Winter 1-2019

Impact of Gender on Acute Aerobic Exercise Induced Brainderived Neurotrophic Factor And Cognitive Function In Older Adults

Madison Leigh Phillips
Cleveland State University

IMPACT OF GENDER ON ACUTE AEROBIC EXERCISE INDUCED BRAIN-DERIVED NEUROTROPHIC FACTOR AND COGNITIVE FUNCTION IN OLDER ADULTS

MADISON LEIGH PHILLIPS

Bachelor of Arts in Exercise Science

Baldwin Wallace University

May 2018

submitted in partial fulfillment of requirements for the degree

MASTER OF EDUCATION IN EXERCISE SCIENCE

at the

CLEVELAND STATE UNIVERSITY

December 2019

We hereby approve this thesis for

MADISON LEIGH PHILLIPS

Candidate for the Master of Education in Exercise Science degree

For the Department of Health and Human Performance and

CLEVELAND STATE UNIVERSITY'S

College of Graduate Studies by

_____

Thesis Chairperson, Dr. Emily Kullman

_____

Department & Date

_____

Thesis Committee Member, Dr. Kenneth Sparks

_____

Department & Date

_____

Thesis Committee Member, Dr. Douglas Wajda

_____

Department & Date

_____

Associate Dean for Academic Programs, Dr. Brian Yusko

_____

Department & Date

Date of Defense: November 27, 2019

AKNOWLEDGEMENT

I would like to thank each of my Thesis Committee Members: Dr. Emily Kullman, Dr. Kenneth Sparks, and Dr. Douglas Wajda for guiding me through my research study. I would like to exceptionally thank Dr. Emily Kullman for her continuous support, motivation, and enthusiasm while completing my master's study and research. With her patience and knowledge, this thesis became possible.

As well, I would like to thank Dr. Kathleen Little for her direction in the creation, language, and dialogue of my research paper.

I also would like to thank all eighteen of my subjects for their dedication and volunteerism to be a part of my study. I enjoyed working with each of you and hearing all of your unique stories about your lives, work, and physical activity journeys.

Lastly, but certainly not the least, I would like to acknowledge my family and friends. Thank you for continuously encouraging me throughout my time of research and reminding me that I can do this. You are who inspired me every day to push forward, thank you.

IMPACT OF GENDER ON ACUTE AEROBIC EXERCISE INDUCED BRAIN-DERIVED NEUROTROPHIC FACTOR AND COGNITIVE FUNCTION IN OLDER ADULTS

MADISON LEIGH PHILLIPS

ABSTRACT

Purpose: The purpose of this study was to examine the impact of gender on acute exercise induced BDNF and cognitive function among older individuals. The hypothesis was that exercise would increase BDNF levels and enhance cognitive processing time post exercise followed by a drop in BDNF and return cognitive processing time to baseline post-30 minutes. It was also hypothesized that women would have higher BDNF values compared to men.

Methods: The subjects consisted of 18 active males (n = 9) and females (n = 9). The subjects took part in an exercise trial and a control trial. The exercise trial entailed riding either a recumbent or upright bike at 75% of their age predicted max heart rate for 30 minutes. The control trial consisted of reading. A Stroop Test was given, and blood samples were obtained before, after, and 30 minutes after exercise and control. Serum was analyzed for BDNF, testosterone, and estrogen using commercially available ELISA kits.

Results: Results showed that there was a significant effect of time in Stroop testing across all subjects. There was a trend ($p = 0.068$) for a decrease in Stroop time from pre to immediate-post timepoints, and a significant decrease ($p = 0.004$) in Stroop time from pre to post-30 timepoints. There was a significant main effect of exercise on BDNF levels, ($p = 0.05$) and females were found to have significantly higher BDNF than males ($p = 0.055$).

Conclusion: There was statistical evidence that acute exercise affects BDNF production in both genders, but not cognitive processing speed among an older active population. Cognitive processing speed continued to improve across all timepoints. As well, women were found to have overall higher BDNF.

TABLE OF CONTENTS

Page

ABSTRACT.....iv

LIST OF TABLES.....vi

LIST OF FIGURES.....vii

CHAPTERS

I. INTRODUCTION.....1

II. LITERATURE REVIEW.....5

III. METHODS.....26

IV. RESULTS AND DISCUSSION.....32

V. SUMMARY AND CONCLUSION.....43

REFERENCES.....46

APPENDIX

A. INFORMED CONSENT.....51

B. AHA/ACSM PRESCREENING QUESTIONNAIRE.....54

C. TICS-M QUESTIONNAIRE.....55

D. RECRUITMENT FLYER.....56

E. STROOP TEST.....57

F. INSTITUTIONAL REVIEW BOARD APPROVAL LETTER.....58

LIST OF TABLES

Table Page

1. Subject Characteristics, Mean ± Standard Deviation.....33

LIST OF FIGURES

Figures Page

1. The incongruent Stroop Test results from both exercise and control trials (pre, post, and post30)....34
2. The effects of acute aerobic (75% of MHR) and control on BDNF levels (1 -pre, 2 - post, 3 - post30). * = ($p < 0.5$) Exercise trial (1 - blue) versus control trial (2 - red)....35
3. Average BDNF levels across all timepoints (pre, post, post30) for exercise and control trials for both groups (males; females)....36
4. Age versus Stroop time pre-exercise....37
5. Age versus Stroop time post exercise....38
6. Age versus Stroop time post-30 exercise....38

CHAPTER I

INTRODUCTION

Brain-derived neurotrophic factor (BDNF) is a naturally created neurotrophin that is distributed throughout many areas of the brain, specifically in the hippocampus which is where high levels of BDNF are found (Adlard, Perreau, Engessar-Cesar, & Cotman, 2004). It has been found in research that within the hippocampus there is an association with learning, memory processes, and neural plasticity (Adlard et al., 2004). BDNF provides support to different subpopulations of neurons in both nuerotrophic and neuroprotective manners during the development of those neurons across the lifespan (Adlard et al., 2004). BDNF levels that are deemed low have been linked to many different types of neuropsychiatric disorders including depression, bipolar disorder, schizophrenia, and neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease (Begliuomini et al., 2007; Ventriglia et al., 2013). In contrast, it has been previously reported that exercise significantly increases the amount of BDNF produced within the brain, in result aiding in cognitive function (Piepmeier & Etnier, 2015).

BDNF is present within the brain as early as fetal life; at birth BDNF intensifies to a maximal level allowing for neuronal outgrowth and differentiation in neonates

(Begliuomini et al., 2007). With aging, the amount of BDNF produced slowly becomes less over time. BDNF is released in both genders, however specific sex hormones released by males and females have an impact on the amount of BDNF produced. Fertile women show significantly higher plasma BDNF levels compared to that of BDNF plasma levels of postmenopausal women, while amenorrhoeic women have the lowest BDNF plasma levels (Begliuomini et al., 2007). There are fewer studies on how sex hormones affect BDNF production in men; however, it has been reported that testosterone, a key factor of androgens, has an encouraging impact on BDNF expression or reproduction (Carbone & Honda, 2012). Both genders are said to experience the same age-related decline of BDNF (Boudewijn et al., 2011).

The tie between sex hormones and that of BDNF production is repetitively found across all forms of research. In this research there is a common link and influence that are further determined by the specific physiological and pathological characteristics of the human subject. Like that of BDNF plasma decreasing with increasing age and weight in both genders suggesting that gender has no effect on BDNF production when individuals are the same age and same weight (Lommatzsch, Zingler, Schuhbaeck, Schloetcke, Zingler, Schuff-Werner, and Virchow 2005). However, these facts should not defer the interest from the knowledge that overall BDNF levels of men versus women are different, women have higher BDNF plasma levels than men overall. This supports the idea that gender, age, weight, and other physiological characteristics do in fact determine the BDNF production of individuals resulting in some having increased interest as to how this can be affected with acute bouts of exercise (Lommatzch et al., 2005).

In reviewing literature, it is evident that there is a surplus of research studies designed to advance knowledge on how exercise, specifically acute bouts of exercise, may affect cognitive performance. Many studies have evaluated specifically cognitive performance while performing acute exercise through the use of rodents. Mu et al. (1999) administered neural injections of BDNF into rats, essentially depriving the rats of their natural secretion of BDNF, in order to prove that BDNF is imperative in aiding in cognitive function and memory. While other studies have assessed BDNF production post-exercise and cognitive performance through human subjects. Wiet (2018) assessed premenopausal and postmenopausal women's aerobic exercised induced BDNF and cognitive production via treadmill running through the Stroop test finding that premenopausal women had a rise in BDNF levels after exercise and postmenopausal women had a decrease in BDNF levels after exercise (Wiet, 2018). The peripheral readings of BDNF levels are conducted as a surrogate indicator due to central BDNF in the hippocampus is not able to ethically be measured. The line of research continues to be active due to all the positive influences BDNF is said to have, in addition to appetite control, regulation of heart rate, and increase insulin sensitivity, on the human brain across all ages and genders (Marosi & Mattson, 2014).

Purpose of the Study

The purpose of this study was to examine the impact of gender on acute aerobic exercise induced BDNF and cognitive function among older individuals.

Hypothesis

The hypothesis of the current study was that acute aerobic exercise would increase BDNF levels and enhance cognitive processing time post exercise followed by

a drop in BDNF and a return of cognitive processing time to baseline post-30 minutes. It was also hypothesized that women would have higher BDNF values compared to men. As for during the control trial, it was hypothesized that the BDNF levels and cognitive processing time would remain constant at each time point of measurement for both genders.

CHAPTER II

LITERATURE REVIEW

Brain Derived Neurotrophic Factor (BDNF)

BDNF is a neurotrophin that is expressed within the central and peripheral nervous system, specifically within the hippocampus, cerebral cortex, and amygdala (Begliuomini et al., 2007). BDNF is a protein that is crucial to the development, maintenance, and plasticity of the central and peripheral nervous systems and plays a key role in learning, memory, and behavior. BDNF provides support to different subpopulations of neurons in both a neurotrophic and neuroprotective manner during their development across the lifespan (Adlard et al., 2004). BDNF is neurotrophic when there are low circulating levels causing neuropsychiatric disorders like that of depression, bipolar disorder, schizophrenia, and neurodegenerative diseases such of that as Alzheimer's disease and Parkinson's disease (Begliuomini et al., 2007). BDNF is also neuroprotective in higher amounts within the brain, which can be boosted prominently by physical activity as well as proper nutrition, sunlight, and living a healthy lifestyle (Begliuomini et al., 2007).

BDNF is existent in large quantities within blood platelets, despite the name "brain-derived," and is also synthesized within the human body's epithelial and vascular

cells, muscle cells, macrophages, and leucocytes (Boudewijn et al., 2011). Research is not clear about bidirectional transit of BDNF across the blood-brain barrier. Regardless, plasma levels of BDNF have been shown to be similar to brain levels. This is supported by recent studies revealing that abnormal levels of BDNF are associated with several mental disorders and appears to be a biochemical marker of such mental disorders (Boudewijn et al., 2011). This has led researchers to utilize plasma BDNF as a biochemical marker for Parkinson's disease and Alzheimer disease. However, the BDNF biochemical markers in patients with neurodegenerative diseases can be due to limited medications effects (Boudewijn et al., 2011).

BDNF initially is synthesized as a precursor protein called pre-proBDNF within the cell's endoplasmic reticulum that is eventually transformed into proBDNF and further processed into mature mBDNF (Marosi et al., 2014). ProBDNF as well is released by neurons, which is altered by the tissue plasminogen activator (tPA) plasmin system to mBDNF (Marosi et al., 2014). The expression and distribution of BDNF is stimulated by excitatory synaptic activity and specific neuropeptides and hormones (Marosi et al., 2014). Glutamate released from the exact same excitatory synapses binds to the receptors on the synaptic membrane, causing an influx of Na^+ and Ca^{2+} through various receptors. Ca^{2+} activates Ca^{2+}-calmodulin-dependent protein kinase (CaMK), protein kinase C (PKC), and mitogen-activated protein kinases (MAPKs) which in result activates the transcription factors cAMP response element-binding protein (CREB) and nuclear factor kB (NF-kB) to prompt BDNF gene transcription (Marosi et al., 2014). BDNF is specifically concentrated in vesicles that are transported into axons, presynaptic terminals, and dendrites from which it is released in response to the glutamate receptor

activation (Marosi et al., 2014). As well derived from dendrites is that of BDNF mRNA, the protein translation can be stimulated by synaptic activity. Local BNDF production and release activates its high-affinity receptor tropomyosin-related kinase B (TrkB) or the low-affinity p75 neurotrophin receptor on synaptic partner neurons and other cells in its immediate vicinity. TRkB is a receptor tyrosine kinase that when activated engages with a number of receptors leading to activation of transcription factors that regulate expression of proteins involved in neural plasticity, stress resistance, neurotransmitter and neuropeptide production and excitability, and cell survival (Bathina and Sas, 2014; Begliuomini et al., 2007; Marosi et al., 2014).

