THE EFFECTS OF INTERMITTENT FASTING ON WORKING MEMORY WITH A COVARIATE OF EXERCISE AMONG THE PERIMENOPAUSAL POPULATION: A RANDOMIZED CONTROLLED TRIAL

by

Karen M. Veltri

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A Dissertation Presented in Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

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ABSTRACT

Intermittent fasting and exercise are tools to improve health. Current literature focuses on their impact on metabolic health and weight loss, leaving a gap in the research examining their effects on working memory during the menopause transition. The purpose of this study was to address this gap by recruiting perimenopausal participants and randomly assigning them to an experimental or a control group. The experimental group followed an 8/16 intermittent fasting regimen for two consecutive weeks. Both groups ate ad libitum without dietary restrictions. Participants completed a pre- and post-study Working Memory Questionnaire and self-reported average hours of exercise per week. An analysis of covariance found no significant mean differences in Working Memory Questionnaire posttest scores across groups with a covariate adjustment for average hours of exercise per week, F (1, 30) = .019, p = .891. The covariate was not significant (p = .538), indicating the groups did not differ in average hours of exercise per week. A Pearson correlation found no significant relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week (r = - .097, n = 34, p =.585). Recommendations for future research include implementing blood tests to determine hormone levels, increasing the number of participants, and monitoring caloric intake and exercise levels. The results of this study contribute to the literature by demonstrating the effects of an 8/16 IF regimen on WM during the MT.

Keywords: menopause transition, perimenopause, intermittent fasting, Working Memory Questionnaire, working memory, exercise, Alzheimer disease

Dedication

This dissertation manuscript is dedicated to my grandfather, the late Raymond Dolan. You were right, “If you haven’t failed, you haven’t tried.” You said a prayer for me, and God must have heard. I felt the answer in my heart. Although He spoke no word, you didn’t ask for wealth or fame, you knew I wouldn’t mind. You asked Him to send treasures of a far more lasting kind. You asked that He’d be near me at the start of each new day to grant me health and blessings and friends to share my way. You asked for happiness for me in all things great and small, but it was for His loving care you prayed the most of all.

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CHAPTER 1: INTRODUCTION TO THE STUDY

Introduction

This study sought to examine the effects of an 8/16 intermittent fasting (IF) regimen on working memory (WM) during the menopause transition (MT) with a covariate of exercise. All women transition through perimenopause to post-menopause, a developmental stage where they spend the last one-third or more of their lives (Maki & Weber, 2021; Mosconi et al., 2021). Due to decreasing estrogen levels, many women in perimenopause experience cognitive functioning decline (Maki & Weber, 2021; Pesonen et al., 2021). Cognitive complaints increase throughout the MT and are associated with reduced performance on WM tests (Jaff & Maki, 2021). The disruption in executive functioning, like WM, has also been linked to other neuropsychiatric disorders, such as Alzheimer's disease (AD), depression, and schizophrenia (Morgan et al., 2018). IF and exercise have consistently been associated with reduced cognitive dysfunction and many non-communicable diseases (Anton et al., 2019; Currenti et al., 2021; Lee et al., 2022; Mahindru et al., 2023). Although multiple studies have shown IF to promote weight loss and reduce prognostic biomarkers of disease, no studies have been conducted to determine whether IF with a covariate of exercise improves WM during the MT.

Background

The MT is a neuro-endocrinological process that occurs over time, typically during midlife (Mosconi et al., 2021). It signifies reproductive senescence through a natural endocrine aging process or medical intervention. The MT is a reproductive and neurological transition, evidenced by neurological symptoms such as sleep disruptions, mood changes, hot flashes, and memory loss (Hampson, 2018).

The MT is associated with a decrease in circulating estrogen in regions associated with memory, such as the prefrontal cortex (PFC), hippocampus (HIPP), and dorsolateral PFC (DLPFC; Eriksson et al., 2015; Garrett & Hough, 2021; Hampson, 2018; Hara et al. 2018). Estrogen is involved in the executive functioning of these regions, and a reduction in hormone levels puts menopausal women at elevated risk of neurodegenerative diseases such as dementia, AD, and a host of other irreversible illnesses (Bortz et al., 2022; Denley et al., 2018). Throughout the MT, estrogen production decreases, along with the functioning of neurotransmitters such as acetylcholine, serotonin, noradrenaline, and glutamate (Denley et al., 2018).

In a review of multiple studies, Gava et al. (2019) acknowledged that longitudinal data representing the MT's impact on cognition and memory functioning are scarce. One observational study of 1,315 women demonstrated that improved verbal memory was associated with a longer fertile period, emphasizing the importance of estrogen production (Gava et al., 2019). Another ongoing study by the Study of Women's Health Across the Nation (SWAN) began in 1996 to mitigate the risk of cognitive decline in perimenopause and observed 3,302 women throughout their MT (El Khoudary et al., 2019). Initial data indicated an impairment in cognitive performance during the MT. Yet another study investigated the effects of estrogen or estrogen-progestin therapy on cognitive function decline in women over the age of 60 and concluded that these interventions offered no such protection (Gava et al., 2019). This study provided an opportunity to explore the potential benefits of IF with a covariate of exercise on WM during a critical time when estrogen levels are fluctuating, causing disruptions in cognitive functioning.

The amount of information stored in the brain is massive (Garrett & Hough, 2021). When the information is recalled into awareness from long-term memory storage, it is temporarily held in WM (Garrett & Hough, 2021). According to a study by Hampson (2018), WM is a short-term control system that temporarily holds information and manipulates it for up to a few minutes. WM is then used to combine recalled information with additional information to make decisions and solve problems.

WM is a cognitive function that declines with age (Hampson, 2018; Hara et al., 2018). While WM is not dependent on one brain region, functional neuroimaging techniques show a core network of frontoparietal sites, including PFC, DLPFC, and HIPP, when WM is activated (Hampson, 2018). A decrease in estrogen in these sites has been correlated with a decrease in WM during the MT (Hara et al., 2018).

Physiological changes resulting from fluctuating hormone levels negatively impact WM functioning (Boyle et al., 2020). Denley et al. (2018) found neurons form cranial nervous tissue architecture and emphasized estrogen as the major proliferative regulator and migratory stimulator needed for adequate functioning. This in-depth examination acknowledged estradiol (E2) as the brain's most significant influencer over estrogenic signaling.

Adan et al. (2019) identified nutritional habits a critical component for improving the physiology and composition of the body and enhancing mood and mental well-being. IF is generally considered less challenging than counting calories and improves cardiometabolic health and induces weight loss (Anton et al., 2019; Santos-Baez et al., 2022). IF improves mental health and cognitive function in adults 65 and older by modulating neuronal plasticity, adult neurogenesis, and brain signaling (Anton et al.,

2019). Currenti et al. (2021) identified nutrition as a modifiable risk factor of disease, reporting that an IF greater than 10 hours decreased cognitive impairment when compared to those with no eating time restrictions.

Li et al. (2020) found that by activating GSK-3b in the HIIPP, IF can improve learning and memory through neuronal differentiation and maturation. In a fasting state when liver glycogen storage is depleted, adipose-cell-derived fatty acids produce ketone body β-hydroxybutyrate (BHB) and acetoacetate (AcAc), which make way for neural networks to adapt to a change in fuel source by providing energy substrates to neurons through the bloodstream (Mattson et al., 2018). This results in promoting neuroplasticity and resistance to brain disease and injury. The implications suggest brain health is positively associated with IF.

IF limits daily nutritional consumption to between 4 and 12 hours per day to extend the time spent in the fasted state (Queiroz et al., 2021). More recent approaches align eating windows with endogenous circadian rhythms. A substantial amount of research evidence that IF and exercise are positively associated with improvements in brain health, disease prevention, and overall wellness.

An abundant supply of evidence boasts exercise's positive biological and psychological effects on human and animal models (Bagit et al., 2021; Chaire et al., 2020). Engaging in regular exercise promotes weight loss, improves body composition, and reduces the risk of nearly all major diseases and premature death, and induces structural and functional changes in the brain, which improves cerebral functioning (Bagit et al., 2021; Chaire et al., 2020; Lee et al., 2022; Mandolesi et al., 2018). According to Mandolesi et al. (2018), exercise reduces the risk of developing dementia,

decreases the deterioration of executive functioning, improves quality of life, and prevents cognitive decline linked to aging.

Exercise protects neurodegeneration and brain plasticity (Chaire et al., 2020; Mandolesi et al., 2018). Physical inactivity is a significant risk factor for the development of sporadic AD, and engaging in regular exercise may prevent or alleviate the neurodegenerative decline observed in AD (Bagit et al., 2021). According to Bagit et al. (2021), a randomized controlled trial (RCT) of 120 older adults demonstrated an increase in HIPP size by 2% in participants who engaged in moderate-intensity aerobic exercise compared to a control group. Another study demonstrated that plasma amyloid-β plaque levels in adults aged 60-95 were lower in those who exercised than those who did not, absent of the apolipoprotein E (APOE) β4 allele (Bagit et al., 2021). Mandolesi et al. (2018) postulated that exercise promotes the release of neurotrophic factors such as brain-derived neurotropic factor (BDNF), increases blood flow, and improves cerebrovascular health. The same research further postulated the ameliorative structural and function of exercise's effects may result from the stimulated blood flow in the neural circuits involved in cognitive functioning.

Exercise induces neurochemical changes in the brain and is considered the cornerstone of non-pharmacological treatment for women during the MT and into post-menopause (Mandolesi et al., 2018). Bagit et al. (2021) and Baranowski et al. (2020) emphasized the important relationship between estrogen, BDNF, exercise, and the MT. A downstream effect of estrogen signaling in the brain is the production of BDNF. BDNF promotes neuronal growth, maintenance, synaptic plasticity, and memory consolidation. When estrogen levels fluctuate and decline during the MT, BDNF decreases. Exercise

increases BDNF production independent of circulating estrogen levels (Bagit et al., 2021; Baranowski et al., 2020). Therefore, exercise-induced BDNF during the MT promotes neural functioning.

A small number of research studies focus on menopause and, more specifically, on the MT. Based on previous research, IF significantly improves metabolic activity which improves cognitive functioning. Exercise also generates a plethora of physical and psychological health benefits. Therefore, because all women are at risk of developing neurodegenerative decline due to a decrease in cognitive functioning during the MT, it was imperative to explore the effects of an 8/16 IF regimen on WM during the MT while controlling for exercise (Conde et al., 2021; Santos-Baez et al., 2022; Seitz et al., 2019).

