The positive effects of physical fitness on cognitive function in elderly individuals: lessons from the elite Masters Athletes

by

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LIST OF SYMBOLS AND ABBREVIATIONS

Symbol	Definition
MCI	Mild cognitive impairment
AD	Alzheimer’s disease
PA	Physical activity
MA	Masters Athletes
NAC	Non-athlete controls
WM	White matter
GM	Grey Matter
EF	Executive functions
ADL	Activities of daily living
MMSE	Mini Mental State Exam
TMT	Trail Making Test
RAVLT	Rey Auditory Verbal Learning Test
CT	Computed tomography
MRI	Magnetic resonance imaging
PET	Positron emission tomography
VO_2max	Maximal aerobic capacity
PFC	Physiological functional capacity
BDNF	Brain-derived neurotrophic factor
HDL	High-density lipoprotein
BMI	Body mass index
PAR-Q	Physical activity readiness questionnaire
ECG	Electrocardiogram
MET	Metabolic equivalent
TMT-A	Trail Making Test-Part A
TMT-B	Trail Making Test-Part B

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data from NAC and MA; F) Individual Phonemic Verbal Fluency data from the NAC and MA; G) Individual RAVLT-LOT data from the NAC and MA;

*Significant difference between NAC and MA, $p < .05$.

ABSTRACT

Cognitive decline is one of the greatest concerns of aging, affecting adults aged 75 years and older (Canadian Institutes of Health Research, 2010). As the proportion of seniors (> 65 years) continues to increase more rapidly than any other age group, the number of cases of cognitive impairment will continue to rise, reaching epidemic levels and placing an enormous burden on the health care system. Physical activity (PA) has been studied as a behavioural factor that has positive effects on age-related cognitive decline. Recent evidence shows that cognitive decline is lower in those who better maintain muscle strength and aerobic fitness with aging (Bherer, Erickson, & Liu-Ambrose, 2013; Colcombe & Kramer, 2003; Heyn, Abreu, & Ottenbacher, 2004; Spirduso & Clifford, 1978); however, the underlying mechanisms responsible for enhancing cognitive function with PA are still unclear. While there is a great amount of information gathered on age-related cognitive decline, there is a notable lack of knowledge on this topic in the older age groups (> 75 years) - where age-related cognitive impairment is so prevalent. The study presented in this thesis is unique because we investigated the relationship between cognitive decline and physical fitness in elderly (> 75 years) study participants. Furthermore, this is one of the only studies to investigate both cognitive and physical function in elderly world-class Masters Athletes (MA). MA are exceptional individuals who maintain higher-than-average PA levels compared to age-matched counterparts, and who train and compete in a variety of sport competitions well into advanced age. As such, the aim of this study was to gain a better understanding of the relationship between cognitive function and physical fitness in a population most susceptible to age-related cognitive decline. We recruited 15 MA and 14 age-sex matched non-athlete controls (NAC) to undergo detailed investigations of physical fitness (maximal aerobic capacity (VO_2max), peak isometric quadriceps strength, and

PA levels), cognitive function (global cognitive function, processing speed and attention, learning and memory, language and verbal fluency, and mental flexibility), and functional capacity (10-repetition chair stand). As expected, we found that MA demonstrated superior indices of cognitive function in areas of global cognitive function, processing speed and attention, and learning and memory, and this superior cognitive function was associated with markers of greater physical fitness (VO_2max and PA levels). Based on our findings, it is clear that greater fitness levels can be beneficial for maintaining cognitive function in an elderly (> 75 years) population.

RESUMÉ

La perte de fonction cognitive est l'un des plus grands enjeux du vieillissement, affectant les ainés Canadiens âgés de 75 ans et plus (Canadian Institutes of Health Research, 2010). La proportion de personnes âgées (> 65 ans) continue d'augmenter, et ce plus rapidement que tout autre groupe d'âge. Ainsi le nombre de cas de déficience cognitive continuera d'augmenter, atteignant des niveaux épidémiques et plaçant un fardeau énorme sur le système de santé. L'activité physique a été étudiée à titre de facteur comportemental ayant des effets préventifs sur la déficience cognitive liée à l'âge. Des données récentes montrent une atténuation de la déficience cognitive chez les individus ayant une plus grande force musculaire et une meilleure capacité aérobie (Bherer, Erickson, & Liu-Ambrose, 2013; S. Colcombe & Kramer, 2003; Heyn, Abreu, & Ottenbacher, 2004; Spirduso & Clifford, 1978); cependant, les mécanismes sous-jacents reliant l'amélioration de la fonction cognitive à l'activité physique sont encore mal connus. Malgré la grande quantité d'informations existante sur la déficience cognitive lié à l'âge, un manque notable de connaissances dans les groupes plus âgés (> 75 ans) subsiste, groupes chez lesquels la plus haute prévalence de déficience cognitive liée à l'âge est observée. Cette thèse présente une étude unique étudiant la relation entre la déficience cognitive et la condition physique chez des participants âgés de 75 ans et plus. De plus, c'est l'une des seules études investiguant, à la fois la fonction cognitive et la fonction physique chez des athlètes maîtres de classe mondiale âgés de plus de 75 ans. Les athlètes maîtres sont des individus exceptionnels maintenant des niveaux d'activité physique élevés comparativement à leurs homologues du même âge, ils s'entrainent et performent dans une variété de discipline sportive, et ce jusqu'à un âge avancé. Ainsi, l'objectif de cette étude était d'acquérir une meilleure compréhension de la

relation entre la fonction cognitive et la condition physique chez le groupe d'âge le plus à risque faces aux déficiences cognitives liées à l'âge. Nous avons recruté 15 athlètes maîtres et 14 participants témoins non-athlètes à se soumettre à des analyses détaillées de la condition physique (capacité aérobie maximale, force du quadriceps, et niveau d'activité physique), fonction cognitive (fonction cognitive globale, vitesse de traitement et attention, apprentissage et mémoire, langage et fluidité verbale et flexibilité mentale) et capacité fonctionnelle (se lever d'une chaise). Comme anticipé, nous avons observé une fonction cognitive supérieure chez les athlètes maîtres (fonction cognitive globale, vitesse de traitement et attention et apprentissage et mémoire). Cette fonction cognitive supérieur était également associée aux composantes d'une meilleure condition physique (capacité aérobie maximale et niveaux d'activité physique). Nos résultats démontrent clairement qu'une condition physique supérieure peut être bénéfique pour le maintien de la fonction cognitive chez une population âgée de plus de 75 ans.

PREFACE & AUTHOR CONTRIBUTIONS

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S. Taran was the primary author with roles in subject recruitment, cognitive function data collection, analysis and interpretation, accelerometer data collection, analysis and interpretation, maximal aerobic capacity data collection, and manuscript preparation.

M.E. Filion had a role in physical fitness and functional capacity data collection, analysis and interpretation.

N.J. MacMillan had a role in maximal aerobic capacity data collection, analysis and interpretation.

S. Spendiff assisted in participant recruitment and management, data collection, interpretation and analysis.

C.M. Sabiston assisted in study design and ethics write up, particularly relating to cognitive aspects, data analysis and interpretation, and preparation of manuscript.

R.T. Hepple assisted in study design, ethics write up, data interpretation and analysis.

T. Taivassalo was the principle investigator on the study and assisted in study design, ethics write up, informed consent, data analysis and interpretation, and manuscript preparation.

CHAPTER 1: INTRODUCTION

1.1 Background

The average age of the population is increasing rapidly as the percentage of seniors (> 65 years) grows faster than other age group. It is estimated that by the year 2026, one in five individuals will be 65 years and older (Seniors, 2002). With aging comes a number of health concerns – an important one being age-related cognitive decline. The risk of cognitive decline increases with advancing age, affecting mental processes such as learning, intuition, language, judgment, memory, and attention. Declines in cognitive function can range from normal age-related decline to mild cognitive impairment (MCI), and to even more severe forms, like Dementia and Alzheimer's disease (AD). Age-related cognitive impairment, along with dementia, affects roughly 25% of Canadians 65 years and older, with a considerable increase in prevalence in adults over 85 years of age (Canadian Institutes of Health Research; CIHR, 2010). As the population ages rapidly, cognitive impairment will continue to be of notable concern, predicted to eventually reach epidemic levels and placing an enormous burden on the health care system (Strout & Howard, 2012).

Researchers over the past 40 years have been investigating the effects and impact of physical activity (PA) on age-related cognitive decline. Bherer, Erickson, and Liu-Ambrose (2013) reported that older adults who participated in PA showed less cognitive decline over time. As well, they described that older adults who had increases in cardiorespiratory fitness as a result of completing a PA intervention program, showed improved cognitive performance. Similarly, Angevaren and colleagues (2008) found that eight out of the eleven reviewed studies investigating aerobic PA programs in individuals over 55 years of age resulted in increased fitness and improved cognition. However, the areas of cognitive function that improved were not the same across each of the eight studies. Daffner (2010) discussed a number of studies, suggesting that higher levels of PA are associated with lower risks of developing cognitive impairment. For example, the Nurses' Health Study included over 18,000 older women (age range 70-81) and found that higher levels of PA were associated with superior cognitive performance on tests of general cognition, verbal memory, verbal fluency, and attention. The purpose of the Honolulu-Asia Aging Study was to examine the distance walked per day in over 2,000 physically able men (age range 71-93). It was found that the men who walked the shortest distance had a 1.8-fold greater risk of dementia compared to men who walked more than two miles per day. Taken together, the evidence that aerobic PA improves cardiorespiratory fitness and benefits cognitive function in older adults adds to the other numerous known benefits of aerobic PA.

It is clear that there is a great amount of information gathered on age-related cognitive decline, however, there is a lack of knowledge on this topic in the older age groups (> 75 years of age). This is an important population to study considering the increasing prevalence of age-related cognitive impairment, with notable increases in individuals over the age of 85. Our study is unique in that it included elderly (> 75 years) study participants. As such, the aim of this study was to get a better understanding of the relationship between cognitive function and physical fitness in a population most susceptible to age-related cognitive decline. Even more uniquely, this is one of the only studies to investigate cognitive and physical function in elderly world-class Masters Athletes (MA). MA are exceptional individuals who spend more time exercise training than the average person, and who continue to compete in elite level sport over the lifespan. They have even been referred to as models of successful aging.

In our study we recruited 15 MA and 14 non-athlete controls (NAC) to undergo detailed investigations of physical fitness, cognitive function, and functional capacity. The two groups were age-sex-matched and all participants were in good health. Comparisons between the groups were made on all measures. The focus of this study was to better understand the link between physical fitness and cognition in an age-population most affected by cognitive decline by comparing MA and NAC, all 75 years of age and older. It was expected that MA would demonstrate healthy brain aging compared to NAC. Based on previous research reporting on the benefits of PA on age-related cognitive decline, the hypothesis of this study was that MA would demonstrate superior cognitive function, and that there would be an association between this greater cognitive function and markers of physical fitness and functional capacity.

It is anticipated that the results from this study will yield important information with respect to improving or prolonging the onset of cognitive decline in elderly individuals through exercise training. This information may be helpful for health care providers when advising elderly individuals about healthy lifestyle factors that promote successful aging.

CHAPTER 2: LITERATURE REVIEW

2.1 Aging and cognition

2.1.1 Population Aging in Canada

Population aging is a growing concern, with the proportion of seniors (> 65 years) increasing more rapidly than any other age group. In 2001, one in eight Canadians was 65 years of age and over. More notably, as the "baby boomers" (those born between 1946 and 1964) age, this number is expected to increase to one in five (approximately 8%) by the year 2026 (Seniors, 2002). The senior population will account for up to half of the growth of the entire Canadian population over the upcoming few decades with the **fastest growth in the senior population being seen among the oldest individuals: those 85 years of age and older**. Currently, this group of oldest Canadians represents 2% of the total population (Statistics Canada, 2012), and this proportion is expected to double by 2041 (Seniors, 2002). These trends are not only being seen in Canada, but worldwide. In almost every country, the percentage of seniors is growing faster than other age group (World Health Organization; WHO, 2012). It is clear that the age structure of the population is changing quickly, with population aging representing one of the greatest achievements of society over the past century. However, this worldwide phenomenon also poses significant challenges to the economy, while trying to ensure optimal health (both physical and mental) and functional capacity of seniors. A growing concern is that the support ratio (the ratio of individuals aged 65 and over to working-age individuals (20-64)) will decline due to low fertility rates (Edwards, 2012), leaving fewer workers to carry the financial burden of the aging population. While medical expenses toward the end of life tend to be highest, pensions and medical care for the elderly are funded by taxes paid by working-age adults. To add to this, as life expectancies are increasing, trends in healthy life expectancy are not as clear. This brings up a great question of whether living longer means living better. Addressing the challenges of the aging population and responding to the needs of older individuals requires a better understanding of aging, disability and interventions. Emphasizing prevention of disease, and promoting a healthy lifestyle, may help to delay disability, dependence, and therefore the need for medical services.