Estrogen, Androgen, and BDNF

Both genders produce and release BNDF within the brain with levels measured in blood plasma. However, recent studies have shown that the specific sex hormones released by males and females impact the amount of BDNF produced. BDNF is present in the follicular fluid, both in women who are cycling normal and in the women undergoing ovulation induction for IVF (Seifer, Feng, Shelden, Chen, Dreyfus, 2002; Seifer, Lambert-Messerlian, Schneyer, 2003). Additionally, BDNF levels in follicular fluid have been shown to be upregulating by gonadotrophin stimulation, since levels of BDNF were 27 times higher in follicular fluid of women going through ovulation induction compared to that of normal cycling women (Seifer et al., 2002). This information along with much more gave reason enough for research on how hormones affect humans BDNF levels, consequently leading Begliuomini et al. to assess BDNF plasma concentrations in female subjects specific to their hormonal status.

Begliuomini et al. (2007) evaluated 60 female subjects for 28 + 2 days to allow the fertile women to go through a full menstrual cycle (Begliuomini et al., 2007). The women were split into three groups, 20 fertile women aged 20-40 years with a BMI between 20-23; 15 amenorrhoeic women, for a minimum of six months, aged 21-42 years with a BMI of 18.5-24; and 25 postmenopausal women aged 48-70 years with a BMI of 21-25 (Begliuomini et al., 2007). Overnight fasting took place and a blood draw from the cubital vein from each subject took place between 7:00 am and 9:30 am to avoid possible circadian variation of blood plasma BDNF concentrations. Five of the 20 ovulatory women were tested every two days, in other normal menstruating women blood was drawn during the follicular phase (days 6-8) and luteal phase (days 20-24), amenorrhoeic women had blood draw every ten days for a total of three times, and after the initial blood drawn ten of the postmenopausal women started on HRT of estradiol valerate and underwent blood draws after six months of treatment (Begliuomini et al., 2007). Blood plasma levels of BDNF were determined with the ELISA method after appropriate dilutions of samples. It was found that fertile women show significantly higher plasma BDNF levels during the luteal phase compared to that of the follicular phase, almost three times as much (Begliuomini et al., 2007). BDNF levels were lowest in the early follicular phase (Days 1-8: from 292.9 pg/mL + 77.4 pg/mL on Day 2 to 541.8 pg/mL + 113.7 pg/mL on Day 8), then increased significantly from Day 10 of the menstrual cycle, and then reached a peak value on Day 14; after ovulation (Days 16-18), BDNF levels decreased and increased again in the mid-luteal phase (Days 20-24), reaching a second peak on Day 24 (1186.4 pg/mL + 190.6 pg/mL); finally a marked fall in BDNF at the end of the cycle on Day 28 expressed values similar to that seen in the early follicular phase

(Begliuomini et al., 2007). Amenorrhoeic women showed the lowest BDNF plasma levels (150.7 pg/mL + 80.7 pg/mL) in comparison to the rest of the subjects (Begliuomini et al., 2007). Lastly, BDNF plasma levels of postmenopausal women were lower in comparison to follicular phase levels of menstruating women (280.6 pg/mL + 116 pg/mL) (Begliuomini et al., 2007). For women who took part in six months of HRT for menopause, BDNF plasma levels returned to that of almost the same as fertile women in the follicular phase. There is also an age-related decrease of BDNF in women, with aged women showing the lowest concentrations (Begliuomini et al., 2007). Concluding, that there is an influence of hormonal status on that of plasma BDNF. Begliuomini et al. (2007) suggest that modifications in BDNF circulating levels during menstruation suggest a potential role by gonadal sex hormones and progesterone in the expression of the nuerotrophin.

When compared with estrogen, fewer studies have been conducted on men and how androgen has an effect on BDNF expression. However, it is suggested that men have the same age-related decline as that of women (Boudewijn et al., 2011). It is reported that females and males do not have a significant difference in the amount of hippocampal BDNF, conversely females do tend to have more BDNF within the prefrontal cortex though (Wei, Y., Wang, S., & Xu, X., 2016). As well, several studies have reported that testosterone, a major component of androgens, is a positive regulator of BDNF expression or reproduction (Carbone et al., 2012), concluding that there is a link between BDNF and sex hormones. However, this link and its potency are further determined by the specific physiological and pathological characteristics of the human,

like that of his or her body weight and composition, hormonal status, and enzyme activities (Carbone et al., 2012).

Those pathological characteristics like body weight and hormonal status in addition to age and gender and how they related to BDNF production are further discussed by Lommatzsch et al. (2005). Lommatszch et al. (2005) examined 140 healthy (72 men, 68 women), adults aging 20-60 years old to discover the impact of age and physical parameters on BDNF levels in human platelets and plasma. Blood was taken between 7 and 10 am to minimize the effects of a possible circadian rhythm of BDNF concentrations (Lommatszch et al., 2005). Total and differential blood cell counts were analyzed by standard hematological procedures and a dedicated analyzer and BDNF and TGF-B1 levels in both serum and plasma were analyzed via ELISA, in addition serotonin, immunoglobulin E (IgE), triglycerides and cholesterol were all measured. Results found that there was a negative correlation between plasma BDNF levels and age. When the data was divided into three groups according to age, those being group A: 20-33 years old, group B: 34-47 years old, and group C: 48-60 years old, there was no significant difference in weight, height or gender between the groups (Lommatszch et al., 2005). With age, it was found that there were decreasing variance of plasma BDNF levels over time. There was a negative correlation between plasma BDNF levels and body weight and there was no significant correlation between weight and platelet BDNF. When evaluating both genders, women had significantly higher BDNF levels in plasma then men. However, women had significantly lower body weight than men (69.3 ± 15.6 kg versus 84.8 ± 11.5 kg respectively) (Lommatszch et al., 2005). When men and women were grouped together based on weight there was no significance in BDNF

plasma levels between women and men. In regards to menstruation, there was no difference between women in the first half of the menstrual cycle and women in the second half of the menstrual cycle (105.5 pg/mL versus 159.3 pg/mL respectively), while there was a significant difference in women that were postmenopausal (60.8 pg/mL) which researchers attributed to greater age and weight (36.0 years versus 37.0 years versus 51.5 years; 68.0 kg versus 61.0 kg versus 69.5 kg respectively)(Lommatszch et al., 2005). To conclude, the data discovered suggests that parameters such as age, weight or gender have specific impacts on stored platelets and circulating plasma levels of BDNF in healthy adults (Lommatszch et al., 2005).

Aging and BDNF

It is well known that with aging there is a decline in cognition function (Rasmussen et al., 2006). However, this decline is not all due to aging. There are other associated factors that may speed up the rate of decline including poor quality of life, decreased social function, and hospitalization (Rassmussen et al., 2006). The hippocampus of the brain is strongly associated with cognitive function, and with it being an important area of the brain the hippocampal volume shrinkage is of concern for those in late adulthood. Specifically, research of what neuromuscular factors trigger the decay in aging humans is attractive due to delaying these factors.

Erickson et al. (2010) performed a cross-sectional study utilizing MRI, enzyme-linked immunosorbent assays (ELISAs), and measures of spatial memory to assess age related decreases in brain volume, plasma BDNF, and memory in older adults. A total of 142 participants between 59 and 81 years of age (mean: 66.5 years, 76% female) were studied upon passing screening for dementia and met criteria for participating in MRI

(Erickson et al., 2010). Erickson utilized MRI in order to look at intracranial volume, looking specifically at the sum of gray, white, and cerebrospinal fluid to compare later to cognition in relation to BDNF levels (Erickson et al., 2010). To test whether BDNF and hippocampal volume would be related to age-related changes in the function of memory, all 142 participants completed a spatial learning computerized task one week prior to the MRI session. The computerized spatial task, performed a total of 40 times, involved following a set of dots for 500 milliseconds that subsequently disappear for 3 seconds (Erickson et al., 2010). During this time the subject is asked to remember the location of the dots, and upon reappearance of the dots they have to acknowledge within 2 seconds if they are in the same spot or have moved (Erickson et al., 2010). Blood sampling as well was collected approximately two-weeks prior to the MRI session. Fasted subjects arrived to the lab to have blood drawn from the antecubital vein and the samples were kept at room temperature for 15 minutes to allow clotting (Erickson et al., 2010). Serum BDNF was quantified using the ELISA. Erickson et al. (2010) found that older adults had significantly lower concentrations of plasma BDNF, small hippocampal volumes, and poorer performance in accuracy and response time on spatial memory tasks compared to that of younger subjects. It was also discovered that regardless of age, if the subject had a smaller hippocampus there was worse memory associated with it, suggesting that levels of BDNF decline with advancing age is to be true, and that a genetic polymorphism of BDNF is related to gray matter volume loss in old age (Erickson et al., 2010). Thus, suggesting that interventions to elevate BDNF might help reduce age-related volume loss in the hippocampus.

Exercise and BDNF Expression

There is a large body of literature supporting the relationship between acute exercise and plasma BDNF (Piepmeier et al., 2015). Research has identified BDNF as playing an instrumental role in the form and function of the brain and is vital for cognitive performance in short term adaptations as well as long term via neural plasticity (Piepmeier et al., 2015). Numerous studies have evaluated acute exercise in relation to BDNF production and cognitive function, with a variety of different exercise protocols and modalities studied (Piepmeier et al., 2015). Since there is a high amount of BDNF located within the hippocampus of the brain, and this part of the brain is widely accepted as being fundamental to memory performance, it appears important to assess cognition in relation to BDNF expression.

Mu, Li, Yao, and Zhou (1999) administered neural injections of BDNF into rats, which essentially deprived the rats of their natural secretion of BDNF. The rats were divided into two groups randomly, BDNF antibody-treated (anti-BDNF, n = 7) and normal sheep immunoglobulin G (IgG) treated control (control, n = 6) (Mu et al., 1999). An osmotic pump containing either the BDNF antibody or normal sheep IgG was placed in the neck subcutaneously. The BDNF antibody was created by vaccination of sheep with recombinant human BDNF (Mu et al., 1999). The rats were placed inside of the Morris water maze to test spatial learning and memory, wherein the swimming pool consisted of a circular tank of 130 cm in diameter and 50 cm in height with an escape platform placed 1 cm beneath the water's surface and 32 cm from the pool's wall (Mu et al., 2012). The surface of the water was covered with 1 cm diameter Styrofoam beads to eliminate view of the escape platform. The rats went through one week of

intraventricular infusion of either the antibody BDNF or control IgG and were subjected to four consecutive trials per block, with two blocks per day for a total of 4.5 days was performed (Mu et al., 2012). The rats were placed in the pool in 4 different locations to find the escape platform in 120 seconds, if not found the trial was terminated and an escape latency was recorded (Mu at al., 2012). The rats were placed in the pool one last time on the last day where the platform was removed and they swam for 2 minutes while the swim distance in each quadrant was calculated for a total distance measurement (Mu et al., 2012). Results showed that the rodents deprived of BDNF experienced declines in cognitive performance being they took more time to find the escape platform compared to that of the controls (74.86 ± 9.80 s, 46.50 ± 4.23 s respectively), thus showing that BDNF is critical for cognitive performance (Mu et al., 1999). The escape latency in control rats dramatically reduced in time in the subsequent trials, reaching a plateau of 11.00 ± 2.53 s, while the antibody-treated rats' average escape latency was much longer than those in the control group (Mu et al., 2012). The results of swimming speed between the control and anti-BDNF-treated groups showed no significant difference (11.9 ± 0.75 cm/s vs 12.1 ± 0.86 cm/s) (Mu et al., 2012). It was concluded that BDNF plays a role in spatial learning and memory, specifically that of short-term.

