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The Relationship between Physical Activity, Depressive Symptoms, and Cognitive Functioning

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The Relationship between Physical Activity, Depressive Symptoms, and Cognitive Functioning

by

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Each person whose signature appears below certifies that this thesis in his/her opinion is adequate, in scope and quality, as a thesis for the degree Doctor of Philosophy.

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CONTENT

FIGURES

Figures Page

TABLES

Tables Page

ABBREVIATIONS

ARCD	Age Related Cognitive Decline
PA	Physical Activity
MCI	Mild Cognitive Impairment
AD^{-}	Alzheimer's Disease
PFC	Prefrontal Cortex
CARDIA	Coronary Artery Risk Development in Young Adult Study
MDD	Major Depressive Disorder
SRPA	Self Reported Physical Activity
HAD	Hospital Anxiety and Depression Scale
PPT	Physical Performance Test
CRF	Cardiorespiratory Failure
AMD	Age Related Macular Degeneration
MMSE	Mini Mental Status Exam
SES	Socioeconomic States
CDC	Centers of Disease Control and Prevention
HAM-D	Hamilton Depression Scale
RAVLT	Rey Auditory Verbal Learning Test
TMT	Trails Making Test
SDMT	Symbol Digit Modalities Test
DV	Dependent Variable
VIF	Variance Inflation Factors
MLR	Multiple Linear Regression

IV	Independent Variable
N	Sample Size
IQ	Intelligence Quotient

ABSTRACT OF THE THESIS

The Relationship between Physical Activity, Depressive Symptoms, and Cognitive Functioning

by

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Dr. Adam Aréchiga, Chairperson

The number of older individuals experiencing age related cognitive decline (ARCD) continues to grow exponentially. Memory, executive functioning, and cognitive processing speed have shown to be particularly sensitive to the effects of aging. The same regions of the brain associated with executive functioning and memory are also associated with mood. Researchers have shown an association between ARCD and depression. Research on physical activity (PA) continues to show a beneficial influence on cognition, physical health, and mood. Developmentally, women and men have normal differences in cognitive functioning. As women and men age, these differences can increase. In addition, researchers have shown that level of PA engagement between men and women can differ. Given these established relationships, continued investigation of how these variables interact is important. The aim of the current study is to use a healthy aging population to investigate the interaction of PA, depressive symptoms, and gender on cognitive functioning. Results showed that the overall optimal linear combination of PA, depressive symptoms, gender, and all interactions accounted for about 6.4% of the variance in memory performance ($p < .05$). Gender was also shown to be a significant predictor of memory performance ($p < .01$). Depressive symptoms were shown to be a

significant predictor of executive functioning performance ($p < .05$). All other models were non-significant.

CHAPTER ONE

INTRODUTION

Age related cognitive decline (ARCD) has become an increasingly prominent issue. On a global level, the number of aging individuals who experience some level of cognitive impairment continues to grow exponentially, which researchers have shown to be a significant risk factor for developing dementia (Ferri et al., 2005). Declines in cognitive functioning can be age-associated (i.e., ARCD) or pathologically associated, the latter being more malignant. Examples of ARCD include non-demented reduction in processing speed; slight reductions in inhibition and organization; and or forgetfulness (Levy, 1994). Levy (1994) also mentioned examples of pathological declines in aging, which can include mild cognitive impairment (MCI) or Alzheimer's Disease (AD). There is an estimated 5.3 million individuals who have AD in America. Hebert, Weuve, Scherr, and Evans (2013) stated that those affected by AD will likely triple by 2050 (Division of Population Health, National Center for Chronic Disease Prevention and Health Promotion, 2015). AD is only one form of a pathological cognitive disease, but is the most common, has the highest mortality rates, and is typically seen in individuals 60 years and older (Alzheimer's Association, 2015; Hebert, Scherr, Bienias, Bennett, and Evans, 2003; Heron, 2012). Being over 65 years old automatically places one at a greater risk for ARCD and developing AD (Alzheimer's Association, 2015). Although the two areas of cognitive decline, ARCD and pathological cognitive declines, are equally important to better understand, the main area of focus for this current study is on ARCD. Much research has been devoted to understanding AD, its risk factors, and biomarkers

because of its high mortality rates and strain on society resources, which is why much of the literature on this topic is mentioned.

Age and Cognitive Decline

Three domains of cognition that have shown to be particularly sensitive to the effects of aging are processing speed, executive functioning, and memory. Cognitive processing speed is a term used to describe how efficiently one is able to examine and complete a simple cognitive task (Deary, Johnson, and Starr, 2010). Salthouse (1996) theorized that processing speed is the underlying, and entirely separate, domain of cognitive functioning that experiences initial decline, which therefore adversely influences other cognitive domains such as executive functioning and memory. Processing speed has been shown to be associated with white matter of the left middle frontal gyrus, bilateral parietal lobes, and bilateral temporal lobes (Turken et al., 2008). Turken et al. (2008) mentioned that white matter fiber tracts have been hypothesized to play an integral role in the transmission of information and control signaling, which are necessary for efficiency in overall cognitive performance tasks. Executive functioning encompasses multiple processes such as regulatory control, working memory, reasoning, problem solving, and planning (Salthouse, Atkinson, and Berish, 2003). It is typically associated with the prefrontal cortex (PFC) in the frontal lobe region of the brain (Stuss and Alexander, 2000). There are various forms of memory such as working memory, short-term memory, and long-term memory. Various brain regions work together to ensure proper memory functioning including the hippocampus, amygdala, cingulate gyrus, thalamus, hypothalamus, epithalamus, and mammillary body. All of these regions

make up the limbic system, which is in the medial temporal lobe of the brain (Erickson, Gildengers, and Butters, 2013; Mastin, 2010). Researchers have shown that the PFC and the hippocampus are particularly impacted by physical activity (PA), and have also been shown to be regions that initially experience atrophy and degeneration with aging (Erickson, Gildengers, and Butters, 2013). Paradoxically, they have also been identified as some of the brain regions with greater propensity for neuroplasticity (Goh and Park, 2009), which is the brain's ability to recognize, adapt, and change in response to various environmental demands and stimuli throughout the lifespan via cell proliferation (Erickson, Gildengers, and Butters, 2013).

