EFFECTS OF HOME-BASED HIGH-INTENSITY INTERVAL TRAINING VERSUS CONTINUOUS WALKING ON COGNITION IN OVERWEIGHT AND OBESE WOMEN

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EFFECTS OF HOME-BASED HIGH-INTENSITY INTERVAL 
TRAINING VERSUS CONTINUOUS WALKING ON 
COGNITION IN OVERWEIGHT AND OBESE WOMEN 

by 

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DISSERTATION 

Submitted in Partial Fulfillment of the 
Requirements for the Degree of 

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EFFECTS OF HOME-BASED HIGH-INTENSITY INTERVAL TRAINING VERSUS CONTINUOUS WALKING ON COGNITION IN OBESE ADULTS

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ABSTRACT

Objective: The purpose of the present study was to determine whether six weeks of home-based high-intensity interval training versus six weeks of moderate-intensity walking improves cognition, depression, and anxiety in women that are overweight or obese. Design: A randomized control trial design. Subjects: Twelve sedentary women characterized as overweight or obese were randomized into either a six-week home-based high-intensity interval training (HIIT, n = 6, 26.6 ± 8.9 years, 37.4 ± 4.9% body fat) group or a six-week moderate-intensity walking (Walk, n = 6, 22.5 ± 3.7 years, 40.2 ± 4.1% body fat) group. Main Measures: Pre- and post-intervention, participants completed the following: 1) Air displacement plethysmography (body fat analysis); 2) Aerobic fitness test (VO₂max); 3) Beck depression inventory-II (BDI-II), state-trait anxiety inventory (STAI-S, STAI-T), three-factor eating questionnaire (TFEQ); and 4) Cognitive performance test battery with functional near-infrared spectroscopy (fNIRS) of the prefrontal cortex. A two-factor repeated measures analysis
of variance (ANOVA) was used to measure each variable of interest. **Results:** No changes in body fat or VO$_2$peak were observed in either group from pre- to post-intervention. No within or between group differences were observed for performance on cognitive tests assessing cognitive interference, processing speed, inhibitory control, or executive function. A significant interaction was observed for episodic memory from pre- to post-intervention suggesting that the walk group (58.7 ± 7.4 to 73.7 ± 2.1), but not HIIT group (62.5 ± 15.5 to 63.3 ± 12.5), improved significantly following the six-week intervention. A significant improvement from pre- to post-intervention in BDI-II was observed in both the HIIT group (12.7 ± 4.3 to 6.0 ± 4.8) and walk group (17.5 ± 10.2 to 9.8 ± 9.0). Similarly, a significant improvement in STAI-S and STAI-T was observed from pre- to post-intervention in the HIIT group (STAI-S: 39.7 ± 8.6 to 28.7 ± 3.1, STAI-T: 45.8 ± 7.7 to 36.8 ± 5.0) and walk group (STAI-S: 37.0 ± 11.3 to 37.0 ± 11.3, STAI-T: 49.2 ± 14.8 to 41.8 ± 10.9). **Conclusion:** Findings from the present study indicate that six-weeks of home-based HIIT did not contribute to cognitive improvements across any cognitive domains assessed. Six-weeks of community-based walking contributed to cognitive improvements only in episodic memory. Both groups saw significant improvements in depression (as assessed with BDI-II) and both state- and trait- anxiety (as assessed with STAI). These results suggest that women characterized as overweight or obese may primarily yield mood but not cognitive-related benefits in response to six-weeks of aerobic exercise at either a high- or moderate-intensity level. Additional research is warranted to explore whether home-based exercise interventions of durations longer than six-weeks promote cognitive improvements.
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SYMBOLS/ABBREVIATIONS

>: greater than
≥: greater than or equal to
<: less than
≤: less than or equal to
±: plus or minus
ADP: air displacement plethysmography
BBB: blood brain barrier
BDI-II: beck depression inventory-II
BDNF: brain derived neurotrophic factor
BF: body fat
BMI: body mass index
CBF: cerebral blood flow
CLGI: chronic low-grade inflammation
cm = centimeter
CNS: central nervous system
CRP: c-reactive protein
CVR: cerebrovascular reactivity
DCCS: dimensional change card sort
eNOS: endothelial nitric oxide synthase
FFAs: free fatty acids
fNIRS: functional near infrared spectroscopy
Hbdiff: hemoglobin difference
HC: hip circumference
HIIT: high intensity interval training
HHb: deoxyhemoglobin
HRmax: maximal heart rate
Il-1β: interleukin-1β
IL-6: interleukin-6
IL-10 interleukin-10
Km: kilometer
LPFC: left prefrontal cortex
LPS: lipopolysaccharide
MICT: moderate intensity continuous training
MRI: magnetic resonance imaging
NIH: national institute of health
NIHTB: national institute of health toolbox
NO: nitric oxide
O$_2$Hb: oxyhemoglobin
PAR-Q+: physical activity readiness questionnaire
PC: pattern comparison
PFC: prefrontal cortex
PGC-1α: peroxisome proliferator-activated receptor gamma coactivator 1-α
PSM: picture sequence memory
RPE: rating of perceived exertion
RPFC: right prefrontal cortex
SCWT: stroop color word test
SD = standard deviation
SMD = standard mean difference
STAI-S: state-trait anxiety inventory-state
STAI-T: state-trait anxiety inventory-trait
TFEQ: three factor eating questionnaire
tHB: total hemoglobin
TNF-α: tumor necrosis factor- α
VEGF-A: vascular endothelial growth factor-A
VO$_2$max: maximal oxygen consumption
VO$_2$peak: peak oxygen consumption
WC: waist circumference
WHR: waist-hip ratio
μmol: micromoles
CHAPTER 1: INTRODUCTION

Obesity is defined as an excessive accumulation of body fat but described as any body mass index (BMI) value of ≥ 30 kg/m² (1). The prevalence of obesity continues to rise with nearly 50% of Americans projected to be obese by the year 2030 (2). The health consequences of this epidemic are tremendous, with obesity contributing to a significant number of preventable deaths in the United States. Obesity is related to a wide-range of health consequences and is a well-established risk factor for neurological and cognitive disorders (3,4). Research suggests that obesity is associated with an increased risk for the development of cognitive impairment and dementia. Obese individuals display poorer cognitive performance than their lean counterparts throughout the lifespan (5–7). These deficits have been observed across a variety of cognitive domains including: executive function (8), learning and memory (9,10), complex attention (11), and perceptual-motor function (11). Importantly, poor cognitive performance is related to increased risk of all-cause mortality (12), reduced quality of life (13), and poor academic performance (14). Further, impairments in cognition may predict the onset of psychiatric disorders (15) and poor adherence to/compliance with various clinical treatments (16,17). Interestingly, the relationship between obesity and cognition may be bi-directional, whereby the cognitive-deficits associated with obesity may further perpetuate weight gain (18), underscoring the importance of preserving cognitive function in an obese population.

Although certain comorbidities of obesity (cardiovascular disease, type II diabetes, sleep apnea) (19–21) are associated with cognitive dysfunction, evidence suggests that an independent relationship exists between obesity and cognitive performance (22). For example, no significant differences were observed in cognitive performance between obese individuals with co-morbid medical conditions (hypertension, type II diabetes, obstructive sleep apnea) and obese individuals without comorbidities (8). In addition, obese individuals
screened for neurological disorders, head injuries, cardiovascular disease, and diabetes showed poorer memory performance than their lean counterparts across adult age groups (age 21-82 years) (9). This independent relationship between BMI and cognition may be explained by structural and functional brain abnormalities in obese individuals. For example, Pannacciulli et al., 2006 used magnetic resonance imaging (MRI) to compare gray matter density across different brain regions in obese and lean young adults. In the obese group, the authors observed significantly lower gray matter density in specific brain regions (cerebellum, post-central gyrus, putamen, medial frontal gyrus, anterior insula) that help regulate inhibition, reward-driven behaviors, and decision making (23). In an 8-year longitudinal study, Cherbuin et al. 2015 note that BMI was not only negatively associated with left and right hippocampal volume in older adults (aged 60-64 years) at the initial assessment, but individuals with a higher BMI showed greater atrophy throughout the follow-up period (24). Importantly, studies have shown a relationship between the volume of certain brain areas and cognitive performance. For example, results from a 2014 meta-analysis suggest a significant direct relationship between prefrontal cortex volume and executive function \((d = .31)\) in healthy adults (25). In addition, Pohlack et al., 2014 found a significant association between hippocampal volume and declarative memory performance in healthy young adult males (26).

While the exact mechanisms causing the functional and structural brain abnormalities in obese individuals remain to be fully understood, several mechanisms have been proposed. One commonly proposed mechanism is the role of chronic systemic inflammation on cognitive performance. Obesity is known to provoke chronic low-grade inflammation as adipose tissue produces and secretes various inflammatory cytokines. Certain cytokines (TNF-α, IL-1β) that are secreted into the blood can cross the blood-brain barrier, invoke neuroinflammation, and disrupt neural circuits involved in cognitive processes (27–29). In
addition to systemic inflammation, cerebrovascular abnormalities are another commonly proposed causative factor to explain the role of obesity in cognitive dysfunction (30). For example, cerebral arterial stiffness, endothelial dysfunction, and reduced small vessel density may cause hypoperfusion of the prefrontal cortex (30). The prefrontal cortex is the brain area central to cognitive processes, thus hypoperfusion to this area is detrimental to normal cognitive functioning (31). Another mechanism that may contribute to obesity-induced cognitive deficits is related to levels of brain-derived neurotrophic factor (BDNF), a protein crucial for neurogenesis and neuronal plasticity (32). Interestingly, decreased levels of circulating BDNF have been observed in adults with obesity compared to their lean counterparts (33). Further, researchers report that low circulating BDNF may mediate the relationship between central adiposity and poor cognitive performance, suggesting a potentially causal role of BDNF in poor cognitive outcomes in individuals with obesity (32). Additional research is needed to confirm and better understand the relative contribution of each mechanism to cognitive dysfunction, as well as explore other potential mechanisms that may impair cognition in obese individuals.

As the prevalence of obesity continues to grow, it is increasingly important to identify strategies to prevent or reverse the cognitive-related deficits associated with this condition. One proposed strategy is to encourage individuals with obesity to participate in regular aerobic exercise (34). The majority of studies examining the effect of aerobic exercise on cognition focus on either adolescent or older adult populations. It is important to note, however, that gray matter shrinkage begins in adolescence and age-related cognitive decline may begin in individuals as early as their late twenties (35). Thus, aerobic exercise may yield cognitive benefits for individuals across the lifespan. For example, Mekari et al., 2020 report a significant improvement in executive function following a 6-week high intensity interval training (HIIT) intervention in healthy young adults (32 ± 8 years) despite no significant
change in BMI or aerobic fitness (36). The effectiveness of aerobic exercise training on
cognition has also been evidenced in clinical populations. For example, results from a 2017
meta-analysis suggest a significant positive effect (SMD = .26, 95% CI = .11, .41) of aerobic
(but not resistance) exercise training on cognition across populations with a variety of
diseases (Alzheimer’s, cancer, mild cognitive impairment) (37). To our knowledge, only
three studies have examined the effectiveness of aerobic exercise on cognition in adults
classified as overweight or obese (38–40). Drigny et al. 2014 reported significant
improvements in cognitive function following a 4-month HIIT program in adults with obesity
(age = 49 ± 8 years) (38). Similarly, Inoue et al. 2020 report similar improvements in
executive function after 6-weeks of both moderate-intensity continuous training (MICT) and
HIIT in men with obesity (age = 30 ± 5 years) (39). Conversely, in an unpublished
dissertation, Lehr et al., 2018 observed no improvements in cognitive function following a
12-week HIIT program in post-menopausal women with obesity (age = 67 ± 6 years) which
may be explained, in part, by low estrogen levels (40). For example, long-term estrogen-
deprivation has been shown to blunt the exercise-induced increase in hippocampal BDNF
observed in a female rodent model (41). Thus, evidence from these studies suggests that
aerobic exercise may improve cognition in young and middle-aged adults with obesity. The
limited number of studies, however, warrants the need for further exploration. Further, it is
unclear whether changes in participant characteristics throughout the intervention may play a
role in cognitive changes. For example, two of the aforementioned studies report no change
in percent body fat (BF%) or BMI (39,40) but significant improvements in indicators of
aerobic fitness including VO₂peak (40) and maximal aerobic velocity (39). In contrast,
Drigny et al., 2014 report a significant change in BMI, total fat mass and VO₂peak (38).
Thus, the role of weight loss and aerobic fitness in terms of cognitive improvements is
ambiguous. In a study comparing a weight loss intervention (diet) with an exercise
intervention, older adults with obesity demonstrated similar cognitive improvements in
response to both interventions. Interestingly, authors report that combined weight loss and exercise provided similar cognitive benefits to exercise alone, suggesting that weight loss may not be necessary to prompt cognitive improvements (42). In a meta-analysis examining the effect of dietary and surgical weight loss interventions on cognition in adults with elevated BMIs ($\geq 25$ kg/m$^2$), weight loss was associated with improvements in cognition in obese, but not overweight individuals (43). Thus, the capacity that weight loss and aerobic fitness play in improving cognition remains unclear.

To determine the ideal exercise prescription to elicit cognitive benefits in obese populations, the optimal exercise intensity must be identified. To our knowledge, only two studies have examined whether cognitive improvements occur in an intensity-dependent manner in overweight and obese individuals (39,44); however, the results from those studies differed. For example, Inoue et al., (2020) reported that 6-weeks of moderate- and high-intensity exercise interventions yielded similar cognitive benefits in sedentary men with obesity (39). In contrast, Oliveira et al., 2021 observed a significant improvement in cognition after 12-weeks of HIIT but not MICT in sedentary men and women classified as overweight (44). Previous investigations suggest that exercise intensity plays an important role in improving cognition in other populations. For example, studies in healthy individuals suggest that high-intensity exercise may be more effective than moderate-intensity exercise for improving cognitive outcomes (36,45) while meta-analytic evidence suggests that low- to moderate-intensity exercise may be more beneficial in clinical populations (37). Thus, additional investigations are needed to determine whether high-intensity and moderate-intensity exercise yield different cognitive improvements in adults with obesity.