Schmolesky, Webb, and Hansen (2013) observed the combined effects of aerobic exercise intensity and duration on serum BDNF levels in healthy men ages 18-25 years old. The study was limited to only males due to reducing variability in BDNF levels that vary across gender and vary with menstrual cycle status in females (Begliuomini et al., 2007). Subjects self-reported their average weekly exercise patterns the past week, per a typical week, and over the past six months in specific sports or physical routines

(Schmolesky et al., 2013). The 45 subjects were then randomly assigned to one of six exercise conditions based on exercise intensity, those included vigorous, moderate, or sedentary, and duration, 20 or 40 minutes, using quota sampling (Schmolesky et al., 2013). The subjects were asked to exercise at the proper duration and intensity assigned to them. Vigorous activity (80% of HRR) and moderate activity (60% of HRR) were carried out on the cycle ergometer (Schmolesky et al., 2013). Heart rate was measured once every minute in order to verify compliance with the program. Antecubital vein blood draws (5 ml) were performed 5 minutes pre-exercise and 2 minutes post-exercise for those exercising and the same blood draws at the same timed points were done on the control subjects who were sedentary watching other subjects exercise for 20 and 40 minutes (Schmolesky et al., 2013). The blood clotted for one hour and then was centrifuged for 10 minutes and analysis was later done via the ELISA (Schmolesky et al., 2013). Results showed that under the conditions set, neither factors of intensity or duration influenced the degree of BDNF increases (pre vs post) that resulted from exercise (Schmolesky et al., 2013). The average pre-post percentage in serum BDNF levels was found to be 25-30% in three of the exercise conditions (Vig20 = 26.38 ± 34.89%, Vig40 = 28.48 ± 19.11%, Mod40 = 30.16 ± 72.11%) and was higher numerically in the fourth condition (Mod20 = 41.23 ± 59.65%) (Schmolesky et al., 2013). Interestingly, the average sum percentage of serum BDNF decreased in both control conditions (Con20 = -14.48 ± 16.50, Con40 = -10.51 ± 26.78) while there was no significant differences between the average sum percentage of serum BDNF values in the two control groups ($t(8) = 0.173$)(Schmolesky et al., 2013). Concluding, that under the conditions set that neither factors of intensity nor duration influenced the degree of

BDNF increase that resulted from exercise (Schmolesky et al., 2013). However, these factors did more than likely play a role in both the probability of a subject achieving a significant BDNF increase and in the volume of circulating BDNF being produced (Schmolesky et al., 2013).

Similar to that of Mu, a study put forward by Adlard (2004) examined the timecourse of induction of BDNF mRNA and protein after 1, 3, 5, 7 ,14 and 28 days of exercise in male rats. Female rats were not used in order to avoid the perplexing effect of cycling hormones. The rats were individually housed in cages with access to food and water ad libitum in a 12-hour dark and 12-hour light varium (Adlard et al., 2004). A subset of rats were set up in cages with a running wheel for either 1, 3, 5, 7, 14, or 28 days (n = 6 rats at each time point) (Adlard et al., 2004). Observation of the number of wheel revolutions was recorded continuously via a computer software attached to each running wheel. Sedentary control rats (n = 12) had been housed for the same amount of time in the same cages as the active wheel running rats. Another subset of rats performed water maze exercise (n = 7 per group), they were exercised 3 weeks prior to and during testing (Adlard et al., 2004). Another sedentary group was tested concurrently (n = 8 per group). The protocol for these rats consisted of two trials per day for six consecutive days, an overhead CCD camera attached to a VCR videotaped all activity. BDNF, in addition to mRNA, was found via micro-dissection of the rats' hemispheres of their brains (Adlard et al., 2004). Results found that the induction of BDNF over the timecourse showed an overall main effect (Adlard et al., 2004). The group of rats given 28 days on the running wheel had a significant upregulation in BDNF compared to that of the sedentary group (271% increase), and this same 28-day rat group had significantly

higher BDNF levels compared to all other timepoints (trend seen at 14 days = 166% compared to sedentary) (Adlard et al., 2004). The exercised rats involved in the water maze trials showed a decreased escape latency compared to that of sedentary rats, there was a significant difference shown after 2 days and from day to day (Adlard et al., 2004). In conclusion, showing that exercise training modulates the induction of BDNF mRNA and protein in a time-depending manner within the hippocampus of the brain at a peak of 28 days, it is suggested that this may contribute to the maintenance of brain health and plasticity (Adlard et al., 2004).

Exercise, Cognition and BDNF

Like that of studies looking specifically at the effects of exercise on BDNF, there are numerous studies that have looked at these two factors and the effects they both have on cognition. The reason researchers believe there is a trend connecting BDNF to improved cognition is that BDNF is thought to play a key role in the health of the central nervous system impacting neuronal survival, growth, and maintenance (Cotman & Engesser-Cesar, 2002), and has been proven to have an interaction in the consolidation in nonhuman animal studies (Mu et al., 1999) and in human studies (Egan et al., 2003) after as little as just one bout of exercise.

Etnier et al. (2016) performed a study to extend previous research and explore dose-response relationships between exercise intensity and memory by testing associations with exercise-induced changes in BDNF. Sixteen young (M = 23.06 years) adult men (n = 9) and women (n = 7) had their learning, episodic memory, short-term memory, and long-term memory assessed via the Rey Auditory Learning Test (RAVLT)(Etnier et al., 2016). Participants were read a primary word list (List A)

consisting of 15 words and were asked to recall as many words as possible in no particular order indicating their short-term memory capability (Etnier et al., 2016). List A was repeated another four times and the participants were asked to recall the words following each trial, the change in performance across those five trials was indicative of their learning (Etnier et al., 2016). After the fifth trial, participants heard a new list of 15 words (List B) and were asked to recall those words (Etnier et al., 2016). Then, without hearing the list again, the participants were asked to recall as many words as they could from List A. Participants were then asked to again recall as many words as possible from List A 30-min later (Etnier et al., 2016). Then the next day participants were contacted via phone to complete a 24-hour recall test where a combination of List A, List B, and 20 distracting words were said and the participants had to identify which group the words belonged providing additional measures of long-term memory (Etnier et al., 2016). Prior to the RAVLT trials 1-7 testing, participants performed a VO_2 max test for session 1 and submaximally exercised for 30 minutes on a treadmill for sessions 2 and 3. Blood samples were taken pre-exercise, post-exercise, and post-memory test to assess BDNF and estradiol in women. BDNF data expressed there was a significant effect for time while exercise intensity and exercise intensity x Time were not significant (Etnier et al., 2016). BDNF serum increased significantly from baseline (M = 15,438.3 ± 1,577.1 pg/mL) to post-exercise (M = 21,502.93, SE = 2,117.42) and then decreased significantly by 30-minutes post-exercise (M = 17,010.20, SE = 1,074.24) (Etnier et al., 2016). Results for short-term memory and long-term memory indicated that there was not a significant difference due to exercise intensity, however there was a nearly significant difference in performance as function of exercise intensity and a significant difference as

function of trials (Etnier et al., 2016). Performance on the memory task increased significantly from Trial 1 (M = 6.74, SE = 0.29) to Trial 2 (M = 9.36, SE = 0.41) and then plateaued expressing no significant difference from Trial 3 to Trial 4 (M = 11.83, SE = 0.28) and Trial 4 from Trial 5 (M = 12.48, SE = 0.38)(Etnier et al., 2016). The overall interaction of exercise intensity x Trial was not significant. Concluding, results of this study support that there is a threshold effect of exercise intensity, higher intensity exercise resulting in significantly better effects than lower intensity exercise, on learning and long-term memory (Etnier et al., 2016).

Similarly, Damirchi, Hosseini, and Babaei (2017) were also interested in how exercise affects BDNF and cognition, and these researchers even looked to see if mental training had an effect as well. The goal of this study was to evaluate the effect of the combination of physical and mental training on cognitive performance, serum BDNF, and irisin level in patients with mild cognitive impairment (MCI)(Damirchi et al., 2017). Of the 101 elderly women who volunteered from Yas adult center, a nonresidential female adult daycare center in Aliabad-e Katul, Golestan Province, Iran, 54 sedentary women were randomized into four groups: physical training (PH; n = 15), mental training (ME; n = 15), PH + ME (n = 15), and control group (CO; n = 9)(Damirchi et al., 2017). Of those 54 elderly women, 44 completed the protocol accurately over the 8-week study. Four cognitive assessments were performed: working memory, processing speed, reaction time, and error number of the computer modified Stroop color-word test. All cognitive measurements were carried out two days prior to and post intervention and 6 months after the last training for testing the maintenance of behavior. Serum BDNF and irisin were measured before and after the ending experiments, a total of two times. Those

participants in the mental training group started exercising with a special program entitled "Modified My Better Mind" partaking in games that worked on visual attention, visual and verbal memory, speed of processing, reasoning and more under the supervision of a physiotherapist for 30 minutes weeks 1 through 6 and for 60 minutes in weeks 7 and 8 (Damirchi et al., 2017). The physical training was 3 days per week and consisted of two sections: 5-minute warm-up followed by 6-minute walking with 55% of heart rate reserve and slowly reaching up 20 minutes with 75% of heart rate reserve by the eighth week; and muscular strength, range of movement (MSROM) Silver Sneakers who partook in group fitness following a similar 5-minute stretching protocol, muscular range of motion exercises coupled with light cardio for 25 minutes total (Damirchi et al., 2017). Those participants within the combined training group participated in both physical and mental training, performing the cognitive training prior to the exercise training (Damirchi et al., 2017). What was discovered was that there was a significant increase in working memory from pretest to post-training in ME and PH + ME (Damirchi et al., 2017). Changes in working memory were significantly higher in ME (21.64%) compared with PH (-0.20%) and CO (-1.16%)(Damirchi et al., 2017). Likewise, there were significant improvements in the post-training scores of processing speed and reaction time in only the ME group when compared with pretest values (Damirchi et al., 2017). Changes in processing speeds were significantly higher in ME (10.24%) compared to PH (-0.42%) and CO (-0.65%)(Damirchi et al., 2017). While improvements in working memory, processing speed, reaction time, and error number were preserved after 6 months of detraining in ME and working memory, the only improved index for PH + ME, decreased significantly after 6 months of detraining (Damirchi et al., 2017). All while BDNF

increased significantly in ME and PH + ME and reduced in PH (Damirchi et al., 2017). Being the physical activity group showed no significant change in cognitive function, BDNF, or irisin researchers attributed this to intensity of exercise which was lower than the intensities used in studies that had positive results. The group that combined physical activity and mental training showed significant changes in working memory and BDNF while the mental training group had improvements in cognitive performance that remained stable for 6 months. In conclusion, the mental training has beneficial effects in older adults and is a useful and safe strategy to prevent cognitive decline via BDNF elevation (Damirchi et al., 2017).