Age and Mood

Richard et al. (2013) reported that depressive symptoms occur in 3% to 63% of aging adults diagnosed with MCI. As stated prior, MCI is a pathological disease, but this does not exclude aging adults who experience ARCD. Late-life depression has been shown to be associated with cognitive impairment and is common in approximately 8% to 16% of the aging population (Blazer, 2003). Researchers have shown there to be phenomenological neurocognitive differences in the profiles of those who develop late-life depression versus those who have recurrent geriatric major depression (Rapp et al., 2005). Late-life depression is characterized with deficits in attention, executive functioning, higher endorsement of anhedonic symptoms, and comorbid cardiovascular morbidity, while recurrent geriatric major depression is characterized by deficits in episodic memory (Rapp et al., 2005). The regions of the brain associated with executive functioning and memory are also associated with mood. Other areas of the brain that have

been shown to be related to depression are the PFC, the left subgenual cingulate cortex, the anterior cingulate, the gyrus rectus, and the orbitofrontal cortex. Identification of the association between dysfunction in these brain areas and depression has greatly contributed to a better understanding of how to conceptualize and treat depression overall (Ballamaier et al., 2004; Botteron, Raichle, Drevets, Health, and Todd, 2002; George, Ketter, and Post, 1994).

The etiology of depression is multifaceted. It can originate from psychosocial factors, organic brain deficits, or an interaction between the two. Treatment of depression is better informed if these brain areas have been identified as having deficits, or if the symptoms are more psychosocially derived. There is inconsistency in the literature regarding the predictive value of depression on MCI, dementia, and overall cognitive decline but researchers have also shown that there is an association between the two (Rapp et al., 2005; Richard et al., 2013; Rock, Roiser, Riedel, and Blackwell, 2014). It remains unclear whether depression precedes cognitive decline, co-occurs, or is the result of other factors. It is likely that all three are plausible. Taken together, these results show support for the importance of assessing depression in aging adults, and especially those experiencing ARCD, since depression can both exacerbate cognitive decline symptoms and exacerbate depression.

Age and Physical Activity

According to the American College of Neuropsychopharmacology (2014), researchers are currently assessing mid-life risk factors that have the potential to be early identifiers of cognitive decline, dementia, and ultimately AD. Researchers have

suggested that certain risk factors can appear a significant amount of time before the actual development of ARCD. In the Coronary Artery Risk Development in Young Adults Study (CARDIA), young adults were followed from young adulthood throughout midlife to assess the predictive value of chronic exposure to cardiovascular risk factors (e.g., high blood pressure, fasting glucose levels, coronary artery and abdominal aortic calcified plaque) and lifestyle behaviors (e.g., diet, exercise) on cognitive decline during midlife. It was found that, collectively, factors related to poor physiological health and sustained low PA were associated with poor cognitive performance later in life (American College of Neuropsychopharmacology, 2014; Reis et al., 2013).

It is well established that various forms of PA have beneficial impacts on cognitive functioning and mood (Angevaren et al., 2008; Bruijn et al, 2013; Buchman et al., 2012; Lee et al., 2013; Netz, Wu, Becker, and Tenenbaum, 2005; Penedo and Dahn, 2005; Penninx et al., 1998; Prakash, Voss, Erickson, and Kramer, 2015; Strawbridge, Deleger, Roberts, and Kaplan, 2002; Weuve et al., 2004). For example, the PA has been shown to buffer against hippocampal atrophy, improve memory function, and reduce depressive symptomology (Erickson, Gildengers, and Butters, 2012). Historically, researchers from different disciplines have been interested in the influence PA has on various domains of cognition and mental health (e.g., depression, anxiety, etc.) since it is a controllable, but difficult to maintain, behavior offering a wealth of physical and mental health benefits. Bluementhal et al. (1999) conducted a 16-week program for aging adults with major depressive disorder (MDD) where they compared the impact of antidepressants versus PA. Results showed that, initially, antidepressants had the most rapid influence, but those who received a combination of medications and exercise

training showed a more rapid response initially than those with severe depression and only receiving antidepressants; therefore, PA was shown to be an effective additive in the augmentation of positive effects for aging adults with MDD. In a longitudinal study that assessed aging adults and the influence varying levels of PA (i.e., frequency of long walks, exercise, sports, and swimming) had on depression (prevalent depression versus incident depression) over a five year time period, more frequent engagement in long walks, exercise, sports, and swimming was shown to be a protective factor for both types of depression (Strawbridge, Deleger, Roberts, and Kaplan, 2002).

In a study that assessed aging adults 65 years and older who were cognitively intact at baseline and followed for 6.2 years, dementia was seen in 13.0 per 1000 persons who self-reportedly exercised three or more times per week and 19.7 per 1000 in persons who exercised less than three times per week (Larson et al., 2006). Netz, Wu, Becker, and Tenebaum (2005) conducted a meta-analysis that showed moderate aerobic PA positively influenced well-being among aging adults without clinical disorders. In terms of PA and cognition overall, there exists a linear relationship between PA and cognitive functioning for the aging population. As PA increases, cognitive functioning has been observed to increase to some degree at all levels of PA, both acute and life-long (Lee, Lee, Rush, and Jolley, 2013; Rimer et al., 2012; Rosano et al., 2005; Wang et al., 2013; Weuve et al., 2004).

The most recent research in this area has looked at both healthy and cognitively declining aging adults at varying severities to better understand the relationships and mechanisms by which PA influences both cognitive functioning and mood. One study showed continued support for a linear relationship between self-reported PA (SRPA) and

aerobic fitness (i.e., an objective measure of PA) and mental health, as operationalized by the Hospital Anxiety and Depression (HAD) scale. In this study, participants were adults with a mean age of 39 years. SRPA predicted mental health and burnout, but not aerobic fitness. For these adults, subjective estimates of regular engagement in physical activity were significantly predictive of better mental health outcomes, which shows the beneficial influence of PA at varying levels of intensity (Lindwall, Ljung, Hadzibajramovic, and Jonsdottir, 2011). For example, regular walking for 30 minutes per day has been associated with preservation of cognitive functioning in older women (age 65 years and older) with vascular conditions (Vercambre, Grodstein, Manson, Stampfer, and Kang, 2011). In general, low to moderate levels of PA are associated with the amelioration of cognitive decline.