In addition, all studies examining the relationship between aerobic exercise and cognition in individuals with obesity have been performed in laboratory-based settings. Laboratory settings provide individuals with optimal exercise conditions and specialized
equipment, thus, results from these studies may not be reproducible when practiced in real-world settings. The use of home-based exercise protocols may be more pragmatic and reflective of adaptations occurring in response to exercise programs performed outside of research study settings. Further, home-based exercise programs may mitigate several barriers to exercise engagement in individuals with obesity including: embarrassment due to negative self-image, lack of access to exercise facilities, and the cost of gym membership (46). Further, the COVID-19 pandemic and resultant need for social-distancing has highlighted the importance of home-based exercise programs. Thus, studies examining the effect of home-based aerobic exercise on cognition in individuals classified as overweight or obese are needed.

Limited evidence suggests that aerobic exercise may improve cognition in obese individuals; however, several gaps in the literature remain. For example, the exact mechanisms that explain aerobic exercise-induced cognitive improvements are not fully understood. In addition, the ideal exercise intensity for obese individuals seeking to gain cognitive benefits remains to be determined. Further, the effectiveness of home-based aerobic exercise interventions on cognition in obese individuals is yet to be explored. Thus, studies addressing these literature gaps are extremely important as the prevalence of obesity continues to increase.

**Problem Statement**

Results from previous research suggest that aerobic exercise as a beneficial effect on cognition in both clinical and healthy populations. A gap remains in the literature regarding the effectiveness of moderate-intensity compared to high-intensity aerobic exercise on cognitive parameters in individuals classified as overweight or obese. In addition, the specific adaptations related to cognitive improvements (i.e., increased brain blood flow, tissue oxygenation, neurogenesis) are currently unknown. Exploratory analyses are needed to
examine whether participants experience improvements in cognitive function, and possible mechanisms for these changes, including changes in aerobic fitness parameters (e.g., increased VO$_2$max), changes in body composition (e.g., reduced body fat), and changes in prefrontal cortex (PFC) oxygenation. In addition, an examination of whether cognitive changes are linked to self-regulation of eating behaviors is warranted.

**Purpose of the Study**

The purposes of the present study were to: 1. Determine if six weeks of aerobic exercise training improves cognitive function among overweight women or women with obesity; 2. Identify if changes in cognition are dependent upon exercise intensity (moderate vs. high); 3. Explore whether cognitive changes after six weeks of aerobic exercise training are associated with any changes found in aerobic fitness, body composition, and/or PFC activation using functional Near Infrared Spectroscopy (fNIRS) during cognitive testing.

**Limitations**

The following limitations were identified in this study:

1. The study sample consisted of women classified as overweight or obese. Therefore, the results of this study may not apply to men or individuals who are not overweight or obese by BMI or have other chronic disease.

2. This study is a randomized control trial design with no non-exercise control group. Thus, results can only be compared between moderate- and high-intensity conditions and from pre- to post-intervention.

3. This study has no planned follow-up after the exercise intervention and, therefore, the long-term changes in cognition cannot be investigated.

**Assumptions**
The following assumptions were identified in this study:

1. All participants completed all exercise sessions following the prescribed intensity (moderate vs. high).

2. Participants did not modify their diet or physical activity levels (outside of the exercise intervention) from pre- to post-intervention.

3. Participants did not perform vigorous exercise for 24-hours, ingest caffeine for 4-hours, or ingest alcohol for 12-hours prior to the pre- and post-intervention visits to the laboratory for testing. In addition, subjects arrived to the lab well-hydrated and after consuming a small meal 2-3 hours prior to the visit.

4. All participants performed at their best effort throughout the study duration.

**Hypotheses**

The following hypotheses were tested in this study:

**Hypothesis 1:** Participants classified as overweight or obese will have improvements in one or more domains of cognitive function (executive function, episodic memory, processing speed) following 6-weeks of moderate- and high-intensity aerobic exercise.

*It has been reported that 6-weeks of moderate intensity continuous training and 6-weeks of high intensity interval training can improve cognitive function in obese men* (39).

**Hypothesis 2:** Six-weeks of home-HIIT will yield significantly greater improvements in aerobic fitness (VO$_2$max) than will moderate-intensity continuous training (walking).

*It has been reported that HIIT training yields greater improvements in VO$_2$max than moderate intensity training in obese men* (47).
Hypothesis 3: Six-weeks of home-HIIT and six weeks of moderate-intensity continuous training (walking) will yield greater prefrontal cortex activation when compared to pre-intervention values.

*It has been reported that participation in an exercise training program leads to improved prefrontal cortex activation during cognitive tasks in overweight and obese adolescents and young adults* (48).

**Scope of study**

Twelve female participants with overweight (BMI = 25 – 29.9) or obesity (BMI ≥ 30 kg/m²) will complete 6-weeks of home-based HIIT (n = 6) or home-based moderate-intensity continuous exercise (n = 6). Cognitive performance (using the NIH toolbox), aerobic fitness (VO₂max), and PFC activation (using fNIRS) will be assessed pre- and post-intervention.

**Significance of study**

The significance of the present study stems from the need to investigate whether home-based aerobic exercise interventions lead to cognitive improvements in adults with obesity. Previous research has established that home-based exercise programs may remove certain barriers to exercise (cost, transportation, self-esteem) (49,50). Therefore, an understanding of whether or not these home-based interventions yield cognitive benefits is needed prior to recommending similar exercise interventions to obese individuals in an effort to improve cognition. Further, if there are cognitive improvements, it is currently unknown whether moderate vs. high intensity exercise will yield greater or equal positive cognitive changes in this population. Findings from this study may contribute to the growing evidence implicating aerobic exercise as a tool to prevent or reduce cognitive dysfunction among clinical populations. Further, results from this study may allow for a broader understanding regarding physiological mechanisms related to aerobic exercise and cognitive improvements.
Definitions

Attention: The ability to selectively focus on relevant stimuli

Brain-derived Neurotrophic Factor (BDNF): A neurotransmitter that supports neurogenesis, neuronal growth, and neuronal survival

Cognitive Flexibility: The ability to selectively switch between mental tasks

Declarative Memory: The ability to recall factual information

Deoxyhemoglobin: The concentration of hemoglobin without oxygen

Dimensional Change Card Sort Test: Cognitive test to assess cognitive flexibility

Episodic Memory: The ability to recall past autobiographical events

Executive Function: Set of cognitive skills that are necessary for the self-regulation of behavior

Flanker Inhibitory Control and Attention Test: Cognitive test to assess executive function

Functional Near Infrared Spectroscopy (fNIRS): Non-invasive brain imaging technique that measures brain activation via hemodynamic changes

Hemoglobin Difference: The concentration of oxyhemoglobin minus deoxyhemoglobin

Inhibitory Control: The ability to suppress the response to goal-irrelevant stimuli

Memory: The ability to recall information

Neurogenesis: The formation of new neurons

Neuroinflammation: Inflammation of the central nervous system
**Oxyhemoglobin**: The concentration of hemoglobin with oxygen

**Pattern Comparison Test**: Cognitive test to assess processing speed

**Picture Sequence Memory Test**: Cognitive test to assess episodic memory

**Prefrontal Cortex**: A region of the frontal lobe implicated in executive function and high-level cognitive control

**Processing Speed**: Time required to perceive and/or respond to stimuli

**Stroop Color Word Test**: Cognitive test used to assess inhibitory control

**Total Hemoglobin**: Total hemoglobin concentration

**Working Memory**: Capacity to temporarily store and use information

**VO\textsubscript{2max}**: The maximum amount of oxygen an individual can take in and use during maximal exercise
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40. Lehr L. The relation between metabolic complications and cognitive functions in obese post-menopausal women: the effect of high intensity interval training. 2018;


CHAPTER 2: LITERATURE REVIEW

The literature review presented in this chapter is planned for submission to the journal of Mental Health and Physical Activity. Authors will be Kelsey Bourbeau, Christine Mermier, Micah Zuhl, Ann Gibson, and Len Kravitz.

Abstract

Obesity is associated with cognitive deficits. With the increasing rates of obesity and negative consequences of cognitive impairments, an understanding of interventions that may reduce cognitive impairment is of utmost importance. One intervention that has been proposed to mitigate cognitive deficits in individuals with obesity is the use of aerobic exercise. Despite the evidence that aerobic exercise may improve cognition in individuals with obesity, the exact mechanisms responsible for the cognitive improvements remain to be elucidated. This review explores three possible mechanisms that contribute to aerobic exercise-induced cognitive improvements in individuals with obesity including: 1) Improved cerebral blood flow, 2) Reduced neuroinflammation, and 3) Increased neurogenesis. Future directions will also be discussed.
Introduction

Impairments in cognitive function are associated with a wide variety of consequences. For example, poor cognitive performance is related to an increased risk of all-cause mortality in adults (1), reduced quality of life in a geriatric population (2), and poor academic performance in middle-school students (3). Impaired cognition may also predict future onset of psychiatric disorders (4) and adherence to clinical treatments (pharmacotherapy, cognitive behavioral therapy) (5,6). Evidence suggests a relationship between obesity (body mass index (BMI) ≥ 30 kg/m²) and deficits in cognitive function, independent of age, sex, or comorbidities of obesity (7,8). Specifically, individuals with obesity have exhibited deficits across several cognitive domains including: executive function (9), learning and memory (7,10), complex attention (11), and perceptual-motor function (11). Obesity is related to structural and functional brain changes that may explain the relationship between weight status and cognition. For example, lower gray matter density has been observed in individuals with obesity in brain regions (cerebellum, post-central gyrus, putamen, frontal gyrus, anterior insula) that help regulate inhibition, reward-driven behaviors, and decision making (12).

In 2016, nearly 13% of adults worldwide were classified as obese, with rates of obesity continuing to rise (13). The consequences of cognitive impairment compounded with the increasing prevalence of obesity warrants the exploration of treatments aimed to mitigate or prevent negative cognitive consequences associated with obesity. The use of aerobic exercise has emerged as a potential method to improve cognition in individuals with obesity. Aerobic exercise is defined by the American College of Sports Medicine as exercise that relies on large muscle groups and is maintained continuously and rhythmic in nature (14). Improvements in executive function have been observed after six-weeks of both moderate-intensity continuous training (MICT) (n=10) and high-intensity interval training (HIIT) (n=10) in men with obesity (mean age = 30 years, mean BMI = 34.4 kg/m²) (15). Similarly, significant improvements in short-term and verbal memory, attention, and processing speed have been reported in adults with obesity (N = 6, mean age = 49 years, mean BMI = 29.7
kg/m$^2$) that participated in a 4-month intervention (90 mins, 3x/week), consisting of HIIT (2 sessions/week), MICT (1 session/week), and resistance training (2 sessions/week) (16). Similar results have been observed in larger randomized controlled trials, comprised of both normal and overweight adults. For example, Masley et al., 2009 report cognitive improvements following a 10-week aerobic exercise intervention (30-45 mins, 5-6x/week) in a sample comprised of both normal and overweight subjects (n = 71, mean age = 47 years, mean BMI = 29.6 kg/m$^2$). Specifically, the researchers report that subjects participating in the exercise intervention showed improved cognitive flexibility compared to a control group (n = 20, mean age = 45 years, mean BMI = 27.5 kg/m$^2$) (17).

In addition, Stern et al., 2019 saw improvements in executive function among overweight adults after a 24-week MICT intervention (n = 66, mean age = 42 years, mean BMI = 27.08 kg/m$^2$, 30-40 mins, 4x/week) compared to a stretching control group (n = 66, mean age = 39 years, mean BMI = 26.33 kg/m$^2$) (18). The beneficial role of aerobic exercise (acute and/or chronic) in facilitation of cognitive improvements is likely due to a variety of mechanisms, represented in Figure 1, including: 1) improved cerebral blood flow (CBF), 2) reduced neuroinflammation, and 3) increased neurogenesis. These mechanisms are not specific to individuals with obesity; however, each may be uniquely impacted by obesity-related pathologies, thereby underscoring the importance of aerobic exercise in this population. Thus, the purpose of this narrative review is to provide a comprehensive examination of the proposed mechanisms that explain the benefits of exercise on cognition among individuals with obesity. Future directions related to the use of aerobic exercise for improving cognition in individuals with obesity will also be discussed.
IL-6, Interleukin-6; IL-10, Interleukin-10; IL-1β, Interleukin-1β; TNF-α, Tumor Necrosis Factor-α; FFAs, Free Fatty Acids; eNOS, Endothelial Nitric Oxide Synthase; NO, Nitric Oxide; VEGF-A, Vascular Endothelial Growth Factor-A; BDNF, Brain-Derived Neurotrophic Factor. Created with BioRender.com.

**Regulation of Cerebral Blood Flow**

One mechanism that may explain the beneficial effects of aerobic exercise training on cognition in adults with obesity is the regulation of CBF. Cognitive tasks increase the metabolic demand of cerebral tissue, resulting in a regional increase in CBF. Reduced CBF in response to cognitive tasks is associated with poorer cognitive outcomes in adults (19–21), and adults with obesity display attenuated regional CBF compared to their lean counterparts (22–24). Importantly, Knight et al., 2021 note that the association between obesity and reduced gray matter CBF was not observed in individuals that report high levels of physical activity, suggesting a protective role of exercise in preserving adequate CBF (24). Aerobic exercise interventions may increase resting CBF
to the frontal lobe and improve executive function in sedentary adults with obesity, with evidence that this occurs independent of weight loss (25).