2.1.2 Cognitive decline with age

Cognitive decline is one of the greatest concerns of aging, with the risk of decline increasing with advancing age (Strout & Howard, 2012). This problem appears as a decline in one or more cognitive processes. Diagnoses can range from normal age-related cognitive decline to mild cognitive impairment (MCI), and to even more severe forms of dementia. Older adults experiencing MCI may experience declines noticeable to those around them; however, the changes may not be severe enough to disrupt daily life or ones independence ("Alzheimer's and Dementia," 2014; Strout & Howard, 2012). Cognitive impairment with aging, including dementia, affects 25% of Canadians over the age of 65, with the incidence rising dramatically to over 65% of adults over the age of 85 (CIHR, 2010). With the increasing rates of aging, the number of cases of cognitive impairment will continue to rise, reaching epidemic levels and placing an enormous burden on the health care system (Strout & Howard, 2012).

Research surrounding aging and cognitive function is growing rapidly, however it seems to include all cognitive information from people 25 years and older (Salthouse, 1991). For this review of the literature, 'cognitive aging' will focus on age-related declines in cognitive performance, or cognition, specifically in older adults (aged 65 and over). The cognitive aging literature covers a vast amount of topics, from pathological cognition to social cognition (Salthouse, 2000), because it generally refers to the effects of aging on all aspects of cognition.

However, for the purpose of clarity in this review, the term cognition, or cognitive function, will refer to the mental or intellectual processes that are of importance in the daily lives of older adults.

2.1.2.1 Cognitive decline and structural brain changes

Cognitive decline, as mentioned above, is a typical feature of aging with onsets beginning as early as 30 years of age – around the time when structural brain changes begin (Colcombe et al., 2003; Salthouse, 2009). These age-related structural brain changes are in the form of tissue loss, with declines in grey and white matter, and several brain cortices. Average volume losses, between the ages of 30 and 90, are approximately 15% of the cerebral cortex (Jernigan et al., 2001) and roughly 25% of the cerebral white matter (WM; Colcombe et al., 2003). Specifically, through childhood and maturation, grey matter (GM) tends to decrease or thin out, while WM expands and replaces it. In a cross-sectional study, Ge and colleagues (2002) investigated grey and white matter changes in healthy adults (age range: 20 – 86 years; *M*: 46 ± 19), and they found that reductions in GM volume began as early as 20 years of age (the age of the youngest study participant), followed by steady and linear declines with advancing age. Similarly, other cross-sectional studies have shown that GM volume peaks around 10 years of age, and then begins to decline during adolescence and early adulthood all the way through to old age (Blanton et al., 2001; Carne, Vogrin, Litewka, & Cook, 2006; Kharitonova, Martin, Gabrieli, & Sheridan, 2013; Pfefferbaum et al., 1994). These GM losses have been shown to be greater in the cortex compared to subcortical structures (Kharitonova et al., 2013). WM, on the other hand, was found to change with advancing age as well, although in a different pattern. WM volume changes were quadratic, rather than linear, with a slight increase from childhood until the ages of 20 to 40 years, followed by a decrease through later life (Ge et al., 2002). WM, which is made up of nerve fibers that connect neurons in different areas of the brain, has recently been thought of as potentially being important for cognition and learning. Since learning involves the strengthening of connections between neurons in the GM, damage to myelin in the WM can impair sensory, motor, and cognitive functions (Fields, 2010). While the exact contributions of grey and white matter to cognitive function are not yet well-known, the literature surrounding cortical brain changes as they relate to cognitive function is more defined.

The frontal cortex is reported to be the most susceptible to atrophy with aging (Colcombe et al., 2003; MacPherson, Phillips, & Della Sala, 2002), and in fact, tissue loss here has been found to be disproportionately greater than other cortical areas. Declines in the temporal cortex are more moderate with smaller declines in the parietal and occipital cortices (Colcombe et al., 2006). The implications of frontal cortex atrophy are emphasized by the fact that this area is essential for carrying out complex cognitive functions, managed by executive functions (EF). In the literature, the link between volumetric decreases in the frontal cortex and declines in executive function is well recognized (Kramer et al., 1999; Park, Polk, Mikels, Taylor, & Marshuetz, 2001). EF can be compared to a "business executive" who doesn't necessarily specialize in one particular area, but instead is responsible for controlling and regulating a variety of cognitive functions (Alvarez & Emory, 2006; Salthouse, Atkinson, & Berish, 2003). These cognitive functions include processes such as working memory (verbal and spatial), inhibition, task-switching, attentional capacity, learning, language, processing speed and long-term memory (Etnier & Chang, 2009; Kramer et al., 1999; Salthouse et al., 2003), and have been defined as "capacities that enable a person to engage successfully in independent, purposive, self-serving behavior" (Lezak, 1993). These brain functions are instrumental in the day-to-day lives of elderly individuals, in order to maintain both physical (walking to the corner store without assistance) and mental (remembering to turn off the stove after using it) independence.

Considering that the ability to carry out activities of daily living (ADL) requires many of the skills controlled by executive functioning, even mild dysfunction of these cognitive processes can have serious implications for ones functional capacity. This relationship between declines in EF with aging and functional impairment has been illustrated in many studies. Specifically, it has been suggested that elderly individuals with lower scores on assessments of EF tend to have greater functional impairment than elderly without executive impairment (Cahn-Weiner, Malloy, Boyle, Marran, & Salloway, 2000; Carlson et al., 1999; Grigsby, Kaye, Baxter, Shetterly, & Hamman, 1998), and therefore greater difficulty with ADL. It has also been shown that intact EF, supported by the frontal cortex, increases the chances that older adults will be functionally independent. This demonstrates that EF are important predictors of functional status, and that they are necessary for planning, organizing, and initiating everyday activities. Royall and colleagues (2004) found that executive dysfunction was a better predictor of functional decline than the Mini Mental State Exam (MMSE), a measure of global cognitive function. Examining EF in older adults has significant implications with regard to identifying those individuals who require long-term care and assistance. As well, implementing interventions to improve both cognitive and physical functioning can only occur once individuals with executive dysfunction have been accurately identified. Given that EF encompass several higher order cognitive functions, its measurement can be difficult. One solution is to incorporate multiple assessments that should, altogether, provide a proper measure of overall cognitive function (Etnier & Chang, 2009).

2.1.3 Neuropsychological assessment

Cognitive assessments have been used cross-sectionally and longitudinally to look at population differences and age-related changes, respectively, in cognitive function (Petersen et al., 2001). Assessments are typically used for screening for cognitive impairment, distinguishing the cause of impairment, rating the severity of the disorder, and monitoring disease progression (Woodford & George, 2007). Considering a number of cognitive processes can be impaired with aging or disease, it is important to assess a variety of cognitive processes, such as executive function, memory, attentional capacity, task-switching, inhibition, learning, language, processing speed, and visuospatial skills (Albert et al., 2011). Typically, standardized pen and paper assessments are used to evaluate cognitive function, and proper clinical judgment is required in order to diagnose Alzheimer's disease (AD) and MCI (Petersen et al., 2001). Administering a battery of validated tests to measure cognitive function can provide valuable information if interpreted correctly.

A variety of cognitive assessments have been developed, ranging from brief screening tools (taking less than a minute to complete), to formal neuropsychological assessments that take up to several hours. Choosing appropriate assessments depends on the purpose of assessment and how much time is available. Some commonly used cognitive assessments for investigating age-related cognitive decline are the MMSE, the Trail Making Tests (TMT; Parts A and B), the Verbal Fluency Tests (Woodford & George, 2007), the Digit Span Test, and the Rey Auditory Verbal Learning Test (RAVLT) (Hodges, 2007). The MMSE is an assessment of global mental status, specifically assessing five areas of cognitive function: orientation, registration, attention and calculation, recall, and language (Folstein, Folstein, & McHugh, 1975). The TMT have been used to assess visual search, scanning, processing speed, and mental flexibility, which can provide a measure of executive function (Tombaugh, 2004). The Verbal Fluency Tests are measures of language, search, and retrieval (Crowe, 1998), as they assess ones ability to generate words belonging to a specific category (semantic verbal fluency), such as animals, or words that begin with a specific letter (phonemic verbal fluency), such as the letter ‘F’. This test can also be used as a measure of EF. The Digit Span Test is used to assess short-term working memory (Richardson, 2007), as digit sequences are verbally presented and then reported back by the subject in the same sequence. The RAVLT can be used as an assessment of several measures of learning and memory, such as immediate and delayed recall, learning rate, verbal learning, recognition of visually presented material, and post-interference recall (Mitrushina, Satz, Chervinsky, & D'Elia, 1991) – all of which are regulated by EF. When incorporating all of the above-mentioned assessments for a comprehensive neuropsychological assessment, the total session length ranges from 60-120 minutes, depending on the participant and their cognitive status.

2.1.4 Neuroimaging

Brain imaging is another great tool for distinguishing the cause of cognitive impairment and for monitoring changes (Petersen et al., 2001). Structural (computed tomography (CT) and magnetic resonance imaging (MRI)) and functional (positron emission tomography (PET) and MRI) methods have been used in both cross-sectional and longitudinal studies to evaluate MCI (Jack et al., 1997). More recently, neuroimaging has been used to investigate the effect of aerobic PA on brain atrophy. In a longitudinal exercise intervention study, Colcombe and colleagues (2006) used a high-resolution MRI structural protocol to show that participation in aerobic PA increased grey and white matter volume in older adults, mainly in the frontal and temporal cortices. As well, Takao and colleagues (2011) used brain imaging in a longitudinal study including adults aged 38 to 82 to show that declines in brain volume accelerate with increasing age. Neuroimaging has helped to accumulate information on age-related declines in brain volume, which has been consistent with age-related declines in cognitive function. Going forward continued work in this area may provide more informative evidence to be able to identify pathologic aging and brain disorders.

2.2 Role of physical activity in preventing cognitive decline

Physical activity (PA) plays an important role in determining physical fitness, with physically active individuals therefore having higher levels of fitness (Wei et al., 1999). Increases in ones physical fitness have been found to be strongly and inversely related to reductions in long-term mortality (Erikssen, 2001), and conversely, low levels of physical fitness are associated with increased risks of all-cause mortality. There are five health-related components that come together to make up physical fitness: 1) cardiorespiratory endurance (aerobic capacity), 2) muscular endurance, 3) muscular strength, 4) body composition, and 5) flexibility (Caspersen, Powell, & Christenson, 1985; Erikssen, 2001). Together, these components of physical fitness impact functional capacity and independent living. Whether or not older individuals are able to live independently and perform ADL depends largely on their aerobic capacity and muscle strength (Fleg et al., 2005).

2.2.1 Age-related declines in aerobic capacity

Cardiorespiratory fitness, as assessed by maximal aerobic capacity (VO_2max), declines progressively with age, beginning as early as 20 years old (Fleg, 2013), followed by the steepest declines after the age of 50 years (Concannon, Grierson, & Harrast, 2012; Yu, Yau, Ho, & Woo, 2011). Data from earlier studies have shown that the rate of decline in VO_2max after the fifth decade of life ranges from 5% to 10% per decade in untrained individuals (Fitzgerald, Tanaka, Tran, & Seals, 1997; Heath, Hagberg, Ehsani, & Holloszy, 1981; T. M. Wilson & Tanaka, 2000;

Yu et al., 2011), and such declines have been associated with factors such as decreases in maximal heart rate and stroke volume (Heath et al., 1981), increases in fat mass or decreases in lean body mass, and decreases in PA (Concannon et al., 2012; Tanaka & Seals, 2003; Yu et al., 2011) – all of which can contribute to a loss of functional capacity, independence, and therefore quality of life with age. For example, tasks that are perceived as being too effortful may be avoided, further reducing aerobic capacity, and further decreasing PA levels.