Heisz, Clark, Bonin, Paolucci, Michalski, Becker, and Fahnestock (2017) came together with a similar purpose like that of Damirchi et al. to examine the combined effects of exercise and cognitive training on memory and neurotrophic factors. However rather than utilizing elderly women, young adults were used. Being that exercise-induced brain plasticity may be dependent on the individual's fitness improvements from exercise training, it was hypothesized that individuals with greater fitness gains from exercise training would show greater increases in high-interferences memory and neurotrophic factors in comparison to individuals with lower fitness gains (Heisz et al., 2017). Ninety-five healthy young adults (58 women, 37 men, age = 21 ± 3 years, range = 17-30 years) partook in the present study and were assigned to three groups: control (n = 7), exercise training (n = 3), and combination exercise and cognitive training (n = 6) (Heisz et al., 2017). Exercise training consisted of 20-minutes of high intensity interval training (HIT) for a total of 6 weeks, 3 times a week (Heisz et al., 2017). Individualized exercise prescriptions based off of preliminary VO_2 max testing were utilized, participants

completed the HIT on stationary cycle ergometers. Combined exercise and cognitive training consisted of the same exercise training plus cognitive training completed on the same day at the same session. Cognitive training consisted of 20 minutes of training on a computerized version of the Concentration Memory Task for a total of 6 weeks, 3 days per week (Heisz et al., 2017). Participants began training at level 1 and that was increased periodically through training and were presented with different numbers of cards each session to remember, cognition training was done prior to exercise training (Heisz et al., 2017). The control participants did not perform either training protocols and were asked to remain sedentary for the whole 6 weeks. The experimental procedure included pre- and post-testing that was done over the span of two days: day 1 started with a 12-hour fasted blood draw, followed be a meal, and then cognitive testing and day 2 the participants completed aerobic fitness training, then pre- and post-testing sessions were separated into the 6-week intervention groups and post-testing was done within 48 hours after intervention completion (Heisz et al., 2017). Kirwan and Stark's mnemonic similarity task was utilized to assess memory function pre- and post-intervention (Heisz et al., 2017). Results showed that for high-interference memory task that there was a main effort of group, high-interference memory improved more for the exercise and the combined training groups than the control group. There were no group differences observed for BDNF levels or recognition memory scores. For recognition memory, a t-test revealed that untransformed pretest (95% CI (-18%, -13%) and posttest (95% CI (-18%, -14%) recognition scores were significantly lower than 100%, suggesting that the effect of group on recognition memory was not due to a ceiling effect (Heisz et al., 2017). Concluding that exercise training selectively enhanced performance on an untrained high-

interference memory task, serum BDNF and IGF-1 levels increased significantly in individuals who exhibited larger aerobic adaptation to exercise training suggesting that due to training level there are differences (Heisz et al., 2017). As well, those high responders to exercise who received cognitive training in addition to exercise training had better high-interference memory than those who exercised only. This suggests that the potential for synergistic effects of combination training may depend on the level of a person's training.

Kim, Lee, Lee, Cho, and Ko (2018) meets Damirchi et al. and Heisz et al. in the middle, and performed a study to evaluate the effects of a cognitive enhancement fitness program (CEFP) on short-term memory and serum BDNF levels according to cognition status in not young, not old, but middle aged women. A total of 30 healthy volunteers that are between the ages of 40-59 years old were divided into two groups: mild cognitive impairment (MCI) and non-MCI. To discover which group these women belonged, volunteers were screened based on the Korean Dementia Screening Questionnaire. A single session of CEFP was performed by each subject and lasted 50 minutes in duration, it consisted of four parts: warm-up, low intensity interval circulation dance exercises, moderate intensity resistance exercises, and a cool-down (Kim et al., 2018). Dance exercises consisted of bounce, side-to-side, twist, swan lake, lady's kick, jump, swerve and shuffle dances and the resistance exercise consisted of bicep curls, chest press, single arm press, lateral raise, overhead pull, good mornings, squat, kicks (Kim et al., 2018). Serum BDNF was taken one hour prior and post-exercise program and were evaluated via ELISA while short-term memory was determined by forward digit/word span test pre and post exercise (Kim et al., 2018). The test consisted of the examinee reading a

sequence of digits, then recalling the digits in the same forward sequence starting at level 1 and attempting all the way till level 10. Results found that after CEFP, forward digit/word span test scores and BDNF levels increased to 119.2%/115.1% and 118.7% respectively (Kim et al., 2018). After CEFP, the MCI and non-MCI groups produced higher forward digit span test scores (from 6.7 ± 1.5 to 7.5 ± 1.4 points and from 6.2 ± 2.0 to 7.0 ± 2.1 points respectively)(Kim et al., 2018). After CEFP, forward word span scores and BDNF levels increased (from 3.5 ± 1.7 to 4.6 ± 1.8 points and from 610.8 ± 221.1 to 757.9 ± 267.9 pg/mL respectively)(Kim et al., 2018). In conclusion, after 50-minutes of CEFP short-term memory and BDNF levels improved in healthy middle-aged women, especially those without MCI (Kim et al., 2018). As well, that short-term memory and BDNF levels after CEFP were found to be negatively correlated with age, but pre- to post-intervention changes in short-term memory and BDNF were not (Kim et al., 2018).

Wiet (2018) as well looked at the effects of exercised induced BDNF levels and cognition, but in premenopausal and postmenopausal women. Assessment of 14 active females, seven premenopausal and seven postmenopausal, was conducted over two different trials, one being an exercise trial and the other a controlled reading trial (Wiet, 2018). The exercise trial consisted of running on a treadmill at 75% of their VO_2 max for a total of 30 minutes while the control trial consisted of a light reading session for the same amount of time. A blood sample to look at plasma BDNF levels and the Stroop test to assess cognition and reaction time was administered before, immediately after, and 30 minutes post-exercise, as well as for the control trial. Results showed that there was an interaction between the two groups in BDNF levels over time. It was discovered that

premenopausal women had a rise in BDNF levels after exercise and postmenopausal women had a decrease in BDNF levels after exercise (Wiet, 2018). Additionally, a correlation was found between age and cognitive performance over each time point, indicating that the postmenopausal group was significantly slower in pre-testing and post-30 minute-testing in both the exercise trial and control trials. This provides evidence for a decline in incongruent choice reaction time because of one's age (Wiet, 2018).

Another study looked into the effect of an acute aerobic exercise session, resistance exercise session, and aerobic resistance exercise session on cognition and BDNF. Paul (2016) observed ten healthy, physically active subjects capable of at least 30 minutes of vigorous activity, five of them males and five females. The Stroop test was used for cognitive assessment where the subject had to name the color of the ink rather than the word, and a lower score was considered a better score (Paul, 2016). A 5 ml blood sample was taken via the antecubital vein at rest, immediately post-exercise, and 30-minutes post-exercise (Paul, 2016). The blood samples were stored in an -80°C freezer until analyzed by a Bio-Tek Synergy plate reader and assessed via ELISA (Paul, 2016). Prior to experimentation body composition was found utilizing the BodPod after subjects over-night fasted, VO_2 maximal testing was done to find the subjects' maximal aerobic power, and 1-RM testing for each exercise was performed in order to find the loads for the resistance workout trial (Paul, 2016). Each exercise condition was performed during the same time of the day, approximately one week apart. Paul (2016) found that all modalities elicited a significant rise in BDNF and cognition improvement (CT (28%) < AT (31%) < RT (45%); CT (~89.5 ms) < AT (~90.5 ms) < RT (~116.4 ms)) immediately after exercise.

CHAPTER III

METHODS

Research Design

This study was a causal comparative research design to observe gender differences in acute exercise induced BDNF production and cognitive function among older individuals. The independent variables were gender, exercise, and time and the dependent variables were BDNF levels and cognitive function (Stroop Test).

Participants

The study was approved by the Institutional Review Board (IRB) at Cleveland State University. Of the 23 potential participants who showed interest and came to CSU to see if they qualified, 18 subjects met the requirements to be eligible for the study. All eighteen subjects, 9 healthy males and 9 healthy females, were asked to volunteer for the study. They were recruited as a convenience sample through flyers, social media, and word-of-mouth. All of the subjects were regularly exercising a minimum of 150 minutes at moderate intensity or 75 minutes at high intensity five days a week for the past three months and were between the ages of 60-85 years old. Those females involved in the study were all postmenopausal. Subjects were required to fast from food and drink, other than that of water, 10 hours prior to each testing session. All the subjects were asked to

complete the American Heart Association (AHA) and American College of Sports Medicine (ACSM) prescreening questionnaire. Only those that were in the low risk category were chosen for the study, unless a doctor's note was provided stating they were cleared to exercise. The TICS-M survey was utilized to assess for early cognitive impairment and limit those who have signs of cognitive decline from the present study. The subjects had to pass the TICS-M with a minimum score of 31 out of 46, this minimum score was determined based off of previous studies. Exclusion criteria consisted of any muscular skeletal injury, cardiovascular disease, hormone replacement therapy (HRT) in both men and women, heart rate altering medication, currently experiencing menopause, recent smoking history, metabolic or endocrine disease, neurological disabilities, color blindness, a percent body fat of > 35% for women and > 23% for men, and the inability to bike for 30 minutes at a moderately high intensity. Before the study, each subject was given an informed consent approved by the IRB.

Body Composition and Anthropometry

Height and body composition were measured upon arrival to the Human Performance Laboratory. Height was measured via a clinically calibrated stadiometer, weight was measured, and body composition and weight were determined using air displacement plethysmography via the BodPod system (Life Measurement Instruments; Concord, California).

Blood Sampling

Serum BDNF, testosterone, and estradiol levels were determined within this study. Blood samples were taken immediately before, immediately after, and 30 minutes after exercise and the control trial. Ten mL of venous blood was drawn with the aseptic

technique from the antecubital vein at each time portion, with a total of 30 mL of blood drawn per session and 60 mL for study total. Only phlebotomy-trained individuals drew blood from the subjects using sterile technique. All supplies used for blood sampling were discarded in accordance with biohazard regulations. Blood was collected in 5 mL serum-separating tubes, with samples allowed to clot for a minimum of 30 minutes at room temperature. The samples were spun in the centrifuge, and the serum was collected and stored in a -80 degrees Celsius freezer until analyzed. BDNF, testosterone, and estradiol levels were measured with commercially available ELISA kits using a Bio-Tek Synergy plate reader.

Cognitive Test

The Stroop Test is a widely used, reliable, and valid test designed to test cognitive performance specifically by testing the subject's selective attention capacity and skills, as well as reaction time. The incongruent style was administered being it is the most relevant test for measuring executive function. The Stroop word-color test consisted of three different trials for both exercise and control (pre, post, and thirty minutes post) via a computer program. The incongruent style of Stroop Test was used which consisted of four different colors: red, blue, green, and black. The subject was asked to name the color of the text rather than the spelling of the word. The subjects were asked to complete the test as quickly and efficiently as possible.

Experimental Protocol

The 18 subjects were assigned for which trial they would complete first based on when they signed up for the study. The participants with an ID number that was odd would exercise first and the participants with an ID number that was even would exercise

on the second visit. Subjects reported to the Human Performance Lab at Cleveland State University on two different occasions and completed those visits as follows:

1st visit	1st visit upon qualification	2nd visit
1. Signed consent form 2. AHA/ACSM questionnaire was completed 3. Blood pressure, heart rate, height and weight were taken 4. TICS-M was performed 5. Body fat assessed via the BodPod 6. Stroop Test was explained 7. Blood draws were explained	1. Practiced Stroop Test 2. Pre-exercise or control blood draw 3. Pre-exercise or control Stroop Test 4. Exercise or control for 30 minutes 5. Post-exercise or control blood draw 6. Post-exercise or control Stroop Test 7. Subjects rested for 30 minutes 8. Post-30 minutes exercise or control blood draw 9. Post-30 minutes exercise or control Stroop Test	*opposite trial of 1st visit 1. Practiced Stroop Test 2. Pre-exercise or control blood draw 3. Pre-exercise or control Stroop Test 4. Exercise or control for 30 minutes 5. Post-exercise or control blood draw 6. Post-exercise or control Stroop Test 7. Subjects rested for 30 minutes 8. Post-30 minutes exercise or control blood draw 9. Post-30 minutes exercise or control Stroop Test

Exercise Protocol

The subjects performed a 30-minute bout of aerobic exercise on either a stationary or recumbent bike of their choice. Subjects were given a five-minute warm up at a speed that allows the subject to reach 75% of their age-predicted maximal heart rate. Percentage of HR_{max} was used rather than performing a VO_2 max test and using that to find intensity being 75% of HR_{max} corresponds to ~60% of VO_2 max. Once this speed was detected, it was initiated for 30 minutes of exercise and altered if their heart rate was too high or too low. After the 30 minutes of exercise, subjects were allowed to cool down and then asked to stop and to rest for the subsequent 30 minutes. Heart rate and rate of perceived exertion were measured throughout the exercise test. Blood draws and Stroop Tests were both initiated prior to exercise, immediately after exercise, and 30 minutes after exercise.

Control Protocol

Subjects in addition to exercise performed a control trial where they read the book, *Endure* by Alex Hutchinson, for 30 minutes in a controlled room with no interruption. After the 30 minutes of controlled reading, subjects were asked to rest for the subsequent 30 minutes like that of the exercise trial. Blood draws and Stroop Tests were both initiated prior to control, immediately after control, and 30 minutes after control.