Other factors of PA (i.e., cardiovascular fitness) may contribute to improvements in cognitive functioning. The way PA is operationalized also plays a role in how influential it may or may not be in a given study. PA was defined in various ways in the studies mentioned above: a modified nine-item Physical Performance Tests (PPT; Tolea, Morris, and Galvin, 2015); self-report measures of frequency of engagement in various forms of light to vigorous PA (e.g., walking, sport play, swimming; Strawbridge, Deleger, Roberts, and Kaplan, 2002; Weuve et al., 2004); cardiorespiratory fitness (CRF) objectively measured with an accelerometer (Burzynska et al., 2015); or physical performance tests (e.g., gait speed, strength, balance; Rosano et al., 2005). PA has been shown to improve mood via multiple mechanisms, therefore assisting in buffering against the natural deterioration of certain cognitive domains, or even helping to strengthen them (neuroplasticity) (Angeyaren, Aufdemkampe, Verhaar, Aleman, and Vanhees, 2008).

Overall, researchers have shown that the effects of acute PA are moderately significant in improving cognitive functioning across all domains (Chang, Labbam, Gapin, and Etnier, 2012).

Gender Differences in Aging Adults

It is important to address gender differences within the aging population since researchers have shown gender to be significantly associated with cognition, depressive symptoms, and PA engagement (Penedo and Dahn, 2005; Schoenberg et al., 2006). For example, cognitive domains in which women have been shown to have more superiority are visuomotor speed and language ability, while men have been shown to demonstrate more superiority in mechanical and visuospatial tasked domains, with these differences becoming more solidified during adolescence up through adulthood (Parsons, Rizzo, Van Der Zaag, McGee, and Buckwalter, 2005). Parsons et al. (2005) showed that aging males have better, and more stable, performance on measures of visuospatial cognitive functioning versus females. Singh-Manoux et al. (2012) showed that cognitive decline can begin as early as 45 years old, and between the ages of 65-70 years both men and women have been shown to experience a significant decline in reasoning ability, with men more sensitive to this decline. In the same study, memory decline was similar between aging men and women, but was not significant (Singh-Manpux, 2012).

It is evident that PA has the potential to benefit aging adults in various ways, but the difference in PA engagement for men versus women widens with age as well. Of particular, PA has been shown to attenuate depressive symptoms and help maintain, or slow down, impairments in cognitive functioning due to ARCD. Natural aging is

accompanied by physical decline; therefore, defining moderate to vigorous PA for the aging population is difficult to clearly determine. Researchers have used different ways to define cut points between low, moderate, and high intensity PA. In general, the level of PA that older adults engage in tends to stabilize after 65 years of age and varies anywhere from 10.8 minutes per day to 106.8 minutes per day (Caspersen, Pereira, and Curran, 2000; Evenson, Buchner, and Morland, 2012), but this population has been shown to be more sedentary than not, with women engaging in less moderate to vigorous PA with age than men (Sun, Norman, and While, 2013). Physiologically, men and women experience a decline in maximal oxygen uptake (VO2max) with age, which impacts their cardiovascular response to PA. Aging naturally causes increased difficulty with cardiovascular function when engaging in PA, and due to women having a naturally higher percentage of body fat, a decline in VO2max is more likely to be seen in sedentary older women (Ogawa et al., 1992).

In terms of depressive symptoms and gender differences in aging adults, men and women present with distinct profiles. In general, women have been shown to experience depressive symptoms, or be diagnosed with depression more in comparison to men (Cole and Dendukuri, 2003; Kockler and Heun, 2002; Nolen-Hoeksema, Larson, and Caria, 1999; Piccinelli and Wilkinson, 2000). This difference can be accounted for by a myriad of factors such as bereavement, employment status, hormonal differences, and women presenting with a more typical depressive profile, therefore increasing the likelihood of women being diagnosed with depression (Edelstein, Bamonti, Gregg, & Gerolimatos, 2015). Given that aging men and women with late-life depression are both at risk for developing pathological cognitive decline diseases such as all-cause dementia, AD, and

vascular dementia (Diniz, Butters, Albert, Dew, and Reynolds, 2013), it is important to investigate how gender may play a role in distinct ARCD profiles.

Understanding the Relationships and Current Study

Aims

Taken together, it is apparent that researchers have consistently shown that (a) PA is associated with attenuating depressive symptoms across the lifespan; (b) PA impacts cognitive functioning via various mediating factors; and (c) generally, ARCD is associated with depressive symptoms among aging individuals. Erickson, Gildengers, and Butters (2013) postulated a bidirectional effect between improved cognitive functioning and mood (see Figure 1).

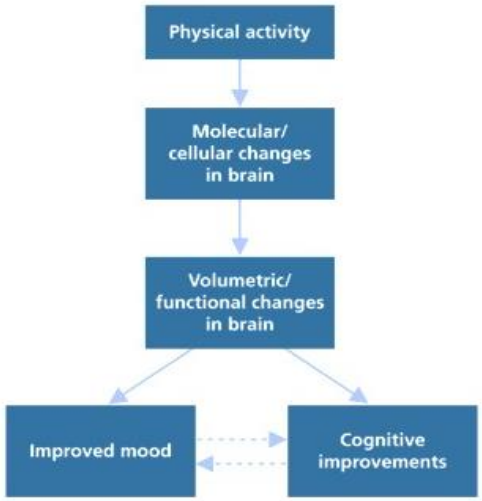

Figure 1. Pathways between Physical Activity, the Physical Brain, Mood, and Cognition (Erickson. Gildengers, and Butters, 2013).

They hypothesized that higher levels of mood can explain cognitive functioning improvement, but that mood improvement can also explain better cognitive functioning. Directionality with regard to this relationship is yet to be fully understood. As described above, the rapidly aging population continues to place a strain on resources in terms of medical care and treatment for deficits related to normal aging, which include ARCD and pathological diseases such as dementia and AD. The aims of this current study are:

i. To better understand the relationship between PA and cognitive decline, specifically processing speed, memory, and executive functioning.
ii. To assess the moderating effects of gender and mood, specifically depressive symptoms, on the relationship between PA and cognition (processing speed, memory, and executive functioning).

Hypotheses

It was hypothesized that:

1. Greater PA would be associated with endorsement of fewer depressive symptoms, being male, and better performance on cognitive measures (measures of processing speed, memory, and executive functioning).
2. Endorsement of fewer depressive symptoms would be associated with better performance on cognitive measures.
3. Being female would be associated with better overall performance on cognitive measures.
4. Women who engage in less PA and endorse more depressive symptoms would have worse performance on cognitive measures than men. Men who engage in more PA

and endorse more depressive symptoms would have better performance on cognitive measures than women.

5. Women who engage in less PA and endorse fewer depressive symptoms would have better performance on cognitive measures than men. There would be no difference in performance for men versus women who engage in more PA and endorse fewer depressive symptoms.