Isaiah 40:31 provides scripture to support life's spiritual and lifestyle changes, "But they that wait upon the LORD shall renew their strength; they shall mount up with wings as eagles; they shall run, and not be weary; and they shall walk, and not faint" (*King James Bible*, 1769/2017). Confiding in Him and asking for strength is a spiritual journey. Implementing lifestyle changes is an opportunity to focus on Him and improve health. Turning to faith for support is a form of self-care and can provide meaning during challenging times. 1 Timothy 4:8 states, "For bodily exercise profiteth little: but godliness is profitable unto all things, having promise of the life that now is, and of that which is to come" (*King James Bible*, 1769/2017). This scripture reminds us that taking care of our physical bodies in the present is essential for future health. 3 John 1:2 reminds us, "Beloved, I wish above all things that thou mayest prosper and be in health, even as thy soul prospereth" (*King James Bible*, 1769/2017). If we take favorable care of our physical body, our mind, heart, and soul will follow.

The current study investigated the impact of IF and exercise on WM in the MT. It was predicted there would not be significant mean differences in WMQ posttest scores across groups (control and intervention) with a covariate adjustment of hours of exercise per week. It was also predicted that there would not be a significant relationship between the WMQ posttest scores and hours of exercise per week.

Problem Statement

Whether natural or medically induced, all women experience the MT. Due to decreasing estrogen levels, cognitive performance, such as WM, declines, particularly in perimenopausal women during the MT, leading to an increased risk of neurological disease (Conde et al., 2021). The reduction of estrogen thereby negatively affects neurotransmitter systems in WM circuitry (Gasbarri et al., 2019). Such neuropathological changes are correlated with serious diseases such as AD and other forms of neurocognitive impairment (Conde et al., 2021). IF is an emerging intervention that increases weight loss, improves mental health and cognition, improves sleep disturbances, and reduces the risk of AD (Anton et al., 2019; Currenti et al., 2021; Ezzati & Pak, 2023). IF has neuroprotective effects, contributing to cognitive resilience and increased neurogenesis (Senderovich et al., 2023). IF improves cognition in adults over the age of 65 with adherence to an IF period of less than 10 hours and eating windows aligned with circadian rhythms improve cardiometabolic health (Anton et al., 2019; Currenti et al., 2021; Queiroz et al., 2021).

An overwhelming number of studies implicate exercise as a modifiable lifestyle factor for which virtually all physical and mental aspects of one's quality of life are improved (Bagit et al., 2021; Baranowski et al., 2020; Chaire et al., 2020; Lee et al.,

2022; Mandolesi et al., 2018). Reducing activity in the sympathetic nervous system and the associated hypothalamic-pituitary-adrenal axis (HPA) improves mood during and after exercise (Hallam et al., 2018). According to Hallam et al. (2018) and Mahindru et al. (2023), the benefits of exercise on brain health are undeniable. The benefits may be obtained through increased activities such as walking or other cardiovascular activities, low-impact activities such as yoga and pilates, or resistance training such as body weight exercises or weightlifting. Although research shows a distinct degeneration of cognition and WM during the MT, no studies have been conducted to evaluate the effects of an 8/16 IF regimen on WM during the MT while controlling for average hours of weekly exercise. It was imperative to identify early preventative interventions that supply cognitive benefits during perimenopause to mitigate the risk of neurological decline. This research study focused on the impact of IF with a covariate of exercise on WM in perimenopausal women, which may potentially mitigate or delay cognitive deterioration by improving WM, thereby reducing severe long-term cognitive diseases such as AD and other forms of dementia.

Purpose of the Study

The purpose of this RCT was to investigate the effects of an 8/16 IF regimen on WM during the MT with a covariate of exercise.

Research Questions and Hypotheses

Research Questions

RQ1: What mean differences are there between perimenopausal women who engage in an 8/16 intermittent fasting regimen for two consecutive weeks in

Working Memory Questionnaire posttest scores with a covariate adjustment of exercise when compared to a control group?

RQ2: What is the relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week?

Hypotheses

*Ho*1: There will be no significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ho*2: There will be no significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

*Ha*1: There will be significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ha*2: There will be significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

Assumptions and Limitations of the Study

When examining the challenges and limitations of this study, it was necessary to anticipate foreseeable barriers that may have compromise the accuracy of the data. When faced with challenges, Philippians 4:13 reminds us, "I can do all things through Christ which strengtheneth me" (*King James Bible*, 1769/2017). Participants were at varying stages of the MT; therefore, their varying circulating estrogen levels may have affected test results. For example, a woman who is beginning the MT may have more circulating estrogen than a woman near the end. A secondary challenge was that participants may

have over- or under-estimated their eating windows or hours of exercise, also leading to inaccurate results. Participants may have experienced difficulty adhering to IF, which led to attrition. Additionally, due to the limitation of social desirability/limitation of self-reported measures, participants may have over-reported good behavior (exercise, IF adherence, etc.).

Theoretical Foundations of the Study

The theoretical framework for this study stemmed from the Capability, Opportunity, Motivation, and Behavior (COM-B) model used to design behavioral change interventions (see Figure 1; Khalilollahi et al., 2023; Yap et al., 2023). The COM-B model provides a comprehensive framework to understand the motivations and barriers to promulgating change in dietary behaviors through the interaction of three components: capability, opportunity, and motivation (see Figure 1; Khalilollahi et al., 2023; Yap et al., 2023). In other words, individuals must have the ability to carry out a new behavior psychologically or physically, an opportunity driven by external social and physical influences, and both the reflective and automatic motivations to engage in the new behavior (Khalilollahi et al., 2023; Yap et al., 2023). This study allows participants to change their behavior and improve their health. They will be required to have both the physical and psychological skills to engage in IF and must be motivated to improve their WM during the MT.

Figure 1

The COM-B Model (Khalilollahi et al., 2023)

To account for the cognitive processing decline seen during normal healthy aging, Ebaid and Crewther (2020) evaluated multiple theories while highlighting the need for a more comprehensive neuroscience approach. Some of the theories included in their review were the Common-Cause Hypothesis, the Information Degradation Hypothesis, and the Scaffolding Theory of Aging and Cognition. One theory highlighted by the authors was the Cognitive Reserve Hypothesis, which postulates those with an enhanced ability to recruit and utilize more brain regions are better equipped to withstand greater levels of age-related decline in neural functioning before an official clinical diagnosis. Participants in this study may have had varying levels of abilities to recruit and utilize more brain regions, so their abilities to cope with age-related cognitive decline may have varied. A second theory that resonates with this study and brought forth by Ebaid and Crewther's (2020) the Frontal Aging Hypothesis, suggests that reduced volume, metabolism, and a concurrent decline in grey and white matter integrity are responsible for cognitive deficits experienced in healthy aging. Participants recruited for this study may have unknowingly possessed varying levels of grey and white matter integrity, exhibiting varying cognitive decline levels. Due to the lack of function and structural

brain imaging capabilities, these varying levels were not considered for this study. Another theory presented by Ebaid and Crewther (2020) relative to this study, the Hemispheric Asymmetry Reduction in Older Age (HAROLD) model, conceptualizes that, as an individual ages, lateralization of brain function declines as observed in fMRI studies in young and older adults during episodic memory and WM tasks. Young adults displayed left PFC activation during WM tasks, whereas older individuals demonstrated bilateral activation of the PFC (Ebaid & Crewther, 2020). Participants in this study were in the MT, so lateralization in brain functioning may not have been as extensive as in older adults, but it may still have been demonstrated. This study did not detect these differences absent brain imaging techniques such as fMRI and PET. Although the average age of participants recruited for this study was relatively similar, it was still not outside of the realm of possibilities that one or more of these theories were present to be accurate. However, it was difficult to prove without proper technologies.

The biblical foundations of this study are supported by scripture. During challenging fasts, scripture can remind us of our dependence on God (2 Samuel 12:15-20, *King James Bible,* 1769/2017). Through the Bible, He provides guidance to support the behaviors necessary to make significant dietary and physical changes for improved health. For example, 1 Corinthians 15:58 states, "Therefore, my beloved brethren, be ye steadfast, unmovable, always abounding in the work of the Lord, forasmuch as ye know that your labour is not in vain in the Lord" (*King James Bible*, 1769/2017).

Definition of Terms

The following is a list of terms used in this study:

Alzheimer's Disease (AD) – A prevalent neurodegenerative disease (Ezzati & Pak, 2023).

Cognitive Decline –- The process of neurodegeneration resulting in increasing cognitive impairment (Basso & Suzuki, 2017).

Cognitive Dysfunction – A disruption in the brain's ability to acquire, process, store, and retrieve information (Khera & Rangasamy, 2021).

Cognitive Reserve Hypothesis – A theory that suggests those with an enhanced ability to recruit and utilize more brain regions are better equipped to withstand greater levels of age-related decline in neural functioning before an official clinical diagnosis (Ebaid & Crewther, 2020).

Diet – The consumption of sufficient macro and micronutrients necessary to support the energetic and physiologic needs of the body (Cena et al., 2020).

Dorsolateral Prefrontal Cortex (DLPFC) – A brain region within the prefrontal cortex involved in working memory, task-switching, inhibition, and planning (Hara et al., 2018).

Estrogens – A group of hormones that support the regulation of a woman's menstrual cycle and the brain, musculoskeletal, and cardiovascular systems (Bortz, 2022; Denley et al., 2018).

Frontal Aging Hypothesis – A theory that suggests reduced volume, metabolism, and a concurrent decline in grey and white matter integrity are responsible for cognitive deficits experienced in healthy aging (Ebaid & Crewther, 2020).

Functional Magnetic Resonance Imaging (fMRI) – A scan used to observe the specific networks of the brain active during a task by tracking blood flow (Hampson, 2018; Martino et al., 2022).

Hemispheric Asymmetry Reduction in Older Age (HAROLD) – A theoretical model that conceptualizes that as an individual ages, lateralization of brain function declines as observed in fMRI studies in young and older adults during episodic and WM tasks (Ebaid & Crewther, 2020).

Hippocampus (HIPP) – A part of the limbic system, each of the two hippocampi are brain structures located within the temporal lobes and are involved in learning and the formation and processing of memories and emotions (Hampson, 2018).