Statistical Analysis

Descriptive statistics were obtained. Repeated measures ANOVAs were conducted to observe changes in BDNF levels and cognitive performance over time and between the two groups. Post hoc pairwise comparison was used to explore any observed

main and interaction effects. Kendall's Tou Correlations were used to assess the relationships between BDNF, cognition, age, gender and hormone status. A One-Way ANOVA was done in order to observe any statistical differences between estrogen and testosterone levels between the two groups. SPSS (version 26) was used for all analyses with .05 used as the level of significance.

CHAPTER IV

RESULTS AND DISCUSSION

A repeated measures ANOVA was done in order to observe any changes in cognition due to exercise. There was a significant difference in Stroop times during all time points (pre, post, post30) in both exercise and control trials ($F = 9.343$; $p = 0.001$) across all subjects. There was no significant difference between exercise or control conditions and no impact due to gender. Pairwise comparisons were also done and showed a trend ($p = 0.068$) for a decrease in Stroop time from the pre to immediate-post timepoints, and a significant decrease ($p = 0.004$) in Stroop time from the pre to post-30 timepoints. There was no significant evidence found, but it was observed that men had slower Stroop times than women throughout each time point for exercise and control (exercise: 1,379.5, 1,322.1, 1,330.6 versus 1,261.7, 1,193.6, 1,167.1; control: 1,484.6, 1,394.6, 1,304.7 versus 1,425.3, 1,311.8, 1,239.8 respectively). There was no significant evidence found to support the finding, however it was observed that overall Stroop times in the control trials were slower than the exercise trials. The results of the study are shown in the following tables and figures.

Table 1. Subject Characteristics, Mean ± Standard Deviation

Measure	All	Males	Females
N	18	9	9
Age (yrs)	67.4 ± 5.8	69.6 ± 6	65.3 ± 5
Height (in)	66.5 ± 3.3	68.3 ± 3.1	64.6 ± 2.3
Weight (lbs)	140 ± 18.3	149.5 ± 16.1	130.6 ± 15.7
Body Fat (%)	19.4 ± 9.5	12 ± 6.3	26.7 ± 5.6
75% of HR_{max} (bpm)	120.6 ± 3.2	119.6 ± 3.3	121.7 ± 2.9
Measured Exercise HR (bpm)	130.6 ± 7.7	127.1 ± 8.1	135.5 ± 6
Estrogen (pg/mL)	74.2 ± 42.3	87.3 ± 51	61.2 ± 32.5
Testosterone (ng/dL)	4.4 ± 4.1	6.8 ± 4.1	1.2 ± 0.6*

*one woman's testosterone results were not included in the averaged results due to being an outlier (greater than two standard deviations above the mean).

Cognitive Assessment

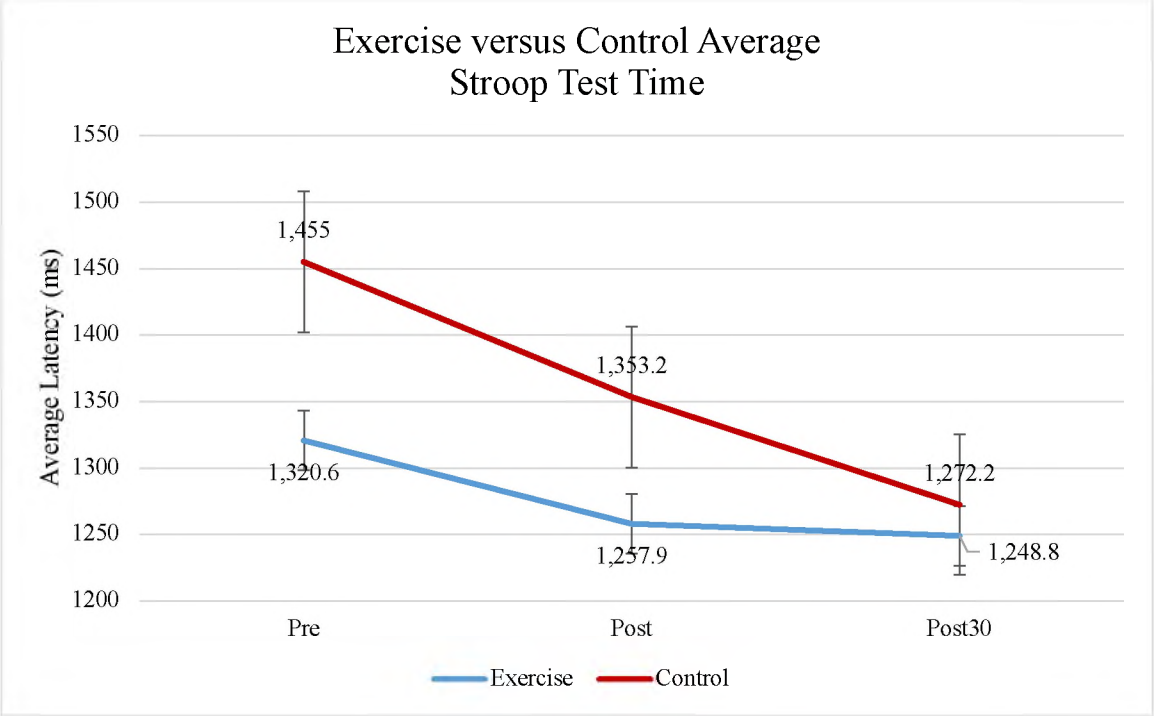


Figure 1. The incongruent Stroop Test results from both exercise and control trials (pre, post, and post30).

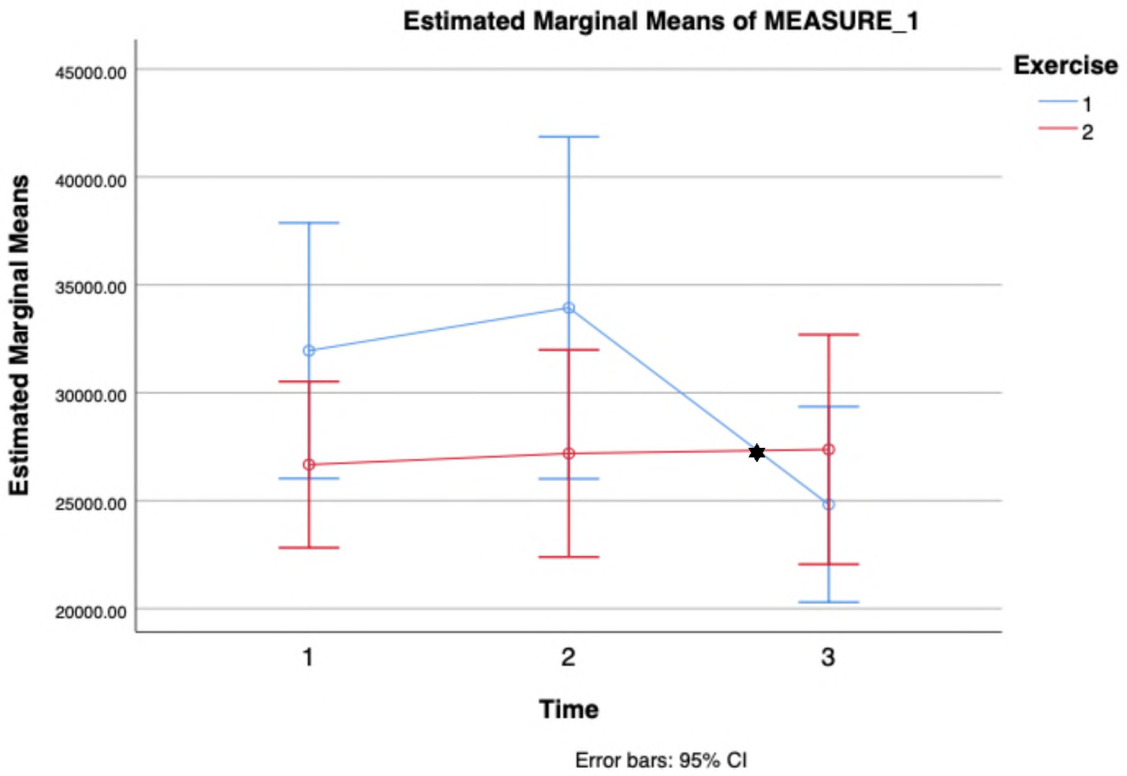


Figure 2. The effects of acute aerobic (75% of MHR) and control on BDNF levels (1 -pre, 2 - post, 3 - post30). * = ($p < 0.5$) Exercise trial (1 - blue) versus control trial (2 - red)

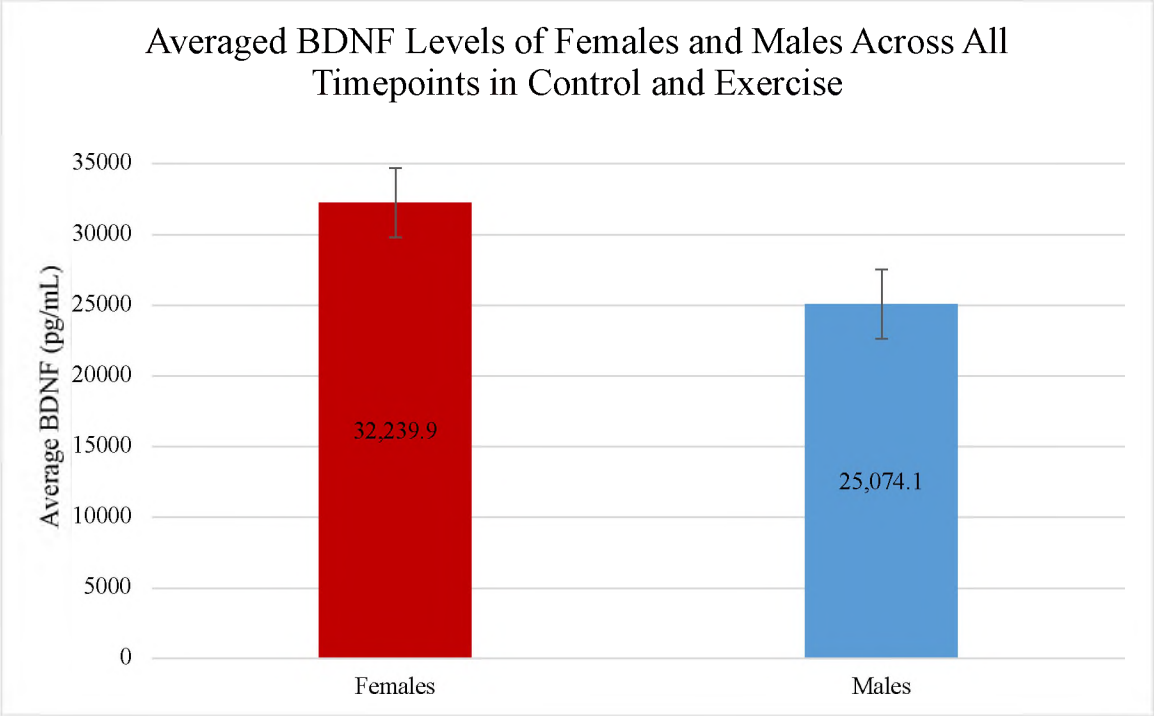


Figure 3. Average BDNF levels across all timepoints (pre, post, post30) for exercise and control trials for both groups (males; females).

A repeated measures ANOVA was done in order to observe any changes in BDNF levels due to exercise. Seen in figure 2, there was a significant interaction between BDNF levels over time due to exercise ($F = 3.268$; $p = 0.05$). A Post Hoc test was done to further investigate this interaction. There was a non-significant drop in BDNF from post to post-30 exercise whereas there was no change in control BDNF from post to post-30. An independent samples t-test was also conducted and expressed that females had significantly higher BDNF than males across all timepoints and conditions (females = 32,239.9 ± 2,446.4 pg/mL; males = 25,074.1 ± 2,446.4 pg/mL; $p = 0.055$).

Correlations with Age

A Pearson Correlations analysis showed significant, positive correlation between age and pre-exercise Stroop time ($p = 0.004$, $r = 0.640$), post exercise Stroop time ($p = 0.002$, $r = 0.676$), and post 30 exercise Stroop time ($p = 0.006$, $r = 0.624$).