CHAPTER TWO

METHOD

Participants

Participants were community-dwelling older adults who were recruited for a larger randomized, single blind, dual center, controlled study under the direction of the Loma Linda University Department of Nutrition. The larger study's aim was to collect baseline and follow-up data in order to assess what impact daily ingestion of walnuts, over a two year time period, would have on ARCD and macular degeneration in a healthy aging population. In brief, walnuts contain long n-3 fatty-acids (LC n-3 PUFA), which have been postulated to be integral during brain development and prevention, or slowing, of ARCD and age-related macular degeneration (AMD). The primary aim of the study was to provide evidence for walnuts helping to prevent or slow down ARCD and AMD in healthy aging adults. The two institutions where the study was conducted were Loma Linda University in Loma Linda, California, United States and Clinic Hospital in Barcelona, Spain. For the current study, only data from the Loma Linda University site was used. Participants were recruited via flyers and posters posted in geriatric clinics, site hospitals, local churches, and community centers. Exclusion criteria included:

- Illiteracy or inability to understand the protocol or undergo neuropsychological tests.
- Morbid obesity (BMI $\geq$ 40 kg/m^2).
- Uncontrolled diabetes (HbA1c >8%).
- Uncontrolled hypertension (on-treatment blood pressure $\geq$150/100 mm Hg).
- Prior cerebrovascular accident.

- Any relevant psychiatric illness, including major depression via self-report of any current psychiatric diagnoses.
- Advanced cognitive deterioration, dementia.
- Other neurodegenerative diseases (i.e., Parkinson's disease).
- Any chronic illness expected to shorten survival (heart failure, chronic liver disease, kidney failure, blood disease, cancer).
- Bereavement in the first year of loss.
- Bad dentures unless fixable dental prostheses are used.
- Allergy to walnuts.
- Customary use of fish oil or flaxseed oil supplements.
- Eye-related exclusion criteria.

Participants were informed about the study protocol at an initial meeting in which informed consent was obtained, clinical history was taken, a physical examination was performed, and the Mini Mental State Examination (MMSE) was administered to screen for potential cognitive impairment. Participants who had a MMSE score < 24 were referred to a physician and were not eligible for participation. At baseline, there were a total of 365 participants (70.2% female) who met inclusion criteria, were recruited, and completed all baseline measurements and testing. Participants were randomly assigned to the experimental group (walnut ingestion group) or control diet group (Sabaté and Rajaram, 2011).

For the current study, only 163 participants (65% female) who completed baseline testing also completed the PA questionnaire and were used in the current analyses. Participants ranged in age from 64 to76 years (M = 69.33, SD = 3.18). Categories of

ethnicity were: Caucasian, Asian, African-American, Hispanic, and "Other." Descriptive statistics showed that 74.2% reported being Caucasian, 9.2% were Hispanic, 8.6% were African-American, 4.9% were Asian, and 0.6% were "Other." Four participants did not report their ethnicity. The majority of participants had either some college or had completed college (M = 16.02, SD = 2.38); 55.7% reported they had completed college, 33.8% reported that they had ≥ 18 years of education, and 10.4% of participants reported that they had completed at least 12 years of education. At baseline, 6.1% of participants had experienced a traumatic event within the past two weeks. Occurrence of a traumatic event was determined via self-report. As part of the introductory questions, participants were asked to subjectively determine whether they experienced anything he or she deemed "traumatic" in the past two weeks. For example, some participants defined a traumatic event as the loss of a loved one, financial issues, or being in some type of accident. It was important to take the experience of a traumatic event into consideration because depending on the severity of the event it could greatly influence performance on test measures.

Materials

Demographic Variables

Participants completed a clinical history questionnaire at the outset of the study, which included age, gender, ethnicity, past and present medical conditions, level of education, and socioeconomic states (SES). These variables were input into the online database (https://ontocrf.grupocostaisa.com/) used for both nutritional and neuropsychological data. Before beginning the neuropsychological examination,

participants also reported whether they slept well the night prior, had breakfast that day, experienced any traumatic events within the past two weeks, handedness, and years of education.

Physical Activity

The Loma Linda University Department of Nutrition gave participants a physical activity questionnaire. The questionnaire consisted of two main sections. The first section included the question, "What type of physical activity do you perform at your work (or in everyday life)?" It offered the participants seven options: (a) basically I am sitting at work and I only take short walks; (b) I am sitting but I do continuous moderate exercise; (c) I walk quite a lot but I do not do vigorous efforts; (d) I walk quite a lot and I do vigorous efforts; (e) I basically do vigorous efforts and a lot of activity; (f) I am basically standing up without moving; or (g) insufficient data. The first section also asked questions about occupation, sedentary behaviors, and average amount of sleep per day. The second section of the questionnaire asked the participants to report the amount, in minutes per day, they engaged in various types of physical activities (walking, stair climbing, gardening, playing sports). It also offered them a free response section in where they were able to respond to the question, "What type of exercise do you do?" (Appendix A). The Centers of Disease Control and Prevention (CDC; 2015) has recommended that older adults 65 years or older should engage in approximately 150 minutes per week of moderate-intensive aerobic activity or 75 minutes per week of vigorous-intensive aerobic activity in order to obtain the desirable health benefits. In the current study, 40% of

participants (M = 163.24, SD = 117.94) met or exceeded the 150-minute per week moderate-intensive aerobic activity recommendation.

Depressive Symptoms

The Hamilton Depression Rating Scale (Ham-D; Hamilton, 1960) was used to assess current presence of depressive symptoms. The Ham-D consists of 21 items. Eight of the items are on a five-point scale (0 = not present, 4 = severe). Nine of the items are on a 0-2 scale. Psychometrically, the Ham-D has been shown to have 86.4% sensitivity and 92.2% specificity (Strik et al., 2001). For the current study, the Ham-D full score was only recorded in the dataset; therefore, Cronbach's Alpha for the current study was not analyzed.

The Ham-D has been shown to be an appropriate, internally consistent depression measure to use in the geriatric population when compared to other depression measures (e.g., Geriatric Depression Scale, Zung Self-Rating Depression Scale; Yesavage et al., 1983). A scale score of zero to seven indicates "normal" levels of depressive symptoms; a score of eight to 13 indicates "mild depression;" a score of 14 to 18 indicates "moderate depression;" a score of 19 to 22 indicates "severe depression;" and a score of 23 or higher indicates "very severe depression" (Hamilton, 1960). In the current study, 5.92% of participants meet the cut off score of eight or more (M = 2.40, SD = 3.23).