Intermittent Fasting (IF) – Periods of abstinence from food intake intervened with periods of normal meal consumption (Senderovich et al., 2023).

Menopause – A state of permanent cessation of menstruation in women (He et al., 2021).

Menopause Transition (MT)/Perimenopause – Neuroendocrinological transition from a reproductive state to a non-reproductive state (Maki & Henderson, 2016).

Exercise –- A planned, structured, and repetitive activity with a final or intermediate objective to improve or maintain one or more components of fitness and includes both aerobic and anaerobic activities (Mandolesi et al., 2018).

Positron Emission Tomography (PET) – A scan that uses a tracer, a radioactive substance, to measure neurological activity in regions of the brain (Mosconi et al., 2021; Zsido et al., 2023).

Prefrontal Cortex (PFC) – A part of the frontal lobe, the PFC is involved in higher-order cognitive processes such as planning, decision-making, reasoning, and memory (Haraet al., 2018).

Working Memory (WM) – A short-term control system that temporarily holds information and manipulates it for up to a few minutes (Hampson, 2018).

Significance of the Study

Early interventions during the MT may decrease or slow the risk of developing cognitive dysfunction. Women are at an increased risk of AD and other types of dementia compared to men and make up two-thirds of all AD cases worldwide (Bortz et al., 2022; Saleh et al., 2023). Cognitive decline negatively impacts the patient, their friends, and family and burdens the healthcare system (Yang et al., 2023).

Studies are needed to understand cognitive decline during the MT and determine interventions to slow neurological degenerative disease. IF and exercise require little to no personal financial strain, no physician's approval, or prescription medication, and have numerous benefits such as weight loss, mental clarity, and improved sleep (Adafer et al., 2020; Mandolesi et al., 2018; Soliman, 2022). Although many studies have explored the effects of IF and exercise separately, to date, no studies have examined the impact of an 8/16 IF regimen on WM during the MT while controlling for a covariate of exercise.

Summary

A relatively small number of research studies focus on menopause and, more specifically, cognitive decline during the MT. Based upon previous research that indicates IF and exercise significantly improve cognitive performance, metabolic activity, and body mass, together with the fact all women are at risk for significant and abrupt cognitive decline related to the decrease in estrogen during the MT, it was imperative to explore the hypothesis of this proposal (Anton et al., 2019; Mandolesi et al., 2018; Santos-Baez et al., 2022).

All women experience the MT, and face increased risks due to estrogen decline (Hampson, 2018). Approximately one-third of a woman's life is spent post-MT when the

chance of experiencing rapid cognitive decline increases with natural aging, and the loss of estrogen hinders the ability to slow rapid decline (Maki & Henderson, 2016). Despite a lack of research that focuses on the WM aspect of cognitive decline and potential mitigating implementations, the benefits of both IF and exercise are known separately to improved cognitive functioning, cardiovascular functioning, and body composition. However, no previous studies have been conducted to whether an 8/16 IF regimen with a covariate of exercise improves WM in perimenopausal women (Bagit et al., 2021; Chaire et al., 2020; Queiroz et al., 2021).

CHAPTER 2: LITERATURE REVIEW

Overview

Due to the number of women entering the menopause transition (MT) each year, along with the increase in health complications implicated in and exacerbated by a decline in ovarian function and circulating estrogen levels, health care practitioners can expect large numbers of patient requests for cost-effective and easy to obtain treatment options (Maki & Weber, 2021). Deterioration in cognitive functioning during the MT, as evidenced by a decline in WM tasks, are ameliorated by lifestyle modifications that may improve current and future health conditions (Jaff & Maki, 2021). Instituting changes such as healthy eating patterns and exercise early in the transition have beneficial physical and neurological effects during and following the MT transition (Maki & Weber, 2021; Mandolesi et al., 2018; Mosconi et al., 2021). Therefore, it is imperative that alternative cost-effective treatment options are available to this massive population.

Description of Search Strategy

The research reviewed in this chapter was found through various databases to include the Jerry Falwell Library at Liberty University, Google, and www.kingjamesbible.com searches. Peer-reviewed journals and textbooks found in journal publications such as Nutrients, Frontiers in Neuroscience, Menopause, Advances in Nutrition, Human Brain Mapping, and World Journal of Psychiatry were utilized to gain a thorough understanding of the current literature. Various keywords and phrases used to locate resources included intermittent fasting, time-restricted eating, working memory, perimenopause, exercise, working memory in perimenopause, menopausal stages, neurological function, and Daniel Fast.

In addition to the search strategies utilized for this study, the biblical implications found in the Daniel Fast from the results of a Google search were also relevant in terms of creating a space to focus on one's relationship with God ("Daniel Fast," 2023). A subsequent search for the terms Daniel Fast, fasting, health, fitness, and food on www.kingjamesbibleonline.com revealed multiple Bible verses relevant to this study. Fasting provides the opportunity to accept grim times and express gratitude about God's creation. Matthew 6:16-18 states, "Moreover when ye fast, be not, as the hypocrites, of a sad countenance: for they disfigure their faces, that they may appear unto men to fast. Verily I say unto you, They have their rewards. But thou, when thou fasted, anoint thine head, and wash thy face; That thou appear not unto men to fast, but unto they Father which is in secret: and they Father, which seeth in secret, shall reward thee openly" (*King James Bible*, 1769/2017). God freely provides us with the nutritional requirements and other essentials necessary to live healthy lives. These essentials allow us to function properly, to flourish in growth, to accept the difficulties faced in intermittent fasting, and to adhere to the implementation of an exercise regimen. 1 Corinthians 6:20 reminds us that our body and spirit belong to Him, "Know ye not that your body is the temple of the Holy Ghost which is in you, which ye have of God, and ye are not your own? For ye are bought with a price: therefore glorify God in your body, and in your spirit, which are God's" (*King James Bible*, 1769/2017).

Review of Literature

The Menopause Transition

All women transition to post-menopause, where they spend at least the last one-third of their lives (Maki & Henderson, 2016). Naturally or medically induced, the

transition from a reproductive state (pre-menopause) to a non-reproductive state (post-menopause) is referred to as perimenopause or the MT. As a neuroendocrinological process, the MT impacts the entirety of the body including the central nervous system (CNS), and occurs in varying lengths, due to fluctuating but overall declining levels of the sex hormone estrogen, thereby initiating disruptions in the menstrual cycle (Bortz et al., 2022; Gava et al., 2019; Grub et al., 2021; Mosconi et al., 2021; Peycheva et al., 2022). Following 12 consecutive months of amenorrhea, the natural transition into post-menopause occurs at an average age of 50-52 though slight variations are shown between ethnic groups (El Khoudary et al., 2019; Mishra et al., 2019). Many studies define perimenopause utilizing the Stages of Reproductive Aging Workshop (STRAW + 10) to identify three stages within the MT, the early MT (Stage -2), late MT (Stage -1), and early post-menopause (Stage +1a) (Kawakita et al., 2023; Metcalf et al., 2023). Stage -2 is defined by changes in the length of a menstrual cycle lasting seven days or more. Stage -1 is defined as amenorrhea for 60 or more days. The final stage, Stage + 1a is defined as 12 or more consecutive months of amenorrhea. The STRAW +10 staging system is not universally used, leading to variability which poses challenges when summarizing literature (Metcalf et al., 2023). Additional vulnerability to misclassification is due to self-assessment of menstrual cycling bleeding patterns that rely on memory rather than calendar tracking (Kawakita et al., 2023).

The natural MT lasts an average of 4-9 years and typically begins in a woman's 40's (Mosconi et al., 2021; Metcalf et al., 2023). Premature menopause occurs if a woman reaches post-menopause before the age of 40 and early natural menopause occurs

between 40-45 years (Mishra et al., 2019). Approximately 5% of women experience early menopause while 12% report sudden amenorrhea (Marlatt et al., 2022).

Accelerated brain aging and dementias later in life have also been associated with early menopause (Zsido et al., 2023). Premature ovarian dysfunction, also known as primary ovarian insufficiency, causes early or premature post-menopause whereas a bilateral oophorectomy, a surgically induced procedure, chemotherapy, pelvic radiation, or spontaneity causes abrupt post-menopause (Marlatt et al., 2022; Russell et al., 2019). Many studies focusing on the MT exclude surgical menopause due to the lack of a transition period (Metcalf et al., 2023). Variability in the natural MT is highly individualistic and is influenced by both genetic and non-genetic factors (Peycheva et al., 2022).

A cohort study of 6,805 women found reproductive health, health behaviors, and socioeconomic characteristics influenced the age of onset of the MT (Peycheva et al., 2022). Circumstances such as social class, a mother who smoked during pregnancy or who had multiple pregnancies, and those who were breastfed one month or less were more likely to undergo early menopause (Mishra et al., 2019; Peycheva et al., 2020). Other influences such as smoking, early menarche, nulliparity, being underweight, and genetics induced a younger MT age while moderate alcohol intake and regular exercise delay the MT (Mishra et al. 2019). A longitudinal study by Grub et al. (2021) collected saliva samples from 127 perimenopausal women aged 40-56 for 13 months and at months 2 and 12 found varying levels of estrogen. All variations in the natural MT experience are not yet fully understood but fluctuation in estrogen levels remains consistent.

Estrogen

The ovaries are the primary source of estrogens and, as a woman progresses through life, the number of ovarian follicles slowly reduce, decreasing levels of circulating estrogen (Bortz et al., 2022; Koebele et al., 2021; Russell et al., 2019; Weber et al., 2021). The fluctuation in hormone levels is associated with a physiological deterioration of hypothalamic-pituitary-ovarian axis (HPO) function (Grub et al., 2019). The HPO axis regulates female reproduction (Mikhael et al., 2019). Estradiol or oestradiol (E2) is produced primarily in the ovaries and the central and peripheral nervous systems by neurons and glial cells and can cross the blood brain barrier (BBB) (Grub et al., 2019). It is known that during ovarian hormone decline in the MT, cognitive functioning is influenced independently of other changes in healthy aging women (Martino et al., 2022). Although sex hormones are powerful modulators of cognitive functions such as learning and memory, less than 0.5% of the neuroimaging-literature considers hormonal transition phases such as the MT (Zsido et al., 2023).

