	
2.	6 - 2 - 9	
	4 - 1 - 5	
3.	3 - 2 - 7 - 9	
	4 - 9 - 6 - 8	
4.	1 - 5 - 2 - 8 - 6	
	6 - 1 - 8 - 4 - 3	
5.	5 - 3 - 9 - 4 - 1 - 8	
	7 - 2 - 4 - 8 - 5 - 6	
6.	8 - 1 - 2 - 9 - 3 - 6 - 5	
	4 - 7 - 3 - 9 - 1 - 2 - 8	
7.	9 - 4 - 3 - 7 - 6 - 2 - 5 - 8	
	7 - 2 - 8 - 1 - 9 - 6 - 5 - 3	

APPENDIX E: 36-ITEM SHORT FORM

Instructions for Completing the Questionnaire

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
O	O	O	O	O

2. Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
O	O	O	O	O

1. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited
a. Vigourous Activities: such as running, lifting heavy objects, participating in strenuous sports	O	O	O
b. Moderate Activities: such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	O	O	O
c. Lifting or carrying groceries	O	O	O
d. Climbing several flights of stairs	O	O	O
e. Climbing one flight of stairs	O	O	O
f. Bending, kneeling, or stooping	O	O	O
g. Walking more than a mile	O	O	O
h. Walking several blocks	O	O	O
i. Walking one block	O	O	O
j. Bathing or dressing yourself	O	O	O

4. During the past 4 weeks, have problems with your physical health caused you to:

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	O	O
b. Accomplish less than you would like	O	O
c. Limit the kind of work you do or other activities	O	O
d. Have difficulty performing work or other activities (for example, it took extra time)	O	O

5. During the past 4 weeks, have problems with your emotional health (such as feeling depressed or anxious) caused you to:

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	O	O
b. Accomplish less than you would like	O	O
c. Do work or other activities <u>less</u> carefully than usual	O	O

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
O	O	O	O	O

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very Severe
O	O	O	O	O	O

8. During the past 4 weeks, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
O	O	O	O	O

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of pep?	O	O	O	O	O	O
b. Have you been a very nervous person?	O	O	O	O	O	O
c. Have you felt so down in the dumps nothing could cheer you up?	O	O	O	O	O	O
d. Have you felt calm and peaceful?	O	O	O	O	O	O
e. Did you have a lot of energy?	O	O	O	O	O	O
f. Have you felt downhearted and blue?	O	O	O	O	O	O
g. Did you feel worn out?	O	O	O	O	O	O
h. Have you been a happy person?	O	O	O	O	O	O
i. Did you feel tired?	O	O	O	O	O	O

10. During the past 4 weeks, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting friends, relatives, etc)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
O	O	O	O	O

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	O	O	O	O	O
b. I am as healthy as anybody I know	O	O	O	O	O
c. I expect my health to get worse	O	O	O	O	O
d. My health is excellent	O	O	O	O	O

APPENDIX F: DEMOGRAPHIC QUESTIONNAIRE

1. How would you rate your health at the present time? ***(circle one option)***
   1. excellent 2. Good 3. Fair 4. Poor

2. How much do health troubles stand in the way of your doing things you want to do?
   1. not at all 2. A little (some) 3. A great deal

3. Do you think your health is better, the same as, or worse than most people your age?
   1. better 2. Same 3. Worse

4. Number of nights you stayed as a patient in the hospital in the past year:
   1. none 2. 1 to 3 3. 4 to 6 4. Over 6

5. What is your average monthly out of pocket cost for physician prescribed medications? _____

---

6. Do you have health insurance?
   1. no
   2. yes

7a. Are you currently receiving Medicare?
   1. no
   2. yes; If yes, are you receiving:
      Medicare: Part A (hospital)
      Medicare: Part B (for doctors)
      Both parts

7b. Do you have a Medicare supplemental plan?
   1. no
   2. yes; If yes, what kind of policy?
      Oschner 65
      Tenet 65
      Other _____

7c. Do you have additional insurance coverage available to you as a retiree of a public or private entity/institution?
   1. no
   2. yes; If yes, what kind of policy?
      State Group PPO
      State Group EPO
      Oschner
      Other _____

7d. Are you carrying a private health insurance policy?