Enhanced cerebrovascular reactivity (CVR) and increased cerebrovascular angiogenesis may explain exercise-induced improvements in CBF. Cerebrovascular reactivity is the ability of cerebrovasculature to respond to vasoactive stimuli, causing either a dilatory or constrictor response. As the metabolic demand of the brain increases (as with neural activity), a well-controlled CVR response prompts local vasodilation to increase regional CBF, ensuring appropriate delivery of oxygen, glucose, and other nutrients. Central to this process are cerebrovascular endothelial cells which sense vasodilatory stimuli and increase endothelial nitric oxide synthase (eNOS) activity to produce nitric oxide (NO), a potent vasodilator (26,27). Endothelial dysfunction is a common consequence of obesity which may explain impaired CBF regulation in this population (28). Acutely, aerobic exercise increases vascular shear stress which is a vasoactive stimulus. When shear stress is sensed repeatedly, as with moderate to vigorous aerobic exercise training, the endothelial cells adapt by increasing eNOS expression and phosphorylation, likely explaining CVR improvements (29–31). Aerobic exercise training may further reduce endothelial dysfunction by improving vascular insulin sensitivity (28). Insulin plays an important vasodilatory role as it activates eNOS to produce NO in insulin sensitive states. In adults with obesity, blunted insulin-induced enhancement of vasodilation has been observed peripherally (32). Rodents with obesity-induced insulin resistance fed a high fat diet showed hypoperfusion of hippocampal vasculature and reduced eNOS which was associated with cognitive deficits (33). Evidence suggests that aerobic exercise training may reverse impaired insulin signaling in the cerebrovasculature of rodents with genetically-induced obesity (34).

Aerobic exercise training may also improve CBF through promoting cerebral angiogenesis. Angiogenesis is a process that involves the formation of new blood vessels, and evidence in rodents suggests that improved CBF to ischemic brain regions is correlated with cerebral angiogenesis (35). The angiogenic stimulus of aerobic exercise training may be especially important for older adults...
with obesity as aging may aggravate obesity-induced cerebral capillary rarefaction (36). Although the mechanisms remain to be fully elucidated, aerobic exercise may stimulate angiogenesis through a lactate-dependent pathway. During high-intensity aerobic exercise, lactate that is released into circulation from the skeletal muscle can cross the blood brain barrier (BBB) (37,38). In rodents, lactate administration to cerebral tissue upregulates vascular endothelial growth factor-A (VEGF-A), a key regulator of angiogenesis (39–41). Human studies examining the role of lactate in cerebral angiogenesis remain to be conducted. To summarize, obesity may lead to reduced CBF as a result of impaired CVR (via endothelial dysfunction) and capillary rarefaction. As displayed in figure 1, aerobic exercise may improve endothelial dysfunction through increases in shear stress during exercise and improved insulin sensitivity. In addition, aerobic exercise may promote cerebral angiogenesis through lactate-dependent increases in VEGF-A.

**Neuroinflammation**

Neuroinflammation can cause neuronal damage and impair neurogenesis, likely contributing to cognitive impairments (42). Individuals with obesity display greater levels of neuroinflammation than lean individuals, and lower levels of neuroinflammation are positively associated with better cognition (43). While this has not yet been examined in humans, results from studies in diet-induced obese rodents indicate that aerobic exercise training may reduce neuroinflammation, contributing to cognitive improvements (44,45). This attenuation in neuroinflammation after aerobic exercise training is likely due reduced systemic inflammation (46). Chronic low-grade inflammation (CLGI) is common in obesity where individuals have chronically elevated levels of systemic inflammation (47,48). Individuals with CLGI have higher levels of circulating pro-inflammatory stimuli including interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), lipopolysaccharide (LPS), and C-reactive protein (CRP) (49). These pro-inflammatory molecules may enter the CNS at areas with a compromised BBB, resulting in pro-inflammatory microglial activation (50). Activated microglia are central modulators of neuroinflammation, as they secrete pro-inflammatory molecules which play a
disruptive role on existing neurons and may decrease neurogenesis (51). Interestingly, evidence suggests that activated microglia play a role in obesity-related cognitive decline (52).

Aerobic exercise inhibits microglial activation through an increase in anti-inflammatory molecules and a decrease in pro-inflammatory molecules (53). For example, IL-6 is a pleiotropic cytokine released from skeletal muscle during acute bouts of aerobic exercise (54). Although initially classified as pro-inflammatory, muscle-derived IL-6 exhibits anti-inflammatory properties through stimulating IL-10 production (55), an anti-inflammatory cytokine that decreases microglial cytokine production (56). Muscle-derived IL-6 may also downregulate the production of circulating pro-inflammatory cytokines TNF-α and IL-1β (57,58). In addition to the acute effects of aerobic exercise on cytokine expression, aerobic exercise training alters circulating levels of certain adipokines. For example, increases in adiponectin and decreases in leptin have been observed following high intensity aerobic exercise interventions in individuals with obesity (59). Not only does adiponectin suppress microglial activation (60), it also may play a role in shifting the pro-inflammatory microglial phenotype towards the anti-inflammatory phenotype (61). In contrast to adiponectin, leptin may modulate pro-inflammatory microglial cytokine release (62). Thus, reduced circulating leptin following high intensity aerobic exercise training in individuals with obesity may reduce neuroinflammation by removing the pro-inflammatory stimulus in the microglia. In addition, aerobic exercise may attenuate pro-inflammatory cytokine expression in the CNS through reducing the levels of circulating free fatty acids (FFAs). Elevated levels of plasma FFAs bind to and activate toll-like receptor 4, a transmembrane receptor that, when activated, mediates the upregulation of proinflammatory cascades in the hippocampus (44,63). Aerobic exercise training (12-weeks, 5x/week) has been shown to decrease fasting plasma FFA levels in individuals with obesity (64), likely as a result of enhanced skeletal muscle uptake of FFAs (65).

Aerobic exercise may further attenuate neuroinflammation by modulating adipose tissue characteristics. Obesity is characterized by adipose tissue expansion which leads to local tissue
hypoxia and consequent expression of pro-inflammatory molecules (IL-6, leptin, and macrophage migration inhibitory factor) (66). Interestingly, a significant increase in VEGF-A, was observed following aerobic exercise training in intra-abdominal adipose tissue of genetically-induced obese male Zucker rats possibly attenuating hypoxic conditions via VEGF-A mediated angiogenesis (67). In insulin-resistant men characterized as overweight or obese, short-term (2-weeks) aerobic exercise training yielded significant increases in adipose tissue vascularization despite no change in %BF (68). Thus, aerobic exercise-induced improvements in adipose tissue vasculature may reduce the pro-inflammatory profile of humans with obesity. To summarize, obesity is associated with increased levels of pro-inflammatory cytokines and stimuli which promote neuroinflammation. As displayed in Figure 1, aerobic exercise may reduce neuroinflammation through an increase in muscle-derived IL-6, which promotes the expression of anti-inflammatory molecules (IL-10) and decreases the expression of pro-inflammatory molecules (IL-1β, TNF-α). Further, aerobic exercise can increase circulating levels of adiponectin (anti-inflammatory) and reduce circulating levels of leptin and FFAs (pro-inflammatory). Lastly, evidence suggests that aerobic exercise may increase VEGF-A in adipose tissue, reducing hypoxia-induced pro-inflammatory cytokine expression.

**Neurogenesis**

One commonly reported mechanism by which aerobic exercise improves cognition is the upregulation of brain-derived neurotrophic factor (BDNF) (69). Brain-derived neurotrophic factor is a protein involved in synaptic plasticity, neuronal survival, and formation of new synapses (70). Meta-analytic evidence suggests that aerobic exercise training increases circulating levels of resting BDNF (71). The literature comparing BDNF in lean vs. adults with obesity is inconsistent. Authors from a recent meta-analysis report no differences in resting plasma or serum BDNF in lean vs. adults with obesity but note that methodological differences between studies makes comparison of results difficult (72). Evidence from a cross-sectional study suggests that, when compared to lean men, those that were overweight or obese had lower resting levels of serum BDNF (73). Low levels of serum
BDNF have been related to cognitive deficits in patients with type II diabetes (74) and schizophrenia (75). Serum BDNF levels may mediate the relationship between abdominal adiposity and cognition as low serum BDNF is related to higher waist-hip ratio and poorer executive function (76).

Aerobic exercise-induced increases in BDNF expression likely contributes to cognitive improvements in individuals with obesity. Several mechanisms have been proposed to explain how aerobic exercise promotes BDNF upregulation. One mechanism is related to the exercise-induced myokine, irisin. Irisin is released into circulation from skeletal muscle during exercise as a downstream protein upregulated through the peroxisome proliferator-activated receptor gamma coactivator 1-α (PGC-1α) pathway (77). Researchers speculate that irisin crosses the BBB and triggers signaling pathways that upregulate cerebral BDNF expression (78,79). In addition, aerobic exercise is thought to promote cathepsin B transcription and secretion from the skeletal muscle. Cathepsin B is a myokine that can cross the BBB and promote upregulation of hippocampal BDNF (80). Further, high-intensity exercise-induced lactate secretion into circulation may play a role in BDNF upregulation, as lactate may cross the BBB and upregulate the PGC-1α signaling pathway ultimately promoting BDNF expression (81). As presented in Figure 1, aerobic exercise may prompt the release of irisin, cathepsin B, and lactate into circulation from the skeletal muscle. These molecules may cross the BBB and increase BDNF expression, promoting neurogenesis.

**Exercise-Induced Cognitive Improvements and the Obese State**

Despite evidence that aerobic exercise training can lead to cognitive improvements in an obese population, the exact mechanisms responsible remain to be fully elucidated. In addition, it remains to be determined whether cognitive improvements induced by aerobic exercise predict weight loss, thereby improving the obese state. Researchers have examined, however, whether baseline cognitive performance is related to weight loss following weight loss interventions in adults with obesity. For example, in bariatric surgery patient’s performance on attention, executive function, and working memory tasks assessed 12-weeks post-surgery showed strong, positive associations with decreased
BMI and higher percent total weight lost at the 36-months post-operative timepoint (82). In addition, adults with higher working memory and self-reported inhibition scores lost more weight when following a multidisciplinary weight loss program (83). Taken together, results from these studies offer several assumptions. First, the accumulation of adipose tissue may be the link between cognitive decline that occurs in the obese state. Chronic excess calorie consumption along with other factors (e.g., environmental, socioeconomic, genetics) likely play a role in mediating this relationship. Second, adults with obesity who display better cognitive performance may be more successful in losing weight in response to weight loss interventions. A similar concept has been observed in older adults, where individuals with higher levels of baseline executive function and self-regulation had greater adherence to an exercise program (84). Thus, if exercise improves cognitive function in the obese population, the cognitive benefits may allow individuals to be more successful in attaining a healthy weight status. Although this remains to be explored with exercise in individuals with obesity, a potential explanation is related to dietary self-regulation. Specifically, if aerobic exercise leads to cognitive improvements, and these improvements result in behavioral modification (e.g., reduced overconsumption of calorie-dense foods), aerobic exercise may reduce obesogenic behaviors, ultimately promoting weight loss via better cognitive control and energy balance through exercise-induced energy expenditure (85).

Conclusion

In the present review, we aimed to examine mechanisms that explain the role of aerobic exercise in attenuating obesity-related pathologies that may contribute to cognitive deficits. Three main mechanisms were explored and include 1) improved CBF, 2) reduced neuroinflammation, and 3) increased neurogenesis. Obesity may impair CBF through endothelial dysfunction-related CVR abnormalities and rarefaction of cerebral capillaries (28,36). Aerobic exercise may reduce endothelial dysfunction via shear stress and improved insulin sensitivity (28,31). Further, aerobic exercise may increase cerebral angiogenesis via lactate-dependent VEGF-A upregulation (39). Obesity may induce neuroinflammation through increased levels of circulating pro-inflammatory stimuli that can cross the
BBB and perpetuate CLGI in cerebral tissue (43,50). Aerobic exercise may alleviate the pro-inflammatory profile by reducing levels of circulating pro-inflammatory cytokines (downstream effects of skeletal muscle-derived IL-6), molecules (FFAs), and adipokines (leptin) (55,59,64). In addition, aerobic exercise is believed to increase the anti-inflammatory adipokine, adiponectin, and increase adipose tissue vascularization, preventing hypoxia-induced release of pro-inflammatory cytokines (59,68). In terms of neurogenesis, the literature is inconsistent regarding whether individuals with obesity have lower levels of BDNF. Despite the inconsistencies, aerobic exercise-induced increases in BDNF are believed to contribute to cognitive improvements. Increased BDNF expression may be the result of skeletal muscle-released irisin, cathepsin-B, and lactate which all may cross the BBB and promote BDNF expression (78,80,81).

Elucidating these mechanisms may help researchers understand why certain individuals (e.g., individuals with obesity that do not have CLGI or reduced CBF) do not show cognitive improvements after participating in aerobic exercise interventions. Additional studies are needed to determine whether a predominant mechanistic change (CBF vs. neuroinflammation vs. neurogenesis) contributes to cognitive changes pre- to post-exercise intervention or whether these mechanistic changes occur in a synergistic manner. Understanding these mechanisms may help researchers determine if one mechanism is more relevant to improvements in cognition and whether a specific exercise intensity or duration best targets that/those mechanisms.
References


CHAPTER 3: RESEARCH MANUSCRIPT

This chapter presents a research manuscript, entitled “Cognitive Effects of Home-based High-Intensity Interval Training compared to Moderate-Intensity Walking in Women with Overweight and Obesity”. This manuscript is authored by Kelsey Bourbeau, Terence Moriarty, Leah Borgerding, Micah Zuhl, Ann Gibson, Len Kravitz, and Christine Mermier.