Three common estrogens are physiologically relevant, E1–- estrone, E2–- 17β-estradiol, and E3–- estriol (Russell et al., 2019). The dominant form of estrogen during reproductive age is E2, also known as oestradiol or estradiol (He et al., 2021). E2 plays a significant role in adequate brain functioning and declines rapidly during the MT (He et al., 2021; Le et al., 2020; Russell et al., 2019). The reduction in circulating estrogen causes a diverse range of symptoms such as hot flashes, sleep disturbances, and brain fog, negatively impacting a woman's quality of life. Eighty percent of women report experiencing at least one symptom (Li & Dreher, 2021). Sex hormones such as E2 can modify systems that regulate functions such as behavior, cognition, memory, sleep, mood, pain, and coordination (Grub et al., 2019; He et al., 2021; Metcalf et al., 2023;

Russell et al., 2019). When the production of E2 decreases, behavioral and emotional aspects of executive functioning are impacted, leading to physical and psychological symptoms (Russell et al., 2019). Vasomotor symptoms include hot flashes and night sweats (Grub et al., 2019; Metcalf et al., 2023; Weber et al., 2021). A disruption in behavioral and emotional aspects are exhibited in sleep disturbances, anxiety, depression, and a reduction in processing speed, attention, concentration, and memory (Bortz et al., 2022; Conde et al., 2021; Grub et al., 2019; Kilpi et al., 2020; Leistikow & Smith, 2022; Russell et al., 2019; Weber et al., 2021). Fluctuating levels of E2 is a significant factor responsible for many physiological and psychological effects associated with the MT (Conde et al., 2021; Seitz et al., 2019).

Estrogen and Neurological Function

It is thought the brain undergoes a structural and biological reorganization during the MT and more specifically in the reorganization of functional memory circuitries (Grub et al., 2019; Konishi et al., 2020). Activation of signaling pathways and gene expression modulation is involved in the molecular and cellular processes that take place during structural and functional changes in the neural system (Gava et al., 2019). Changes at the structural and cellular levels result from decreasing E2 levels as evidenced largely in non-human studies (Gava et al., 2019; Russell et al., 2019). Estrogen fluctuations significantly impact the CNS through neurotropic and neuroprotective effects, evidenced by the significant role E2 plays in both cortical and subcortical structures of the brain (Gava et al., 2019; Grub et al., 2019).

Estrogen Receptors

The neurobiology of cognitive functioning is supported by circulating estrogen due to estrogen receptors (eRs), abundant in multiple regions of the brain that support memory and executive function such as the PFC, basal forebrain, and HIPP (Le et al., 2020; Metcalf et al., 2023; Morgan et al., 2018; Nunez et al., 2020). E2 has the highest number of intracellular eRs, eRα and Erβ. Erβ has been found and expressed mostly in the PFC and HIPP while eRα is found in magnocellular cholinergic neurons of the basal forebrain (Gava et al., 2019; Grub et al., 2019; Russell et al., 2019). The complex nature of executive functioning suggests interconnectivity between various regions of the brain (Morgan et al., 2018).

eRs are responsible for initiating intracellular and extracellular actions both in the nuclei and along the membranes at synapsis, spine, and mitochondria sites, inducing a cascading or trophic effect required for proper executive functioning (Gava et al., 2019; Grub et al., 2019; Le et al., 2020; Morgan et al., 2018). It has been demonstrated that E2 induces a trophic effect for memory and executive functions in the basal forebrain and HIPP (Grub et al., 2019). eRs exert action by enhancing synaptic plasticity, neurite growth and neurogenesis, and by protecting against neural injury (Gava et al., 2019). eRs also may play a potential role in demyelinating diseases by providing regulation in myelin formation in the glia (Grub et al., 2019).

When eRs are expressed, E2 regulates physiological processes to include docosahexaenoic acid (DHA) metabolism, BBB integrity, and the utilization of macronutrients (Saleh et al., 2023). Cellular changes elicited by a reduction in circulating E2 include a decrease in synapses, cell proliferation, synaptic density, myelination, axon growth, and dendritic spines (Gava et al., 2019). In high energy required sites, estrogen

improves mitochondrial function by enhancing adenosine triphosphate (ATP) production and mitochondrial respiration (Gava et al., 2019). By regulating glucose transport, aerobic glycoses, and mitochondrial function, estrogen generates ATP which is found in multiple regions such as the medial temporal, posterior cingulate, and the PFC, known to support cognitive functioning (Gava et al., 2019). Neuroprotective effects of estrogen include decreased inflammation, modulation of neuropeptides, modulation of neurotransmitters, and neurosteroid synthesis and activity, a reduction in cell apoptosis, antioxidant properties, reduced formation of amyloid-β, modulation of the brain immune system, and modulation of mitochondrial activity (Gava et al., 2019; Mosconi et al., 2021). Estrogen also interacts with other neurotransmitter systems that support executive functioning, learning, and memory such as serotonergic, GABAergic, dopaminergic, and glutamatergic pathways (Le et al., 2020; Leistikow & Smith, 2022).

Structural changes post-menopause includes a reduction in gray matter volume (GMV) in the superior temporal gyrus, inferior frontal gyrus, olfactory cortex, and supplementary motor area (Russell et al., 2019; Zsido et al., 2023). Liu et al. (2021) utilized resting-state functional magnetic resonance imaging (rs-fMRI) to evaluate the effects of sex hormones on amplitude of low-frequency fluctuation (ALFF) in regions of the brain related to cognition in 25 perimenopausal women and 25 premenopausal women. An indicator used to measure physiological states and to locate spontaneous neural activity in regions of the brain, ALFF measures the intensity of fluctuations in the blood oxygen level-dependent signal. The study concluded when compared to premenopausal women, perimenopausal women showed significant ALFF increase in the left gyrus rectus and decreases in the left superior temporal gyrus, left inferior frontal

gyrus, and left insula. It was also determined the GMV values of both the left gyrus rectus and left superior temporal gyrus were reduced in perimenopausal women. These findings concluded E2 levels were negatively correlated with the ALFF value of the left gyrus rectus in women in the MT. This reduction in GMV and increase in ALFF display the neurological changes influenced by fluctuating hormone levels during perimenopause.

Studies performed only in ovariectomized rats show hormones produced by the ovaries, E2 and progesterone, modulated neurotransmission, facilitated synaptogenesis, and increased rate of neurogenesis (Konishi et al., 2020; Martino et al., 2022). Estrogens repair DNA, promoting antioxidant effects, and were linked to impaired cognitive function through their association with increased levels of an inflammation marker, C-reactive protein (Gava et al., 2018). Degeneration in the HIPP was reversed and spatial memory enhanced in rodents when estrogen was replaced (Konishi et al., 2020).

Through a literature review, Li and Dreher (2021) found estrogen replacement had positive effects on PFC-dependent cognitive functions throughout the MT such as mental flexibility, inhibition control, planning, and working memory (WM). Seitz et al. (2019) also found a multitude of previous cognitive literature demonstrating the impact of E2 replacement on cognitive functioning such as memory performance and memory circuitry.

Hormone Replacement Therapy

Hormone replacement therapy (HRT) is a treatment used to relieve undesirable menopausal symptoms, producing conflicting evidence on its effects on executive functioning (Boyle et al., 2020; Le et al., 2020; Weber et al., 2021). HRT is prescribed in

various forms such as tablets, cream, vaginal ring, and skin patches and requires an ongoing financial constraint (Seitz et al., 2019). The replacement of estrogen through exogenous administration improved executive functions in some studies however, in large, randomized placebo-controlled trials, HRT was shown not to be effective in improving cognition in post-menopausal women (Conley et al., 2022; Le et al., 2020; Weber et al., 2021).

The MT has been referred to as the "critical window" (Bortz et al., 2022; Metcalf et al., 2023) and a 'window of vulnerability' (Jaff & Maki, 2021). The critical window hypothesis refers to studies which evidence varying outcomes in HRT treatment during the MT and that HRT may only be effective when administered during certain windows to prevent cognitive dysfunction (Morgan et al., 2018). Some studies show whether HRT enhanced or impaired a cognitive task was dependent on the metabolic status of the brain area utilized during specific tasks (Prakapenka & Korol, 2021). Research suggests HRT may provide improvements during the MT, early in post-menopause, or when E2 and eRs initially begin to decrease (Bortz et al., 2022; Conde et al., 2021). Interest in the perimenopausal stage or MT suggests this time may provide a therapeutic window while others consider this window both a risk and opportunity for women's health (Bortz et al., 2022; Morgan et al., 2018). In Matyi et al. (2019), it was shown women who initiated HRT within 5 years of menopause improved cognition when compared to those initiating HRT 6 or more years later.

HRT protects against osteoporosis, heart disease, and dementia; however, research continues to evaluate the benefits of HRT on stress reduction, cardiovascular health, and delayed onset of dementia (Boyle et al., 2020; Weber et al., 2021). In one

study, 81 women were given HRT during the MT and performed better on verbal fluency and memory tasks than untreated women (Jaff & Maki, 2021). The same women who received HRT also performed better years later. Comparable results were found in women who underwent oophorectomies (Jaff & Maki, 2021). However, two other studies, the Women's Health Initiative (WHI) and Women's Health Initiative Memory Study (WHIS) did not support those findings (Gava et al., 2019; Jaff & Maki, 2021). Li and Dreher (2021) found women who received less than and up to 10 years of HRT had fewer changes in GMV in the PFC and better performances in executive functioning than those receiving HRT for more than 10 years where PFC deterioration was present.

Although animal studies have offered insight on HRT for treatment of cognitive dysfunction during the MT, methods include ovariectomized rodents rather than those with natural follicle depletion (Duarte-Guterman et al., 2015; Metcalf et al., 2023). The MT is better represented during normal ovarian follicle and endogenous estradiol decrease (Metcalf et al., 2023). Utilizing an ovarian toxin, vinylcyclohexan dieposide (VCD), estradiol administered in VCD-treated rodents did show an improvement in WM when compared to control but increased errors in WM tasks (Koebele et al., 2020). In another VCD animal study, rodents receiving both synthetic progestin (levonorgestrel) presented improved WM when compared to those receiving estradiol only and progesterone treated rodents displayed a decrease in WM when compared to other hormone treatments and control (Koebele et al., 2021).