1. no
2. yes; If yes, what kind of policy?
   - Blue Cross
   - PPO
   - HMO
   - Aetna
   - Other _____

   If yes, did you obtain this policy through your employer/union:
   1. No
   2. Yes

8. Your marital status:
   1. never married
   2. married
   3. Divorced or separated
   4. Widowed

   If married, for how many years? _____

9. What has been your usual occupation or job – the one you have worked at the longest?

   Job/occupation

   Type of industry or business (what does the company do or make)

   Your usual activities or duties in the job

   Years in this job

   [__][__] Years *(Don't know – record 99)*

10. If married, what has been your spouses' usual occupation or job?

    Job/occupation

    Type of industry or business (what does the company do or make)

    Your usual activities or duties in the job

    Years in this job

    [__][__] Years *(Don't know – record 99)*

2. Years of Education:

SELF: ____ years
(circle one option)
- Less than 7th grade
- 7th-9th grade
- 10th-11th grade
- High School graduate
- Partial college or specialized training (at least 1 yr)
- College or university graduate
- Graduate degree

IF MARRIED, SPOUSE: ____ years
(circle one option)
- Less than 7th grade
- 7th-9th grade
- 10th-11th grade
- High School graduate
- Partial college or specialized training (at least 1 yr)
- College or university graduate
- Graduate degree

12. How many clubs or social organizations do you belong to? (include church and other community activities)
    1. none
    2. 1 to 3
    3. 4 to 6
    4. over 6

13. How many hours per week do you spend outside of your home?
    1. none
    2. 3 to 5 hours
    3. 6 to 12 hours
    4. 13 to 19 hours
    5. over 19 hours

14. How satisfied are you with the overall support you get from other people for dealing with personal or day-to-day problems:
    1. very satisfied
    2. fairly satisfied
    3. a little satisfied
    4. not satisfied at all

15. Do you have a confidant, someone you can talk to about issues that concern you?
    1. yes
    2. no

APPENDIX G : SOCIAL SUPPORT QUESTIONNAIRE

Name: _____

Date: _____

Highest degree held (check one):
- □ High school diploma
- □ Some college/Associate's degree
- □ Bachelor's degree
- □ Master's degree
- □ Doctorate

Your Gender: (check one):
- □ male
- □ female

Marital Status (check one):
- □ single (never married)
- □ married
- □ divorced
- □ widowed

Ethnicity: (check one):
- □ African American or Black
- □ Caucasian or White
- □ American Indian or Alaska native
- □ Hispanic or Latina(o)
- □ Asian
- □ Native Hawaiian or other Pacific Islander
- □ Other
- □ Multiracial

Age: _____

For each question listed below, please place a checkmark next to the response you feel is most appropriate.

3. How many clubs or social organizations do you belong to? (include church and other community activities)

□ none
□ 1 – 3
□ 4 – 6
□ more than 6

4. How many hours per week do you spend outside your home?

□ none
□ 3 – 5
□ 6 – 12
□ 13 – 19
□ more than 19 hours

5. How satisfied are you with the overall support you get from other people for dealing with personal or day-to-day problems?

□ very satisfied
□ a little satisfied
□ fairly satisfied
□ not satisfied at all

6. Do you have a confidant, someone you can talk to about issues that concern you?

□ yes
□ no

The questions below refer to activities and experiences that may occur to most people. For each question, there are two possible answers, "yes" or "no". Please mark the answer you choose for each item.

	Yes	No
7. Do you have access to a telephone or computer in your household?	□	□
8. Have you made a personal call in the last week?	□	□
9. Have you written a personal letter or email in the last week?	□	□
10. Do you subscribe to a weekly or monthly magazine or journal?	□	□
5. Do you attend religious services, or religious gatherings or meetings?	□	□
6. Did you vote in the last local, regional, or national elections?	□	□
7. Have you been on vacation in the last year?	□	□
8. Are you planning to go on vacation in the next year?	□	□
9. Do you use the public library?	□	□
10. In the past month, have you attended a meeting, or gathering of any club, organization, society, or group?	□	□

The two questions below ask you to evaluate the level of social support you have received in the past month. Please select the response you deem most appropriate for each item.

During the past month…	None	Almost none	Some	A lot	Very much
11. How sufficient was the social support you received?	□	□	□	□	□
12. How satisfied are you with the support you received?	□	□	□	□	□

The questions on this page ask you about your level of everyday activity. For each item, please place a checkmark next to how often you perform the following activities.

In the last <u>3 months</u> how often have you engaged in the following activities?