Memory

The Rey Auditory Verbal Learning Test (RAVLT; Rey, 1941) was used to assess memory. In this measure, a list of 15 unrelated words are repeated five times (List A).

Between each trial, the participant is asked to repeat as many words as he or she can recall. An additional list of 15 unrelated words are read after the multiple repetition of the original list, and the participant is asked to repeat as many words as he or she can recall from this new list (List B). The participant is then asked to recall as many of the words from the original list as he or she can without repetition from the administrator. After a 30-minute interval, the participant is asked to verbally repeat, and visually recognize, as many words as he or she can recall from the original list once more. Psychometrically, the RAVLT has been shown to have good validity and reliability with a Cronbach's Alpha coefficient of 0.80 (de Sousa Magalhães, Fernandes Malloy-Diniz, and Cavalheiro Hamdan, 2012). The RAVLT has also been shown to be effective in early identification of AD in individuals with subjective memory complaints, and in differentiation between preclinical phase AD patients, MCI individuals, and normal aging individuals (Estévez-González et al., 2003). In a healthy population between the ages of 24-81 years, performance on the RAVLT was shown to decrease with age, but females and participants with a higher education tended to perform better compared to males and participants with lower education, across all age ranges (Van der Elst, van Boxtel, van Breukelen, & Jolles, 2005). For the current study, the RAVLT Delayed Recall List (M = 10.49, SD = 2.97), which is a single score measure, was used to measure memory.

Executive Functioning

The Trails Making Test (TMT) was used to assess executive functioning. This measure is a widely used neuropsychological test of visual attention and task switching. Participants are asked to connect dots numbered one to 25 (TMT A) as quickly and as

accurately as possible. Participants are then asked to connect dots sequentially alternating between numbers (1-13) and letters (A-L) as quickly and as accurately as possible (TMT B). TMT B is used as a measure of executive functioning, as participants are required to organize information efficiently and rapidly in order to complete the task successfully (Tombaugh, 2004). Psychometrically, the TMT has been shown to have good retest reliability for both TMT A (0.76-0.89) and TMT B (0.86-0.94) (Wagner, 2011). Tombaugh (2004) also showed that the TMT was significantly negatively correlated with age and level of education, but not with gender. For the current study, TMT B (M = 93.41, SD = 48.30), a single score measured in seconds, was used to measure executive functioning.

Processing Speed

The Symbol Digit Modalities Test (SDMT; Smith, 1968; Smith 1982) was used to assess cognitive processing speed. The SDMT was developed to assess for neurological impairment. It is also widely used to assess attention, visual scanning, and motor speed (Sheridan et al., 2006). The participants are instructed that they will have 90 seconds to pair specific numbers with given symbols (a key of which numbers match to any given symbol is listed at the top of the page). Sheridan et al. (2006) reported this single score measure to have a test/retest reliability and correlation with the Wechsler Digit Symbol Test, a similar measure, of .80 in a normal sample. Benedict et al. (2012) also reported the SDMT to have a test/retest reliability of .80.

Statistical Analysis

SPSS 20.0 was used to perform all statistical analyses. To obtain the main predictor "PA" variable, overall minutes per week of PA engagement (walking, stair climbing, gardening, and playing sports) were summed. Depressive symptoms and gender were the two variables being tested for their moderating influence. The total raw score for the Ham-D was used as the depressive symptoms score. The raw scores for the RAVLT Delayed Recall (memory measure), TMT B (executive functioning measure), and SDMT (processing speed measure) were used as the separate dependent variables (DVs) for the three models that were tested. Descriptive statistics were computed for PA, depressive symptoms, memory, and executive functioning.

Outliers were checked for using the calculated leverage (.085), discrepancy (± 2), global influence (DFFITS > 1.3636), and specific influence values (DFBETA > ± .1562). If any participant exceeded these cut off scores on more than one outlier measure, that participant was deleted. Multicollinearity was also checked. Nonessential multicollinearity, or high correlations between main effects and interaction terms, can change the regression coefficients' magnitude and sign, standard errors can become large, and interpretation of coefficients or significance tests can become less accurate (Morrell, 2013). The variance inflation factors (VIF) and Tolerance scores for each predictor variable in all models were assessed for evidence of nonessential multicollinearity. An acceptable, but lenient, cut off for VIF values are scores exceeding seven, and for Tolerance values, scores less than .10 (Morrell, 2013).

Assumptions of multiple linear regression (MLR) include linear relationship between X and Y variables, correct specification of independent variables (IVs), no

measurement errors in IVs, homoscedasticity, independence of residuals, and normality of residuals (Cohen, Cohen, West, and Aiken, 2003; Morrell, 2013). If these assumptions were not met, results can be been at risk for Type I or Type II error, or over/under estimation of significance and or effect size (Osborne and Waters, 2002). Linear relationship between X and Y is the assumption that each IV and each DV has been specified correctly. To check for this, scatterplots of X on Y residuals with a superimposed fit line were created. Correct specification of IVs is the assumptions that all important variables are included in the regression. The variables in this current study have been chosen based on previous research, theory and practice in order to minimize violation of this assumption. No measurement error in IVs is the assumption that all IVs are measured without error. To check for this, evaluation of reliability of used measurements were reported. Because the DV measures used were single score measures, test/re-test reliability analyses were not performed in this current study due to lack of re-test data. Homoscedasticity is the assumption that the amount of error variance in X is constant. To check for this, Y residuals were plotted against each IV in separate scatterplots to assess whether there was any indication of heteroscedasticity, which would violate this assumption. Independence of residuals is the assumption that errors are not correlated across observations. Clustering, systematic change over time, or serial dependency can increase the risk for violation of this assumption. In this current study, participants were measured at one time, therefore eliminating any likelihood of systematic changes over time or serial dependency. In addition, there was no reason to believe that characteristics of the participants were significantly different based on time of study entry. Each participant was offered the same incentive and recruited in the same

way. Normality of residuals is the assumption that residuals are normally distributed for every value of X. To check for this, Normal Q-Q plots were created to assess for any non-normal distributions of residuals (Cohen, Cohen, West, and Aiken, 2003; Morrell, 2013; Osborne and Waters, 2002).