Current clinical guidelines suggest HRT until the age of average menopause for women (50-52 years) who experience premature or early menopause (Mishra et al., 2019). It is customary practice when prescribing estrogen replacement that a progestin is

also used to mitigate the risk of uterine hyperplasia and cancer, but patients who have undergone hysterectomy with or without ovary removal do not need a progestin component (Seitz et al., 2019). While numerous studies acknowledge additional RCTs are needed to fully understand HRT's specific role in cognition during the MT due to lack of current evidence, the North American Menopause Society does not currently recommend HRT as a viable treatment for cognitive dysfunction during the MT (Metcalf et al., 2023).

Memory

When a memory is stored in the brain, a physical representation of the memory is consolidated and made permanent (Garrett & Hough, 2021). According to Garrett and Hough (2021), during the consolidation process, memories process into one of three categories: short-term memory (seconds to hours), long-term memory (hours to months), and long-lasting memories (months to lifetime). Each stage of memory serves an important and different role, executed in various orchestrated regions of the brain such as the HIPP, cerebellum, and PFC (Mosconi et al., 2021; Seitz et al., 2019; Zhang et al., 2022). Memory systems include recall memory, visual memory, episodic memory, associative memory, WM, and others (Seitz et al., 2019).

The advancing age of the population brings with it a multitude of age-related health challenges such as interruptions in memory. Of the total aging population, approximately 75% report memory-related impairments (Seitz et al., 2019). Evidence shows education level, stress, income levels, nutrition and other dietary choices, and genetics play varying roles in the differences among age-related memory disruptions (Martino et al., 2022). In additional to normal aging symptoms, women in the MT

experience a steeper decline in memory function compared to their male counterparts due to declining levels of estrogen, and experience them in conjunction with other MT related symptoms (Conde et al., 2021; Eriksson et al., 2015; Martino et al., 2022; Metcalf et al., 2023).

Most of the scientific literature focuses on factors of reproductive aging such as stress, depression, sleep habits, exercise, and diet to explain changes in memory, however, studies surrounding the MT and its effects on WM have fallen short (Bortz et al., 2022; Martino et al., 2022; Metcalf et al., 2023). Limited population-based studies show 44-62% of women report memory disruption during the MT (Conde et al., 2021; Mosconi et al., 2021). Other research shows 30-60% of women in both perimenopause and post-menopause report memory disruption (Conde et al., 2021). Difficulty remembering where items were left, what someone had told them, and whether they already told another person something are examples of WM impairments and were reported in half of women in the MT (Metcalf et al., 2023).

Working Memory

WM is a key process in complex cognitive tasks and considered a mental sketchpad utilized to temporarily retain, update, and manipulate information (Eriksson et al., 2015; Hampson, 2018; Plaschke et al., 2020; Yoshimura et al., 2023). WM is thought to be a temporarily accessible state of representation, despite the type (e.g., verbal, visual, auditory, spatial, etc.) and includes procedures or action sequences such as following a recipe (Eriksson et al., 2015). Eriksson et al. (2015) found WM remained stable between 10 and 50 years but declined from age 55-60 to 75-80 years. WM is highly limited in the amount of information that can be held simultaneously active (Eriksson et al., 2015).

According to Eriksson et al. (2015), a capacity limit of 3-4 simple items is estimated among healthy young adults, although functional limits are dependent upon the nature of the demands imposed by the required WM task. In this study, performance on high level cognitive tasks in areas such as abstract reasoning, mathematics and language abilities, fluid intelligence, and overall academic performance strongly predicted an individual's WM capacity. Lower capacities indicated a difficulty in ignoring distracting information whereas higher capacity individuals were faster at disengaging attention from information deemed irrelevant. It was concluded that efficiently deploying attentional control during overloading tasks seemed to explain an individual's ability to perform multiple complex cognitive tasks simultaneously.

Age-related neurodegenerative decline produces a disruption in WM, impacting quality of life (Conde et al., 2021; Seitz et al., 2019). Functional tests of WM have shown forgetting appointments or purpose of behavior, losing train of thought, or difficulty retrieving numbers or words decline rapidly in some while others display slow impairment (Conde et al., 2021; Martino et al., 2022; Mosconi et al., 2021; Seitz et al., 2019). While WM and episodic memory were two types of memory found to be most affected by the normal aging process, WM was found to be a common complaint associated with the MT (Hampson, 2018).

Working Memory during the Menopause Transition

During premenopausal years, women outperform men in most cognitive domains to include verbal and associative memory tasks, however, memory dysfunction in women increases during the MT due to the reduction in circulating E2, indicating estrogens protective effects on memory decline (Conde et al., 2021; Konishi et al., 2020).

Weber et al. (2021) found memory to be the most affected cognitive domain by the MT and was evident in neuropsychological (NP) tests insensitive to subtle decline. The Japan Nurses' Health Study (JNHS) also found of the 12,507 participants who responded to a 4-year survey, poor memory or forgetfulness was the most common complaint among 21 menopausal symptoms asked on a self-administered questionnaire (Kunihiko et al., 2022).

In the limited literature, NP battery tests displayed significant heterogeneity in WM during the MT (Weber et al., 2021). Although many cognitive dysfunction studies have been conducted on the postmenopausal population, recent underpowered trials completed in the perimenopausal sample suggested deficits in processing speed, attention, and WM (Metcalf et al., 2023). More postmenopausal women reported cognitive complaints than premenopausal women, however, memory impairment was more often reported during the MT phase than in post-menopausal (Conde et al., 2021; Greendale et al., 2020). While declines in attention, WM, and verbal memory are associated with the MT, Weber et al. (2021) acknowledged significant individual differences. Martino et al. (2022) analyzed reproductive aging on executive functioning in 100 premenopausal, perimenopausal, and postmenopausal women and found no differences between groups in WM. Additionally, the JNHS found a peak prevalence of memory dysfunction during the MT and a gradual decrease after age 55. Forgetting names or words, losing objects, and losing track of what information was previously shared or received from others indicates a decline in memory as evidenced by 50% of female participants in SWAN (Hayashi et al., 2022; Leistikow & Smith, 2022). The SWAN was a longitudinal study initiated in the 1990's in the United States and has

shown vulnerability to fluctuating estrogen levels and the increased risk of memory dysfunction during the MT.

Estrogen's Role in Working Memory

In the last 10-15 years, both human and non-human primate (NHP) studies have provided substantial evidence that estrogens play a leading role in the functioning of WM in the adult female brain (Hampson, 2018). The decline of E2 in the MT coincides with changes in cognition, particularly memory (Bortz et al., 2022). When levels of circulating E2 decrease, the range of cognition, especially in verbal memory, semantic memory, and processing speed, decline in women who undergo an oophorectomy (Weber et al., 2021). Estrogen replacement reversed the verbal memory deficits in the same oophorectomy patients, suggesting E2's contribution to changes in memory during the MT. Hampson (2018) concluded E2 may modulate frontal regions involved in cognitive control by promoting functioning of WM. The modulatory role of estrogen in the executive control process of the WM system are apparent in other behavioral, functional imaging, and cellular/molecular studies (Hampson, 2018). Hampson (2018) was one of the first to uncover an association between an increase in estrogen and improvements in WM function. It was also shown in animal studies that the combination of E2 and levonorgestrel (progestin) may decrease or alleviate WM symptoms (Metcalf et al., 2023). During the MT and into post-menopause, glucose metabolism starts to decline due to widespread expression of eRs and bioenergetics throughout the brain (Metcalf et al., 2023). The proper modulation of circulating estrogens in women ensures adequate functioning of the WM system despite neural atrophy associated with natural aging, occurring mostly in prefrontal and HIPP regions (Hampson, 2018; Konishi et al.,

2020). Fluctuating levels of E2 throughout the menstrual cycle correlate to verbal memory performance, HIPP volume, and a disruption in the functional activity and connectivity of the memory circuitry (Konishi et al., 2020).

Neural Substrates of Working Memory

Research has demonstrated the complex interaction among several substrates involved in WM by providing conflicting evidence in cognitive changes seen during the MT (He et al., 2021; Liu et al., 2021; Mosconi et al., 2021; Metcalf et al., 2023; Seitz et al., 2019; Zhang et al., 2022). Although it has been determined that specific areas involved in WM are dependent on the task, nature of information, and stage of processing components such as the delay period, response phase, or encoding, the DLPFC, inferior parietal lobule (iPAR), anterior cingulate cortex (ACC), and HIPP are implicated in memory circuitry and have relatively dense gonadal hormone receptors (Eriksson et al., 2015; Konishi et al., 2020; Seitz et al., 2019). Over the MT, WM performance shifts from reliance on the DLPFC and iPAR to the DLPFC and HIPP, indicating the significant impact that the MT has on the aging of memory circuitry (Konishi et al., 2020). While the WM circuitry engages multiple regions and no one neural structure is unique, a combination of processes and other constellations synchronize to ensure the WM process works efficiently (Seitz et al., 2019).

The cerebral cortex is the largest portion of the brain and considered the outermost portion responsible for retrieving memories (Denley et al., 2018; Garrett & Hough, 2021). The PFC is a region of the cerebral cortex, covering the front part of the frontal lobe, susceptible to environmental, pathological, and physiological stimuli such as E2. Due to eRs essential role in the activation of specific brain regions, their responses

are extremely sensitive to dosage and reproductive stage (Denley et al., 2018). E2 binds with eRα and eRβ to influence neural activity in the CNS (Hampson, 2018).

To locate the region of WM in the human brain, fMRI has been used to show activation sites such as the PFC (Hampson, 2018). Hampson (2018) found the PFC to be associated with high load conditions during the N-back test and other WM tasks when post-menopausal women received E2 supplementation and when compared with placebo. In this delayed match-to-sample task to study of WM, cell activity in the PFC increased during a delay and continued to increase despite introduced distractions. Damage to the PFC inhibited the ability to recall a stimulus during the delay period.

When WM demands increase, greater upregulation of frontal cortex activity was seen in younger adults whereas older adults displayed elevated PFC recruitment during WM maintenance (Eriksson et al., 2015). It was also shown during maintenance tasks, fMRI data displayed a weaker increase in blood-oxygen-level-dependent (BOLD) signal in DLPFC in older adults than those younger, indicating a less efficient frontal cortex. In another study reviewed by Eriksson et al. (2015), post-menopausal women not receiving E2 supplementation were found to have activation in the DLPFC during N-back testing, indicating similar activation as men rather than premenopausal women. Following the determination that circulating E2 modulated neural activation in the PFC during WM processing in the same study, the neurotransmitter mechanisms responsible for the mediation of the WM effects were called into question.