Such low levels of cardiorespiratory fitness have been associated with an increased risk of all-cause mortality. Meyers and colleagues (2002) showed that the risk of all-cause mortality in individuals whose aerobic capacity was less than 5 MET (17.5 ml/kg/min) was approximately two times greater than in individuals whose aerobic capacity was 8 MET (28 ml/kg/min). As well, it has been suggested that VO_2max values between 15-20 ml/kg/min are the minimum levels necessary to support independent living, and sedentary individuals may reach this point by the age of 80-85 years (Concannon et al., 2012). These deleterious effects of physical inactivity and sedentary behavior are even more pronounced in an aging population. Older adults tend to spend more time engaging in sedentary behavior, and it has been found that all-cause death rates increase with increased daily sitting time in adults over the age of 60. In addition to that, sedentary behavior has been found to be negatively associated with successful aging, such that those who engage in more sedentary activities are less likely to age successfully (Dogra & Stathokostas, 2012). On the other hand, Paterson and colleagues (1999) concluded that a healthy but sedentary older adult (67 years old) can improve his or her VO_2max by roughly 3.8 ml/kg/min after participating in 4-5 months of moderate intensity PA, three times per week. Additionally, endurance-trained older adults tend to have higher levels of physiological functional capacity, and lower risks of premature death compared to sedentary adults (Fleg, 2013; Yu et al., 2011). This is illustrated by one of the very few studies assessing aerobic capacity in octogenarian athletes and non-athletes (Figure 1; Trappe et al., 2013). Maintaining higher habitual PA levels is a key determinant to maintaining overall health, and also for reducing functional disability.

2.2.2 Muscular strength and aging

Maintaining muscle mass and strength with age is essential for carrying out day-to-day activities (Chodzko-Zajko, Schwingel, & Park, 2009). Muscle strength and muscle mass, even in healthy individuals, begins to decline around 25 years of age (Concannon et al., 2012), especially in the leg and back muscles (Tanaka, 2009). Exponential decreases then occur between the ages of 65 and 80, at which point up to 50% of muscle mass can be lost. This age-related decline in muscle mass and strength is known as sarcopenia. Sarcopenia has been characterized by a decrease in type II (fast-twitch) muscle fibers, which affect the strength and speed of movements. These changes in muscle strength with aging can lead to functional decline and disability, causing loss of balance, increased falls, and functional dependence (Tanaka, 2009). More specifically, it has been shown that the number of falls in older adults increases by 35-40% after the age of 60 (Milanović et al., 2013). Similar consequences of reduced muscle mass were demonstrated by Baumgartner and colleagues (1998), who found that elderly individuals with low muscle mass were three to four times more likely to develop a disability, loss of balance, and the need to use an assistive device for walking. Muscular strength and aerobic capacity, independently and together, are important determinants of physical fitness and functional capacity.

2.2.2.1 Role of muscle strength in maintaining functional capacity

Physiological functional capacity (PFC) is the ability to perform ADL, and the ease of doing these activities. Roughly 10% of healthy community-dwelling adults 75 years and older lose independence and require assistance to carry out basic ADL (Ploutz-Snyder, Manini, Ploutz-Snyder, & Wolf, 2002) – indicating low PFC. Lower limb muscle strength, specifically quadriceps strength, is an essential factor limiting ones ability to rise from a chair, walk at an appropriate speed, and go up and down a flight of stairs - all of which are ambulatory activities performed daily. Rising from a chair is an essential functional task for independent living and one of the most significant measures of physical function. It has been suggested that a threshold level of muscular strength is required to perform certain physical tasks, such as rising from a chair, and that a lack of strength can hinder individuals from carrying out ADL that are important determinants of independence. A peak isometric torque to body weight ratio (STR/BW, Nm/kg) of 3.0 has been found to be necessary in order to walk at an appropriate speed and to go down a flight of stairs. A higher ratio of roughly 3.5 is necessary to successfully rise from a chair (Ploutz-Snyder et al., 2002). Additionally, there is increasing evidence that these ambulatory activities, along with grip strength and balance, not only characterize physical capability but also current and future health status. In a meta-analytic review by Cooper, Kuh, & Hardy (2010), lower performance on measures of grip strength, walking speed, chair stand, and standing balance was associated with all-cause mortality. On the other hand, it has been demonstrated that individuals who engage in regular PA are able to carry out these physical tasks more easily than their sedentary counterparts. Chou and colleagues (2012) have shown that PA positively influences physical function, specifically gait speed and balance, as well as the performance of ADL in frail older adults. Wroblewski and colleagues (2011) showed that regular PA helped to preserve lean muscle mass in MA, aged 40-81, and that fat infiltration of muscle was prevented.

As well, Brill and colleagues (2000) found that men and women with greater strength had a lower prevalence of functional limitation, assessed using a 10-question assessment focusing on their ability to perform recreational, household, daily living, and personal care tasks. There is a clear relationship between PA and PFC. Although PA cannot stop the aging process, regular aerobic and strength training can help to increase and/or maintain physical function and reduce dependence on assistance in performing ADL.

2.2.3 Benefits of physical activity

There are many physical and mental health benefits associated with regular PA. As mentioned above, PA has been shown to reduce the risk of a variety of chronic diseases, including cardiovascular disease, hypertension, obesity, joint diseases (osteoporosis and arthritis), and cancer (King, Taylor, Haskell, & DeBusk, 1989; Rolland, Abellan van Kan, & Vellas, 2010; Sabiston & Brunet, 2012), and has been linked to a variety of psychological benefits, such as enhanced mental performance and concentration, improved self-esteem and confidence, improvements in sleep quality, energy levels, mood, and stress levels, and decreased anxiety and depression (Fox, Stathi, McKenna, & Davis, 2007; King et al., 1989; Ruuskanen & Ruoppila, 1995). The benefits of PA on brain function have not been studied as extensively as the aforementioned diseases, however, more recently, PA has been shown to contribute to healthy brain aging (Rolland et al., 2010) and reduce the risks of AD and cognitive decline (Buchman et al., 2012). More specifically, a physically active lifestyle has been linked to improved cognitive performance in older adults, especially for executive functioning (Concannon et al., 2012). These improvements in cognitive function have also been found in individuals with known cognitive impairment or dementia (Heyn et al., 2004). Regular PA is a key component to healthy and successful physical and cognitive aging.

2.2.4 Physical activity rates in elderly

Despite the many known benefits of PA, many people have yet to adopt a physically active lifestyle. In fact, over the past several decades, PA and fitness levels of Canadians have actually decreased (Tremblay et al., 2011). According to Canadian Physical Activity Guidelines, older adults (65 years and older) should be accumulating at least 150 minutes of moderate-to-vigorous aerobic PA per week, in bouts of 10 minutes or more, along with muscle strengthening activities and flexibility exercises (Canadian Society for Exercise Physiology, 2011; Tremblay et al., 2011). The Canadian Health Measures Survey (2013) provided data on direct measures of PA through the use of activity monitors. Data collected from 2007 to 2011 showed that only 11% of older adults (aged 60-79) were meeting the PA guidelines. To make matters worse, not only are older adults not getting enough PA, the majority of their waking hours are spent sedentary. Older individuals accumulate, on average, 10 hours of sedentary time per day, which is the most compared to younger age groups (Statistics Canada, 2013). Prior to 2007, physical inactivity rates among seniors were reported as being as high as 62% (Aging, 2006), and notably, this rate has worsened since 2001. Overall, the physical inactivity trends, especially in elderly individuals, seem to be worsening over time. In order to increase PA levels to meet the recommended guidelines, older adults can incorporate PA into their daily routine through transportation, recreation, planned exercise sessions, or community activities (Tremblay et al., 2011). Going forward, it would be valuable to have a better definition of the type, intensity, and amount of PA that is beneficial to healthy aging, and specifically to improve cognitive outcomes for this aging population.

2.2.5 Physical activity and cognitive decline

Pharmacological interventions have been recognized as being less effective than hoped in delaying or halting the onset of dementia or other age-related cognitive disorders. Therefore, an emphasis has been placed on understanding behavioural factors that may impact cognitive decline and dementia. PA has been studied as a behavioral factor for several decades, most notably by Spirduso and colleagues (1978), who investigated the relationship between aerobic fitness and cognition. In their cross-sectional study, they compared young and old racquet players, runners, and sedentary individuals on cognitive tasks and found that the older athletes performed significantly better than the older sedentary adults, and had a similar performance to the young sedentary adults. As well, according to a meta-analytic study by Colcombe and Kramer (2003), similar results were obtained from longitudinal studies investigating aerobic fitness and cognition in non-demented adults 55 years and older. They found that the aerobically trained individuals outperformed the non-aerobically trained controls on a variety of cognitive tasks, with EF showing the largest benefits of improved fitness. EF, compared to other cognitive functions, tend to show substantial age-related declines (Colcombe et al., 2006). Interestingly, Colcombe and Kramer (2003) also found that the greatest effects of training were seen when PA programs combined aerobic training with strength and flexibility training. Heyn and colleagues (2004) showed similar findings from their meta-analysis examining the benefits of exercise (including low intensity exercise, strength and resistance training) in individuals with dementia and cognitive impairment. However, contrary to these findings, other observational studies (Wilson et al., 2002; Yamada et al., 2003) did not find the same relationship between aerobic training and cognition, and instead found no effects of PA levels on cognitive function or dementia later in life. There are clearly discrepancies between these findings, and likely many reasons why different associations were observed. Overall, PA has been shown to have many positive effects on age-related cognitive decline, as well as brain structure. In a longitudinal study, Kramer and colleagues (2006) used MRI to assess changes in the brain structure of older adults who participated in either an aerobic training program or a nonaerobic control group. They found that older adults who were assigned to an aerobic training group had significant increases in GM volume in the frontal and temporal lobes of the brain, compared to the control group. These findings suggest that even short (6 months) PA programs can restore some of the age-related brain volume losses. Intervention studies have implied a causal relationship between PA and improved cognitive function, more efficient brain function, and spared brain volume in older adults, however there are still many unanswered questions. Not much is known yet about how much PA, and the type of PA, that is needed to have the greatest effects on cognitive function, or how long these effects can last after stopping a PA program. As well, the underlying mechanisms responsible for enhancing cognitive function with PA are still unclear. Additional studies are needed to further examine the relationship between PA and cognitive function, and perhaps potential moderators of this relationship.

2.2.6 BDNF: a moderator of healthy brain aging

Brain-derived neurotrophic factor (BDNF) has received a lot of attention as a potential moderator of the cognitive function-PA relationship over the past decade. BDNF, an important growth factor, is expressed throughout the brain, with transport occurring in both directions across the blood-brain barrier. BDNF plays a critical role in neuronal health, (Vaynman, Ying, & Gomez-Pinilla, 2004), cellular maintenance, and activity-dependent plasticity in the adult brain (Adlard, Perreau, & Cotman, 2005), through activities such as learning and PA. PA, which has been shown to be beneficial to cognitive function and brain structure, has also been thought to increase the availability of BDNF in the brain, particularly in the hippocampus - a structure involved in cognitive functions such as learning and memory (Cotman, Berchtold, & Christie, 2007). Knowing the importance of BDNF for synaptic plasticity and learning and memory, it has been suggested that the increase in hippocampal BDNF through exercise might underlie the ability of exercise to improve cognitive function – although the exact mechanisms responsible for causing the exercise-induced improvement in cognitive function still remain unclear.