ABSTRACT

Purpose: Overweight and obesity are well-established risk factors for neurological and cognitive impairments. In addition, individuals who are overweight or obese by BMI are at increased risk for anxiety and depression. Aerobic exercise has been proposed as a strategy to prevent or reverse cognitive and mood-related consequences of overweight and obesity. Several gaps in the literature regarding this relationship exist. For example, the ideal exercise intensity for individuals that have high BMI values and are seeking to gain cognitive and mood benefits remains to be determined. In addition, the effectiveness of home-based aerobic exercise interventions on cognition in this population is yet to be explored. Thus, the purpose of the present study was to determine whether six weeks of home-based high-intensity interval training versus six weeks of moderate-intensity walking improves cognition, depression, and anxiety in women that are overweight or obese. Methods: Twelve sedentary women characterized as overweight or obese were randomized into either a six-week home-based high-intensity interval training (HIIT, n = 6, 26.6 ± 8.9 years, 37.4 ± 4.9% body fat) group or a six-week moderate-intensity walking (Walk, n = 6, 22.5 ± 3.7 years, 40.2 ± 4.1% body fat) group. Pre- and post-intervention, participants completed the following: 1) Air displacement plethysmography (body fat analysis); 2) Aerobic fitness test (VO_{2peak}); 3) Beck Depression Inventory-II (BDI-II), State-Trait Anxiety Inventory (STAI-S, STAI-T), Three-Factor Eating Questionnaire (TFEQ); and 4) Cognitive Performance Test Battery with functional near-infrared spectroscopy (fNIRS) of the prefrontal cortex. A two-factor repeated measures analysis of variance (ANOVA) was used to assess each variable of interest. Results: No changes in relative body fat or
VO2peak were observed in either group from pre- to post-intervention. No within- or between-group differences were observed for performance on cognitive tests assessing cognitive interference, processing speed, inhibitory control, or executive function. A significant pre- to post-intervention interaction was observed for episodic memory where the Walk group (58.7 ± 7.4 to 73.7 ± 2.1), but not HIIT group (62.5 ± 15.5 to 63.3 ± 12.5) improved significantly. A significant improvement from pre- to post-intervention in BDI-II was observed in both the HIIT group (12.7 ± 4.3 to 6.0 ± 4.8) and Walk group (17.5 ± 10.2 to 9.8 ± 9.0). Similarly, a significant improvement in STAI-S and STAI-T was observed from pre- to post-intervention in the HIIT group (STAI-S: 39.7 ± 8.6 to 28.7 ± 3.1, STAI-T: 45.8 ± 7.7 to 36.8 ± 5.0) and Walk group (STAI-S: 37.0 ± 11.3 to 37.0 ± 11.3, STAI-T: 49.2 ± 14.8 to 41.8 ± 10.9). **Conclusion:** Findings from the present study indicate that six-weeks of home-based HIIT did not contribute to cognitive improvements across any cognitive domains assessed. Six-weeks of community-based walking contributed to cognitive improvements in only episodic memory. Both groups, however, saw significant improvements in depression (as assessed with BDI-II) and both state- and trait- anxiety (as assessed with STAI) scores. These results suggest that women characterized as overweight or obese by BMI may primarily see mood but not cognitive-related benefits in response to six weeks of aerobic exercise at either a high- or moderate-intensity level. Additional research is warranted to explore whether home-based exercise interventions of durations longer than six weeks promote cognitive improvements.
INTRODUCTION

Overweight and obesity are chronic conditions defined by the World Health Organization (WHO) as “abnormal or excessive fat accumulation that may impair health”. Adults with body mass index (BMI) values $\geq 25 – 29.9 \text{ kg/m}^2$ and $\geq 30 \text{ kg/m}^2$, are classified as overweight and obese, respectively (1). The prevalence of these chronic conditions continues to rise with worldwide obesity rates in adults nearly tripling since 1975 (2). Overweight and obesity are related to a wide variety of health consequences and are well-established risk factors for neurological and cognitive impairments (3–6). When compared to their lean counterparts, individuals with obesity have displayed poorer performance across several cognitive domains including: learning and memory (7,8), executive function (9), and complex attention (10). Importantly, worse cognitive performance is associated with all-cause mortality and reduced quality of life in older adults (11,12), and may predict the onset of psychiatric disorders (13). Further, evidence suggests that cognitive abilities may play a role in healthy lifestyle behaviors. For example, weaker inhibitory control (executive function) may predict increased saturated fat intake in normal and overweight males and females (14).

The relationship between weight status and cognition may, in part, be explained by structural and functional brain abnormalities in individuals with overweight or obesity. Lower gray matter in brain areas related to reward-driven behaviors and decision making has been observed in individuals with obesity when compared to normal weight individuals (15). In addition, individuals with obesity may have attenuated cerebral blood flow during cognitive challenges when compared to normal weight individuals (16,17). The relationship between cognition and obesity is likely bidirectional where obesity may impair certain
cognitive functions and, in turn, these impaired cognitive functions may contribute to excessive caloric intake (18). The increased prevalence of cognitive impairments in overweight and obese populations compared to normal weight counterparts is concerning given the negative impacts associated with each of these disorders independently. Thus, an understanding of interventions that may attenuate obesity-associated cognitive impairments is of great importance.

Aerobic exercise has been proposed as a strategy to prevent or reverse the cognitive consequences associated with overweight and obesity. Several studies report improvements in cognition in overweight or obese individuals following aerobic exercise interventions (19–21). Despite well-established evidence that aerobic exercise may benefit cognition, an ideal aerobic exercise prescription to promote cognitive improvements in this population remains to be elucidated. To our knowledge, only three studies have examined the impact of exercise intensity on cognition in this population with differing results between the studies (22–24). The relationship between aerobic exercise and improved cognition in overweight and obese adults may be related to cerebral blood flow (CBF). Cognitively challenging tasks increase the metabolic demand of cerebral tissue which is met by a regional increase in CBF as a means to increase oxygen delivery (25). Individuals unable to meet the increased metabolic demand (e.g., individuals with obesity), may present with cognitive deficits (26). Thus, one proposed mechanism that may explain how aerobic exercise yields cognitive improvements in overweight or obese adults is related to changes in cerebral oxygenation, specifically the improved ability of the body to deliver adequate oxygen to the prefrontal cortex (PFC). Researchers often use functional near-infrared spectroscopy (fNIRS) to measure cerebral oxygenation and blood flow responses. Using this non-invasive method allows for the
measurement of oxyhemoglobin (O$_2$Hb), deoxyhemoglobin (HHb), and total hemoglobin (tHb). In addition, hemoglobin difference (Hbdiff) can be quantified (O$_2$Hb-HHb) to represent oxygen extraction. Increases in O$_2$Hb are proportional to increases in regional CBF whereby providing a measure of PFC activation (27). To our knowledge, no previous studies have utilized fNIRS to investigate cerebral hemodynamic changes during cognitive tasks following a HIIT compared to MICT exercise intervention in overweight or obese adults.

The lack of agreement in the literature warrants further exploration of whether cognitive improvements occur, and if so whether they occur in an intensity-dependent manner in individuals with BMIs $\geq$26 kg/m$^2$. In addition, the specific mechanisms (e.g., change in aerobic fitness, body fat, PFC activation) responsible for potential cognitive changes remain to be determined. Additionally, previous studies examining aerobic exercise-induced cognitive changes in overweight and obese individuals have largely been performed in laboratory-based or supervised settings. While valuable, these settings provide individuals with specialized equipment and optimal exercise conditions which may not be reproduced in real-world settings. Thus, the purpose of the present study is to: 1) Determine whether a 6-week home- or community-based aerobic exercise intervention impacts cognition in overweight or obese women, 2) Determine whether cognition is impacted differently by HIIT vs. MICT, 3) Explore whether significant cognitive changes are associated with changes in aerobic fitness, body composition, or prefrontal cortex activation.

METHODS

Participants

Twelve sedentary women categorized as overweight or obese (BMI $\geq$25 kg/m$^2$) between the ages of 18-45 were recruited for the present study. Participants were excluded if
they had any of the following characteristics: 1) Not classified as sedentary (≥30 min moderate-intensity exercise, ≥3 days/week, ≥3 months), 2) not classified into the ‘poor’ or ‘very poor’ category for body composition as measured by air displacement plethysmography (ADP) (28), 3) history of neurologic brain disease, 4) age <18 or >45 years, 5) diagnosis of metabolic disease other than obesity, 6) currently taking any medications known to impact heart rate or blood pressure or, 7) had any existing physical injury or were under active care of a medical provider for conditions that may interfere with safe participation in the study protocol. Participants gave written consent and completed a health history and physical activity readiness questionnaire (PAR-Q+) prior to participation in the study protocol. After written consent, participants were randomized into either a HIIT group (n = 6) or a Walk group (n = 6). Participant characteristics are displayed in Table 1. The study was approved by the university’s Institutional Review Board (approval #22-0057). All research methods were carried out in accordance with the Declaration of Helsinki.

**Experimental Protocol:**

The study protocol is represented in Figure 1. Participants reported to the Exercise Physiology laboratory at the University of Northern Iowa for two separate visits (baseline and post-intervention). During the baseline visit, written consent was obtained, participants were screened for eligibility and asked to complete the health history and PAR-Q+. After, participants completed a series of questionnaires and anthropometric, cognitive, and aerobic fitness evaluations (see below). After the baseline data collection, participants were randomized into either a community-based moderate-intensity walking group (Walk, n = 6) or a home-based high-intensity interval training group (HIIT, n = 6). Prior to leaving the lab, participants in the Walk and HIIT group were informed of their respective intervention
protocol and the corresponding exercise intensity. Participants were given a GPS-based fitness wrist watch and instructed on how to use the device to monitor exercise intensity. Each participant was asked to complete 18 exercise sessions across 6-weeks (3x/week). Within 72 hours of the final exercise session, participants reported to the lab for the post-intervention data collection which was comprised of the same questionnaires, anthropometric, cognitive, and aerobic fitness procedures performed at the baseline visit.

Figure 1. Outline of study protocol

PAR-Q+ = Physical Activity Readiness Questionnaire, %BF = Percent Body Fat, WC = Waist Circumference, HC = Hip Circumference, BDI-II = Beck Depression Inventory-II, STAI = State-Trait Anxiety Inventory, TFEQ-R18 = Three Factor Eating Questionnaire, fNIRS = Functional Near Infrared Spectroscopy, VO₂max = Maximal Oxygen Uptake, HIIT = High-Intensity Interval Training

**Testing Procedures:**

**Anthropometric Data Collection:**

Anthropometric data were collected at the pre- and post-intervention visits. Participants were instructed to arrive to the laboratory in a hydrated state after abstaining from alcohol for 24 hours, vigorous exercise for 24 hours, and caffeine for 4 hours prior to arrival. To calculate BMI, participant’s barefoot-standing height and weight were recorded using a stadiometer (Shorrboard Measuring Board, Shorr Productions, Olney, MD) and an electronic scale (Seca 770, Seca, Chino, CA), respectively. Next, waist circumference (WC)
and hip circumference (HC) measures were obtained using World Health Organization
standardized sites (29). Afterwards, body fat was estimated using air displacement
plethysmography accounting for measured thoracic gas volume (Bod Pod, Software version
5.4.3, Cosmed, Rome, Italy). Prior to body fat analysis, subjects were instructed to void and
dress in form-fitting clothing. Participants were asked to wear the same or similar clothes in
the Bod Pod at the pre- and post-intervention visits.

*Functional Near Infrared Spectroscopy (fNIRS) Recording:*

A dual wavelength (760 and 850 nm) portable fNIRS device (OctaMon, Artinis
Medical Systems, Elst, The Netherlands) was used to monitor prefrontal cortex (PFC)
oxygenation during cognitive testing. The fNIRS device consisted of a head-worn sensor
probe embedded in a flexible headband with eight optodes and two receivers, with an
interoptode distance of 3.5 cm. The headband was placed in the center of the forehead, 2 cm
above the nasion site with four LED optodes and one receiver placed over the right prefrontal
cortex (RPFC) and over the left prefrontal cortex (LPFC) regions (4x2 configuration, 8 total
channels). Optode placement was based on the modified international electroencephalogram
10-20 system (30). The signal sampling rate was 10 hz. Once the headband was positioned
properly, participants were instructed to remain seated with minimal movement for 2-
minutes, allowing for resting fNIRS values to be obtained. After the 2-minutes of rest,
participants began the series of cognitive tests. The raw data obtained from the fNIRS was
averaged in both PFC regions and analyzed after filtering it with a lowpass 0.1 Hz filter in
order to eliminate any data points with high frequency due to physiological changes (e.g.
heart rate, respiration, and speaking).
Cognitive Testing:

Cognitive testing was performed at the baseline and post-intervention visits. A computerized version of the Stroop Color Word Test (SCWT) and the NIH toolbox (NIHTB) Cognition Battery were employed to assess cognition. All cognitive tests were delivered in a quiet room with 1-2 members of the research team present to limit participant distractions. The SCWT was delivered on a desktop computer and the NIHTB Cognition Battery was delivered via an iPad device. The NIHTB consisted of 4 separate tests including: 1) Pattern comparison test, 2) Picture sequence memory test, 3) Flanker inhibitory control and attention test, and 4) Dimensional change card sort test. Fully corrected T-scores (adjusting for key demographic variables such as age, sex, race/ethnicity, and educational background) allowed for individual domain scores of processing speed, episodic memory, executive function, and attention. A score of 50 indicates performance at the national average for the demographic information of the participant.

Stroop Color Word Test (SCWT)

An internet-based version of the SCWT was used to assess the inhibitory control subdomain of executive function. The test was developed using code provided by PsyToolkit (31,32). The task consisted of 16 warm-up trials followed by 80 test trials. Participants were instructed to respond with the color of a presented stimulus by typing the first letter of the color of the stimulus. The stimuli in this task are written colors (‘Blue’, ‘Green’, ‘Yellow’, ‘Red’). Incongruent stimuli are stimuli that are displayed in a color different from the written stimulus color. Congruent stimuli are stimuli where the color of the word matches the written word itself. Response times were recorded by the computer in milliseconds. Stroop effect
was calculated as average response time for incongruent stimuli minus average response time for congruent stimuli. This test takes 2 minutes to complete.

**NIHTB Pattern Comparison Test (PC)**

The NIHTB Pattern Comparison test was used to assess processing speed. During this test, participants were presented with a series of side-by-side images. Participants were asked to determine, as quickly as possible, whether two images are the same or different. This test takes 90 seconds to complete.

**NIHTB Picture Sequence Memory Test (PSM)**

The NIHTB Picture Sequence Memory test was used to assess episodic memory. During this test, participants were presented with a number of images that were displayed in a fixed sequence on the screen. After all images have been displayed, they move from their fixed position to a random array and participants must move each image to its initial fixed sequence location. This test takes 7 minutes to complete.

**NIHTB Flanker Inhibitory Control and Attention Test (Flanker)**

The NIHTB Flanker inhibitory control and attention test was used to assess executive function and attention. During this task, participants were asked to focus on a central target (an arrow) surrounded by arrows pointing in the same direction (congruent) or opposite direction (incongruent). Participants were instructed to indicate the direction of the central target as quickly and accurately as possible. This task takes approximately 4 minutes to complete.