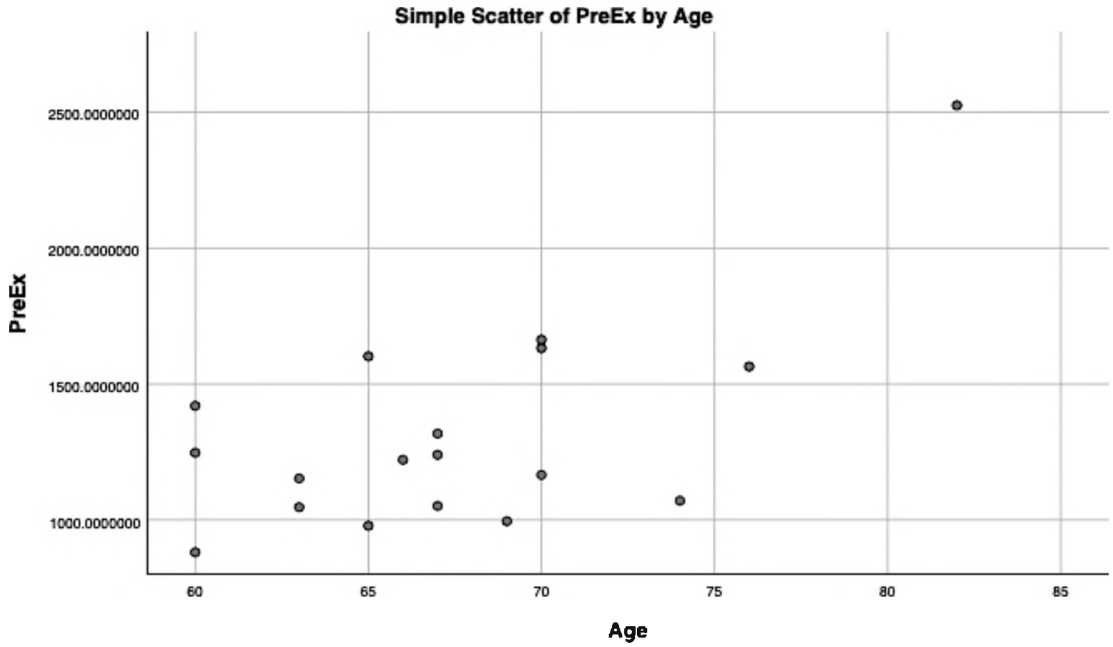


Figure 5. Age versus Stroop time pre-exercise

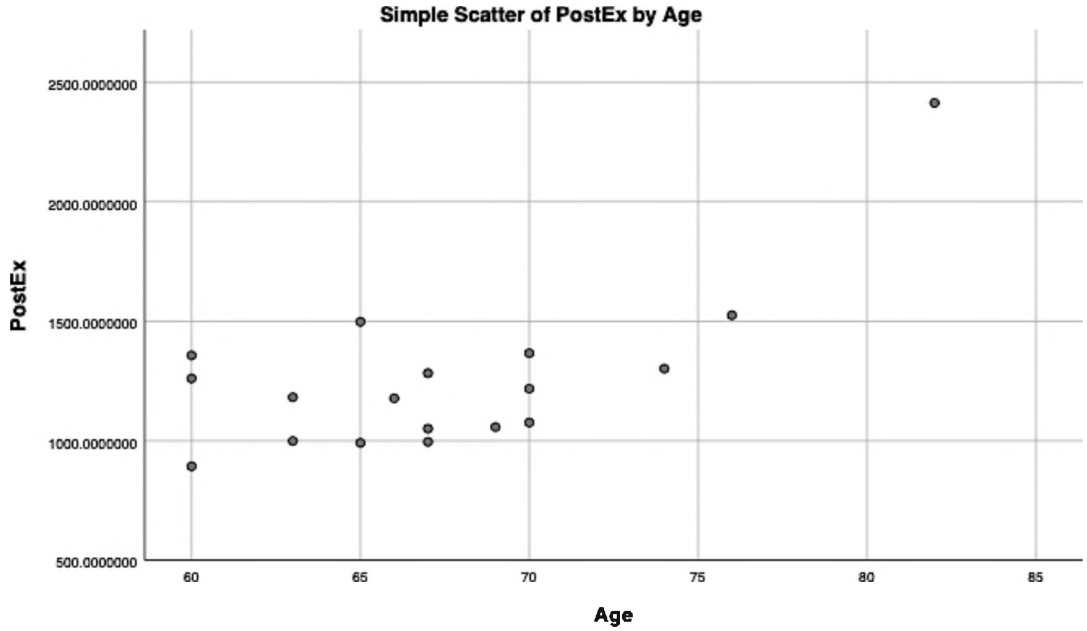


Figure 6. Age versus Stroop time post exercise

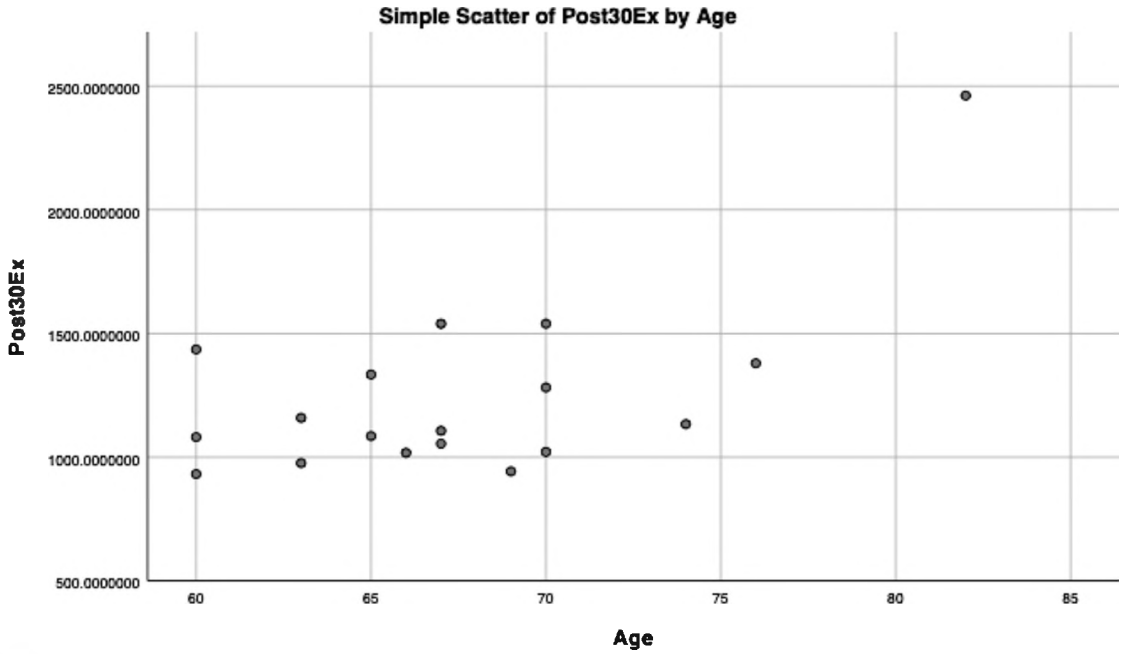


Figure 7. Age versus Stroop time post-30 exercise

Hormone Levels and Body Composition

An independent samples t-tests was conducted and expressed that males had significantly higher testosterone than females ($p = 0.007$), and significantly lower body fat ($p < 0.001$). However, there is no significant relationship between hormones and BDNF.

Discussion

It was discovered that there was a significant difference in cognitive processing time via the Stroop Test at all time points (pre, post, post30) in both exercise and control trials ($p = 0.001$) across all subjects. Additionally, there was a trend ($p = 0.068$) for a decrease in Stroop time from the pre to immediate-post timepoints, and a significant decrease ($p = 0.004$) in Stroop time from the pre to post-30 timepoints. Some research, like that of Wiet (2018) who tested premenopausal women and postmenopausal women and Paul (2016) who tested subjects based on mode of exercise, found an acute improvement in Stroop Test cognitive processing time post-exercise which then returns to baseline 30 minutes after exercise. In the present study it was discovered that with each time point the cognitive processing time continued to improve in both exercise and control, which can likely be attributed to a learning effect. Being our subjects are of the older population, extra familiarization time with the Stroop Test may have been necessary to avoid this.

Another potential contributing factor to the unexpected Stroop Test reaction times, may be the role epinephrine plays when the subjects know they are about to exercise. Ahmadiasl, Alaei and Hänninen (2003) investigated the effects of exercise on learning and memory, long-term potentiation and levels of epinephrine in treadmill

trained rats over the span of ten days. They discovered that physical activity produced a significant enhancement in spatial learning, with decreased path length and latency to the platform in the Morris water maze with significantly increased levels of epinephrine (Ahmadiasl et al., 2003). This would make sense as to why for some individuals, but not all, there was the trend seen of constant improvement in cognitive processing times, and a faster cognitive processing time in the exercise trials compared to the control trials.

Lastly, another theory of why the elderly population improved over all three timepoints in the exercise trial for cognitive function may be due to the intensity of the mode of exercise. Etnier et al. (2016) tested the dose-response effects of exercise intensity of memory performance and found that there was no significant difference in short-term memory as a function of condition, meaning the various intensities of exercise the subjects endured did not differentially influence how many words participants were able to recall following exposure to the word list initially. This was unexpected by Etnier et al. (2016) due to their research that found that there should have been a small positive effect on short-term memory due to acute exercise; however, Etnier et al. never performed a control group with subjects so they were unable to draw the conclusion from the results as to whether exercise influenced short-term memory. Etnier et al. (2016) did although make a suggestion based off of the evidence by Chang, Labban, Gapin, and Etnier (2012) that there is an association between exercise intensity and cognitive performance assessed post-exercise based on the timing of cognitive testing. Chang et al. (2012) states that exercise at lower intensities has been shown to be the most beneficial for cognitive performance assessed immediately after exercise while exercise at higher intensities is better for cognitive performances assessed after a delay. With that being

said, the intensity level of the current study may have not been low enough to benefit short-term cognition specifically but high enough to benefit long-term cognition as reaction times continued to improve at each timepoint in our active elderly adults.

It was also found that there was a significant main effect between BDNF levels over time due to exercise ($p = 0.055$). The exercise hypothesis was based off of Etnier et al. (2016) who found that BDNF serum increased significantly from baseline to post-exercise and then decreased significantly by 30-minutes post-exercise in both genders of young adults. The results of the current study showed a significant interaction when looking at BDNF based on condition, not considering gender of the elderly adults, where there was a non-significant drop in BDNF following exercise in the exercise trial while there was no change in BDNF in the control trial similar to that of Etnier et al. These results do not support past literature showing that a single bout of exercise increases peripheral levels of BDNF, which may be due the level of intensity the subjects worked at when riding either the recumbent or stationary bike. Ferris, Williams, and Shen (2007) determined there is a relationship between exercise intensity and BDNF responses when they tested their subjects' production of BDNF when they performed a graded exercise test to determine their VO_2max and ventilatory threshold on a cycle ergometer, in which the subjects cycled two subsequent 30-minute endurance rides performed at 20% below ventilatory threshold and 10% above ventilatory threshold (Ferris et al., 2007). They discovered that BDNF levels increased from baseline after exercise at 10% above ventilatory threshold and the graded exercise test, while there were no significant changes in BDNF from baseline after exercise at 20% below ventilatory threshold (Ferris et al., 2007). Concluding, that possibly the reason that in the present study the subjects did not

produce evidence that acute aerobic exercise does induce BDNF production was due to exercise intensity not being high enough for our active population.

Lastly, it was exposed that females had significantly higher BDNF than males. These findings are similar to that which was found in Lommatszch et al. (2005) where the sedentary young females expressed higher levels of BDNF plasma in comparison to that of the sedentary young males. It has been found that estradiol levels of young fertile women in comparison to young fertile men were 996-1,377 pg/mL and 10-82 pg/mL respectively (Begliuomini et al., 2007; Yamamoto, Hibi Katsuno, and Miyake, 1995) and being that our older males and females had no difference in estrogen, and higher BDNF levels still persisted in the females within our current study like that of Lommatszch et al.'s study suggests that there may be an estrogen-independent relationship to BDNF. Begliuomini et al. (2007) inferred that hormonal status does have an influence on that of plasma BDNF when he discovered that sedentary postmenopausal women had much lower plasma BDNF in comparison to that of sedentary women in the mid-luteal phase of their menstrual cycle, roughly a 1,000 pg/mL difference, in BDNF production. However, what was discovered in the current study may be a novel finding that suggests looking into other factors outside of estrogen as the relating cause to elevated BDNF in older women.