After evaluation for outliers likely to skew results, nine cases were deleted from the memory model (N = 154), eight cases from the executive functioning model (N = 155), and 11 cases from the processing speed model (N = 152). Centering of all continuous predictor variables reduced nonessential multicollinearity, and all predictors had VIF and Tolerance values that did not indicate problems with multicollinearity. Non-linear relationships were corrected for after diagnostics indicated non-linear relationships in each model. Each type of linear transformation (square root, log, and inverse transformations) was created to assess which was best for each model. A log transformation was used for the memory model, a square root transformation for the executive functioning model, and an inverse transformation for the processing speed model. Because each model also showed evidence of heteroscedasticity for some variables, these linear transformations were performed to help remedy this as well.

Pearson's *r* correlational analyses for each model were conducted to assess for significant associations among variables. Three separate hierarchical MLR analyses were conducted to investigate the three cognitive domains (memory, executive functioning, and processing speed) under current analysis. Before analysis, each continuous X variable was centered, and gender was contrast coded (.5 = male, -.5 = female) to increase meaningful interpretation of results. Centering the predictor variables ($X_i - \overline{X}$) helped to remove nonessential multicollinearity and reduce correlations among

predictors. It also helped to create a more meaningful interpretation. For each model, PA was entered at step one; depressive symptoms and gender at step two; the interaction between PA and depressive symptoms, the interaction between PA and gender, and the interaction between gender and depressive symptoms at step three; and the three-way interaction between PA, depressive symptoms, and gender at step four. The first MLR model tested the following equation:

$$\text{Memory} = B_0 + B_1(\text{PA}) + B_2(\text{Depressive Symptoms}) + B_3(\text{Gender}) + B_4(\text{PA x Gender}) + B_5(\text{PA x Depressive Symptoms}) + B_6(\text{Gender x Depressive Symptoms}) + B_7(\text{PA x Depressive Symptoms x Gender}).$$

The second MLR model tested the following equation:

$$\text{Executive functioning} = B_0 + B_1(\text{PA}) + B_2(\text{Depressive Symptoms}) + B_3(\text{Gender}) + B_4(\text{PA x Gender}) + B_5(\text{PA x Depressive Symptoms}) + B_6(\text{Gender x Depressive Symptoms}) + B_7(\text{PA x Depressive Symptoms x Gender}).$$

The third MLR model tested the following equation:

$$\text{Processing speed} = B_0 + B_1(\text{PA}) + B_2(\text{Depressive Symptoms}) + B_3(\text{Gender}) + B_4(\text{PA x Gender}) + B_5(\text{PA x Depressive Symptoms}) + B_6(\text{Gender x Depressive Symptoms}) + B_7(\text{PA x Depressive Symptoms x Gender}).$$

CHAPTER THREE

RESULTS

Pearson's *r* correlation analyses were conducted to test the first three hypotheses. For the memory model, results showed that the relationship between performance on the RAVLT Delayed Recall (*M* =10.49, *SD* = 2.97*)* and gender was significantly negative (*r* = -.230, *p* < .01), meaning that male group membership was associated with a .230 decrease in number of words recalled on the RAVLT Delayed Recall. The relationship between minutes per week of engagement in PA (*M* =167.42, *SD* = 123.08) and gender was significantly positive (*r* = .177, *p* < .05), meaning that male group membership was associated with a .177-minute increase in engagement in PA per week. The relationship between scores on the Ham-D (*M* = 2.45, *SD* = 3.31*)* and gender was significantly negative (*r* = -.159, *p* < .05), meaning that male group membership was associated with a .159-point decrease in scores on the Ham-D. For the executive functioning model, results showed that the relationship between performance, in seconds, on the TMT B (*M* = 93.41, *SD* = *48.29*) and scores on the Ham-D (*M* = 2.42, *SD* = 3.22) were significantly positive (*r* = .191, *p* < .05), meaning that, for every one second increase on the TMT B there was a .191-point increase in Ham-D scores. For the processing speed model, results showed that the relationship between minutes per week of engagement in PA (*M* = 165.15, *SD* = 125.27) and gender was significantly positive (*r* = .228, *p* < .01), meaning that male group membership was associated with a .228-minute increase in engagement in PA per week. See Table 1 for a summary of results.

Table 1. Correlations among physical activity, gender, depressive symptoms, and cognitive domains.

	1	2	3	4	*M*	*SD*
Memory model (*n* = 154)						
1.Memory[a]	-	.598	.136	.136	.10.49	2.97
2. Physical activity[b]	-	-	.177*	-.114	167.42	123.08
3. Gender	-	-	-	-.159*	-	-
4. Depressive symptoms	-	-	-	-	2.45	3.31
Executive functioning model (*n* = 155)						
1.Executive functioning[c]	-	- .126	.010	-.191*	93.41	48.28
2. Physical activity	-	-	.157	-.059	163.24	117.94
3. Gender	-	-	-	-.138	-	-
4. Depressive symptoms	-	-	-	-	2.42	3.22
Processing speed model (*n* = 152)						
1. Processing speed[d]	-	- .041	-.076	-.085	49.14	8.74
2. Physical activity	-	-	.228*	-.111	165.15	125.27
3. Gender	-	-	-	-.153	-	-
4. Depressive symptoms	-	-	-	-	2.40	3.23

*$p < .05$. **$p < .01$.

[a]Memory measured using raw RAVLT Delayed Recall scores, maximum score = 15.

[b]Physical acitivty measured using Physical Activity Questionnaire, in minutes per week.

[c]Executive functioning measured using raw TMT B scores, in seconds.

[d]Processing speed measured using raw SDMT scores, higher scores indicate better performance.

Multiple linear regression (MLR) was used to test the predictive value of PA on cognition (memory, executive functioning, and processing speed), and the moderating influence of gender and depressive symptoms within these relationships. For the memory model, a linear log transformation of raw RAVLT Delayed Recall scores was used as the "memory" outcome variable (higher scores indicated better performance). For the executive functioning model, a linear square root transformation of raw TMT B scores was used as the "executive functioning" outcome variable (lower scores indicated better performance). For the processing speed model, a linear inverse transformation of raw SDMT scores was used the "processing speed" outcome variable (higher scores indicated better performance).