**NIHTB Dimensional Change Card Sort Test (DCCS)**
The NIHTB Dimensional Change Card Sort test was used to assess the cognitive flexibility subdomain of executive function. During this test, participants sorted images by shape or color depending on a word cue (e.g., “shape” or “color”) located at the top of the screen. This task takes approximately 4 minutes to complete.

**Maximal Exercise Test:**

The women performed a maximal exercise test on a motorized treadmill (Precor, C966, Woodinville, WA) to determine aerobic fitness by measuring maximal oxygen consumption (VO$_2$max). Participants were familiarized with the Borg$_{6-20}$ rating of perceived exertion (RPE) scale prior to beginning the test (33). During the test, gases were sampled and continuously monitored breath-by-breath using a calibrated metabolic cart (Parvomedics, TrueOne 2400, Sandy, Utah). Initial treadmill speed was 5.5 km/hr and increased by .5 km/hr every minute until the participant reached volitional fatigue (24). Heart rate (HR) was continuously monitored during exercise by a Polar heart rate monitor (Polar Electro, model FS1, Lake Success, NY) and the maximal recorded heart rate (HRmax) was used to create individualized target HR ranges for the exercise intervention intensity prescription. To determine that a true VO$_2$max was attained, ≥2 of the following criteria must have been met: 1) maximal respiratory exchange ratio (RER) ≥ 1.10; 2) HRmax within ±10 beats of age-predicted HRmax (208 -.7 x age) (34); 3) RPE ≥17; and 3) increase in oxygen uptake ≤ 150 mL/min between the final two stages of the test. VO$_2$max value was recorded as the highest value using an 11-breath running average.
Questionnaires

**Beck Depression Inventory II:**

Depression symptoms and severity were measured using the 21-item Beck Depression Inventory II (BDI-II) (35). Scores range from 0-63 with higher scores indicating greater depression severity. Raw scores of 0-13 indicate minimal depression, 14-19 indicates mild depression, 20-28 indicates moderate depression, and 29-63 indicates severe depression. The BDI-II is the most widely used, psychometrically valid self-report measure of depression and is recommended for use in obese populations (36).

**State Trait Anxiety Inventory:**

Anxiety levels were measured using the 40-item State Trait Anxiety Inventory (STAI) (37). The STAI consists of two 20-item subscales (state anxiety and trait anxiety). Scores for each subscale can range from 20-80 with higher scores indicating higher levels of anxiety. Raw subscale scores of greater than 30 indicate the presence of anxiety, 31-49 indicate intermediate levels of anxiety, and scores greater than or equal to 50 indicate high levels of anxiety.

**Three Factor Eating Questionnaire-Revised 18 items (TFEQ-R18)**

The TFEQ-R18 is a widely used to assess eating behavior in obese adults. This 18-item questionnaire yields three behavior subscales: cognitive restraint (6 items), uncontrolled eating (9 items), and emotional eating (3 items). Each item is answered on a four-point scale with higher scores indicating more of the behavior (38).
**Exercise Protocols:**

The interventions were completed by participants in an unsupervised location of their choosing. To monitor training compliance and adherence, participants were given a Polar Watch (Polar M200) and used the Polar Beat mobile application on their smart phones. Following each exercise session, heart rate data was automatically uploaded to a cloud storage website (flow.polar.com) which was accessed by a member of the research team to confirm the appropriate exercise intensity was achieved during each session. Participants were contacted a minimum of 1x/week to enquire about progress and discuss any issues with the exercise intervention. Participants were considered ‘adherent’ to the intervention if they participated in at least 16/18 total sessions.

*Walk Group:*

Individuals in the Walk group performed indoor or outdoor walking 3x/week for 6 weeks. After a warm-up (5 minutes of dynamic stretching), participants were instructed to walk at a moderate intensity using RPE (12-13) and advised to achieve 64-76% HRmax, as determined during the baseline VO2max test. During the first week of the intervention, participants continuously walked for 25/min per session and increased by 5 minutes each week, up to a maximum of 50 min/session during week 6.

*High-Intensity Interval Training Group (HIIT):*

Participants in the HIIT group performed a bodyweight interval exercise protocol 3x/week for 6 weeks. Videos were created for each week of the intervention and participants were asked to follow along with the video throughout each exercise session. In addition, participants were provided with a training diary that included detailed information about the
exercises included in the protocol and data collection forms for reporting exercise intensity. Prior to each exercise session, participants were instructed to complete a warm up for 5 minutes (dynamic stretching, easy walking). The HIIT protocol is displayed in Figure 2 and consisted of 6-8 intervals at a 1:1 work:rest ratio. Each work interval was comprised of two different bodyweight exercises performed for 30 seconds each with no rest in between. During each work interval, participants were instructed to exercise at a vigorous intensity by achieving an RPE of 14-17 and a heart rate between 77-95% HRmax as determined during the baseline VO₂max test. During the active rest period, participants stepped slowly in place for one minute. The number of intervals performed during each session progressively increased throughout the intervention with participants completing six intervals during weeks 1-2, increasing by one interval every 2-weeks, up to a maximum of eight intervals. Immediately after each exercise session interval, participants were asked to record their average session RPE in their training diary.
Figure 2. High-Intensity Interval Training Protocol and Progression.
Statistical Analysis

Sample size was determined based on a priori calculation for repeated measures designs with power set to .80 and alpha level of .05 (G*power, Dusseldorf, Germany). The sample size calculation was based on detecting a change in Stroop effect from pre- to post-intervention. A minimum sample size of n=4 was required for each group to reach statistical power (1-β) of .80 established from previous works by (23) who report a large effect size (Cohen’s d = .80) for faster Stroop effect following a HIIT intervention in overweight/obese adults. An independent samples t-test was used to compare age at the pre-intervention time point between HIIT and Walk groups. A two-factor repeated measures analysis of variance (ANOVA) was used to measure each variable of interest (VO₂max, cognitive test performance, %BF, BMI, fNIRS parameters, TFEQ-R18 subscales, BDI-II, STAI). The two-factor repeated measures ANOVA is based on the two independent variables, time (pre, post) and condition (HIIT vs. Walk). If a significant main effect was found, between group difference was assessed using Bonferroni test. Equality of variance was assessed using Mauchly’s test. All data are reported as mean ± standard deviation, unless otherwise noted, with a significance level set to a probability value less than 0.05.

Results

Participant characteristics

Twelve female participants completed the present study. Fourteen participants consented; however, two participants did not complete the study due to unrelated health issues. The remaining 12 participants were randomized into the HIIT (n = 6) or walk (n = 6) group. Participant characteristics separated by group are displayed in Table 1. At the pre-
intervention timepoint, participants in the HIIT group had an average percent body fat of 37.4 ± 4.9% and participants in the Walk group had an average percent body fat of 40.2 ± 4.1% categorizing both groups as ‘very poor’ (28). In the HIIT group, 4 participants had BMIs categorizing them as obese while 2 participants had BMIs categorizing them as overweight. In the Walk group, 5 participants had BMIs categorizing them as obese while 1 participant had a BMI categorizing them as overweight. were categorized as obese and 2 were categorized as overweight. In the Walk group, 5 participants were categorized as obese and 1 was categorized as overweight. Only 3 participants in the HIIT group and 3 participants in the Walk group met the criteria for achieving VO\textsubscript{2}{max}; therefore, VO\textsubscript{2}{peak} is reported. At pre-intervention, participants in the HIIT group had an average VO\textsubscript{2}{peak} of 35.3 ± 3.3 ml/kg/min classifying them as ‘fair’. Participants in the Walk group had an average VO\textsubscript{2}{peak} of 30.9 ± 4.7 ml/kg/min classifying them as ‘poor’. Despite being in different classification categories, no significant difference between groups was observed at the pre-intervention timepoint in VO\textsubscript{2}{peak}. A significant difference (\(p = .011\)) in participants’ age was detected at the pre-intervention time point between the HIIT (26.6 ± 8.9 years) and Walk (22.5 ± 3.7 years) group. No significant between- or within-group differences (\(p > .05\)) were observed from pre- to post-intervention in weight, body mass index (BMI), percent body fat, waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), or peak oxygen uptake (VO\textsubscript{2}{peak}).
Table 1. Participant Characteristics. N = 12.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIIT n = 6</th>
<th>Walk n = 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Pre: 26.6 ± 8.9</td>
<td>Post: -</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>87.2 ± 4.9</td>
<td>88.3 ± 5.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.6 ± 1.6</td>
<td>30.9 ± 1.8</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>37.4 ± 4.9</td>
<td>35.9 ± 4.9</td>
</tr>
<tr>
<td>WC (in)</td>
<td>37.5 ± 3.0</td>
<td>37.4 ± 2.9</td>
</tr>
<tr>
<td>HC (in)</td>
<td>44.3 ± 2.6</td>
<td>44.5 ± 2.7</td>
</tr>
<tr>
<td>WHR</td>
<td>.849 ± .087</td>
<td>.844 ± .086</td>
</tr>
<tr>
<td>VO₂peak (ml/kg/min)</td>
<td>35.3 ± 3.3</td>
<td>35.6 ± 4.2</td>
</tr>
</tbody>
</table>

* = p < .05 compared to HIIT group; HIIT = High-Intensity Interval Training, kg =kilograms, BMI = Body Mass Index, kg/m² = kilograms/meters², WC = Waist Circumference, HC = Hip Circumference, in = inches, WHR = Waist-Hip Ratio, VO₂peak = Peak Oxygen Uptake, ml/kg/min = milliliters/kilograms/minute

**Exercise Session Characteristics**

All participants met adherence criteria (completed at least 16/18 sessions).

Participants in the HIIT group completed an average of 17.7 ± .52 exercise sessions and participants in the Walk group completed an average of 17.0 ± .89 sessions over the 6-week intervention. On average, participants in the HIIT group exercised at an RPE of 15.5 ± .84 and 84.0 ± .04% of their maximal heart rate attained during the VO₂peak test. Participants in the Walk group exercised at an average RPE of 12.5 ± .55 and 66.0 ± .09% of their maximal heart rate attained during the VO₂peak test.

**Cognitive Performance**

Pre- and post-intervention cognitive scores for both groups are displayed in Table 2. For the SCWT, Stroop Effect (incongruent response time – congruent response time) is reported in milliseconds. For the NIHTB tests, t-scores for each test are reported. No significant within- or between-group effects were observed for Stroop Effect, Pattern Comparison, Flanker or Dimensional Change Card Sort (p > .05). A significant improvement
in Picture Sequence Memory performance was observed from pre- to post-intervention in the Walk group but not the HIIT group (F (1,10) = 14.222; p = .007, ηp² = .532) (Figure 3).

Table 2. Cognitive test score summary table for HIIT and Walk at pre- and post-intervention timepoints. N = 12.

<table>
<thead>
<tr>
<th>Cognitive Test</th>
<th>HIIT n = 6 Mean ± SD</th>
<th>Walk n = 6 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Stroop Effect (ms)</td>
<td>121.8 ± 89.1</td>
<td>110.2 ± 122.3</td>
</tr>
<tr>
<td>Pattern Comparison</td>
<td>53.5 ± 15.9</td>
<td>66.5 ± 10.4</td>
</tr>
<tr>
<td>Picture Sequence</td>
<td>62.5 ± 15.5</td>
<td>63.3 ± 12.5</td>
</tr>
<tr>
<td>Flanker</td>
<td>39.7 ± 8.9</td>
<td>42.7 ± 7.9</td>
</tr>
<tr>
<td>Dimensional Change</td>
<td>53.2 ± 12.6</td>
<td>53.2 ± 6.6</td>
</tr>
</tbody>
</table>

# = p < .05 compared to HIIT, * = p < .05 compared to pre-intervention time point; HIIT = High-Intensity Interval Training, SD = Standard Deviation, ms = milliseconds

Figure 3. Picture sequence memory at pre- and post-intervention time points in the HIIT (n = 6) and walk (n = 6) groups. N = 12.

# = p < .05 significantly different from HIIT; * = p < .05 significantly different from pre- to post-intervention; HIIT = High-Intensity Interval Training
**PFC Oxygenation during Cognitive Testing**

Changes in \( \text{O}_2\text{Hb}, \text{tHb}, \text{and Hbdiff} \) responses in the right prefrontal cortex (RPFC) and left prefrontal cortex (LPFC) during cognitive testing at pre- and post-intervention timepoints are displayed in Tables 3 and 4, respectively. No significant within- or between-group differences were observed in any parameter (\( p > .05 \)).

Table 3. Pre- and post-intervention summary table for change in right prefrontal cortex (RPFC) oxyhemoglobin (\( \text{O}_2\text{Hb} \)), total hemoglobin (\( \text{tHb} \)), and hemoglobin difference (\( \text{Hbdiff} \)) responses during cognitive testing. \( N = 12 \).

<table>
<thead>
<tr>
<th>Cognitive Parameter</th>
<th>Timepoint</th>
<th>HIIT n = 6</th>
<th>Walk n = 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>( \text{O}_2\text{Hb} ) Mean ± SD</td>
<td>( \text{tHb} ) Mean ± SD</td>
</tr>
<tr>
<td>SCWT</td>
<td>Pre</td>
<td>0.49±1.07</td>
<td>0.22±1.11</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>0.82±1.76</td>
<td>0.81±1.83</td>
</tr>
<tr>
<td>PC</td>
<td>Pre</td>
<td>1.82±1.61</td>
<td>1.79±1.6</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>1.58±2.17</td>
<td>1.54±2.13</td>
</tr>
<tr>
<td>PSM</td>
<td>Pre</td>
<td>2.39±2.05</td>
<td>2.52±2.66</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>2.04±2.54</td>
<td>1.66±2.19</td>
</tr>
<tr>
<td>Flanker</td>
<td>Pre</td>
<td>2.55±2.19</td>
<td>2.77±2.95</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>2.14±2.91</td>
<td>1.71±2.37</td>
</tr>
<tr>
<td>DCCS</td>
<td>Pre</td>
<td>2.43±2.29</td>
<td>2.98±3.75</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>2.17±3.37</td>
<td>1.98±3.25</td>
</tr>
</tbody>
</table>

RPFC = Right Prefrontal Cortex, \( \mu\text{mol} \) = micromoles, HIIT = High-Intensity Interval Training, SD = Standard Deviation, SCWT = Stroop Color Word Test, PC = Pattern Comparison, PSM = Picture Sequence Memory, DCCS = Dimensional Change Card Sort, \( \text{O}_2\text{Hb} \) = Oxyhemoglobin, \( \text{tHb} \) = total Hemoglobin, Hbdiff = Hemoglobin difference.
Table 4. Pre- and post-intervention summary table for change in right prefrontal cortex (RPFC) oxyhemoglobin (O$_2$Hb), total hemoglobin (tHb), and hemoglobin difference (Hbdiff) responses during cognitive testing. N = 12.