CHAPTER V

SUMMARY AND CONCLUSION

Conclusion

The purpose of this study was to examine the impact of gender on acute aerobic exercise induced BDNF and cognitive function among older individuals. It was found that there was statistical evidence that acute exercise affects BDNF production in both genders, but not that of cognitive processing time. Additionally, women were found to have higher overall levels of BDNF. The hypothesis of the current study was that acute aerobic exercise would increase BDNF levels and enhance cognitive processing time post exercise and then BDNF and cognitive processing time would return to baseline 30 minutes post exercise in both genders, with women having overall higher BDNF levels than that of the men. Statistical evidence was not able to show the increase in cognitive processing time performance post acute aerobic exercise. Rather statistical evidence showed a decrease in cognitive processing time at post-30 minutes. Therefore, the exercise and BDNF hypothesis was partially supported that we saw a drop in BDNF after exercise as compared to the control condition. However, we did not see the exercise-induced BDNF increase. As for the cognitive processing speed, this was not affected by exercise. Our hypothesis that females would have higher BDNF than males was

supported. With that being said, there were observations that support the need for further investigation in this area of research.

Future Research

Suggestions for future research would be to have a larger sample size. Different modes of aerobic exercise could reveal different results, an example could be that of swimming or running contrasting from biking. Increasing or decreasing the intensity of the aerobic exercise of the study may elicit a different response of BDNF and show improvements in cognitive performance in either short-term cognition and long-term cognition respectively. If utilizing the Stroop Test or any other cognitive assessment test with this population age range, a suggestion to give more time for familiarization with the test is suggested in hopes that results of reaction time would normalize. It would be interesting to compare the results found from regularly active individuals to that of sedentary and how that affects the production of BDNF post-exercise. It as well would be interesting to compare two groups of elderly adults, one group exercising at low-intensity while the other exercises at high-intensity to see the effects of exercise intensity on BDNF production and short-term and long-term cognitive function. There is a need for further exploration as to how BDNF reacts with estrogen, testosterone and other factors that could potentially influence BDNF production.

Limitations

All participants in the study were regularly active males and females. Activity role does play a role, as found by Adlard et al. (2004), on BDNF levels and could even play a role on cognitive performance. Within this study riding either a recumbent or stationary bike were the only forms of aerobic exercise used. The mode of exercise itself

was low intensity and low impact, and potentially an even lower or higher intensity would have elicited different BDNF and cognitive results. Other forms of aerobic exercise like that of running or swimming could elicit a different response both in BDNF levels and cognitive performance. The only cognitive test used in the study was the Stroop Test, possibly another cognitive assessment could have examined a different aspect of cognition. The study had a small sample size. Although it was controlled to the best of the researcher's ability, the lab that the participants exercised and took the Stroop Test in had a constantly changing environment with people coming in and out of the room and temperature changing that could have had an effect on results. Diet was not controlled other than that of fasting.

REFERENCES

Adlard, P., Perreau, V., Engessar-Cesar, C., & Cotman, C. (2004). The timecourse of induction of brain-derived neurotrophic factor mRNA and protein in the rate hippocampus following voluntary exercise. *Neuroscience Letters*, 363, 43-48.

Ahmadiasl, N., Alaei, H., Hänninen, O. (2003). Effects of exercise on learning, memory and levels of epinephrine in rats' hippocampus. *The Journal of Sports Science and Medicine,* 2(3): 106-109.

Bathina, S., Das, U.N. (2014). Brain-derived neurotrophic factor and its clinical implications. *Archives of Medical Science*, 11(6), 1164-1178.

Begliuomini, S., Casarosa, E., Pluchino, N., Lenzi, E., Centofanti, M., Freschi, L., Pieri, M., Genazzani, A.D., Luisi, S., and Genazzani, A.R. (2007). Influence of endogenous and exogenous sex hormones on plasma brain-derived neurotrophic factor. *Human Reproduction*, 22, 995-1002.

Boudewijn, A., Bus, A., Tendolkar, I., Franke, B., De Graaf, J., Den Heijer, M., Buitelaar, J., Oude Voshaar, R. (2011). Serum brain-derived neurotrophic factor: Determinants and relationship with depressive symptoms in a community population of middle-aged and elderly people. *The World Journal of Biological Psychiatry*. 13, 39-47. 10.3109/15622975.2010.545187.

Carbone, D. L., Handa, R. J. (2012). Sex and stress hormone influences on the expression and activity of brain-derived neurotrophic factor. *Neuroscience*, 239, 295–303. doi:10.1016/j.neuroscience.2012.10.073

Chang, Y.K., Labban, J.D., Gapin, J.I., & Etnier, J.L. (2012). The effects of acute exercise on cognitive performance: A meta-analysis. *Brain Research*, 1453, 87–101. PubMed doi:10.1016/j.brainres.2012.02.068

Damirchi, A., Hosseini, F., Babaei, P. (2017). Mental training enhances cognitive function and bdnf more than either physical or combined training in elderly women with mci: A small-scale study. *American Journal of Alzheimer's Disease and Other Dementias.* DOI: 10.1177/1533317517727068

Dietrich A., Audiffren M. (2011). The reticular-activating hypofrontality (RAH) model of acute exercise. *Neuroscience & Biobehavioral Reviews.* 35:1305-25.

Erickson, K.I., Prakash, R.S., Voss, M.W., Chaddock, L., Heo, S., McLaren, M. (2010). Brain-derived neurotrophic factor is associated with age-related decline in hippocampal volume. *The Journal of Neuroscience.* 30:5368-75.

Etnier, J.L., Wideman, L., Labbon, J.D., Piepmeier, A.T., Pendleton, D.M., Dvorak, K.K., Becofsky, K. (2016). The effects of acute exercise on memory and brain-derived neurotrophic factor (BDNF). *The Journal of Sport and Exercise Physiology.* 38:331-340.

Ferris, L.T., Williams, J.S., & Shen, C.L. (2007). The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. *Medicine and Science in Sports and Exercise*, 39(4), 728–734. PubMed doi:10.1249/mss.0b013e31802f04c7

Kim, H.J., Lee, S.Y., Lee, H.G., Cho, Y.H., Ko, E.M. (2018). Effects of a single-session cognitive enhancement fitness program on serum brain-derived neurotrophic

factor levels and cognitive function in middle-aged women. *The Journal of Sports Science and Medicine.* 17, 110-116.

Heisz, J.J., Clark, I.B., Bonin, K., Paolucci, E.M., Michalski, B., Becker, S., Fahnestock, M. (2017). The effects of physical exercise and cognitive training on memory and neurotrophic factors. *The Journal of Cognitive Neuroscience.* 29(11):1895-1907.

Lommatzsch, M., Zingler, D., Schuhbaeck, K., Schloetcke, K., Zingler, C., Schuff-Werner, P., Virchow, J.C. (2005). The impact of age, weight and gender on bdnf levels in human platelets and plasma. *The Journal of Neurobiology of Aging.* 115-123.

Marosi, K., Mattson, M. (2014). BDNF mediates adaptive brain and body responses to energetic challenges. *Trends In Endocrinology and Metabolism,* 25, 89-98.

Mu, J.S., Li, W.P., Yao, Z.B., Zhou, X.F. (1999). Deprivation of endogenous brain-derived neurotrophic factor results in impairment of spatial learning and memory in adult rats. *Brain Research,* 835:259-65.

Paul, D.N. (2016). *Effect of an acute aerobic vs resistance vs aerobic resistance exercise bout on cognition and brain-derived neurotrophic factor (BDNF)* (Master's thesis). Cleveland State University, Cleveland, Ohio.

Piepmeier, A.T., Etnier, J.L. (2015). Brain-derived neurotrophic factor (BDNF) as a potential mechanism of the effects of acute exercise on cognitive performance. *Journal of Sport and Health Science,* 4(1), 14-23. doi:10.1016/j.jshs.2014.11.001

Rassmussen, H., Bagger, Y., Tanko, L., Qin, G., Christiansen, C., & Werge, T. (2006).

Cognitive impairment in elderly women: the relative importance of selected genes, lifestyle factors, and comorbidities. *Neuropsychiatric Disease and Treatment*, 2(2), 227-233.

Seifer, D.B., Feng, B., Shelden, R.M., Chen, S., Dreyfus, C.F. (2002). Brain-derived neurotrophic factor (BDNF): A novel human ovarian follicular protein. *The Journal of Clinical Endocrinology and Metabolism,* 87, 655-659.

Seifer, D.B., Lambert-Messerlian, G., Schneyer, A.L. (2003). Ovarian brain-derived neurotrophic factor is present in follicular fluid from normally cycling women. *Fertility and Sterility,* 79, 452.

Schmolesky, M.T., Webb, D.L., & Hansen, R.A. (2013). The effects of aerobic exercise intensity and duration on levels of brain-derived neurotrophic factor in healthy men. *Journal of Sports Science & Medicine,* 12(3), 502-11.

Tangen, G.G., Engedal, K., Bergland, A., Moger, T.A., Mengshoel, A.M. (2014). Relationships between balance and cognition in patients with subjective cognitive impairment, mild cognitive impairment, and alzheimer disease. *Physical Therapy*, 94(8), 1123–1134. https://doi.org/10.2522/ptj.20130298

Ventriglia, M., Zanardini, R., Bonomini, C., Zanetti, O., Volpe, D., Pasqualetti, P., Bocchio-Chiavetto, L. (2013). Serum brain-derived neurotrophic factor levels in different neurological diseases. *BioMed Research International*, 2013:901082. doi:10.1155/2013/901082

Wiet, R. (2018). *The effects of acute aerobic exercise on BDNF levels and cognition in postmenopausal women* (Master's thesis). Cleveland State University, Cleveland, Ohio.

Wei, Y., Wang, S., & Xu, X. (2016). Sex differences in brain-derived neurotrophic factor signaling: Functions and implications. *Journal of Neuroscience Research,* 95(1-2), 336-344. doi:10.1002/jnr.23897

Yamamoto, M., Hibi, H., Katsuno, S., Miyake, K. (1995). Serum estradiol levels in normal men and men with idiopathic infertility. *International Journal of Urology,* 2(1), 44-46. doi.org/10.1111/j.1442-2042.1995.tb00619.x

APPENDIX A: INFORMED CONSENT

Cleveland State University

College of Education and Human Services

Department of Health and Human Performance

INFORMED CONSENT FOR PARTICIPATION

IMPACT OF GENDER ON ACUTE EXERCISE INDUCED BRAIN-DERIVED NEUROTROPHIC FACTOR AND COGNITIVE FUNCTION IN OLDER ADULTS

Introduction

Thank you for your interest in this study. My name is Madison Phillips and I am working on my Master's Thesis at Cleveland State University. This study will be led under the supervision of Dr. Emily Kullman, Associate Professor of Exercise Science in Health and Human Performance, Dr. Kenneth Sparks, Associate Professor of Exercise Science in Health and Human Performance, and Dr. Douglas Wajda, Associate Professor of Exercise Science in Health and Human Performance.

The purpose of this study is to examine the impact of gender on the effect of acute aerobic exercise on brain-derived neurotrophic factor (BDNF) and cognition among older individuals. We will look at BDNF, estrogen, testosterone levels and cognition. BDNF is a protein that helps protect neurons. This study will provide information on how aerobic exercise effects BDNF levels and cognition. The research study will be conducted in the Human Performance Laboratory (HPL) at Cleveland State University (CSU).

Procedures

BDNF, estrogen, and testosterone will be measured through blood draws from your arm. Cognition will be measured using the Stroop test. For this test, you will be shown color words in a different ink than the actual text. You will name the color of the ink of each word as quickly and accurately as possible. We will recruit 10 healthy female and 10 healthy male subjects, who regularly exercise. Subjects will complete an American Heart Association/American College of Sports Medicine questionnaire to determine medical history. The information will be used to determine eligibility for the study. A test will be given as well to assess if there is delayed cognition (TICS-M).