Brain concentrations of BDNF cannot be easily studied in humans; therefore circulating levels of BDNF have been measured for studies involving humans. Previous cross-sectional studies (Komulainen et al., 2008; Swardfager et al., 2011) of seniors have shown that circulating levels of BDNF have been associated with cognitive assessment scores; although one of these studies included women only. In studies using animal models, BDNF levels were shown to increase progressively with regular PA over a period of two months, and these elevated levels of BDNF were able to be re-induced with a bout of PA after a two-week sedentary period (Intlekofer & Cotman, 2013). This suggests that there may be a "memory" for BDNF, and that a reduction in PA frequency may still be sufficient to maintain the accumulated BDNF levels. Animal studies have also found that the greatest responses of exercise-related increases in BDNF have been in the hippocampus (Adlard et al., 2005; Ferris, Williams, & Shen, 2007), however, studies with older animals have shown that these increased BDNF levels are maintained for shorter periods (Intlekofer & Cotman, 2013). With the approaching shift towards a more elderly population, there is a critical need to better understand the underlying mechanisms linking PA and improved brain function, as well as a need to tackle neurodegenerating processes. Through the induction of neurotrophins, which enhance neuroplasticity, PA is a key strategy to help lessen neurodegeneration and cognitive decline caused with aging. In all, these findings indicate that BDNF has an important role with aging. The moderating effects of BDNF on the relationship between PA and cognitive function should be further investigated in order to optimize healthy brain aging.

2.3 Masters Athletes as models of superior aging

2.3.1 History of Masters Athletics

For most of the 20th century, rest or gentle exercise was considered the norm for elderly individuals. Strenuous activity requiring overexertion was thought to be too demanding for the aging body, and sports were seen as inappropriate or not enjoyable for elderly people (Dionigi, 2006). However, the increase in the aging population was paralleled by an increase in athletics participation and the term "Masters Athletics" was coined to describe participation of individuals aged 35 years or over in competition. The exact birth of Masters sport is not quite known, however, it can be traced back to sometime in the mid-1960's. Some credit the Los Angeles Seniors Track Club, launched in 1966 by high school coach, Howard Barnes, for sparking Masters in the United States. This club, which featured over-40 events, quickly expanded to over 100 members and led to the creation of San Francisco and San Diego divisions. Others credit University of Oregon Track coach, Bill Bowerman, for the organization after he witnessed an over-40 running group in New Zealand. Some speculate that Canadian Don Farquharson started the Masters movement with the long distance Veteran running club competitions in the 1970's. Veterans track and filed competitions were organized according to "Ability classes 1-5" rather than age groups (Olson, 2000). It was David Pain, a runner from La Jolla, California, who introduced the idea of age-group competitions for track-and-field. In 1966, Pain invited other runners to a meeting to propose the idea of having a "special mile run for men over 40". He called the first event 'Masters Mile' because he felt the term 'Masters' was a better description for these middle-aged athletes than Seniors or Veterans (Baker, Horton, & Weir, 2009). This term eventually grew to be accepted as the description of older track and field athletes, and 'Masters Miles' became incorporated into track meets all over the United States.

With the concept of 'Masters' competitions becoming more popular, the first Masters U.S. Track and Field Championships were held in 1968, with 130 competitors, all of whom were men (Baker et al., 2009). Pain created this event because he felt that senior runners were starting to prove that they too could be in great physical shape. The cut-off age to participate was decided to be 40 years, based on the age of most of the interested (male) athletes. The Masters soon began to demonstrate that older athletes were able to take part in all of the established track-and-field disciplines, leading to the subsequent U.S. Masters Track and Field Competitions. The increased interest in Masters-only competition eventually led to the creation of world-class Masters competitions. The first World Masters Championships was held in Toronto in 1975 and included 1400 competitors. Following this, the first World Masters Games was also held in Toronto in 1985. This international event, a venue for world-class competition for seniors, is held every four years. It has become the largest multi-sport event of its kind, bringing together up to 30, 000 men and women aged 35 and over. In 2010, the first World Masters Winter Games took place in Bled, Slovania (Baker et al., 2009), and included a number of sports such as alpine and cross-country skiing, ice hockey, speed skating, etc. These Masters Athletics events are becoming increasingly popular, with the number of participating competitors increasing steadily over time.

2.3.2 What it means to be a Masters Athlete

When studying optimal aging, MA can be considered ideal subjects. MA are unique individuals 35 years and older who train and compete in a variety of sport competitions. Compared to a typical aging individual, elderly MA (>65 years) spend more time exercising and training, and have better health indicators (Ransdell, Vener, & Huberty, 2009; Shephard, Kavanagh, Mertens, Qureshi, & Clark, 1995). In fact, MA typically maintain higher-than-average PA levels (Baker et al., 2009), and continue to compete well into old age. It has been suggested that individuals who compete in sport at an older age may be "resisting the dominant negative stereotypes associated with aging and feeling empowered to live a fulfilled and healthy life" (Dionigi, 2006). As well, MA have even been referred to as models of successful aging as the physiological changes that occur with normal aging have been found to be less severe in MA (Baker et al., 2009). Today, the number of older athletes is higher than it ever was, and all of the research to date shows that MA are the best preserved in their age groups.

2.3.3 The physiology of an elderly MA

Masters Athletes, through PA, can maintain a healthy weight and body composition, a high level of fitness, and a reduced risk of chronic disease. These are a few of the problem areas which many aging individuals face. Studies on MA have found that weight and body composition changes do occur with age, however, their overall body composition remains superior compared to age-matched sedentary controls. Ryan and colleagues (1996) compared female MA to a group of younger sedentary controls, and found that the female MA had a lower percent body fat and fat mass. In addition to maintaining a lower fat mass, MA have also been shown to preserve lean (muscle) mass compared to age-matched untrained counterparts. Wroblewski and colleagues (2011) studied MA aged 40 to 81 years and observed a preservation of muscle mass and a lack of fat infiltration in their muscles (Figure 2). More importantly, there was no difference in quadriceps strength among the MA until they reached the 60-year age mark. However, among the 60 to 70 to 80 year-old age-groups, there was no significant difference in quadriceps strength. This suggests that although there was a decline in strength beginning around the age of 60, the decline did not significantly increase with further aging in these MA. These findings were comparable to those of McCrory and colleagues (2009) who found that senior (>60 years) athletes had significantly greater thigh muscle strength than healthy controls. Being physically fit and maintaining a lean body composition can also act as a powerful strategy to reduce the risk of cardiovascular disease. For example, MA have been found to have lipid profiles that are comparable to younger adults, with high-density lipoprotein (HDL) levels even greater than younger comparison groups (Seals et al., 1984). PA is not only beneficial to maintain health with age, but also to maintain physical performance. Interestingly, highly trained endurance athletes have a reduction in the percent decline of VO_2max compared to non-athletes. Heath and colleagues (1981) studied the effect of consistent, high-level PA on VO_2max, and compared the physiological effects in highly trained older and younger MA. They found that the older MA had a VO_2max only 15% lower than the younger athletes, suggesting a decline of <5% per decade in this group, rather than the typical 10% decline. This demonstrates that individuals with highly active lifestyles can have significantly higher VO_2max values than age-matched sedentary counterparts. Maintaining such high PA levels in later life can also be very beneficial to ones overall health. MA, in general, tend to be rather healthy and extremely physically fit, and this has translated into decreased risk of all-cause mortality. In a 16-year longitudinal study in Finland (Kettunen, Kujala, Kaprio, & Sarna, 2006), male track and field MA were compared to healthy male controls to investigate different aspects of health with aging. It was found that the MA had a lower risk of chronic disease than the controls, lower body mass index (BMI) at both baseline and follow-up, and none of the MA had diabetes at follow-up while 10% of the controls reported having diabetes. There are many health advantages associated with participation in regular PA with aging. As the number of MA competing in elite athletic events continues to rise, and as the general population continues to increase in age, there is accumulating research on MA and the benefits associated with being physically active into older age. A more recent area of interest is related to cognitive function in this fascinating group of older individuals.

2.3.4 Cognitive function in elderly MA

Considering MA have been illustrated as the 'physical elite' in their age groups, they have become the focus of many studies examining issues related to aging, physical and cognitive functioning, and health (Baker et al., 2009). Up until recently, cognitive function in elderly (>75 years of age) MA had not been studied. Tseng and colleagues (2013) investigated cognitive function and regional brain volume in 12 MA with an average age of 72.4 (±5.6) years. They found significant differences between MA and sedentary controls on assessments of verbal fluency, as well as greater grey and white matter volumes in the right parietal and occipital lobes of MA. This study showed that cognitive function was preserved in the elderly MA. Prior to this study, cognitive function was studied in elderly marathon runners and compared to age-matched non-athletes ($M_{age} = 66 \pm 4$) (Winker et al., 2010). The elderly marathon runners had a significantly greater performance on a test of nonverbal fluency and almost a significantly greater performance on a test of interference capability, both of which are measures of executive function. These findings were similar to those of Colcombe and Kramer (2003), which also demonstrated the benefits of PA on EF in older adults. As the population continues to age over time, MA will continue to be used as models of successful physical and cognitive aging as there are still many unanswered questions with regards to the relationship between PA and healthy brain aging.

2.4 Conclusion

Cognitive impairment is a major threat for the rapidly aging population as it negatively affects independence and quality of life. It is therefore a public health priority to identify preventive measures to reduce its deleterious effects. There is increasing evidence in the literature demonstrating that PA is a lifestyle behavior associated with decreases or improvements in cognitive decline with aging. However, although this association between PA and cognitive function exists, few studies have investigated this relationship in older aged adults- those greater than 75 years of age- who are most affected. As well, there is a lack of knowledge about the chronic protective effects of long-term exercise training on cognitive function. Considering that advancing age is accompanied by changes in brain health and function, and that the number of older adults will continue to increase over time, more research is needed to better understand the benefits of long-term exercise training on cognitive decline with aging. One way of doing this is by studying older (>75 years of age) MA, who continue to train and participate in elite level athletic competitions.

Figure 1. VO_2max data from octogenarian athletes and healthy untrained athletes

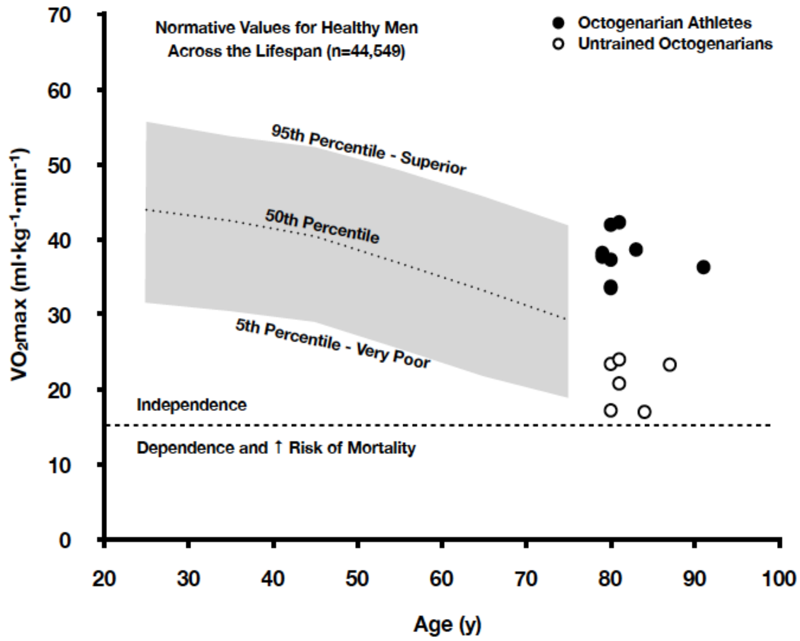
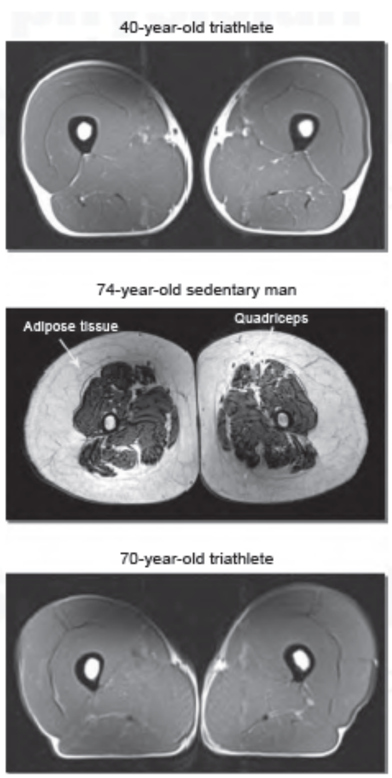


Figure 2. Quadriceps MRI scans of a 40-year-old triathlete, 74-year-old sedentary man, and 70-year-old triathlete.