<table>
<thead>
<tr>
<th>LPFC = Left Prefrontal Cortex(µmol)</th>
<th>Cognitive Parameter</th>
<th>Timepoint</th>
<th>HIIT n = 6 mean ± SD</th>
<th>Walk n = 6 mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>O$_2$Hb</td>
<td>tHb</td>
</tr>
<tr>
<td></td>
<td>SCWT</td>
<td>Pre</td>
<td>1.18±1.43</td>
<td>1.39±1.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>0.28±0.67</td>
<td>0.25±0.73</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>Pre</td>
<td>2.17±1.63</td>
<td>2.43±1.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>1.3±0.76</td>
<td>1.42±0.87</td>
</tr>
<tr>
<td></td>
<td>PSM</td>
<td>Pre</td>
<td>3.28±2.1</td>
<td>3.66±2.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>2.27±1.33</td>
<td>2.19±0.94</td>
</tr>
<tr>
<td></td>
<td>Flanker</td>
<td>Pre</td>
<td>3.55±2.59</td>
<td>4.03±3.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>2.55±1.74</td>
<td>2.49±1.09</td>
</tr>
<tr>
<td></td>
<td>DCCS</td>
<td>Pre</td>
<td>3.19±2.05</td>
<td>3.76±2.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>2.44±1.77</td>
<td>2.67±1.42</td>
</tr>
</tbody>
</table>

LPFC = Left Prefrontal Cortex, µmol = micromoles, HIIT = High-Intensity Interval Training, SD = Standard Deviation, SCWT = Stroop Color Word Test, PC = Pattern Comparison, PSM = Picture Sequence Memory, DCCS = Dimensional Change Card Sort, O$_2$Hb = Oxyhemoglobin, tHb = total Hemoglobin, Hbdiff = Hemoglobin difference.

**Questionnaires**

**Depression and Anxiety**

Levels of depression (BDI-II), state anxiety (STAI-S), and trait anxiety (STAI-T) at pre- and post-intervention are displayed in Table 5 and Figures 4-6. A significant within-group effect for time was observed in BDI-II (F (1,10) = 21.204; p = .001, $\eta^2_p = .680$), STAI-S (F (1,10) = 14.016; p = .004, $\eta^2_p = .584$), and STAI-T (F (1,10) = 8.593; p = .015, $\eta^2_p = .462$) scores indicating reduced mood disorder symptoms in both groups following the 6-week intervention. No significant between-group effect was observed suggesting that the HIIT and walk intervention reduced symptoms to a similar degree.
Table 5. Pre- and post-intervention summary table for depression and anxiety questionnaires. N = 12.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIIT (n = 6)</th>
<th>Walk (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre mean ± SD</td>
<td>Post mean ± SD</td>
</tr>
<tr>
<td>BDI-II</td>
<td>12.7 ± 4.3</td>
<td>6.0 ± 4.8**</td>
</tr>
<tr>
<td>STAI-S</td>
<td>39.7 ± 8.6</td>
<td>28.7 ± 3.1**</td>
</tr>
<tr>
<td>STAI-T</td>
<td>45.8 ± 7.7</td>
<td>36.8 ± 5.0*</td>
</tr>
</tbody>
</table>

* = p < .05 compared to pre-intervention, ** = p = <.01 compared to pre-intervention; HIIT = High-Intensity Interval Training, SD = Standard Deviation, BDI-II = Beck Depression Inventory-II, STAI-S = State-Trait Anxiety Inventory-State, STAI-T = State-Trait Anxiety Inventory-Trait

Figure 4. Beck Depression Inventory-II values pre- and post-intervention time points in the HIIT (n = 6) and Walk (n = 6) groups. N = 12.

* = p < .05 significantly different from pre- to post-intervention; BDI-II = Beck Depression Inventory-II, HIIT = High-Intensity Interval Training
Figure 5. State-Trait Anxiety Inventory-State subscale values pre- and post-intervention time points in the HIIT (n = 6) and Walk (n = 6) groups. N = 12.

* = p < .05 significantly different from pre- to post-intervention; STAI-S = State-Trait Anxiety Inventory- State subscale, HIIT = High-Intensity Interval Training

Figure 6. State-Trait Anxiety Inventory-Trait subscale values pre- and post-intervention time points in the HIIT (n = 6) and walk (n = 6) groups. N = 12.

* = p < .05 significantly different from pre- to post-intervention; STAI-T = State-Trait Anxiety Inventory- Trait subscale, HIIT = High-Intensity Interval Training
Three-Factor Eating Questionnaire-R18 (TFEQ-R18)

Scores from the three TFEQ-R18 subscales are displayed in Table 6. No significant within- or between-group effect was observed for uncontrolled eating (TFEQ-UE), or emotional eating (TFEQ-EE). A significant within-group effect was observed for cognitive restraint (TFEQ-CR, Figure 7) \( F(1,10) = 5.141; p = .047, \eta_p^2 = .340 \) suggesting that both exercise interventions improved cognitive restraint to a similar magnitude.

Table 6. Pre- and post-intervention summary table for TFEQ-R18 subscales. \( N = 12 \).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIIT (n = 6)</th>
<th>Walk (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre mean ± SD</td>
<td>Post mean ± SD</td>
</tr>
<tr>
<td>TFEQ-CR</td>
<td>14.8 ± 4.1</td>
<td>17.2 ± 2.1*</td>
</tr>
<tr>
<td>TFEQ-UE</td>
<td>20.8 ± 4.9</td>
<td>19.2 ± 5.3</td>
</tr>
<tr>
<td>TFEQ-EE</td>
<td>9.2 ± 1.8</td>
<td>7.5 ± 1.5</td>
</tr>
</tbody>
</table>

\* = \( p < .05 \) compared to pre-intervention; HIIT = High-Intensity Interval Training, SD = Standard Deviation, TFEQ-CR = Three Factor Eating Questionnaire- Cognitive Restraint, TFEQ-UE = Three Factor Eating Questionnaire-Uncontrolled Eating, TFEQ-EE = Three Factor Eating Questionnaire-Emotional Eating

Figure 7. Three factor eating questionnaire-cognitive restraint subscale values pre- and post-intervention time points in the HIIT (\( n = 6 \)) and Walk (\( n = 6 \)) groups. \( N = 12 \).

\* = \( p < .05 \) significantly different from pre- to post-intervention; TFEQ-CR= Three Factor Eating Questionnaire-Cognitive restraint subscale, HIIT = High-Intensity Interval Training
Discussion

The present study investigated a variety of cognitive tests to assess whether 6-weeks of home-based HIIT or moderate-intensity walking (Walk) impacted various domains of cognition in overweight and obese women. The main findings from the present study indicate that neither the HIIT or Walk intervention yielded significant changes from pre- to post-intervention in the executive function subdomains (inhibitory control or cognitive flexibility). Similarly, no significant differences from pre- to post-intervention were observed in either group in the attention subdomains (selective attention or processing speed). In contrast, a significant improvement in the learning and memory subdomain (episodic memory) was observed in the Walk but not the HIIT group from pre- to post-intervention. Significant improvements in dietary cognitive restraint, depression, and anxiety was observed from pre- to post-intervention in both groups. No significant relationships were observed between change in cognition and change in aerobic fitness (VO$_2$peak, percent body fat, or prefrontal cortex [PFC]) activation.

To our knowledge, this is the third study to examine the impact of a high-intensity exercise intervention compared to a moderate intensity continuous training (MICT) exercise intervention on cognition in overweight or obese adults (23,24). In contrast with the present findings, Inoue et al., 2020 report significant improvements in executive function (inhibitory control) following 6-weeks of both HIIT (n = 10) and MICT (n = 10) in men with obesity (30 ± 5 years, BMI = 34.3 ± 3.6 kg/m$^2$) (24). In addition, Oliveira et al., 2021 note significant improvements in executive function (inhibitory control) following 12-weeks of HIIT and 12-weeks of aerobic exercise at a self-selected intensity but not after 12-weeks of MICT (23). It is important to note that the aforementioned studies report significant increases in aerobic
fitness from pre- to post-intervention across all groups which may explain the contrasting results with the present study. Aerobic fitness has been reported to play a role in the cognitive performance of adults. For example, middle-aged adults (N = 362, 42 ± 9 years, BMI = not reported) with moderate and high levels of aerobic fitness display better inhibitory control than individuals with low levels of aerobic fitness (39). Similarly, evidence in young, lean, adults (N = 72, 20 ± 2 years, BMI = 22.5 ± 2.7 kg/m²) suggests that a higher level of aerobic fitness is associated with increased cognitive flexibility (40). Another potential explanation behind the conflicting results of the present study is the study sample recruited. Specifically, one of the aforementioned studies recruited only male participants (24) while the other study recruited a mixed sex sample (38% male participants) (23). Previous study results suggest that biological sex may impact the cognitive-related gains associated with aerobic exercise. For example, Stern et al., 2019 report that 24-weeks of aerobic exercise (intensity progression from 55% to 80% HRmax, 4x/week) yields significantly greater executive function improvements in men (n = 19, 38 ± 10 years, BMI = 28.1 ± 4.1) compared to women (n = 47, 43 ± 13 years, BMI = 26.6 ± 5.3 kg/m²) (41). In addition, authors from a 2020 meta-analysis report lower exercise-induced cognitive benefits in studies with a higher percentage of female participants (42). While the exact mechanisms remain unknown, these sex differences may be related to hormone-related impacts on cognition. For example, Pletzer et al., 2017 report that attention task performance varies based on hormonal changes associated with the menstrual cycle (43). In addition, in vivo evidence suggests that estrogen may regulate brain-derived neurotrophic factor (BDNF) expression (44). As the present study did not control for menstrual cycle phase across the 6-week intervention, individual
variability related to hormonal fluctuations may have obscured the likelihood of finding a significant difference in cognition.

In contrast to the lack of change observed in executive function subdomains, we observed a significant improvement in episodic memory in the Walk, but not the HIIT group. To our knowledge, no previous studies have compared the effect of HIIT versus MICT on episodic memory in overweight or obese adults. Researchers have, however, performed cross-sectional studies exploring the impact of aerobic training on episodic memory. For example, Lehr et al., 2018, examined the impact of 12-weeks of high-intensity aerobic exercise on episodic memory and executive function in sedentary post-menopausal women with obesity (N=19, 67 ± 6 years) (45) Results from this study suggest that the exercise intervention did not impact executive function and resulted in a decrease in episodic memory performance. The author speculates that increased anxiety at the post-testing timepoint may have impacted cognitive test results due to participants recalling difficulties during pre-testing (45). Taken together, results from the present study and Lehr et al., 2018 suggest that high-intensity exercise may not promote episodic memory enhancements in overweight or obese women. As episodic memory is thought to play a role in satiety, dietary selections, and cognitive restraint, further research is warranted to determine whether episodic memory is impacted in an intensity-dependent manner (46,47).

In the current study, PFC activation during cognitive testing did not change following 6-weeks of home-based exercise (for both the HIIT and walking groups). This may not come as a surprise, given that differences in PFC activation often co-occur with improvements in cognitive performance. Whereas the present findings do not support differences in PFC oxygenation following a 6-week exercise intervention, they do provide new insight into the
cortical activation in females with overweight and obesity. It is also important to highlight that exercise intervention studies that have assessed PFC activity during cognitive testing have yielded mixed results. Xu et al. (2017) found that overweight/obese adolescents and young adults who underwent a 4-wk fitness intervention, had higher \(O_2Hb\) in the left ventrolateral and bilateral dorsolateral PFCs during the Stroop effect (a measure of executive function) and lost more weight than those participants with lower activation in the targeted neural regions. Moriarty et al. (2020) also report individuals with cardiovascular disease had increased PFC activation (Hbdiff and \(O_2Hb\)) during various cognitive tests following 6 weeks of cardiac rehabilitation (48). It is also noted that a variety of inverse correlations between changes in PFC activation and changes in cognitive test scores could indicate improved neural efficiency (less PFC activation for a given output). Conversely, Talamonti et al., 2022 investigated cognitive and brain oxygenation changes over a 1-year period in physically active individuals with and without mild cognitive impairment (49). They found that cognitive performance improved while cortical oxygenation during the cognitive component of a dual-task walking was decreased (included a single cognitive task, a single motor task, and a dual-task condition); individuals with mild cognitive impairment showed the greatest improvements. Nishiguchi et al., 2015 also reported that decreased brain activation was associated with short-term memory improvements in the PFC following a 12-week exercise intervention among older adults (50). It should be noted that the application of different cognitive tasks and/or exercise interventions (varying intensity, duration, and mode) might have contributed to the heterogeneity of the results. In addition, since all participants were healthy, it may be that both cognitive performance and PFC activation were influenced by a ceiling effect, whereby the cognitive test was maximized and further brain activation not
required from the outset. Future research may aim to focus on different brain regions, utilize alternative channel configurations, or the use of simultaneous devices (e.g., fNIRS and electroencephalogram) to explore thoroughly the neural basis of cognitive performance in overweight and obese female adults.

Despite minimal findings regarding cognitive performance effects of either exercise intervention, results indicate that participants in both the HIIT and Walk group displayed improvements in dietary cognitive restraint, depression, and anxiety. Dietary cognitive restraint describes the ability to consciously restrict food intake in an effort to control body weight (51). Evidence suggests that individuals with higher levels of cognitive restraint are more successful at maintaining weight loss. Further, increases in dietary cognitive restraint as a result of weight-loss interventions is a robust predictor of weight loss and reduction in percent body fat (52). Our findings that both home-based HIIT and moderate-intensity walking significantly increase dietary cognitive restraint may provide rationale for the use of exercise interventions in weight loss treatments for reasons outside of simply achieving caloric deficits. In addition, these results suggest that individuals may perform their preferred aerobic exercise intensity (high vs. moderate) in home-based settings and achieve similar improvements in dietary cognitive restraint.