You will be asked to come to the HPL 2-3 separate times. Each session will last about 1.5-2 hrs and will require a 10 hour fast prior to testing. The total study time commitment is around 4.5-6 hrs spread over 2 weeks. During session one, basic measurements will be taken. These include height, weight, BMI, body composition, resting heart rate, and blood pressure. You will be allowed to practice the Stroop test. We will measure body composition using the BodPod. The BodPod is a machine that measures your body composition comfortably by air pressure in a locked cubicle and takes 5 minutes to complete. You will be asked to dress in a bathing suit, or form-fitting clothes.

The order of the last two sessions will be random. One session will be 30 minutes of biking at 75% of age-predicted max heart rate. The other will be a reading session. A blood sample and Stroop test will be obtained before, immediately after, and 30 minutes after each trial. There will be a total of 3, 10 mL blood draws for each exercise session. A total of 30 mL of blood per session. All storage and analysis of blood will be done at the HPL by study personnel and not used for genetic testing. Those taking blood are Dr. Emily Kullman, Dr. Kenneth Sparks, or Dr. Douglas Wajda, all trained phlebotomists. will be done at the same time of day.

Risks

Risks of these tests are minimal and do not exceed those of normal exercise. Risks associated with this study include muscle soreness, shortness of breath, fatigue, heart attack, or acute injuries resulting from the exercise. This risk would be the same experienced from a normal exercise routine. The needle stick may hurt. There is also a small risk of bruising, a rare risk of infection, or lightheadedness. Every effort will be made to minimize these risks. Understand that the laboratory is equipped with an Automated External Deregulator (AED). All lab personnel are certified in CPR and First Aid. Emergency procedures include calling EMS (x911) stating to the dispatcher: "We have a medical emergency in the Human Performance Laboratory PE Building-Room B60". Cardiopulmonary Resuscitation (CPR)/First aid will be administered until EMS arrives. In the event you are injured as a result of participation in this research, please notify the research team and seek medical attention by your primary care physician. The costs of such medical care will be billed to you or your insurance company. There are no plans to provide compensation for lost wages, direct or indirect losses. Cleveland State University will not voluntarily provide compensation for research related injury. Understand that you can stop at any time.

Benefits

I understand that there are no direct benefits for participating in the study other than engaging in an exercise session and body composition. However, the results of this study will be beneficial to individuals seeking to improve their brain health through exercise.

Confidentiality

To protect privacy, any data and information obtained will be confidential. It will not be disclosed to anyone without consent. A number will be assigned to each subject in place of a name. The information may be used for a statistical or scientific purpose with the right of privacy retained. Dr. Emily Kullman and Madison Phillips will be the only witnesses of the information being presented. Data will be stored in the Human Performance Lab PE-60B in a locked filing cabinet. Blood samples will be unidentifiable when in the locked cabinet and will be kept for 3 years for potential future research.

Participation

I understand that participation in this project is by choice. I have the right to withdraw at any time with no consequences. I attest and verify that I have no known health problems that could prevent me from completing the testing. If I have any questions about the procedures, I can contact Dr. Emily Kullman at (216) 687-4854 or Madison Phillips at (419) 577-5195.

I understand that if I have any questions about my rights as a research subject, I can contact Cleveland State University's Review Board at (216) 687-3630.

Participant Acknowledgement

The procedures, purposes, known discomforts and risks, possible benefits to me and to others have been explained to me. I have read the consent form and I understand it. I also understand that all data will be stored in a secured file in the HPL for at least 3 years then shredded.

I agree to participate in this study and that I am at least 18 years old. I have also been given a copy of this consent form.

Signature: _____ Date: _____

Name Printed: _____

Witness: _____ Date:_____

APPENDIX B: AHA/ACSM PRESCREENING QUESTIONNAIRE

AHA/ACSM Health/Fitness Facility Preparticipation Screening Questionnaire

Assess your health status by marking all *true* statements

History
You have had:
___ a heart attack
___ heart surgery
___ cardiac catheterization
___ coronary angioplasty (PTCA)
___ pacemaker/implantable cardiac
___ defibrillator/rhythm disturbance
___ heart valve disease
___ heart failure
___ heart transplantation
___ congenital heart disease

Symptoms
___ You experience chest discomfort with exertion.
___ You experience unreasonable breathlessness.
___ You experience dizziness, fainting, or blackouts.
___ You take heart medications.

Other health issues
___ You have diabetes.
___ You have asthma or other lung disease.
___ You have burning or cramping sensation in your lower legs when walking short distances.
___ You have musculoskeletal problems that limit your physical activity.
___ You have concerns about the safety of exercise.
___ You take prescription medication(s).
___ You are pregnant.

If you marked any of these statements in this section, consult your physician or other appropriate health care provider before engaging in exercise. You may need to use a facility with a **medically qualified staff.**

Cardiovascular risk factors
___ You are a man older than 45 years.
___ You are a woman older than 55 years, have had a hysterectomy, or are postmenopausal.
___ You smoke, or quit smoking within the previous 6 months.
___ Your blood pressure is >140/90 mm Hg.
___ You do not know your blood pressure.
___ You take blood pressure medication.
___ Your blood cholesterol level is > 200 mg/dL.
___ You do not know your cholesterol level.
___ You have a close blood relative who had a heart attack or heart surgery before age 55 (father or brother) or age 65 (mother or sister).
___ You are physically inactive (i.e., you get <30 minutes of physical activity on at least 3 days per week).
___ You are > 20 pounds overweight.

If you marked two or more of the statements in this section you should consult your physician or other appropriate health care provider before engaging in exercise. You might benefit from using a facility with a professionally qualified exercise staff to guide your exercise program.

___ None of the above

You should be able to exercise safely without consulting your physician or other appropriate health care provider in a self-guided program or almost any facility that meets your exercise program needs.

APPENDIX C: TICS-M QUESTIONNAIRE

TICS-M

Orientation (1 pt each)

1. (i) What day of the week is it? ___Day of the week
   (ii) What is today's date? ___Day ___Month ___Year
   (iii) What season are we in? ___Season
2. What is your age? ___Age
3. What is your telephone number? ___Telephone Number

Registration/Free Recall (1 pt each)

4. I'm going to read you a list of 10 words. Please listen carefully and try to remember them. When I'm done, tell me as many as you can in any order. Ready? Now tell me all the words you remember.

___Cabin	___Watch
___Pipe	___Whip
___Elephant	___Pillow
___Chest	___Giant
___Silk	___Theatre

Attention/Calculation

5. Please take 7 away from 100. Now continue to take 7 away from what you have left over until I ask you to stop. (1 pt each)

___93	___72
___86	___65
___79	

6. Please count backwards from 20 to 1 (2 pts) ___No Mistakes

Comprehension, Semantic, and Recent Memory (2 pts each)

7. What do people usually use to cut paper? ___ Scissors
8. What is the prickly green plant found in the desert? ___ Cactus
9. Who is the president now? ___Correct Name
10. Who is the vice president now? ___Correct Name
11. What is the opposite of east? ___West

Language/Repetition

12. Pleas say this: "Methodist Episcopal" (2 pts)___Exactly Right

Delayed Recall (1 pt each)

13. Please repeat the list of 10 words I read earlier

___Cabin	___Theatre
___Pipe	___Watch
___Elephant	___Whip
___Chest	___Pillow
___Silk	___Giant

ID_____ Date_____ ___/ 46, Minimum of 31

APPENDIX D: RECRUITMENT FLYER

VOLUNTEERS WANTED FOR AN EXERCISE STUDY

Cleveland State University

If you have exercised regularly for the past three months you may qualify

Participants will receive free extensive body composition testing, and will have the opportunity to ask professionals questions to further their knowledge on fitness and own body composition

Volunteers will be asked to come to the CSU Human Performance Lab on two occasions for exercise assessments; each visit will last roughly 1.5-2 hours

Do you bike or exercise on a regular basis?

Are you 60-85 years of age?

Are you interested in learning more about your physical fitness and body composition?

The CSU Human Performance Lab is recruiting for a study observing cognition and hormones after exercise according to gender!

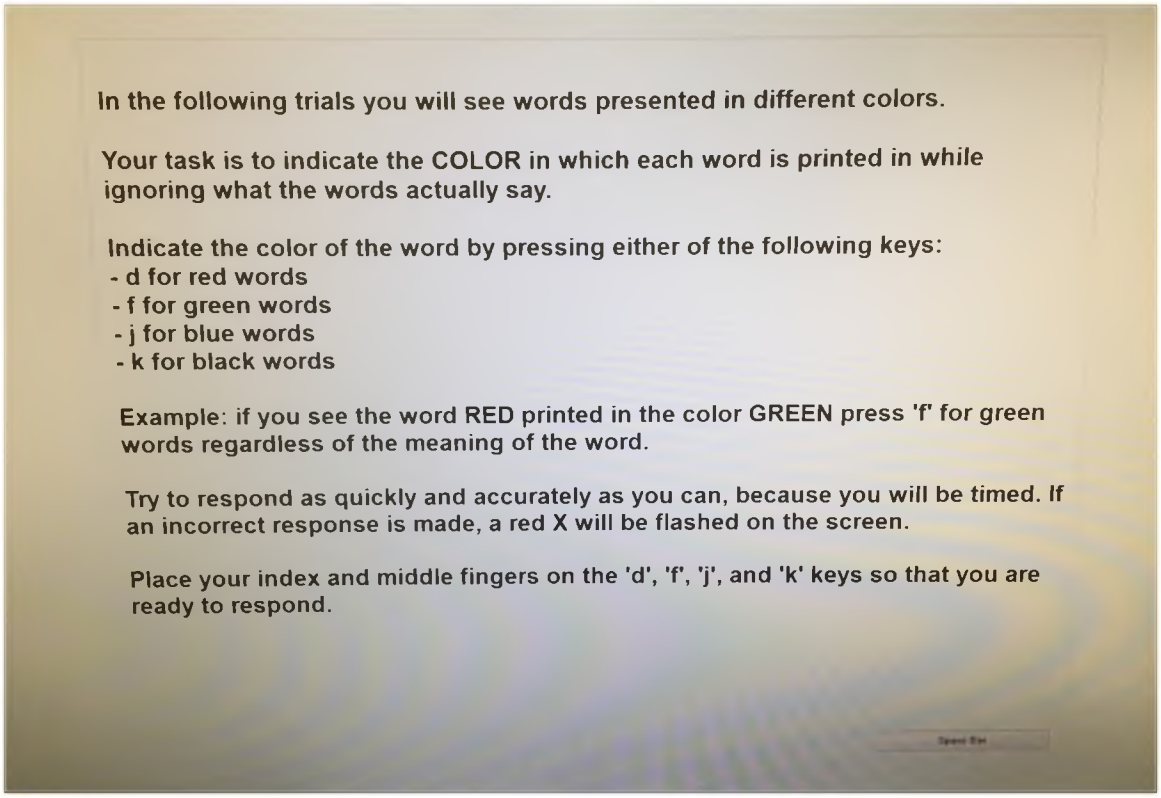
Interested?

Contact Madison Phillips
(419) 577-5195
m.l.phillips55@vikes.csuohio.edu

or

Dr. Emily Kullman
(216) 687-4854
e.kullman@csuohio.edu

APPENDIX E: STROOP TEST



APPENDIX F: INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

June 13, 2019

Dear Emily Kullman,

RE: IRB-FY2019-228
IMPACT OF GENDER ON ACUTE AEROBIC EXERCISE INDUCED BRAIN-DERIVED NEUROTROPHIC FACTOR AND COGNITIVE FUNCTION IN THE ELDERLY

The IRB has reviewed and approved your application for the above named project under the category noted below.
Application renewal is not necessary unless indicated below.

Approval Category: Expedited Category 2a, 4, 7
Approval Date: June 13, 2019
Expiration Date: --

By accepting this decision, you agree to notify the IRB of: (1) any additions to or changes in procedures for your study that modify the subjects' risk in any way; and (2) any events that affect that safety or well-being of subjects. Notify the IRB of any revisions to the protocol, including the addition of researchers, prior to implementation.

Thank you for your efforts to maintain compliance with the federal regulations for the protection of human subjects. Please let me know if you have any questions.

DO NOT REPLY TO THIS EMAIL. IF YOU WISH TO CONTACT US, PLEASE SEND AN EMAIL MESSAGE TO cayuseirb@csuohio.edu.

Sincerely,

Mary Jane Karpinski
IRB Analyst
Cleveland State University
Sponsored Programs and Research Services
(216) 687-3624
m.karpinski2@csuohio.edu