CHAPTER 3: EXPERIMENTAL ARTICLE

3.1 Introduction

Lifespan has increased significantly over the past few decades, leading to the aging population growing rapidly. It is projected that by 2056, 1 in 4 Canadians will be 65 years and older, and 1 in 10 will be 80 years and over – three times the proportion of older seniors in 2005 (Cranswick & Dosman, 2008). As aging underlies cognitive decline, cognitive decline is anticipated to be one of the greatest health threats of the 21st century (Benedict et al., 2013). Specifically, cognitive decline will have a significant impact on health and independence (Kramer et al., 2003). Adults aged 75 years and older are proposed to be the most affected by age-related cognitive decline. As such, it is important to better understand cognitive function and related mechanisms that explain decline in these older old age adults.

Cognitive decline with aging is paralleled by declines in muscular mass and strength as well as cardiorespiratory fitness. Declines in both cognitive performance and muscle cross-sectional area tend to accelerate around 50 years of age (Angevaren et al., 2008; Lexell, 1995). Cognitive decline and physical dependence have been found to be lower in those who better maintain strength and/or aerobic fitness with aging (Colcombe & Kramer, 2003; Slingerland et al., 2007). Exercise is a promising mechanism to assist in the maintenance or improvement in muscular strength, endurance, and fitness among older adults (Tanaka, 2009). Regular exercise has been shown to improve muscle strength, balance, cardiorespiratory fitness, activities of daily living and prevent functional and cognitive decline in the elderly, even in those in their eighties and nineties (Ciolac, 2013; Tanaka, 2009). Larson and colleagues (2006) studied more than 1750 adults over the age of 65 years during a six-year period and found those who exercised at least three times per week were less likely to develop serious cognitive impairment later in life.

Fitness levels, irrespective of exercise habits, have also been associated with better cognition in older age adults (Barnes et al., 2003). Similar results have been reported in both observational and intervention studies (see Colcombe & Kramer, 2003 for review) suggesting fitness levels and exercise habits may buffer against the development of cognitive impairment. The strongest effects have been noted for cognitive tasks involving executive control processes such as the goal-directed actions of scheduling, planning, working memory, interference control, task coordination, and multi-tasking (Colcombe & Kramer, 2003; Hillman et al., 2008). Furthermore, the greatest effects of training may be observed when exercise programs combine aerobic training with strength and flexibility training (Kramer, Erickson, & Colcombe, 2006) and with at least 30 minutes of exercise duration (Colcombe & Kramer, 2003). While the association between exercise and cognition has been elucidated, few studies focus on older aged adults (those greater than 75 years of age who are most affected by cognitive and physical declines), and little is known about the chronic protective effects of long-term exercise training on cognitive function. Elite Masters Athletes (MA) may be a particularly valuable population in the understanding of chronic training effects on cognitive function. MA train and compete in elite-level athletics up to and over the age of 100 years old. There is limited understanding of cognitive function in elite-level MA.

The purpose of this study is to examine cognitive function in world-ranking elite MA aged 75 years or older compared to a group of age- and sex-matched non-athletic adults. A secondary aim is to examine predictors of cognitive function in adults aged 75 years and older. It was hypothesized that MA would demonstrate superior cognitive function compared to the non-active healthy controls (NAC), and that superior cognitive function would be associated with markers of greater physical fitness.

3.2 Methods

3.2.1 Participants

As part of the "Superior Aging: Lessons from the Masters Athletes" study, fifteen elite track-and-field MA (including six world-record holders) with an average of 20 years of competition experience were recruited from International Masters Athletic competitions. Based on eligibility criteria, MA were 75 years of age or older, free from major physical or mental health problems (i.e., diagnosed dementia or depression, heart, lung and/or central nervous system disease, anemia or low platelet count, if they were taking blood thinning or anti-coagulant medication), ranked top three in the world in their respective age category within two years from the start of the study, were in good health without any physical restrictions for walking or doing exercise, and were willing and able to provide informed consent. Fourteen healthy, age- and sex-matched NAC were recruited through advertisements in local press and postings at local hospitals and recreation centers. These subjects were also free of the above mentioned health problems, and represented a spectrum of health and activity levels seen in the general population. All participants were screened for eligibility following initial contact with the researchers. In order to assure age- and sex-matching of study participants, some men and women were excluded after initial screening if they were not of a certain age or sex. Volunteers completed a medical history and exercise experience form, as well as the Physical Activity Readiness Questionnaire (PAR-Q; Appendix I). Following clearance for participation, volunteers signed an informed consent form (Appendix I) and were scheduled for laboratory visits. The Faculty of Medicine Institutional Review Board (research project # A08-M66-12B) approved this study.

3.2.2 Procedures

All participants were requested to complete three laboratory visits at McGill University. On the first day, anthropometric measures, socio-demographic data, current physical activity levels, and physical and mental health information were gathered on a self-report questionnaire. On the second visit, participants performed an incremental cycle exercise test to exhaustion to obtain measures of peak aerobic fitness, strength testing on the Biodex 4 Pro dynamometer to obtain peak isometric quadriceps strength, and the 10-repetition chair stand to obtain measures of functional capacity. On the third visit, participants underwent five standardized modern cognitive function assessments. All assessments were conducted in a single session by the same examiner, in a room with a quiet and controlled environment, and lasted approximately 90 minutes. The tests were presented in a fixed order, and the examiner provided standard instructions to all participants. Following the cognitive assessments, participants were provided instructions on the use of an ActiGraph Accelerometer to measure physical activity levels.

3.2.3 Experimental Measures

3.2.3.1 Anthropometric measures. Height was measured using a drop-down tape measure and weight was measured using a digital scale by a trained technician. Body mass index (BMI) was calculated by dividing weight, in kilograms (kg) by the square of the height, in meters (m^2).

3.2.3.2 Peak aerobic fitness. To determine peak aerobic capacity (VO_2max, ml/kg/min), participants performed a continuous incremental exercise test on a stationary electronically-braked, pedal rate-independent cycle ergometer (Ergoline 800s) until volitional exhaustion, usually indicated as breathlessness or leg fatigue. Testing followed the guidelines of the American Thoracic Society and American College of Chest Physicians (2003), beginning with three minutes of rest, followed by a warm-up of three minutes of unloaded cycling. Immediately after the warm-up, the workload was increased by 20 watts, every two minutes, until the participant reached the point of symptom limitation. Using a Viasys/CareFusion Encore 29C cardiopulmonary exercise testing system, standard metabolic, respiratory, breathing pattern, and pulmonary gas exchange parameters were collected on a breath-by-breath basis while participants breathed through a rubber mouthpiece and low-resistance flow transducer with nasal passages occluded by a nose clip. Cardiovascular hemodynamic parameters, including blood pressure, heart rate, and stroke volume were measured continuously during exercise and for 10-minutes following exercise. Blood pressure was measured manually by auscultation of the brachial artery using a sphygmomanometer with an arm cuff at rest, every two minutes during exercise, at the end of exercise, and two minutes post exercise. Heart rate was monitored with a standard 12-lead electrocardiogram (ECG). The Borg 0-10 scale was used throughout exercise to provide ratings of perceived exertion in terms of breathlessness (dyspnea) and leg fatigue. Ratings were taken at rest, within the first 30 seconds of every second minute during exercise, and at the end of exercise.

3.2.3.3 Peak muscle strength. The multi-joint system Biodex 4 Pro dynamometer (Biodex, Atlas Medic) was used to quantitatively assess peak isometric quadriceps strength (Nm). Participants were seated with their knees angled at 90° and they were instructed to push as hard as they can, using their dominant leg, against the stationary arm of the machine for four seconds at a time. This was repeated three times. Participants were familiarized with the equipment and proper exercise technique and were warmed up prior to the assessment.

3.2.3.4 Functional capacity. The 10-repetition chair stand test was used to assess physical functionality related to performing activities of daily living (ADL). Participants were seated in a chair and instructed to stand up and sit back down as fast as they could for 10 repetitions, without using their arms (Bohannon, 2012). Each assessment was timed using a stopwatch, beginning on the command "go" and stopping when participants sat down after the 10^{th} repetition. Higher times indicated lower functional capacity.

3.2.3.5 Cognitive function. Five cognitive assessments were performed on all participants, investigating functions such as global cognitive function, learning and memory, visual search, processing speed, verbal fluency and language, and executive function.

3.2.3.5.1 Global cognitive function. The Mini Mental State Exam (MMSE; Folstein, Folstein, and McHugh, 1975) was used to assess mental status. Five areas of cognitive function are assessed on 11 items/tasks: orientation, registration, attention and calculation, recall, and language. A sample task would be: "Take the paper in your right hand, fold it in half, and put it on the floor". This task is scored out of three, with one point per action performed correctly. The maximum possible score for the MMSE is typically 30, however, for this study, questions 1 and 2 were eliminated, making the maximum possible score 20. Questions 1 and 2 referred to the time, date, and place of testing. Considering that all study participants were healthy, free from any diagnosed dementia, and consented to take part in this study, it was assumed that they were aware of where they were and what time of year it was. As well, the cognitive assessment room was away from the main study area, therefore to ask the participants "what floor are we on?" was a slightly tricky question. A score of 14 or lower was used as an indicator of potential cognitive impairment (Escobar et al., 1986). The MMSE has been validated and used extensively in both clinical practice and research (Fountoulakis, Tsolaki, Chantzi, & Kazis, 2000).

3.2.3.5.2 Executive function. The Trail Making Test (TMT) is a timed paper-and-pencil task that consists of two parts (Reitan, 1955). Part A (TMT-A) involves drawing a line sequentially connecting encircled numbers (i.e., from 1 to 25). Part B (TMT-B) is similar to Part

A, except there is the added task of connecting numbers and letters in an alternating progressive sequence (i.e., 1 to A to 2 to B). Participants are instructed to connect the circles as quickly as possible, without lifting the pencil from the paper. The test is demonstrated for the participant using a sample sheet prior to starting. If an error is made during the test, the examiner points it out immediately and allows the participant to correct it. Errors affect the total score only in that the correction of errors is included in the completion time for the task. Results for both TMT-A and TMT-B are reported as the number of seconds required to complete the task; therefore, higher scores reveal greater impairment. Performing the TMT successfully requires a variety of abilities, including visual search, scanning, speed of processing, and mental flexibility (Tombaugh, 2004). As such, the TMT was used as a measure of executive function in the current study, with higher scores indicating lower cognitive function.

3.2.3.5.3 Verbal Fluency. Verbal fluency is the ability to generate words belonging to a specific category. Two frequently used time-limited verbal fluency tasks were administered in this study. Both of these tasks require strategies of search and retrieval (Crowe, 1998). The Semantic Verbal Fluency Test requires giving words that belong to a restricted category, such as animals (Rosen, 1980). Participants were instructed to “say the names of as many animals as you can think of”. This task lasted for 60 seconds. The Phonemic Verbal Fluency Test requires giving words that begin with a specific letter (Spreen, 1977). Participants were given the letter “F” and instructed to “say as many words as you can think of, beginning with the letter “F”. This task lasted for 60 seconds. Responses from both tasks were transcribed as they were said aloud. Answers were considered invalid if they had already been mentioned, or if the word did not belong to the animal category or begin with the letter “F” (Crowe, 1998). Responses were scored as either correct or incorrect and the number of correct words generated was summed. Typically, a cut-off score of 14 is used for the detection of mild dementia (Sager, Hermann, La Rue, & Woodard, 2006). The more words recalled reflect higher cognitive function.

3.2.3.5.4 Verbal working memory. Measures of forward and backward digit span are well established and have been used frequently to assess short-term verbal memory (Richardson, 2007; Woods et al., 2011). In both cases, digit sequences are presented to the participants beginning with a length of three digits, in both the forward and backward order. All digit sequences were presented at a rate of one digit per second, in a monotone voice, without putting emphasis on any specific digits. Participants were instructed to report the digit sequence first in the forward order, followed by the backward order. Testing ceased when the participant failed to accurately report the digit sequence, or when the maximal list length was reached (seven digits forward, seven digits backward). The maximal list length was set at seven digits since seven digits in the forward span is considered to be the normal memory span (Woods et al., 2011). To score the Digit Span test, the total number of forward sequences and backward sequences reported correctly was summed, producing a total possible score out of 10. Higher scores reflect better cognitive function.