In addition to improved cognitive restraint, both groups in the present study displayed significant reductions in depressive, state-anxiety, and trait-anxiety symptoms. Meta-analytic evidence suggests that adults with depression have a 37% increased risk of becoming obese (53). Further, evidence suggests that overweight individuals or individuals with obesity have significantly higher rates of anxiety than normal weight individuals (5). In older adults with diabetes mellitus, higher anxiety and depression levels were associated with poorer
adherence to medication and physical activity routines (54). In addition, cross-sectional evidence suggests that overweight or obese adults with moderate to severe depression are more likely to drop out of weight loss interventions (55). Findings from the present study suggest that home-based HIIT or moderate-intensity walking may reduce depression and anxiety symptoms. Perhaps similar, short-term, exercise interventions prior to beginning weight loss treatments in individuals with elevated symptoms of anxiety or depression may act as a primer to increase adherence to the treatment. Additional studies are necessary to explore whether a priming effect is evidenced by increased adherence to future treatments.

Several limitations exist in the present study. First, the sample was comprised of only overweight and obese women recruited from the University of Northern Iowa. Results may not be generalizable to the overweight and obese male population or populations that are not affiliated with Midwest university settings. In addition, the exact setting in which the exercise sessions were performed was not controlled. For example, participants may have performed the exercise indoors or outdoors which may alter the cognitive or mood-related impact of the interventions. Specifically, outdoor exercise may enhance the psychological benefits of exercise when compared to indoor exercise (56,57). Another limitation of the present study is that several subjects did not attain a true VO\textsubscript{2max} during the pre-intervention session. As the maximal heart rate from the VO\textsubscript{2max} test was used to prescribe heart rate ranges for each intervention, the prescribed heart rate range may not be indicative of the true maximal heart rate which may have resulted in exercise sessions of lower intensity than planned. In addition, no non-exercise control group was employed and no follow-up timepoint was examined to investigate whether long-term improvements in mood, cognition, or dietary behaviors were observed.
In summary, results from the present study suggest that neither 6-weeks of home-based HIIT or moderate-intensity walking improved cognition across domains of executive function or attention in overweight or obese women. Episodic memory, however, may be improved after 6-weeks of moderate-intensity walking in this population. In addition, these interventions may not be potent enough to prompt changes in PFC oxygenation, aerobic fitness, or body fat percent. Alternatively, cognitive restraint, symptoms of depression, and symptoms of anxiety may be improved independent of the intensity of the exercise intervention. These results warrant future investigations into whether longer interventions of a similar nature prompt cognitive improvements. In addition, future research should examine whether specific physiologic mechanisms (e.g., change in aerobic fitness, adiposity, or PFC oxygenation) are required to promote changes in cognition.
References


45. Lehr L. The relation between metabolic complications and cognitive functions in obese post-menopausal women: the effect of high intensity interval training. 2018;

46. Francis HM, Stevenson RJ. Higher reported saturated fat and refined sugar intake is associated with reduced hippocampal-dependent memory and sensitivity to interoceptive signals. Behavioral neuroscience. 2011;125(6):943.


CHAPTER 4: SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Summary

This study is the first research study done to compare the cognitive changes and prefrontal cortex oxygenation responses to 6-weeks of home-based high-intensity interval training (HIIT) and moderate-intensity continuous walking in women with overweight and obesity. Specifically, we investigated whether cognitive changes occur in an intensity-dependent manner across several domains of cognition. The literature review presented in Chapter 2 is a brief review entitled “Mechanisms of Aerobic Exercise in Attenuating Obesity-Induced Cognitive Impairments”. This review explores the mechanistic role that aerobic exercise may play in reducing cognitive-related consequences of obesity. The research manuscript entitled, “Cognitive Effects of Home-based High-Intensity Interval Training compared to Moderate-Intensity Walking in Overweight and Obese Women” presented in Chapter 3 provides evidence that suggests 6-weeks of HIIT is not sufficient enough to prompt changes across any cognitive domain examined. In contrast, 6-weeks of moderate-intensity continuous walking resulted in episodic memory improvements in overweight and obese women. Furthermore, 6-weeks of HIIT and 6-weeks of continuous walking resulted in improved cognitive restraint (related to eating behaviors), reduced symptoms of depression (BDI-II), and reduced symptoms of state and trait anxiety (STAI-S, STAI-T).

Conclusions

In women with overweight and obesity, moderate-intensity continuous exercise may yield superior episodic memory improvements when compared to HIIT. Episodic memory is related to dietary behaviors, making these findings especially relevant for women with
overweight or obesity. It is important to note that neither exercise intervention significantly improved aerobic fitness or percent body fat suggesting that interventions of a longer duration may be more beneficial in this population, as these variables are thought to impact cognition. In addition, both exercise interventions yielded improved cognitive restraint, depressive, and anxiety symptoms suggesting that moderate-intensity continuous walking exercise may be sufficient to prompt these benefits. In a sedentary, overweight or obese population, exercising at a high-intensity may be somewhat intimidating. These results highlight the fact that exercise does not need to occur at a high-intensity to yield mood-related benefits. Further, exercise at a moderate-intensity may be more beneficial for episodic memory which is related to dietary choices and satiety. Based on our data, we conclude the following:

- Engaging in moderate-intensity walking was found to be superior to HIIT in terms of episodic memory improvements.
- Six weeks of home-based HIIT and moderate-intensity continuous walking did not improve aerobic fitness, percent body fat, or PFC oxygenation which may, in turn, fail to yield executive function or attention improvements in overweight and obese women.
- Both HIIT and moderate-intensity continuous walking improved depression, anxiety, and cognitive restraint in overweight and obese women.

**Recommendations**

Based on these findings, future investigations should be done to:
1. Examine the impact of longer duration (> 6-weeks) home-based HIIT and moderate-intensity continuous exercise on cognitive performance across a variety of cognitive domains.

2. Compare the effects of a similar exercise intervention in men and women to determine if sex-dependent differences exist.

3. Identify whether differential mechanisms for the role of aerobic exercise exist, specific to the cognitive domain examined.

4. Explore the long-term effects of similar exercise interventions on cognitive restraint and whether it relates to anthropometric changes over time.

5. Explore the long-term effects of similar exercise interventions on mood parameters (depression and anxiety) and whether they relate to anthropometric and cognitive changes over time.
APPENDICES

A. Informed Consent

B. Data Collection Sheets

C. Training Diaries
APPENDIX A.

UNIVERSITY OF NORTHERN IOWA
HUMAN PARTICIPANTS REVIEW
INFORMED CONSENT

Project Title: Effects of home-based high intensity interval training versus continuous walking on cognition in overweight and obese adults

Name of Investigators: Kelsey Bourbeau, Terence Moriarty, Leah Borgerding

Invitation to Participate: You are invited to participate in a research project conducted through the University of Northern Iowa. The following information is provided to help you make an informed decision on whether or not to participate.

Nature & Purpose: The purpose of this study is to examine how six weeks of home-based exercise (walking or bodyweight exercises) impacts cognition and brain function in overweight or obese adults.

Explanation of Procedures: If you agree to participate you will be asked to visit the University of Northern Iowa (UNI) Exercise Physiology Lab for an initial visit before starting a 6-week exercise regimen which you will perform 3 times/week at any location of your choosing. After you complete the 6-weeks of exercise, you will visit the UNI Exercise Physiology Lab for a post-testing visit. All visits to the lab will take approximately 90 minutes. The details of the visits are presented below.

- Initial Visit. You will arrive to the lab in a hydrated state after abstaining from alcohol for 24 hours, vigorous exercise for 24 hours, and caffeine for 4 hours. You should consume a small meal 2-3 hours prior to arrival. 7 measurements/procedures will take place:
  - Paperwork. You will fill out paperwork that will determine your eligibility for the study including: an informed consent form, COVID-19 screening form, health history questionnaire, and a physical activity readiness questionnaire.
  - Height and Weight. We will measure your height and weight using a stand-on-scale and vertical ruler.
  - Questionnaires. You will complete a series of questionnaires including: Beck Depression Inventory II (BDI-II), State Trait Anxiety Inventory (STAI), and the Three Factor Eating Questionnaire (TFEQ-R18). COVID-19 screening form.
  - Body Fat Test. We will measure your body fat percentage using a piece of equipment called the Bod Pod. You will sit inside the device for 5-10 minutes while following breathing instructions on the screen.
Cognitive Tests. You will complete a 20-25 minute cognitive test administered by a member of the research team. The cognitive tests will take place in a quiet room with only one member of the research team present. These tests will be administered using an iPad and include tests that measure processing speed, memory, and attention. Before starting the cognitive tests, you will be fitted with a headband that will cover your forehead. This band will be connected to several wires and is used to measure brain blood flow during cognitive tests. You will sit quietly for 1 minute while the activity in your brain is measured using light waves. This is painless and only measures the amount of oxygen your brain is using. This measurement is called a functional near-infrared spectroscopy (fNIRS). After the 1 minute of sitting quietly, you will begin the series of cognitive tests.

Treadmill test. You will complete treadmill oxygen consumption test, which will last approximately 8-12 minutes. In this test, you will walk and/or run on a treadmill and either speed or incline will be increased every minute until you can no longer continue. When your maximal effort is reached you will hand signal and grab treadmill safety rails indicating your desire to stop. During this test, you will wear a mouthpiece and a nose clip for us to capture the air that you have breathed out. In addition, you will be connected to a device that monitors your heart rhythms and heart rate response to exercise.

Exercise Introduction. You will be selected to participate in 6-weeks of either home-based high intensity interval training (HIIT) or home-based continuous walking. You will be familiarized with the exercises that you will be performing and given a fitness watch to use while performing the sessions remotely. You will be familiarized with what exercise intensity you should be performing your sessions at using a rating of perceived exertion (RPE) scale and a heart rate range determined during the treadmill test. A member of the research team will write your target heart rate range on your training diary. In addition, you will be shown how to warm-up and cool-down before and after each exercise session.

Exercise Sessions. You will be randomly selected for either the HIIT or walking group intervention. Each group will exercise 3 times per week for 6-weeks. These exercise sessions can be performed on any day of the week, but should be separated by at least one day, if possible. Both groups will be given a training diary that includes detailed information about the protocol and exercise session data collection forms that should be completed after each exercise session. Group-specific information is below.

HIIT Group. The HIIT protocol consists of 6-8 rounds of 1-minute work bouts (high intensity body weight exercise) interspersed with 1-minute rest bouts (active rest, walking in place or around room).
Your exercise sessions can be completed in a location of your choice. You will be provided with the link to an exercise video that you can follow throughout each exercise session.

Before each exercise session, you will put on your fitness watch and set the watch to record your exercise session.

Your first 2 exercise sessions will be performed while remotely supervised via zoom by a member of the research team present, to help ensure that you are doing the exercises correctly.

Prior to each exercise session, you will perform a 5-minute warm up (dynamic stretching easy walking).

Each work bout consists of two different body weight exercises performed for 30 seconds each with no rest in between. You will follow the instructions and example on the video to ensure proper form and correct timing.

Each work bout should be performed at an RPE between 14-17 and a HR between 77-95% of your maximal heart rate observed during your treadmill test.

Each rest bout consists of walking in place or around the room for 1 minute.

During your first 2 weeks, you will perform 6 rounds of HIIT. The number of rounds will increase by 1 round every 2-weeks, up to a maximum of 8 rounds during week 6.

After each exercise session, you will end recording on the fitness watch and cool down for 5-10 minutes by walking slowly in place or around the room.

Walking Group. The walking protocol consists of indoor or outdoor walking, 3x/week for 6 weeks. These exercise sessions can be performed on any day of the week, but should be separated by at least one day, if possible.

Before each exercise session, you should warm up for 5 minutes by stretching dynamically.

Prior to starting your exercise, you should put on your fitness watch and set it to record.

During the first week of the intervention, you will walk continuously for 25-minutes.

You will increase the time spent walking by 5-minutes per week after the first week, up to a maximum of 50-minutes per session during week 6.

All exercise sessions should be performed at an intensity of 12-13 using the RPE scale and heart rate should remain between 64-76% of your maximal heart rate observed during the treadmill test.
After each exercise session, you will end recording on the fitness watch and cool down for 5-10 minutes by walking slowly in place or around the room.

- Post-testing Visit. During this visit, you will perform the same tests as the initial visit. These tests will include: Measurement of height and weight (5 minutes), measurement of body fat (5-10 minutes), questionnaires (BDI-II, STAI, TFEQ-R18; 10-15 minutes), treadmill test (20-25 minutes). This visit should last between 60-90 minutes.

Privacy and Confidentiality: Information obtained during this study which could identify you will be kept confidential in locked files, available only to authorized members of the research team for the duration of the study. To protect your information, you will receive a subject ID number with no link to your name on any study materials. Any personal identifying information and any record linking information to subject ID number will be destroyed upon completion of the study. For any information entered into a computer, the only identifier will be the unique subject ID number. All health history information will be disclosed to the research team only. The purpose of this disclosure is to determine your eligibility for the study. The summarized findings with no identifying information may be published in an academic journal or presented at a scholarly research conference.

Discomfort, Risks, & Costs:

Exercise risk. There are risks associated with maximal/submaximal exercise testing including the following: brief feelings of nausea, lightheadedness, muscle cramps, or dizziness. There is a very low risk (approximately 1 per 10,000 hours of testing) for having a heart related event when a healthy subject performs exercise. The exercise sessions will be stopped immediately if you become injured or do not feel well. To minimize this risk, the research team members are CPR certified. Juice and snack bars will be available after exercise if needed.

Mental stress. You may have some frustration during the cognitive tasks. These tasks are designed to challenge your memory and ability to recall facts in a certain amount of time. If you become upset during the concentration tasks then the test will be stopped.

Bod Pod: You may experience mild anxiety while sitting in the enclose capsule. Should this become overwhelming, you can press a cancel button located inside the device that will cancel the test.

Brain cap. You may have some redness or irritation on the forehead area from the cap itself. For example, some people report minor irritation at the electrode site. We will adjust the gear to be as comfortable as possible.