For each model, a hierarchical MLR strategy was used to regress memory, executive functioning, and processing speed on PA (step one); depressive symptoms and gender (step two); the interaction between PA and depressive symptoms, the interaction between PA and gender, and the interaction between gender and depressive symptoms (step three); and, the three-way interaction between PA, depressive symptoms, and gender (step four). Results indicated that the overall optimal linear combination of all predictors in the "memory" model accounted for approximately 6.4% of the variance in memory performance (R^2_{adj} = .064, $F(7, 145) = 2.485$, $p < .05$). In addition, there was a significant change in model fit after controlling for PA in step two of the memory model (R^2_{change}= .089, $F_{\text{change}}(2, 149) = 7.349$, $p < .01$). Individual analyses of each predictor variable indicated that gender, holding the influence of all other predictor variables constant, was the only significant predictor of memory performance. More specifically, the difference between the mean memory performance of men, and the mean memory

performance of women was -.169 (B = -.169, t = -2.878, p < .01, 95% CI [-.286, -.053]). Males recalled .169 fewer words, on average, than females, after controlling for all other predictors in the model. Gender uniquely accounted for approximately 5.1% of the total variance in memory performance (sr^2 = .0511).

Results indicated that the optimal linear combination of all predictors in the "executive functioning" model did not account for a significant amount of the variance in executive functioning performance (p > .10). There was a significant change in model fit after controlling for PA in step two of the executive functioning model (R^2_{change} = .041, $F_{change}(2, 151)$ = 3.286, p < .05). The optimal linear combination of minutes per week of PA, depressive symptoms, and gender accounts for about 3.2% of the variance in executive functioning performance (R_{adj}^2 = .051, $F_{(3, 151)}$ = 2.719, p < .05) in the step two model. Individual analyses of each predictor variable in the step two model indicated that depressive symptoms, holding the influence of all other predictor variables constant, was the only significant predictor of executive functioning performance. More specifically, for every one point increase in depressive symptoms on the Ham-D, number of seconds taken on the TMT B increased by 879.742 (B = 879.742, t = 2.469, p < .05, 95% CI [175.704, 1583.780]). Depressive symptoms uniquely accounted for about 3.8% of the total variance in executive functioning performance (sr^2 = .038). Results indicate that the optimal linear combination of all predictors in the "processing speed" model did not account for a significant amount of the variance in processing speed performance (p > .50). In addition, all main effects and interactions were non-significant (p > .05). See Table 2 for a summary of all final regression models.

Table 2. Summary of final regression models for variables predicting cognitive functioning.

Model	*B*	*SE B*	β	95% Confidence Interval for *B* Lower Bound	95% Confidence Interval for *B* Upper Bound
Memory[a]					
Physical activity (PA)	.000	.000	-.075	-.001	.000
Depressive symptoms (DS)	.027	.015	.276	-.002	.056
Gender	-.169**	.059	-.246**	-.286	-.053
PA x DS	.000	.000	-.178	-.001	.000
PA x Gender	.000	.001	-.082	-.002	.001
Gender x DS	.040	.029	.207	-.018	.099
PA x DS x Gender	.000	.000	-.192	-.001	.000
$R^2_{adjusted}$	.064				
F	2.485*				
Executive functioning[b]					
PA	-25.830	13.642	-.212	-52.791	1.130
DS	909.149	620.206	.204	-316.523	2134.821
Gender	2631.649	2572.804	.087	-2452.812	7716.110
PA x DS	-11.218	7.347	-.248	-25.737	3.301
PA x Gender	-29.134	27.285	-.119	-83.056	24.787
Gender x DS	-127.938	1240.412	-.014	-2579.283	2323.406
PA x DS x Gender	-16.673	14.694	-.185	-45.711	12.365
$R^2_{adjusted}$	.027				
F	1.605				
Processing speed[c]					
PA	-2.610E-006	.000	-.082	.000	.000
DS	.000	.000	-.111	.000	.000

Gender	6.279E-005	.001	.007	-.001	.002
PA x DS	-1.475E-006	.000	-.121	.000	.000
PA x Gender	-3.219E-006	.000	-.050	.000	.000
Gender x DS	-.001	.000	-.251	-.001	.000
PA x DS x Gender	1.149E-006	.000	.048	.000	.000
$R^2_{adjusted}$	-.003				
F	.918				

Note. Linear transformations have been used for all outcome variables; unstandardized B values represent directionality of relationship.

[a]Memory measured using raw RAVLT Delayed Recall scores, maximum score = 15. Log transformation used for memory variable.

[b]Executive functioning measured using raw TMT B scores, in seconds. Square root transformation used for executive functioning variable.

[c]Processing speed measured using raw SDMT scores, higher scores indicate better performance. Inverse transformation used for processing speed variable.

*$p < .05$, ** $p < .01$; memory model ($n = 154$), executive functioning model ($n = 155$), processing speed model ($n = 152$).

CHAPTER FOUR

DISCUSSION

The current study showed partial support for some hypotheses, but a greater proportion of hypotheses were not supported, likely due to multiple factors. The first hypothesis was that greater PA would be associated with endorsement of fewer depressive symptoms, being male, and better performance on cognitive measures (measures of processing speed, memory, and executive functioning). Results showed that engagement in increased minutes per week of PA was associated with being male. Endorsement of fewer depressive symptoms was also associated with being male. The second hypothesis was that endorsement of fewer depressive symptoms would be associated with better performance on cognitive measures. Results showed that endorsement of more depressive symptoms was associated with worse performance on the executive functioning measure. The third hypothesis was that being female would be associated with better performance on cognitive measures. Results did not specifically support this hypothesis, but did indicate that worse performance on the memory measure was associated with being male. The last two hypotheses were associated with tests of three-way interactions. The fourth hypothesis was that women who engage in low PA and endorse more depressive symptoms would have worse performance on cognitive measures than men. Men who engage in more PA and endorse more depressive symptoms were hypothesized to have better performance on cognitive measures than women. The fifth hypothesis was that women who engage in less PA and endorse fewer depressive symptoms would have better performance on cognitive measures than men, and that there would be no difference in performance for men versus women who engage

in more PA and endorse fewer depressive symptoms. Neither hypothesis four nor five was supported, given that the interaction effects were non-significant across all regression models.

Overall, results showed that predicting memory performance was the only significant model. However, for both the memory and executive functioning models, there was a significant change in model fit after controlling for PA in the second step of the hierarchical MLR. This means that the optimal linear combination of gender and depression accounted for a significant proportion of the variance above and beyond the effect of physical activity. Gender predicted memory performance, and more depressive symptoms predicted worse executive functioning performance. Neither of the three-way interactions hypothesized were supported, but the significant main effects of gender and depressive symptoms showed some promising support for future directions of study when determining what factors influence cognitive functioning.