The DLPFC plays an integral part in manipulating information held in short-term storage required in WM tasks such as mental arithmetic (Yoshimura et al., 2023). eRα has been confirmed in primate brains in the DLPFC. fMRI has also been used to observe

the network of frontoparietal sites supported in WM where Martino et al. (2022) found greater activity in the left DLPFC during a WM task in women during the MT.

The role of the HIPP region in WM was also evident using fMRI during memory testing and was found to work with other brain regions (Hampson, 2018). According to Hampson (2018), the HIPP and surrounding temporal cortex are used to form long-term memories. In the same study, as words or photographs were presented to human subjects, researchers could watch consolidation occur in the HIPP and adjacent cortex. Brain scans such as PET have also been used to determine the HIPPs involvement in memory retrieval (Zsido et al., 2023). The HIPP is also involved in consolidation and retrieval of information in long-term storage (Garrett & Hough, 2021). The HIPP is rich in ER's and greater hippocampal volume was found in some studies to be associated with E2-dominant menstrual cycle phases (Zsido et al., 2023).

Estrogen replacement during the MT enhanced hippocampal and PFC functioning in neuroimaging studies when verbal memory tests were performed (Bortz et al., 2022). Bortz et al. (2022) also found fMRI scanning displayed impaired hippocampal activity and connectivity during memory tasks associated with decreased circulating estrogen during the MT. Martino et al. (2022) discussed the PFC's role in mental processes such as WM, flexibility, inhibitory control, verbal fluency, and planning. While fluctuating hormones during the MT influenced these executive functions, bilateral HIPP connectivity was enhanced in postmenopausal women (Konishi et al., 2020; Martino et al., 2022). Consistent with other studies, reproductive aging was associated with a failure to disengage the HIPP during a WM N-back task (Konishi et al., 2020).

The parietal cortex also plays a role in WM and more specifically, the superior parietal cortex (Eriksson et al., 2015). Eriksson et al. (2015) found this area to be associated with selective attentional control and executive aspects of WM. It is thought to play an active role in WM capacity. As the number of items to remember increases and reaches a limit of 3-4 items, activity leveled out. Lateralization towards the right hemisphere was seen in impairments of special WM when the right parietal cortex was lesioned, however, lesions to the left parietal cortex did not show impairment (Eriksson et al., 2015).

NHPs are used in studies surrounding WM due to similarities with human brains. During human neuroimaging studies and single-cell recordings in monkeys, the PFC displayed sustained neural activity during the delay period of WM tasks (Eriksson et al., 2015). In other studies reviewed by Eriksson et al. (2015), noninvasive magnetic or electrical stimulation of the PFC influenced the performance of WM and demonstrated the ventral PFC was involved in verbal WM whereas the DLPFC was active in other WM tasks such as the manipulation tasks, not maintenance tasks.

In other animal studies, according to Garrett and Hough (2021), rats who learned where a platform was located that would remove them from a water tank were later injected with a glutamate-blocking drug. During subsequent testing and when compared to a control group, it was determined the receptors for the neurotransmitter glutamate in the HIPP were temporarily disabled when the rats lacked the ability to remove themselves via the same platform. When the same rats were given the same drug during testing, their recall was impaired, suggesting the HIPP plays a role in memory

retrieval. The HIPP in both human and NHPs are especially vulnerable to the pathology of AD and other forms of dementia (Morgan et al., 2018).

Dementia and Alzheimer's Disease

Approximately 50 million people worldwide live with dementia (Le et al., 2020). The prevalence of dementia across the world is a growing public health epidemic with rates expected to triple by 2050 (Morgan et al., 2018). First discovered in 1906 by Alois Alzheimer, AD accounts for 60-70% worldwide of cases of dementia, negatively affecting the quality of life for patients and caregivers (Bortz et al., 2022). AD is the leading neurodegenerative cause of dementia and is a progressive neurodegenerative condition characterized by a loss in memory, difficulty in every-day tasks, and impaired spatial recognition (Boyle et al., 2020; Bortz et al., 2022; Martino et al., 2022). AD diagnosis is based on the presence of amyloid-β plaque and neurofibrillary tangles in the brain (Nasaruddin et al., 2020).

Due to cognitive decline in midlife, women are especially susceptible to mild cognitive impairment (MCI) caused by a loss of estrogen due to its involvement in the cellular pathways required for proper functioning (Martino et al., 2022). The combination of endocrine aging and the MT are implicated in pathological conditions and cognitive decline leading to advanced neurological dysfunction (Russell et al., 2019)**.** When normal cognitive functioning begins to deteriorate into MCI, further dysfunction transitions into dementia (Conde et al., 2021). Those diagnosed with MCI have a nine-fold increased risk of dementia, the fifth leading cause of death categorized as a severe form of cognitive functioning impairment (Le et al., 2020). The disruption in cognitive functioning has also

been linked to other neuropsychiatric disorders in addition to AD and other dementias (Morgan et al., 2018).

Although age plays a role in the risk of AD, it is important to note the prevalence is higher in women than in men, representing two-thirds of cases worldwide (Bortz et al., 2022; Saleh et al., 2023; Zsido et al., 2023). Biological variables such as the loss of estrogen have become a controversial factor to explain the discrepancy in susceptibility and has emerged as the main etiological basis for the larger prevalence of AD in women (Bortz et al., 2022; Saleh et al., 2023). Boyle et al. (2020) found a woman's risk for memory dysfunction and increased risk for AD were directly associated with declining levels of estrogen during the MT. Executive functioning was found to be crucial for protecting against AD and other forms of dementia (Martino et al., 2022). In a 12-year population-based study conducted in Cache County, Utah, endogenous estrogen exposure (EEE) was positively associated with cognitive status and a longer duration of HRT was also positively associated with cognitive status (Matyi et al., 2019).

The neurodegenerative processes are associated with AD decreases in the presence of E2 (Morgan et al., 2018). The MT increases a woman's risk of AD-related changes in neuroimaging studies (Mosconi et al., 2021; Metcalf et al., 2023; Morgan et al., 2018). E2 decreases the hyperphosphorylation and deposition of amyloid-β (Morgan et al., 2018). According to Mosconi et al. (2021), estrogens play a key role in the protection of free radicals and trafficking of cholesterol, and clears the presence of amyloid-β, implicated as a precursor to the development of AD. AD is thought to be caused by the overproductions and failure of amyloid-β clearance, leading to its accumulation (Nasaruddin et al., 2020).

A recent study suggests women in the MT had a higher amyloid-β load brain-wide than premenopausal women and the presence of E4 isoform of APOE heightened this effect (Metcalf et al., 2023). By increasing the number of antioxidants, E2 is believed to decrease the amount of amyloid-β in the brain (Morgan et al., 2018). In a longitudinal brain imaging study, 59 women were assessed for risk factors associated with AD and found women in the MT showed an increase in amyloid-β deposition and hypometabolism in the PFC during the 3-years between baseline and follow-up MRI and PET scans when compared to premenopausal women and men of similar age (Mosconi et al., 2021). Several observational studies demonstrated a positive effect of HRT on AD, showing a 29% reduction in AD (Gava et al., 2019). Prior to the onset of AD, neuropathological changes were also observed in the brain, accompanying subtle cognitive decline, indicating the need to test for WM consistently to adopt early interventions to decrease cognitive decline during the MT (Mosconi et al., 2021).

Tests of Working Memory

Questionnaires such as the Working Memory Questionnaire (WMQ) are also validated self-administered subjective measures of WM deficits (Vallat-Azouvi et al., 2012). According to Vallat-Azouvi et al. (2012), the WMQ specifically addresses participants' self-report of three sections of WM: short-term storage, attention, and executive control. The first, short-term storage, is the ability to maintain information for a brief time. The second, attention, includes questions based on distractibility, mental fatigue, mental slowness, and dual-task processing. The third domain, executive control, relates to questions regarding planning ahead and decision making. Questions are scored on a five-point Likert-type scale, ranging from 0 (no problem at all) to 4 (very severe

problem in everyday life) with a total possible score of 120 where higher scores correspond to more self-reported WM difficulties/complaints.

Intermittent Fasting

A unique, cost-effective, and safe diet intervention, intermittent fasting (IF), is an eating pattern found to prevent and manage cognitive decline and improve a multitude of health conditions and neurodegenerative diseases (Ezzati & Pak, 2023; Gudden et al., 2021; Manoogian & Panda, 2017; Senderovich et al., 2023). According to Senderovich et al. (2023), requirements of IF include periods of prolonged abstinence from food intake, alternated with periods of normal meal consumption. Varying protocols of IF methods include alternate-day fasting (ADF), time-restricted eating (TRE), modified fasting regimens, and religious fasting such as during Ramadan for Muslims and Sustenance in China (Nasaruddin et al., 2020; Queiroz et al., 2021; Xie et al., 2022). Sustaining a robust eating-fasting cycle without additional restrictions may also reverse chronic diseases characteristic of aging (Gudden et al., 2021; Manoogian & Panda, 2017).

Diets such as IF are effective lifestyle modifications that improve blood glucose, reduce insulin, blood pressure, inflammation, and heart rate, depletes or reduces glycogen storage, mobilizes fatty acids, and generates ketones (Anton et al., 2019; Gabel et al., 2022; Mattson et al., 2018; Senderovich et al., 2023; Xie et al., 2022). No serious side effects were documented in previous studies of IF (Xie et al., 2022).