***3.2.3.5.5 Learning and memory**.* The 15-word Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1964) was used to assess several measures of learning and memory, such as immediate and delayed recall, learning rate, verbal learning, recognition of visually presented material, and post-interference recall (Mitrushina et al., 1991). Participants were orally presented with a list of 15 words, in the same order, over five trials, at a rate of one word per second (Lezak, 1983). At each trial, they were instructed to free-recall the word-list in any order, immediately after presentation of the entire list. Following the five word-recall trials, a 15-word 'interference list' was presented to participants, at a rate of one word per second, and they were instructed to free-recall words from this list. After recalling the interference word-list, participants were instructed to recall words from the original 15-word list, without any additional presentation of those words. Between each trial, participants were allowed a 10-second rest. The last recall trial was followed by a three-minute break, during which participants were allowed to have a drink of water, or a snack. After the three-minute break, there was a 'delayed recall' trial where participants were asked to once again recall words from the original 15-word list, without additional presentation of the words. To end the test, a list of 30 words was given to the participant, along with a pencil, and they were asked to circle all words that they recognized as being part of the original 15-word list. For each free-recall trial, all responses were recorded, in the order they were recalled. To score each trial, the number of correctly recalled words was summed, excluding any repeated words. Words that were recalled but that were not part of the 15-word list were marked as 'error'. Words that were correct, but that were recalled more than once, were marked as 'repeat'. The RAVLT has been widely used in the assessment of memory disturbances caused by a variety of diseases or injury, and has also been found to be an effective tool to investigate memory deficits with aging (Mitrushina et al., 1991). Higher scores on the RAVLT reflect better cognitive function.

3.2.3.6 Physical activity levels. Physical activity patterns were directly assessed using accelerometry (Actigraph GT3M) which provides objective measures of physical activity, such as information about the amount, frequency, and duration, and can also assess non-exercise physical activity, such as activities of daily living (Murphy, 2009). For collection of physical activity data in this study, participants wore accelerometers for seven consecutive days, 24-hours a day. During waking hours, the accelerometer was worn around the waist, aligned directly with the knee on the dominant side of the body, and secured with an elastic belt that was provided.

The accelerometer was also worn while sleeping, however participants were instructed to remove the accelerometer from their waist and wrap it around their wrist, just before going to sleep. An accelerometer time log was provided to each participant to record wake time, time accelerometer was placed around waist, bed time, time accelerometer was switched from waist to wrist. Participants could also record times that they went swimming or bicycling since the accelerometer does not capture these activities.

3.2.4 Data analysis

Sample size was determined based upon a desired power of 0.8 and an alpha of 0.05, equating to 10-17 participants per group (calculated using Sigmaplot software). All statistical tests were performed using statistical package for social sciences (SPSS) software (IBM© SPSS© Statistics Version 20). Descriptive statistics (means and standard deviation) were used to characterize the participants. Comparisons between groups (MA and NAC) on the cognitive function outcomes were performed using Student's t-tests. Pearson product moment correlation coefficients were estimated among physical activity, fitness, and the cognitive function outcomes across participants, regardless of MA or NAC status. In all cases, statistical significance was set at $p < .05$.

3.3 Results

3.3.1 Participant characteristics

Twenty-nine participants completed the study. Descriptive information for the MA (n=15) and NAC (n=14) are presented in Table 1. A greater percentage of MA had a university degree (86% vs 50%; X^2 (1) = 4.61, $p < .05$) and were married/common-law (66% vs 28%; X^2 (1) = 4.23, $p < .05$) compared to the NAC. MA had an average BMI of 22.5, which was significantly lower than the BMI of the NAC ($M_{MA} = 22.5 \pm 2.7$ kg/m^2 vs $M_{NAC} = 26.9 \pm 3.7$ kg/m^2, $t(27) = 3.77$, $p < .05$).

3.3.2 Mean Differences

3.3.2.1 Physical fitness. MA demonstrated superior performances on measures of physical fitness. As seen in Figure 3, MA had a significantly higher peak aerobic capacity (VO_2max; 34 ±9 ml/kg/min, $t(27) = 5.71$, $p < .05$) than the NAC (19±3 ml/kg/min). Peak isometric strength of the quadriceps muscle was significantly higher in the MA compared to NAC (167 ± 59 Nm vs 119 ± 35 Nm, respectively, $t(27) = 2.66$, $p < .05$). In addition, functional capacity as reflected by the 10-repetition chair stand was higher in the MA compared to NAC ($t(27) = 4.62$, $p < .05$) whereby the MA were able to complete 10 chair stands in almost half of the amount of time (14 ± 3 sec) compared to NAC (25 ± 8 sec).

3.3.2.2 Cognitive function. As seen in Figure 4, MA scored significantly higher on tests of global cognitive function (measured using the MMSE; $t(27) = 3.02$, $p < .05$); visual search and processing speed (measured using the TMT-A; $t(27) = 2.09$, $p < .05$); and learning and memory (measured using the RAVLT; $t(26) = 2.77$, $p < .05$). No significant differences between MA and NAC were found when assessing mental flexibility (measured using the TMT-B, $t(27) = 1.4$, $p = .17$); digit span (measured using the Digit Span Test, $t(27) = 1.43$, $p = .89$); or language and verbal fluency (measured using the Semantic and Phonemic Verbal Fluency tests, $t(27) = 1.08$, $p = .29$ and $t(27) = 1.79$, $p = .09$, respectively), however MA still outperformed the NAC on these assessments.

3.3.2.3 Physical activity levels. Individual data and group means (± SD) are presented in Figure 5. As shown, MA had significantly higher levels of PA compared to NAC, reflected by a 3-times greater daily step count ($M_{MA} = 8341 \pm 3573$ vs $M_{NAC} = 2731 \pm 984$, $t(21) = 3.17$, $p <$

.05) and over six times greater participation in daily MVPA (MA 38 ± 22 minutes vs NAC 6 ± 3 minutes, t(21) = 2.30, p = .03).

3.3.3 Relationships among fitness, functional capacity, physical activity, and cognitive function

For all tests of association, the MA and NAC groupings were collapsed. Higher VO_2max was associated with better general cognitive function (assessed using the MMSE; $r(27) = .47$, $p < .05$) and verbal learning and memory (assessed using the RAVLT; $r(27) = .38$ to 0.53, $p < .05$). Higher physical activity levels were associated with greater cognitive function. Specifically, number of steps per day was associated with better general cognitive function (MMSE; $r(20) = .45$, $p < .05$), and the number of minutes spent in MVPA was associated with greater global cognitive function (MMSE; $r(20) = .51$, $p < .05$) and greater verbal learning and memory (RAVLT Trials 3-5; $r(20) = .47$ to .56, $p < .05$). Correlation coefficients can be seen in Table 2.

Table 1.

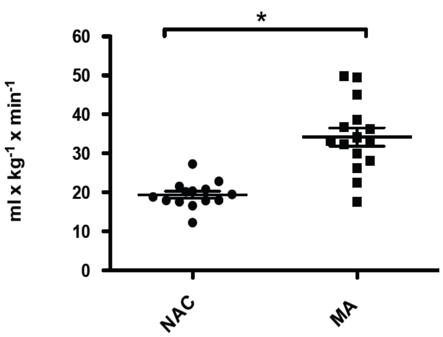
Participant Characteristics for NAC and MA

Variable	NAC	MA	Total Sample
Age (y)	80 ± 4	79 ± 5	80 ± 4
Height (cm)	164 ± 12	166 ± 11	165 ± 2
Weight (kg)	72 ± 11	62 ± 13*	67 ± 13
BMI (kg/m^2)	27 ± 4	22 ± 3*	25 ± 4
Education (years)	14 ± 2	15 ± 1	14± 2
Education (% university)	35%	73%	55%
Marital status (% married)	28%	60%	45%

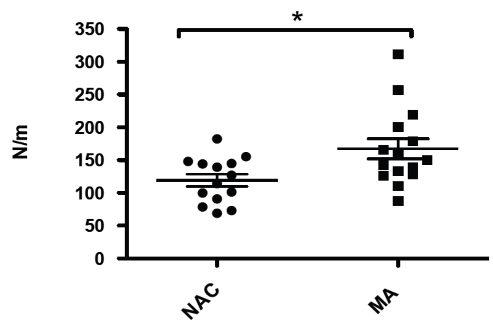
Data are presented as means ± SD. NAC: non-athlete controls. MA: Masters Athletes. BMI: Body Mass Index.
*Significant difference between NAC and MA groups, p < .05.

Figure 3. Differences in Physical Fitness between NAC and MA

A. VO_2max



B. Isometric Quadriceps Strength



C. Time Required to do 10 Chair Stands

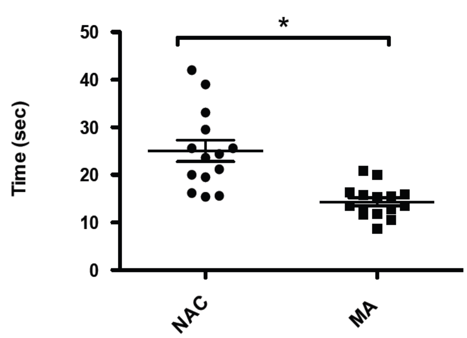
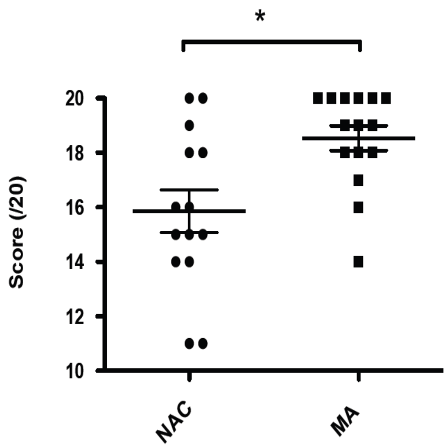
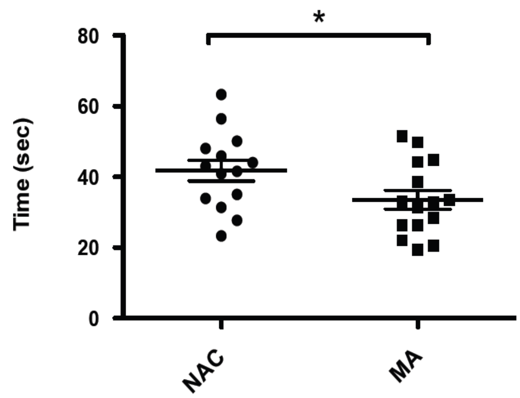