It is your responsibility to notify the researcher if you experience dizziness, nausea, lightheadedness, unusual pain, or any response that you find unusual or unexpected during or
after exercise/interview. You must do what you think is safe and not push yourself too far. The researchers will create the safest environment possible. In the unlikely event that any injury or illness occurs as a result of participation in this research, you will be responsible for the cost of medical care.

**Benefits and Compensation:** Each participant will receive $50 in gift cards upon completion of the post-testing (following the 6-week intervention). You will also find out your body fat % and current fitness level. If requested, a member of the research team will also share and explain results of the cognitive tests. There are no other direct benefits to you from participating in this study. However, it is hoped that information gained from this study will help us investigate and identify the mechanisms of how physical activity may improve cognitive function and brain oxygenation in overweight or obese individuals.

**Right to Refuse or Withdraw:** Your participation is completely voluntary. You are free to withdraw from participation at any time or to choose not to participate at all, and by doing so, you will not be penalized or lose benefits to which you are otherwise entitled from. The researcher also has the right to terminate or restrict your participation at any time. You may request at the time of withdrawal that all of your data be excluded from the research.

**Questions:** If you have any questions about the study or desire information in the future regarding your participation or the study generally, you can contact Kelsey Bourbeau at (319)-273-5673 or kelsey.bourbeau@uni.edu. You can also contact the office of the IRB Administrator, University of Northern Iowa, at 319-273-6148, for answers to questions about the rights of research participants and the study review process.

**Agreement:** I am fully aware of the nature and extent of my participation in this project as stated above and possible risks arising from it. It is my responsibility to notify the researcher if I experience dizziness or nausea, lightheadedness, unusual pain or any response that I find unusual or unexpected during or after exercise. I hereby agree to participate in this project. I acknowledge that I have received a copy of this consent statement. I am 18 year of age or older.

__________________________        ______________
(Signature of participant)        (Date)
__________________________
(Printed name of participant)
__________________________
(Signature of investigator)        (Date)
__________________________
(Printed name of investigator)
APPENDIX B.

Data Form

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<tr>
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<td>Stroop incongruent (ms): ____________</td>
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<tr>
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<td>Stroop Effect (ms): ____________</td>
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<td>HRmax: ____________</td>
<td>Stroop Effect (ms): _______</td>
</tr>
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**Health and Medical History Questionnaire**

**Demographic Information**

Date of Birth: ____/____/____  
Age: _______  
Sex: _______

Email address: ________________________________________________

Phone number: ________________________________________________

Best time to contact: ____________________________________________

Emergency contact (name, phone #) _________________________________________________________

**Medical History**

Physical injuries (muscle, joint, other): _________________________________________________________

Limitations___________________________________________________________________________

Have you ever been told that you had any of the following illnesses? Please check all that apply.

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Do you currently have any other medical condition not listed? ____ Yes ____ No

Details:

Are you currently prescribed any medications by a physician? ____ Yes ____ No

Details:
Exercise

Aerobic Training
Times per week (circle one): 1-3 3-5 6-8
Minutes/Day (circle one): 30-60 min 60-90 min >90 min
Training background (circle one): 1-3 months 4-6 months >6 months

Resistance training
Times per week (circle one): 1-3 3-5 6-8
Minutes/Day (circle one): 30-60 min 60-90 min >90 min
Training background (circle one): 1-3 months 4-6 months >6 months

Other
Do you participate in other sports or physical activities?
Describe:
EXERCISE PHYSIOLOGY LABORATORY
VO₂MAX DATA SHEET

AGE: _____ WT: _____(lbs)_______(kg) HT:______(in.)_________(cm)

Technicians(s): ____________________________________

VO₂max (11-breath): ______

HRmax: ______

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<th>RPE</th>
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</table>
BODPOD

DATE____/____/____  TIME: AM  PM  GENDER  M ___  F ____  AGE______

HEIGHT _______ (in) \( \times 2.54 = _______ \) (cm)

Clothing description:

Weight (lb): ______________

TGV (L): ______________

PERCENT FAT: ______________%  

FAT WEIGHT (FW): ______________

LEAN BODY WEIGHT: ______________

TESTED BY: ________________________________________________________________________________

Comments:_____________________________________________

____________________________________________________________________________________________________________

____________________________________________________________________________________________________________

____________________________________________________________________________________________________________

____________________________________________________________________________________________________________

____________________________________________________________________________________________________________

____________________________________________________________________________________________________________
Baseline Data Collection Checklist

- Informed Consent
- COVID screening
- PAR-Q
- Health History
- Height
- Weight
- BMI calculation
- Waist Circumference
- Hip Circumference
- BodPod with TGV
  - Document clothes
  - Void if necessary
  - Check category (poor or very poor required)
- Exclusion criteria check
  - BMI >26
  - Sedentary (≥30 min moderate intensity, ≥3 days/week, ≥3 months)
  - No neurologic or metabolic disease
  - No meds that impact HR or BP
  - Not under active care of clinician for conditions that interfere with study protocol
  - Access to smartphone
- Polar m200 familiarization
  - Download flow app on subject’s phone
  - Create profile, pair phone
  - KB invite subject to be athlete
- BDI-II
- STAI
- TFEQ-R18
- fNIRS set up
  - Edge of cap ~2 cm above nasion, ~1 cm above brow line
  - Baseline fNIRS for 1 min
- Cognitive Tests
  - Stroop Interference
    - Psytoolkit.org: Kelsey.bourbeau@uni.edu
    - Password: 69028
    - Practice Round
    - Start time: _____________
    - End time: _____________
    - Record Stroop data
  - NIH Toolbox
    - Pattern Comparison
      - Start time: _____________
      - End time: _____________
    - Picture Sequence Memory
      - Start time: _____________
      - End time: _____________
    - Flanker Inhibitory Control
      - Start time: _____________
      - End time: _____________
    - Dimensional Change Card Sort
      - Start time: _____________
      - End time: _____________
☐ VO2max
  ☐ Set up HR monitor and make sure m200 is worn
  ☐ Familiarize with RPE
  ☐ Collect HR monitor after test

☐ Training Diary
  ☐ Record HR zones
  ☐ If HIIT, give video link
  ☐ Familiarize with exercises

☐ Schedule follow-up (24-48 hrs after last exercise session)
  ☐ Contact preference: ____________________________

Post Visit Data Collection Checklist:

☐ Height
☐ Weight
☐ BMI calculation
☐ Waist Circumference
☐ Hip Circumference
☐ BodPod no TGV
  ☐ Document clothes
  ☐ Void if necessary
  ☐ Check category (poor or very poor required)

☐ BDI-II
☐ STAI
☐ TFEQ-R18
☐ fNIRS set up
  ☐ Edge of cap ~2 cm above nasion, ~1 cm above brow line
☐ Baseline fNIRS for 2-minutes

☐ Cognitive Tests
  ☐ Stroop Interference
    ☐ Psytoolkit.org: Kelsey.bourbeau@uni.edu Password: 69028
    ☐ Practice
    ☐ Start time: ____________
    ☐ End time: ____________
    ☐ Record Stroop data

  ☐ NIH Toolbox
    ☐ Pattern Comparison
      • Start time: ____________
      • End time: ____________
    ☐ Picture Sequence Memory
      • Start time: ____________
      • End time: ____________
    ☐ Flanker Inhibitory Control
      • Start time: ____________
      • End time: ____________
    ☐ Dimensional Change Card Sort
      • Start time: ____________
      • End time: ____________

☐ VO2max
  ☐ Set up HR monitor
  ☐ Familiarize with RPE
  ☐ Collect HR monitor after test

☐ Collect Polar m200
☐ Collect training diary
☐ Payment and signature
APPENDIX C.

High Intensity Interval Training Diary

Start week:

End week:

Follow up visit:
Packet Contents:

This packet provides you with a detailed description of all exercises that you will perform. It also includes the steps you should take before, during, and after your exercise session.

Outline of training program:

You should train 3 times per week at any location of your choosing. You can perform the exercise on any day of the week but it is recommended that you have a rest day between sessions.

Outline of Exercise Session:

1. Record date and time in your training diary
2. Ensure you are wearing your charged polar wrist watch snugly on top of your wrist, just behind the wrist bone. The sensor on the back of the watch must be in constant contact with your skin but the wristband should not be too tight to prevent blood flow.
3. Click the right button until you see ‘training’ and then hold the right button until you see the HIIT training profile
4. Press and hold right button until you see ‘training started’
5. Start the exercise video created for your current week
6. After the exercise session, press and hold the left button on the watch to stop recording your training session
7. Save the training session by hitting the right button
8. Record the average RPE (excluding the warm up and cooldown) using the table below and any relevant notes in your training diary

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<thead>
<tr>
<th>Rating</th>
<th>Perceived Exertion</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
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<tr>
<td>7</td>
<td>Extremely light</td>
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<td>Hard</td>
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<td>Very hard</td>
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<tr>
<td>19</td>
<td>Extremely hard</td>
</tr>
<tr>
<td>20</td>
<td>Maximal exertion</td>
</tr>
</tbody>
</table>
Exercise Descriptions:

### Squats

**Form:**
- Start with feet hip width apart, toes forward
- Hands behind head or arms crossed in front of body
- Keep back straight and weight on heels at all times
- Bend knees while lowering hips towards ground
- Continue lowering until thighs are parallel to floor
- Repeat

**Modification:**
- Remove explosive jump from above

### Jumping Jacks

**Form:**
- Start with arms at sides and feet together
- Jump to second position by raising arms above head and widening legs to a comfortable position
- Return to first position
- Repeat

**Modification:**
- Replace jumping movement with a stepping movement, widening legs to a comfortable position

### Side Lunges

**Form:**
- Start with hands on hips and feet shoulder-width apart
- Step directly to the left, leaving right foot in place
- Bend left knee moving left thigh parallel to the ground
- Right leg should be completely straight
- Return to starting position
- Repeat on opposite side
- Repeat

**Modification:**
- Replace jumping with a stepping movement

### High Knees

**Form:**
- Begin jogging in place, lifting knees as high as possible
- Keep core tight to support your back
- Repeat

**Modification:**
- Replace jogging with walking
### Forward Lunge

**Form:**
- Stand upright with hands behind head or at sides
- Take one step forward into a split stance
- Lower yourself towards ground by bending knees until front thigh is parallel to ground
- Push up from the balls of your feet to move forward back to starting position
- Repeat on opposite side

**Modification:**
- Remove jumping component from above directions

### Shadow Boxing

**Form:**
- Stand upright with tight core and left leg forward
- Bring hands to shoulder level, make tight fist with hands
- Throw a left jab by extending left hand straight in front of you and immediately retracting
- Repeat for 15 seconds
- Switch sides by moving your right foot forward
- Throw right jabs by extending right hand in front of you and immediately retracting
- Repeat
Set 1
- Squats
- Jumping Jacks
- Active Rest

Set 2
- Side Lunge
- High Knees
- Active Rest

Set 3
- Forward Lunge
- Shadow Boxing
- Active Rest
Cooldown:
- Progressively recover by leisurely walking around the room for ~ 3 minutes.
- Finish your cooldown with some total body stretches, holding each for 15-30 seconds (on each side, if necessary)
- It’s okay to use a wall to stabilize while performing the stretches
- Example stretches:
Training Diary

Week 1:

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<td>F. Lunge &amp; Boxing</td>
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<td>S. Lunge &amp; High Knees</td>
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<td>S. Lunge &amp; High Knees</td>
<td>F. Lunge &amp; Boxing</td>
<td>Squats &amp; Jumping Jacks</td>
<td>S. Lunge &amp; High Knees</td>
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<th>Notes</th>
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<td>F. Lunge &amp; Boxing</td>
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**Day One**

**Day Two**

**Day Three**

**Week 4:**

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**Day One**

**Day Two**

**Day Three**
### Week 5:

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<td>Day Three</td>
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Walking Training Diary

Start week:
End week:
Follow up visit:
Outline of training program:

You should perform your walking exercise 3 times per week at the target intensity written in your packet. You can perform the exercise on any day of the week but it is recommended that you have a rest day between sessions. You can complete each exercise session in a location of your choosing (including indoors and outdoors).

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<tr>
<th>Week 1</th>
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<tbody>
<tr>
<td>Week 2</td>
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<td>Week 3</td>
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<tr>
<td>Week 5</td>
<td>45 minutes</td>
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<tr>
<td>Week 6</td>
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</table>

Outline of Exercise Session:

9. Record date and time in your training diary
10. Check the duration that you need to walk for, based on the week.
11. If walking outside, make sure you walk half the duration in one direction and half the duration back towards your starting point.
12. Ensure you have appropriate footwear/clothing for the environmental conditions
13. Perform a 3-5 minute warm-up by walking in place or around the room
14. Ensure you are wearing your charged polar wrist watch snugly on top of your wrist, just behind the wrist bone. The sensor on the back of the watch must be in constant contact with your skin but the wristband should not be too tight to prevent blood flow.
15. Go to Training on the watch and press and hold the right button
16. Navigate to the Walking Sport Profile and press and hold the right button to start recording your training session
17. Begin your walk, following the correct duration for the current week. Make sure you are staying within the target intensities prescribed to you.
18. After the exercise session, press and hold the left button on the watch to stop recording your training session and confirm ‘save’
19. Using the table below, record your average Rating of Perceived Exertion (RPE, excluding the warm up and cooldown).

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<tr>
<th>Rating</th>
<th>Perceived Exertion</th>
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<tr>
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<tr>
<td>7</td>
<td>Extremely light</td>
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<td>Extremely hard</td>
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<tr>
<td>20</td>
<td>Maximal exertion</td>
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</table>
Cooldown:
- Progressively recover by leisurely walking around for ~ 3 minutes.
- Finish your cooldown with some total body stretches, holding each for 15-30 seconds (on each side, if necessary)
- It’s okay to use a wall to stabilize while performing the stretches
- Example stretches:
### Training Diary

#### Week 1: 25 minutes

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#### Week 2: 30 minutes

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Week 3: 35 minutes

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Week 4: 40 minutes

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### Week 5: 45 minutes

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<table>
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### Week 6: 50 minutes

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