According to Manoogian and Panda (2017), epidemiology studies show inconsistent eating patterns increase the risk for diseases characteristic of aging such as cognitive decline. Irregular eating-fasting cycles incongruent with circadian rhythms disrupt the temporal coordination of metabolism and physiology. Protection from breast

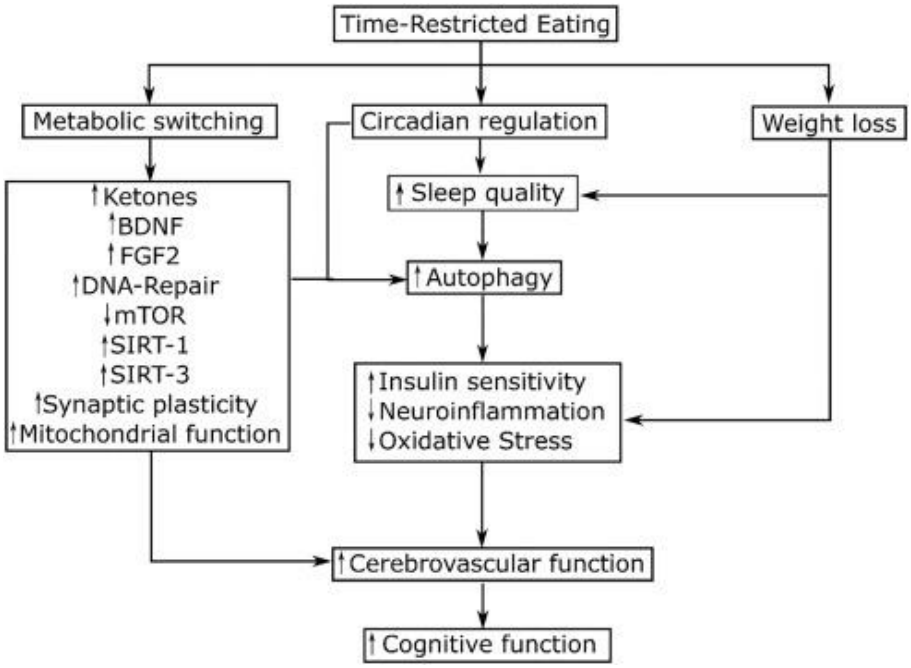
cancer was also correlated with sustained eating-fasting cycles or prolonged overnight fasting. Senderovich et al. (2023) evidenced IF has neuroprotective effects by increasing neurogenesis in the HIPP and thereby improving cognitive resilience and found IF to be a safe intervention with no adverse effects found in the 9 RCTs reviewed that assessed the impact of IF on cognition. Moreover, adhering to a defined eating pattern in accordance with the timing of external cues can maintain a robust circadian clock and may prevent or improve disease (Manoogian & Panda, 2017).

Another benefit of IF, adult neurogenesis, is the generation of new neurons produced by neural stem cells in the nervous system and occurs in human hippocampal formation (Kim et al., 2020). The HIPP is a key region in memory circuitry and is one of the few regions in the brain that continues to undergo neurogenesis during the aging process (Konishi et al., 2020). In rodents, according to Kim et al. (2020), adult hippocampal neurogenesis (AHN) is required in recognition memory and the ability to identify previously encountered stimuli. In adult mice, AHN was reported in IF and restricted daily caloric intake regimens. To test the effects of intermittent and caloric restriction on human hippocampal neurogenesis-related cognition, Kim et al. (2020) was the first to conduct a RCT in humans, investigating the association between energy restriction and neurogenesis-associated cognitive function. It was determined energy restriction may enhance HIPP-dependent memory and may benefit those in an aging population with declining cognition. Multiple rodent studies have also shown AHN can be modulated by nutritional cues such as continuous energy restriction (CER) or a reduced daily caloric intake and intermittent energy restriction (IER) or the drastic reduction of caloric intake for varying periods of time (Kim et al., 2020).

Modern conveniences have also allowed societies to consume food three or more times each day than in the past without allowing sufficient time for metabolic switching which produces the ketone BHB and occurs 12-36 hours following the initiation of fasting (see Figure 2; Ezzati & Pak, 2023; Xie et al., 2022). This is problematic because synaptic plasticity is improved by the upregulation of BDNF expression in neurons because of BHB production (see Figure 2; Ezzati & Pak, 2023; Xie et al., 2022).

Figure 2

Time-Restricted Eating Neuroprotective Benefits (Ezzati & Pak, 2023)



Konishi et al. (2020) evidenced that BDNF and sex steroid hormones play a significant neuroprotective role in memory circuitry in postmenopausal women. During a fasting state, ketones are produced from adipose-cell-derived fatty acids when liver glycogen is depleted, creating a metabolic switch in cellular fuel source, and optimizing brain health through the increase in ketones, BDNF, fibroblast growth factor-2 (FGF2), and autophagy of DNA damaged cells, resulting in enhanced cerebrovascular and

cognitive functioning (see Figure 2; Ezzati & Pak, 2023; Gabel et al., 2022; Mattson et al., 2018). Ezzati and Pak (2023) found IF protects the brain from neurodegenerative diseases such as AD by preventing the dysfunction and degeneration of neurons by reducing glucose, leptin, insulin, inflammatory cytokines, and the mammalian target or rapamycin (mTOR) pathway activity (see Figure 2). This adaptation allows for cellular and molecular changes in neural networks which enhance functionality and increase resistance to stress, injury, and disease. The metabolic switching process occurring in IF shows promise for the optimization of brain functioning and resilience throughout the lifespan by impacting signaling pathways to promote neuroplasticity and resistance to potential brain injury and disease (Mattson et al., 2018). According to Mattson et al. (2018), in both healthy and at-risk human populations, IF has emerged as a common alternative to traditional dietary strategies.

Sutton et al. (2018) was the first study to test the benefits of IF independent of weight loss. This 4-week crossover experiment also constituted the first RCT to be aligned with circadian rhythms in metabolism. The research demonstrated IF in humans improves aspects of cardiometabolic health and that the effects are not solely due to weight loss. Participants included 12 prediabetic men randomized to a 6/18 IF regimen or a control and found IF improved insulin sensitivity, β cell responsiveness, blood pressure, oxidative stress, and appetite. Zouhal et al. (2020) investigated the effects of Ramadan IF (RIF) on 28 males with obesity randomized to a 30-day fasting group or control group. This study demonstrated improved systematic inflammation biomarkers in males with obesity who fasted for 30 days with an adherence of 100%.

In animal studies, IF has shown neuroprotective benefits leading to neurogenesis in the HIPP, thereby reducing stroke and other neurodegenerative diseases (Gudden et al., 2021; Mattson et al., 2018; Senderovich et al., 2023). IF in animal models displayed a preventative tool to influence amyloid-β production in AD (Nasaruddin et al., 2020). The prevention of mitochondria decay and synthesis of new mitochondria, a proposed mechanism of IF called mitochondriogenesis, improved overall health to include cognition (Senderovich et al., 2023). In other animal models, and likely in humans, the mechanisms of IF suggest the prevention of obesity, improvement in insulin sensitivity and inflammation, mitochondrial metabolism, and autophagy and a reduction in hepatic fat, and stress responses (Gudden et al., 2021). Gudden et al. (2021) found benefits of IF in epilepsy, multiple sclerosis (symptoms and progress), and AD. Hernandez et al. (2022) also determined 12 months of time-restricted feeding (TRF) in animal studies improved cognition and altered microbiome composition regardless of macronutrient composition. In additional animal studies, positive outcomes were shown in Parkinson's Disease, autism spectrum disorder, mood and anxiety disorders, and ischemic stroke because of IF, but it was also recognized total caloric intake, intake of specific nutrients, and variations in fasting patterns may be relevant components of IF success (Gudden et al., 2021).

Adherence to Intermittent Fasting

Findings concerning adherence rates vary according to behavioral, biological, environmental, and psychosocial factors (O'Connor et al., 2022). Anton et al. (2019) conducted a study with 84% adherence of 10 overweight and sedentary adults 65 years and older who fasted for 16 hours a day. Participants experienced weight loss, clinically

meaningful changes in walking speed, improvements in quality of life, and fewer adverse events. This study demonstrated that fasting for 16 hours per day displayed acceptable and feasible eating patterns for participants to follow.

O'Connor et al. (2022) and Jefcoate et al. (2023) identified social events, feelings of hunger and sluggishness, inadequate diet quality during eating windows, family life, misalignment with other 24-hour activity behaviors, the need to mitigate negative feelings, difficulties with self-monitoring, flexible work/school schedules, and baseline eating patterns as barriers of adherence to IF that were largely influenced by other lifestyle factors. Those who adhered to IF protocols found the ability to consume ad libitum during eating windows and simplicity to be among the key factors (O'Connor et al., 2022). A systematic review by Adafer et al. (2020) identified 494 articles from six nutrition journals and five general databases between January 2014 and September 2020 that evaluated the effects of IF in human subjects and adherence rates. Of the articles collected, 23 were utilized for analysis and found an 80% adherence rate to the IF regimen, presenting the ease of following an IF regimen. Additionally, and although caloric restriction was not a factor, 3% of fat mass and weight loss was attributed to an IF diet during the same review. Jefcoate et al. (2023) found an adherence rate estimated between 63% and 100% to IF protocols during a review of studies but acknowledged potential inaccuracies of reporting. O'Neal et al. (2023) found adherence rates ranged from 47% to 95%, however, after conducting their own analysis, the researchers found adherence rates to average approximately 61% per week and approximately 63% after 5 weeks. While it is imperative to acknowledge difficulties related to adherence of

intermittent fasting, this review would be incomplete if nutritional components were also not addressed.

Chrono-Nutrition

The Latin *circa diem,* or "about a day," refers to the coordination of biological, metabolic, and behavioral processes that occur throughout a 24-hour period known as the circadian cycle (Queiroz et al., 2021). This cycle anticipates and adapts to internal daily rhythmic changes (Manoogian & Panda, 2017). Since the invention of electrical lighting, humans can choose their sleep-wake pattern according to their schedule and often no longer abide by their internal natural diurnal rhythms (Manoogian &Panda, 2017). According to Queiroz et al. (2021), environmental cues such as irregular or abnormal eating times alter the genetic machinery of the body's internal clock. These disruptions, along with a fat-rich Western diet conveniently served 24-hours a day, play a causative role in a variation of chronic diseases (Xie et al., 2022). Altered circadian rhythms along with disruptions in eating and fasting cycles, cause chrono-disruptors that compromise health (Adafer et al., 2020; Queiroz et al., 2021; Xie et al., 2022). Other chrono-disruptors include shift work, jet lag, artificial lighting, and nutrient deficient foods (Queiroz et al., 2021). Prior to the abundance of food and light sources around the clock, circadian systems enhanced neural plasticity in response to the changing of lighting and food sources and provided a natural adaptation to varying seasons (Manoogian & Panda, 2017).