Figure 4. Cognitive Function Differences Between NAC and MA

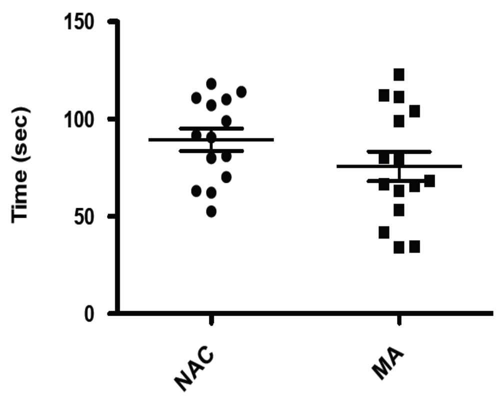
A. Mini Mental State Exam



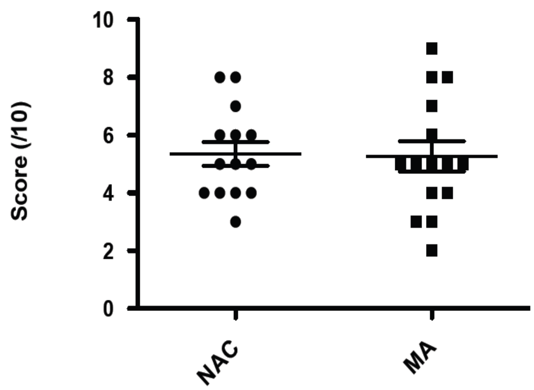
B. Trail Making Test – Part A



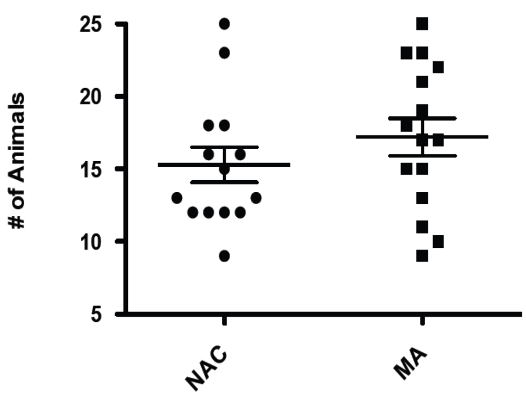
C. Trail Making Test – Part B



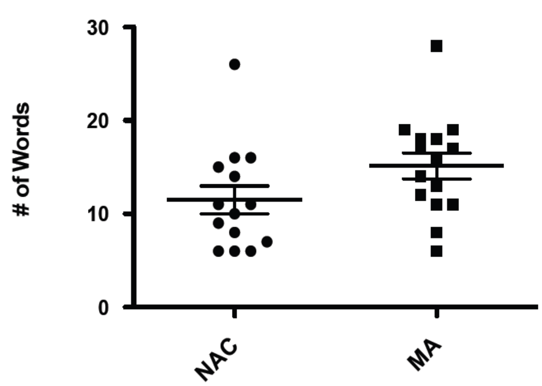
D. Digit Span



E. Semantic Verbal Fluency



F. Phonemic Verbal Fluency



G. Rey Auditory Verbal Learning Test – Learning Over Trials (LOT)

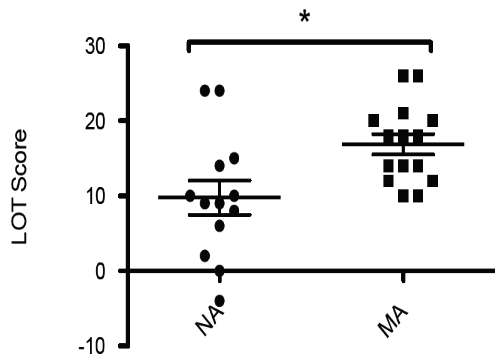
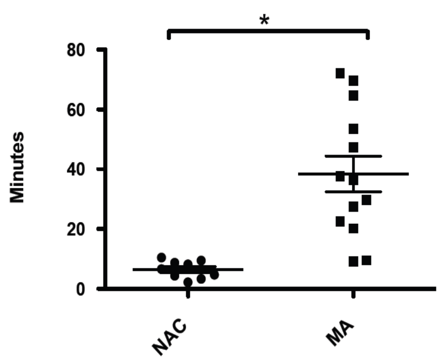


Figure 5. Differences in Physical Activity levels between MA and NAC

A. Daily MVPA



B. Daily Steps

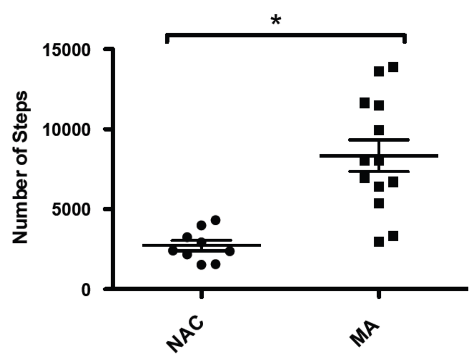


Table 2.

Correlation between markers of physical fitness and cognitive function

	VO_2max	Strength	Chair	MVPA	Steps
1. VO_{2max}	1				
2. Quadriceps Strength	.31	1			
3. Chair Stands	-.52*	-.21	1		
4. MVPA	-.12	0	.28	1	

5. Daily Steps	-.18	-.05	.38	.93*	1
6. MMSE	.47*	.27	-.28	.51*	.45*
7. TMT-A	-.18	-.30	.32	-.22	-.21
8. TMT-B	-.11	-.25	.13	-.39	-.36
9. Digit Span	-.12	.33	.12	.23	.12
10. VF-Semantic	.17	.32	-.15	.01	-.14
11. VF-Phonemic	.15	-.08	-.28	.05	-.03
12. RAVLT1	-.05	.45*	.02	.23	.09
13.RAVLT2	.11	.34	-.03	.37	.29
14. RAVLT3	.47*	.35	-.24	.50*	.41
15.RAVLT4	.37*	.39*	-.29	.47*	.36
16. RAVLT5	.49*	.45*	-.30	.56*	.45*
17. RAVLTB	.45*	.37	-.59*	.39	.32
18. RAVLT6	.27	.28	-.18	.34	.24
19. RAVLT - LOT	.37*	.22	-.32	.29	.35

Data are presented as Pearson correlation coefficients. VO_2max: maximum oxygen consumption (ml/kg/min). Quadriceps Strength: Quadriceps Isometric Strength (N/m). MVPA: moderate to vigorous physical activity (minutes/day). MMSE: Mini Mental State Exam. TMT-A: Trail Making Test Part A. TMT-B: Trail Making Test Part B. VF-Sem: Verbal Fluency – Semantic. VF-Phon: Verbal Fluency- Phonemic. RAVLT: Rey Auditory Verbal Learning Test (trial number indicated). RAVLT - LOT: Rey Auditory Verbal Learning Test – Learning Over Trials. *Significant difference between NAC and MA groups, $p < .05$.

3.4 Discussion

This study is the first, to our knowledge, to investigate both cognitive and physical function in an age group (≥ 75 years of age) that is most affected by age-related cognitive and physical declines. Although many previous studies have examined MA, a group of individuals who represent a unique model to healthy aging, there is a lack of knowledge surrounding this group of athletes who represent an age associated with the most physical and cognitive impairments. Consistent with our hypothesis, MA demonstrated superior indices of cognitive function, and this superior cognitive function was associated with markers of greater physical fitness. More specifically, compared to aged NAC, aged MA demonstrated superior indices of global cognitive function (MMSE), verbal learning and memory (RAVLT), and processing speed and attention (TMT-A); and as expected, they had greater physical activity levels (steps/day and minutes of moderate-to-vigorous physical activity), physical fitness (VO_2max and quadriceps strength) and functional capacity (chair stands).

Our first hypothesis, that MA would have greater performances on cognitive function assessments compared to NAC, was confirmed. MA outperformed the NAC on a number of cognitive assessments (Figure 4), showing agreement with previous findings demonstrating that physical activity has preventive effects on age-related cognitive decline (Klusmann et al., 2010) and can lead to improvements in cognitive function with aging (Cooper et al., 2010). Specifically, MA had superior performances on assessments focusing on tasks such as processing speed, attention, memory, and learning – all of which are controlled by executive functions. Executive functions tend to show notable age-related declines; however, interestingly, they also show the largest benefits from physical activity (Colcombe et al., 2003; Colcombe et al., 2006). Considering that MA had significantly higher physical activity levels compared to

NAC (Figure 5), these findings are in line with many other observations, that cognitive processes that are most susceptible to age-related decline can be protected by regular, consistent physical activity.

The MA were long-term exercisers with an average of 20 years of competition experience and still competed in elite athletic competitions at the time of testing. The healthy, age-sex-matched NAC had no history of structured exercise beyond activities of daily living, demonstrated by the ~4600 fewer steps per day in the NAC compared to MA (Figure 5B). According to Tudor-Locke et al. (2011), this low step count of the NAC can be classified as "limited activity", compared to the higher step count of the MA, classified as "somewhat active". As well, the MA accumulated almost three times the number of minutes of MVPA per day (Figure 5A). However, when looking at the total number of minutes per day spent doing light activity, there is not much of a difference between the MA and NAC (285.3 ± 46.3 and 234.3 ± 72.1, respectively), showing that the NAC are not completely inactive, and do continue to engage in activities of daily living.

While a progressive decline in VO_2max with age is well established, participation in regular physical activity can greatly affect VO_2max, even in older adults. Endurance-trained individuals have been shown to attenuate declines in VO_2max with aging, compared to untrained individuals (Mikkelsen et al., 2013; Tanaka, 2009). In our study, this was demonstrated by the highly active MA who had 78% higher VO_2max than NAC. Their high aerobic capacity (34 ±9 ml/kg/min) is comparable to findings from Trappe and colleagues (2013) who reported VO_2max values of 38 ±1 ml/kg/min (range: 34-42 ml/kg/min) for nine male octogenarian athletes. Harridge and colleagues (1997) also reported on the VO_2max of five men > 80 years of age with a history of lifelong endurance training, however, they had an average VO_2max of 27 ±5 ml/kg/min, which is 25% lower than the MA in this study. Three of the MA in our study had VO2max levels greater than 45 ml/kg/min, classified as “good/excellent” in adults aged 30-39 years (American College of Sports Medicine, 2013) – about 50 years younger than the average age of the MA. According to a summary of 21 studies (Trappe et al., 2013), the average VO_2max for untrained men and women > 80 years of age was 21 ±4 ml/kg/min and 18 ±4 ml/kg/min, respectively - values that are very similar to those of the NAC in this study. Seven of the 14 NAC in this study had VO_2max values between 15-20 ml/kg/min, which is the threshold value of independent living and disability (Concannon, Grierson, & Harrast, 2012; Myers et al., 2002), and one NAC had a VO_2max below this threshold. MA who continue training into older age are typically free from confounders affecting the general aging population, such as increased body fat, reductions in lean mass, and chronic diseases. These findings emphasize the importance of maintaining physical activity, and therefore aerobic capacity, with age in order to preserve physical independence and reduce the risks of all-cause mortality.

As expected, MA had significantly greater quadriceps strength than NAC, which was reflected in their superior performance on the 10-repetition chair stand – an essential functional task for independent living. A loss of muscle strength with age, commonly referred to as sarcopenia, has a direct effect on the performance of ADL in the elderly (Tanaka, 2009); however, resistance training can improve muscle strength in older adults (Maharam, Bauman, Kalman, Skolnik, & Perle, 1999), and even help to alleviate the associated functional consequences of muscle loss (Concannon et al., 2012). This concept has been demonstrated by the MA who incorporate resistance training into their weekly exercise sessions, and accordingly had 40% greater quadriceps strength than NAC. The NAC, on the hand, had comparable results on the 10-repetition chair stand assessment to mobility-limited community dwelling older individuals (Bean et al., 2002) – suggesting that the NAC may have more noticeable physical effects of aging. Overall, low functional capacity with age can contribute to increased risk of disability, increased risk of falls, and increased risk of dependence (Tanaka, 2009).

Our second hypothesis, that the superior cognitive function of MA would be associated with markers of greater physical fitness and functional capacity, was partially confirmed. MA had significantly higher PA levels, aerobic capacity (VO_2max), quadriceps strength and greater functional capacity as seen with the chair stand, which were all positively associated with cognitive function, except for functional capacity (Table 2). The cardiovascular fitness hypothesis has been proposed to explain the relationship between cognitive function and aerobic capacity: suggesting that aerobic fitness is a physiological factor mediating the many health benefits of physical activity (North, McCullagh, & Tran, 1990). This would mean that gains in aerobic fitness through participation in regular physical activity mediate the resulting cognitive function benefits. However, Etnier and colleagues (2006) tested the viability of the cardiovascular fitness hypothesis as an explanation for the relationship between physical activity and cognitive performance and their results do not support this concept. While the benefits of physical activity for cognitive function are well established, the underlying moderators of this relationship have not yet been fully identified. Underlying physiological mechanisms, such as brain structure (Colcombe et al., 2003), cerebral blood flow, or neurotrophic factors (Etnier et al., 2006) have been suggested as potentially moderating the relationship between physical activity and cognitive function, with neurotrophic factors recently receiving the most attention. Physical activity has been thought to increase the availability of brain-derived neurotrophic factor (BDNF) in the hippocampus – a brain structure involved in learning and memory (Cotman et al., 2007). It is perhaps this increase in hippocampal BDNF through physical activity that may underlie the relationship between physical activity and cognitive performance. The exact mechanism responsible for the exercise-induced cognitive improvements still remains unclear and requires further investigation.