Lack of Sample Variability

The sample used in this current study included only "very healthy" aging adults. These adults were screened for any major medical or psychological health problems. The majority of participants included in the current study were Caucasian men and women with a college degree or higher. The CDC currently recommends that men and women 65 years of age and older maintain a 150-minute per week PA regimen of moderate intensity level aerobic activity. The PA mean in the current study exceeded this recommendation. It is likely that individuals who engage in moderate to high levels of frequent PA in various forms also engage in other healthy living habits such as eating foods high in

vitamins, protein, and nutrients; consuming a low calorie diet; more frequent socialization; and or engagement in brain stimulating games/activities (e.g., crossword puzzles). Higher levels of education are shown to be correlated with higher levels of cognitive reserve and a higher overall intelligence quotient scores (IQ; Schoenberg et al., 2006). The fact that the majority of participants had a high likelihood of increased cognitive reserve, based on their high level of education, also contributes to the lack of variability and potential lack of detecting any significant effects. In addition, only about 5% of the sample met criteria on the Ham-D for any level of depression, again decreasing the likelihood of detecting a truly significant effect if it exists.

Methodological Concerns

Deary, Johnson, and Starr (2010) mentioned that because there is no methodological way to establish directionality of causal relationships, there is no way to establish meaningful conclusions when using cross-sectional data. There are several methodological concerns that should be considered when interpreting the results of the current study. The use of archival data meant that study design and how each variable of interest was measured were predetermined. Because the main IV of interest was PA, only those participants who completed the baseline PA questionnaire were included in the study, which eliminated approximately half of the sample. Lindwall, Ljung, Hadzibajramovic, and Jonsdottir (2011) mentioned that older adults who perceived themselves to be engaging in an appropriate amount of PA had beneficial outcomes in comparison to those who engaged in more actual PA. As mentioned above, there was a lack of heterogeneity in the sample due to the rigid exclusion criteria of the WAHA

Study. Approximately 5%-7% of the sample in each model consisted of outlier participants, and even after deletion, non-linear relationships and threats to homoscedasticity were encountered. Including the main three-way interaction term that was tested in this current study, and three two-way interactions for each possible IV interaction, placed each analysis at risk for not having enough statistical power, which also contributed to the problems encountered in this study. These interactions may have been non-significant due to lack of statistical power instead of being truly non-significant.

Current Research and Future Directions

Several potentially important variables were not included in the current study due to lack of measurement or lack of power to include more variables in the models. Some researchers have shown that variables such as level of education and IQ to influence performance on measures of memory and processing speed (Salthouse, 2011; Schoenberg et al., 2006), while other researchers have shown that greater cognitive reserve is not a significant predictor of processing speed later in life (Ritchie et al., 2013). Processing speed is an important domain that is in need of further research.

The main area of interest in the current study was the assessment of the effects of PA on cognitive functioning, and identification of potential underlying factors that may strengthen or weaken this relationship. Sofi et al. (2011) were the first to conduct a meta-analysis on non-demented aging adults and the relationship between PA and cognitive decline. They mentioned that the literature was "controversial" by stating that results are contradicting at times and or the populations used were not generalizable. Also, the level

of PA intensity was sometimes stated to matter in the literature and other times not. In the current study, PA was not a significant predictor in predicting performance on any of the cognitive measures. This could be due to the fact that all participants who were included engaged in at least a moderate amount of PA each week. As Colcombe and Kramer (2003) mentioned in their meta-analysis of fitness on cognitive functioning in aging adults, the relationship between PA and cognitive functioning can be moderated by many programmatic and methodological factors.

Future researchers wanting to better assess the influence of PA on cognitive functioning would benefit from use of more specific measures, and use of more controlled study designs (i.e., use of a control group versus a PA group over a specified time span), while keeping in mind the three main challenges when studying how PA, or cardiorespiratory fitness (CRF), influences brain functioning in aging adults outlined by Burzynska et al. (2015). The first challenge mentioned by these authors is that it is not clear how sedentary lifestyles impact brain functioning even though light to no PA accounts for most of waking hours for the majority of individuals. The second challenge is that the relationship between CRF and PA has yet to be teased apart (i.e., Does PA always directly impact CRF? Is it CRF or PA that accounts for more variance in brain function?). The third challenge is that the way in which each construct is measured could underlie the difference between finding significant differences or not. Although Burzynska et al. (2015) mentioned challenges more related to brain functioning and not necessarily cognitive functioning, the same challenges arise when investigating cognitive functioning in aging adults.

Conclusion

The underlying mechanisms between PA and cognitive functioning need continued research. The current study has several limitations such as homogeneity of sample, poor methodological study design, and low power. However, it was shown that gender and depressive symptoms directly influence memory and executive functioning above and beyond the effects of PA. Processing speed is an important construct that needs to be better understood. It is likely that processing speed ability explains, or even predicts, the function of other cognitive domains, and therefore should be tested as a mediator rather than an outcome variable in future studies of the effect of PA on cognitive functioning. As ARCD continues to be a prominent global concern, finding ways to better operationalize the variables under investigation in this current study will help with further understanding of what factors predict cognitive decline and promote its viability in order to optimize future detection and treatment for aging adults.

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APPENDIX

PHYSICAL ACTIVITY QUESTIONNAIRE

What type of physical activity do you perform at your work (or in everyday life)?

- ☐ Basically I am sitting at work and I only take short walks (civil servant, desk work)
- ☐ I am sitting but I do continuous moderate exercise (cashier, etc.)
- ☐ I walk quite a lot but I do not do vigorous efforts (shop counter, commercial, etc.)
- ☐ I walk quite a lot and I do vigorous efforts (postman, carrier, etc.)
- ☐ I basically do vigorous efforts and a lot of activity (masonry/painting, shipper, etc.)
- ☐ I am basically standing up without moving
- ☐ Insufficient data

What is your job? _____

How many hours are you watching TV, at a computer, at a video game on a business day? (outside work) _____

How many hours are you watching TV, at a computer, at a video game on a non-working day? (outside work) _____

How many hours do you sleep every day? _____

BRIEF PHYSICAL ACTIVITY QUESTIONNAIRE

Please indicate below the amount of each activity that you perform during a standard week

For one week:

How many days do you walk fast?	_____	How many minutes per day?	_____
How many days do you take a walk at a leisurely pace	_____	How many minutes per day?	_____
How many days do you walk cross-country, go on excursions?	_____	How many minutes per day?	_____
How many days do you climb stairs?	_____	How many floors per day?	_____
How many days do you work in the garden or yard?	_____	How many minutes per day?	_____
How many days do you exercise and practice sports outdoors or at home or at the gym?	_____	How many minutes per day?	_____

What type of exercise do you do? _____

_____

_____