13. Preparing main meals:
____never ____< 1 time/week ____1 – 2 times/week ____ most days

14. Washing up:
____never ____< 1 time/week ____1 – 2 times/week ____ most days

15. Washing clothes:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

16. Light housework:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

17. Heavy housework:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

18. Local shopping
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

19. Social outings:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

20. Walking outside for more than 15 minutes:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

21. Actively pursuing a hobby:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

22. Driving a car or bus travel:
___never ___< 1–2 times in 3 months ___3–12 times in 3 months ___1 or more times/week

In the last <u>6 months</u> how often have you engaged in the following activities?

11. Outings/car rides:
___never ___< 1–2 times in 3 months ___3–12 times in 6 months ___1 or more times/week

12. Gardening:
___never ___< 1–2 times in 3 months ___3–12 times in 6 months ___1 or more times/week

23. Household/car maintenance:
___never ___< 1–2 times in 3 months ___3–12 times in 6 months ___1 or more times/week

Please read the following questions. These questions refer to your social experiences and personal feelings. Please mark the answer you choose for each item.

24. How many persons within one hours travel (of your home/from here) do you feel you can depend on or feel very close to? Do not include members of your own family.

Number: _____

	never	1	2	3	4	5	6	7+
25. How many times during the past week did you spend some time with someone who does not live with you? For example, you went to see them or they came to visit you, or you went out together?	□	□	□	□	□	□	□	□
26. How many times did you talk to someone – friends, relatives or others – on the telephone in the past week? (either they called you, or you called them).	□	□	□	□	□	□	□	□
27. How often did you go to meetings of social clubs, religious meetings, or other groups that you belong to in the past week?	□	□	□	□	□	□	□	□

	hardly ever	some of the time	most of the time
5. How often do your family and friends (i.e., people who are important to you) understand you?	□	□	□
6. How often do you feel useful to your family and friends?	□	□	□
7. How often do you know what is going on with your family and friends?	□	□	□
8. When you are talking with your family and friends, how often do you feel you are being listened to?	□	□	□

9. How often do you feel you have a definite role (place) in your family and among your friends?	□	□	□
10. How often can you talk about your deepest problems with at least some of your family and friends?	□	□	□

	very dissatisfied	**somewhat dissatisfied**	**satisfied**
28. How satisfied are you with the kinds of relationships you have with your family and friends? *IF NO FAMILY OR FRIENDS*, how satisfied are you with not having any of these relationships?	□	□	□

****THANK YOU FOR PARTICIPATING IN THIS SURVEY. ****

APPENDIX H: ABBREVIATION LIST

1. **APOE:** Apolipoprotein
2. **BDS:** Backward Digit Span
3. **CHRONIC:** Objective Health/Chronic Condition Index
4. **FDS:** Forward Digit Span
5. **HKR:** Hurricanes Katrina and Rita
6. **LHAS:** Louisiana Healthy Aging Study
7. **MCS:** Mental Health Composite Score of the 36-Item Short Form
8. **MMSE:** Mini-Mental State Exam
9. **MMSE-R:** Mini-Mental State Exam-Recall Domain
10. **PBRC:** Pennington Biomedical Research Center
11. **PCS:** Physical Health Composite Score of the 36-Item Short Form
12. **SF-36:** 36-Item Short Form
13. **SJS:** Size Judgment Span Score
14. **SJS-PROP:** Size Judgment Span-Proportion Score
15. **SS-4:** Social Network Characteristics Measure
16. **SS-4/CLUBS:** Social Network Characteristics Measure -Clubs Question
17. **SS-4/HOURS:** Social Network Characteristics Measure-Hours Question
18. **SS-4/SUPPORT:** Social Network Characteristics Measure-Support Question
19. **VOCAB:** Vocabulary Score
20. **YPAS:** Yale Physical Activity Survey

VITA

Jennifer Lee Silva grew up in Somerville, Massachusetts, and graduated from Somerville High School in 1999. Jennifer attended the University of New Hampshire (UNH) during her undergraduate career and graduated with a Bachelor of Arts in 2003. Jennifer started her graduate training at UNH and graduated with a Master of Arts in 2005. She enrolled at Louisiana State University and worked with Dr. Katie Cherry and the Louisiana Healthy Aging Study investigating the determinants of successful aging. After graduation, Jennifer will be an Assistant Professor of Psychology at Drury University in Springfield, Missouri.