Quadriceps strength was also found to be associated with a measure of cognitive function, specifically learning and memory (Table 2). Previous studies (Boyle, Buchman, Wilson, Leurgans, & Bennett, 2009; Nakamoto et al., 2012) have also found this association between cognitive function and strength, and more specifically have found that greater muscle strength was associated with lower risks of developing cognitive impairment. Boyle and colleagues (2009) investigated the association between muscle strength and the risks of developing AD in community-dwelling older adults and found that individuals with greater strength showed slower rates of cognitive decline over time. Although little information is available on the association between exercise-related changes in muscle strength and cognitive function, a few studies do provide evidence for the positive effects of resistance training on maintaining or improving cognitive function (Kramer et al., 2006; Özkaya et al., 2005). Assessing muscle strength in older individuals may be useful for identifying the onset of cognitive impairment and for identifying those who may benefit most from a physical activity intervention which incorporated both aerobic and strength training.

Functional capacity was not found to be associated with cognitive function, however it was noted that the 10-repetition chair stand was associated with VO_2max. This is not surprising, as aerobic fitness is a key determinant of functional capacity. This relationship between VO_2max and functional capacity suggests that there is also an association between cognitive function and functional capacity. Intact cognitive function is necessary to carry out everyday physical functions, however this relationship has not been studied extensively.

The results of this study should be interpreted within the context of its limitations. The main limitation of this study was its cross-sectional design. This design didn't allow for us to track changes in cognitive function over time, meaning that no cause-effect conclusions can be made. Follow-up data would provide more insight into the benefits of physical activity on cognitive function with aging. Another limitation is that the findings from this study were based on a small sample size. Moreover, our cross-sectional data represent a sample bias because of voluntary participation, most likely including NAC who are healthier than the average population. However, our healthy control group, who were not inactive but rather maintained a range of physical activity, allowed us to study the effects of healthy aging. Although this was not a methodological flaw in the case of the MA -because our intention was to show an optimal model of aging from a physiological point of view- the findings from studying highly active elderly MA may not be generalizable to the rest of the aging population. Furthermore, the superior cognitive function observed in the MA cannot be attributable to exercise alone. There are other factors, such as genetics and environment, which need to be taken into account as well when interpreting these findings. In addition, despite our efforts to optimally recruit and match MA and NAC on age and sex, it was difficult to match for level of education. A unique aspect of our study is that we studied both cognitive and physical function in individuals who were all 75 years of age and older. This is a strength knowing that cognitive and physical decline is increasingly prevalent and burdensome in this age group.

3.4.1 Conclusion

In conclusion, this study demonstrates that high aerobic fitness, as seen in MA, can be beneficial for maintaining cognitive function with age. Given that the MA have been competing for an average of 20 years, this suggests that long-term exercise training is important for the maintenance of high aerobic fitness and therefore cognitive function. The MA had superior performances on all cognitive assessments, physical fitness assessments, and functional capacity assessments. Specifically, MA had significantly greater scores on cognitive assessments measuring executive functions, which have been shown to be more susceptible to age-related declines. When looking at the relationship between cognitive function and markers of physical fitness and functional capacity, cognitive function was positively associated with aerobic capacity, PA levels, and quadriceps strength.

Many unanswered questions still remain with regard to the relationship between cognitive function and PA. Future research is needed to examine different exercise training protocols that are most beneficial for successful brain aging, as well as exercise programs that are feasible for elderly individuals. Evidently, aerobic exercise, along with resistance training, has positive effects on reducing normal age-related declines; however, the frequency, type, and intensity of exercise that is required to produce these positive effects is still unclear. Additionally, more work is needed in understanding the moderators of this cognitive function-physical activity relationship. Animal studies have suggested that exercise increases brain-derived neurotrophic factor in the hippocampus, along with enhanced angiogenesis, may slow or reverse brain aging (Tseng et al., 2013). While PA may improve growth factor levels in the brain and/or in the periphery, more human studies are needed to identify the underlying physiological mechanisms. Work in this area is especially important considering the increasing rates of elderly individuals in the population, and therefore, the increasing rates of cognitive decline. Cognitive decline has been associated with negative functional and emotional outcomes, thus exercise promotion should be a primary method of treatment (or even better, prevention) from health care providers to the elderly. Optimizing exercise protocols is of great interest for future research in order to improve the health and quality of life in individuals with cognitive decline or impairment.

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APPENDIX I: PAR-Q & INFORMED CONSENT

PAR-Q:

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	**Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2.	**Do you feel pain in your chest when you do physical activity?**
☐	☐	3.	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4.	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5.	**Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6.	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7.	**Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME ____

SIGNATURE ____ DATE ________________________

SIGNATURE OF PARENT ________________________________ WITNESS ________________________
or GUARDIAN (for participants under the age of majority)

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

PARTICIPANT INFORMED CONSENT FORM:

1. I am aware that this is a research study
2. I have read all the pages of the consent form. The research personnel have explained the information and procedures involved in the study. I have had the opportunity to ask questions and they have been answered to my satisfaction. I have been given time to consider the information carefully and to decide whether or not to participate in this study.
3. I have been informed that my participation in this study is entirely voluntary and that I may refuse to participate or withdraw at any time.
4. I will be given a copy of this informed consent to keep for my own information, once it is signed.
5. I do not give up any of my legal rights by signing this form nor am I freeing the investigator or the establishment where the study takes place from their legal and professional responsibilities.
6. I agree to the option of participating in Dr. Jensen's ongoing data collection of breathing muscles involving an esophageal catheter insertion ☐ Yes ☐ No
7. My signature below indicated that I voluntarily agree to take part in this study.

Participant's signature	Participant's name (please print)	Date
Signature of Person Administering Informed Consent	Name (please print)	Date

<u>Statement of study investigator:</u>

I, or one of my trainees, have carefully explained to the participant the nature of the above research study. I certify that, to the best of my knowledge, the participant understands clearly the nature of the study and demands, benefits, and risks involved to him/her in this study.

Signature of Principal Investigator (Tanja Tavaissalo, Ph. D.) or Russ Hepple, Ph. D. — DATE

APPENDIX II: CANDIDATES LIST OF AWARDS, PUBLICATIONS AND PRESENTATIONS

LIST OF AWARDS

1) **Bloomberg Manulife Fellowship –** 2014-2015
   Department of Kinesiology and Physical Education
   Value: $22,500 / year

2) **Fond de la Recherche en Sante du Quebec** 2014-2017
   Doctoral Award
   Value: $20,000 / year

3) **CIHR Institute Community Support – Travel Award** 2014
   Value: $1000

4) **Graduate Research Enhancement and Travel (GREAT) Award** 2014
   Value: $500

5) **Education Graduate Student's Society (EGSS)** 2013
   Faculty of Education Travel Award
   Value: $500

6) **R.E. Wilkinson Award – Graduate Award** 2013
   Value: $800

7) **Graduate Research Enhancement and Travel (GREAT) Award** 2013
   Value: $500

8) **Adriano Tassone Internship Award** 2012
   Value: $4000

LIST OF PUBLICATIONS

1) Brunet, J., **Taran, S.,** Burke, S., Sabiston, C.M. (2013). *A Qualitative Exploration of Barriers and Motivators to Physical Activity Participation in Women Treated for Breast Cancer*. Disability and Rehabilitation.

2) Taivassalo, T., Spendiff, S., MacMillan, N., Filion, M.E., **Taran, S.,** Konokhova, Y., Sabiston, C., Allen, M., Power, G., Rice, C.L., Doherty, T.J., Capri, M., Franceschi, C., Narici, M.V., Garagnani, P., Pirazzini, C., Giuliani, C., Erskine, R., Morais, J.A., and Hepple, R.T. (In preparation). *Superior Aging in World Class Ocotgenarian Athletes is Characterized by Neuroprotection and Higher Serum BDNF.*

LIST OF PRESENTATIONS

1) **Taran, S.,** Filion, M-E., Spendiff, S., MacMillan, N., Sabiston, C.M., Hepple, R.T., and Taivassalo, T. (2014). *Positive Association Between Cognitive Function and Indices of Physical Fitness in the Very Old: Lessons from the Masters Athletes.* Poster presentation at the Inaugural PERFORM Centre Research Conference, Montreal, Quebec. Concordia University.

2) **Taran, S.,** Filion, M-E., Konokhova, Y., Spendiff, S., MacMillan, N., Sabiston, C.M., Hepple, R.T., and Taivassalo, T. (2014). *Positive Association Between Cognitive Function and Indices of Fitness in the Very Old: Lessons from the Elite Masters Athletes.* Poster presentation at the International Conference on Frailty and Sarcopenia Research, Barcelona, Spain.

3) **Taran, S.,** Taivassalo, T., Sabiston, C.M. (2013). *The Neuroprotective Effects of Long-Term Exercise Training in Older Adults: A Look at World-Ranking Elite Masters Athletes.* Oral presentation at the annual meeting of the Canadian Society for Psychomotor Learning and Sport Psychology Conference, Kelowna, British Columbia.

4) **Taran, S.,** Taivassalo, T., Sabiston, C.M. (2013). *Long-Term Exercise Contributions to Healthy Brain Aging: Insights From Elite Masters Athletes Aged 75 Years and Older*. Oral presentation at the Eastern Canada Sport and Exercise Psychology Symposium, St. Catharines, Ontario. Brock University.

5) Brunet, J., **Taran, S**., & Sabiston, C.M. (2013). *Weight Fluctuation During Adulthood Can Be Detrimental to Breast Cancer Survivors' Psychological Well-Being*. Poster presentation at Society of Behavioural Medicine, San Francisco, California.

6) **Taran, S**., Sabiston, C.M. (2012). *Body-Related Emotions and Depression in Breast Cancer Survivors: Does Being Inactive or Overweight Matter?* Oral presentation at the annual meeting of the Canadian Society for Psychomotor Learning and Sport Psychology Conference, Halifax, Nova Scotia. Dalhousie University.

7) **Taran, S.,** Cousin, J., Carver, T., Andersen, R., Musci, I., Ferland, D., Baran, D., Cantarovitch, M., Jensen, D., & Taivassalo, T. (2012). *The Feasibility and Efficacy of Continuous Exercise Training in Kidney Transplant Recipients*. Poster presentation at the McGill Undergraduate Research Conference, Montreal, Quebec. McGill University.

8) **Taran, S.,** Sabiston, C.M. (2012). *Weight Fluctuation and Exercise Motivation in Breast Cancer Survivors.* Oral presentation at the 16th Annual Eastern Canada Sport and Exercise Psychology Symposium, London, ON. Western University.

9) Brunet, J., **Taran, S.,** Sabiston, C.M. (2011). *A Qualitative Analysis of Motives, Barriers and Enablers to Engaging in Physical Activity.* Poster presentation at the annual meeting of the Canadian Society for Psychomotor Learning and Sport Psychology, Winnipeg, Manitoba.

APPENDIX III: SUPLPEMENTAL DATA

Table 3. Physical Activity and Physical Fitness in NAC, MA and Total Sample

Variable	NAC	MA	Total Sample
Daily steps	2731 ± 984	8341 ± 3573*	6045 ± 3954
Daily MVPA (min)	6 ± 3	38 ± 22*	25 ± 23
VO_2max ($ml \cdot kg^{-1} \square min^{-1}$)	19 ± 3	34 ± 9*	27 ± 10
Quadriceps strength (Nm)	119 ± 35	167 ± 59*	144 ± 54
Chair stands (sec)	25 ± 8	14 ± 3*	20 ± 8

Data are presented as means ± SD. MVPA: moderate-to-vigorous physical activity. VO_2max: Maximal oxygen consumption. Chair stands: Time in seconds to do 10 chair stands. *Significant difference between NAC and MA groups, $p < .05$.

Table 4. Cognitive Function in NAC, MA and Total Sample

Test	NAC	MA	Total Sample
MMSE	15 ± 2	18 ± 1*	17 ± 2
TMT-A	38 ± 13	33 ± 10*	38 ± 11
TMT-B	89 ± 22	76 ± 29	82 ± 26
Digit Span	5 ± 1	5 ± 2	5 ± 1
VF - Semantic	15 ± 4	17 ± 5	16 ± 4

VF - Phonemic	11 ± 5	15 ± 11	13 ± 5
RAVLT - LOT	9 ± 9*	17 ± 5	13 ± 8

Data are presented as means ± SD. MMSE: Mini Mental State Exam. TMT-A: Trail Making Test Part A. TMT-B: Trail Making Test Part B. VF: Verbal Fluency. RAVLT-LOT: Rey Auditory Verbal Learning Test – Learning Over Trials.

*Significant difference between NAC and MA groups, $p < .05$.