A regularly repeated occurrence or external stimulus, such as the temperature or daylight, serves to synchronize the body's internal biological clock mechanisms. These external stimuli, called zeitgebers, modify circadian synchronization in conjunction with

the self-sustaining and autonomous circadian rhythms generated by the central and peripheral oscillators in the body (Manoogian & Panda, 2017). According to Queiroz et al. (2021), cues such as irregular or abnormal eating times alter the genetic machinery of the body's internal clock. The 24-hour oscillations in circadian rhythms are found at a molecular, physiological, and behavioral level and tune functioning of the digestive, immune, endocrine, and cardiovascular systems as well as several brain regions and metabolic organs (Xie et al., 2022). Oscillations optimize energy expenditure, synchronize metabolic pathways to reduce build-up of toxins, and separate incompatible biochemical or physiological processes (Queiroz et al., 2021).

The hypothalamus houses the suprachiasmatic nucleus (SCN) which is considered to be the mammalian master circadian system clock, while several secondary clocks distributed throughout the brain (extra-SCN) and in other organs such as the liver, pancreas, adipose tissue, and skeletal muscle (Queiroz et al., 2021). According to Queiroz et al. (2021), the mammalian circadian system acts as the central/master clock, along with the secondary clocks, and are responsible for generating self-sustained oscillations. The autoregulatory feedback loops function via a set of proteins called clock proteins (Queiroz et al., 2021). The SCN also plays a significant role in eating behaviors, due to its centralized pacemaker regulated by light shone through the retinohypothalamic tract (Queiroz et al., 2021). According to Queiroz et al. (2021), the light-dark cycle controls the master clock, and peripheral tissues respond to eating. Circadian oscillators of peripheral tissues, mostly the liver and adipose tissue, are influenced by temporal food consumption patterns and dietary macronutrients (Manoogian & Panda, 2017). Involved

in the regulation of food intake is the arcuate nucleus and, together with the SCN, neuroanatomical connections mediate circadian food intake (Queiroz et al., 2021).

According to Queiroz et al. (2021), the food clock is a secondary brain clock which influences the timing system, participates in circadian eating cycles, and controls food anticipation. Multiple factors directly influence the effectiveness of the food clock such as body temperature, hormonal signals such as cortisol and melatonin, and both the sympathetic and parasympathetic systems in the autonomic nervous system (ANS). The food clock is also impacted indirectly through the eating-fasting, sleep-wake, and resting-activity cycles. The development of circadian rhythmicity supports physiological processes at propitious moments and functions using the central clock, food clock, peripheral oscillators, and zeitgebers.

The disruption of natural circadian rhythms accentuates the pathogenesis of metabolic disease (Queiroz et al., 2021). For example, unlimited and uninterrupted access to high energy density and low nutritional quality food contribute to multiple adverse health outcomes (Queiroz et al., 2021). Although the mechanisms and exact relationships are unclear, circadian disruption is correlated to neurodegenerative diseases such as AD and Parkinson's Disease (Queiroz et al., 2021). It has also been postulated that because neurogenesis is influenced by circadian rhythms, the disruption of circadian rhythm in aging contributes to AD (Manoogian & Panda, 2017). In support of this putative mechanism, research has shown that cognitive deficits in hippocampal learning and memory in rodent models can be induced by chronic circadian disruption (Manoogian & Panda, 2017). In the same study, the dendrite length and neuronal complexity in the prelimbic PFC in these mice also showed a decrease in functioning. By temporarily

coordinating cellular and tissue function and behavior, circadian rhythms optimized physiology and health in the mice. For these reasons, it is important to optimize eating patterns according to circadian clocks to prevent disease. By aligning the internal processes of central and peripheral clocks with external stimuli such as the eating-fasting cycle, the prevalence and burden of cognitive decline during the MT may be mitigated (Queiroz et al., 2021; Xie et al., 2022).

According to Adafer et al. (2020), food timing, circadian rhythm, and chrononutrition are used interchangeably to refer to various forms of IF. IF based on chrononutrition principals has been found to be a well-tolerated and simple diet that results in improved health. Eating times based on endogenous circadian rhythms have grown in popularity and a substantial amount of evidence has shown IF to be beneficial in weight loss, improved biomarkers, and brain health (Ezzati & Pak, 2023). The disruption of known estrogen-regulated systems such as sleep, circadian rhythms, depression, thermoregulation, and cognitive decline are neurological in nature (Queiroz et al., 2021). Whereas estrogen is considered the master regulator of the metabolic system of the female brain and body, the circadian system is a master integrator of internal states of an organism and external interactions with ambient light and nutrition (Mosconi et al., 2021).

By synchronizing the supply of food to the body to the times the body is best prepared to receive it is aligning IF's eating-fasting cycle with circadian rhythms and autophagy (Ezzati & Pak, 2023). Ezzati and Pak (2023) and O'Neal et al. (2023) found IF shows potential benefits in optimizing the body's circadian rhythms, coordinating metabolism and physiological functions such as glucose utilization, insulin sensitivity,

energy expenditure, inflammation, sleep, and lipid levels. According to Ezzati and Pak (2023), the complex interactions between circadian biology, human metabolism, and nutritional profiles may provide enhanced health and cerebrovascular cognitive functioning.

Despite the benefits IF has evidenced, it is important to recognize the strength of the effects are dependent on individual physiological needs, and on existing conditions such as genetics, stress, sleep patterns, dietary consumption, preexisting conditions, etc. (Manoogian & Panda, 2017; Queiroz et al., 2021; Xie et al., 2022).

Intermittent Fasting and Cognition

Metabolic Switch

Although there are variants of IF that differ in the duration of fasting, people who fast between 12 to 36 hours experience a metabolic switch when the body's glucose levels drop (Anton et al., 2021; Gudden et al., 2021; Schuppelius et al. 2021). When glucose levels drop, the body switches from the utilization of energy through glycogenolysis (the breakdown of glycogen into glucose) to lipolysis (the breakdown of stored fat in the form of lipids from adipose tissue; Gudden et al., 2021). Once this occurs, the lipids are metabolized into free fatty acids (FFAs), transformed into Acetyl CoA in the liver, and subsequently turned into ketones BHB and AcAc. BHB and AcAc are then transported from the blood into the brain where the preferred fuel for the brain becomes the ketones (Gudden et al., 2021). This metabolic switch, demonstrated in both animal and human pilot studies increased levels of ketones, BDNF, fibroblast growth factor-2 (FGF2), Sirtuin 1&3, and autophagy, thereby optimizing cerebrovascular and cognition function (see Figure 2; Ezzati & Pak, 2023). Additionally, the switch may

decrease glucose, leptin, insulin, mammalian target of rapamycin (mTOR) pathway activity, and inflammatory cytokines, resulting in improved cognition and the prevention of dysfunction and degeneration of neurons which protects the brain from diseases like AD (see Figure 2; Ezzati & Pak, 2023).

Enhanced neuroplasticity and protection against oxidative and metabolic stress is a result of lower levels of circulating insulin in the blood due to IF (Currenti et al., 2021; Ezzati & Pak, 2023; Gudden et al., 2021). Autophagy is also stimulated due to lower levels of circulating glucose which reduces the activity of the mTOR pathway (see Figure 2; Ezzati & Pak, 2023). In animal models, BHB upregulates the expression of BDNF, thereby promoting cellular stress resistance, synaptic plasticity, DNA repair, and the promotion of mitochondrial health (see Figure 2; Ezzati & Pak, 2023; Gudden et al., 2021; Mattson et al., 2018). It is also postulated that increased BDNF levels in humans leads to increased levels of BDNF in the brain (Gudden et al., 2021). The benefits of IF are neuroprotective, improve sleep quality, and increase weight loss as seen in Figure 2 (Ezzati & Pak, 2023; Schuppelius et al., 2021).

Circadian Rhythms

As previously discussed, the SCN in the human brain is involved in the regulation of the circadian clock, where hormonal secretion, gene transcription, and protein levels oscillate on a 24-hour basis (Currenti et al., 2021; Gudden et al., 2021; Schuppelius et al., 2021). Secondary clocks found in peripheral tissues, such as the liver, are regulated by meal timing and food intake outside of normal eating dampen the amplitude and knock peripheral clocks out of phase with central oscillators (Gudden et al., 2021; Schuppelius et al., 2021). Advancing age and individuals with ADHD, AD, hemorrhagic stroke

vulnerability, and mood disorders have increased amplitudes of peripheral circadian oscillations (Currenti et al., 2021; Gudden et al., 2021; Schuppelius et al., 2021). IF resets secondary oscillators and shift peripheral oscillators to match the phase of central oscillations (Gudden et al., 2021; Schuppelius et al., 2021). Engaging in IF decreases insulin levels which leads to overall increased insulin sensitivity and is beneficial because glucose metabolism decays with age and are associated with AD, even before disease onset (Currenti et al., 2021; Ezzati & Pak, 2023; Gudden et al., 2021; Schuppelius et al., 2021). It is known that IF enhances cognitive functioning therefore, it is reasonable to believe that IF will also show positively effect on WM during the MT.

Exercise

Exercise is not limited to organized sports but also includes dance, martial arts, swimming, walking, running, boxing, weightlifting, yoga, etc. (Mahindru et al., 2023; Posadski et al., 2020). Exercise is a planned, structured, and repetitive exercise which has a final or intermediate objective to improve or maintain one or more components of fitness and includes both aerobic and anaerobic activity measured by frequency, duration, and intensity (Mandolesi et al., 2018). Anerobic-based exercise such as resistance training preserves or increases lean muscle mass and aerobic-based exercise such as running or walking promotes metabolism and the reduction of fat mass (Parr et al., 2020).

According to Posadski et al. (2020) and Mandolesi et al. (2018), exercise significantly reduces the risk of medical conditions such as heart disease, stroke, osteoporosis, cancer, and diabetes. A plethora of studies have shown regular exercise improves sleep, substance abuse, mortality rates, pain and disability, muscle and bone strength, psychiatric disorders such as depression and anxiety, and cognition (Lee et al.,

2022; Mahindru et al., 2023; Mandolesi et al., 2018; Posadski et al., 2020). A review of public health in Sweden by Malm et al. (2019) found the health benefits of exercise through sports improved psychosocial and personal development and reduced alcohol consumption.

Neural Impacts

A strong gene modulator, exercise induces functional and structural changes in the brain, providing enormous biological and psychological benefits (Mandolesi et al., 2018). Gelfo et al. (2018) reported numerous studies demonstrating how exercise is linked to the prevention of cognitive decline related to aging, reduces the risk of developing dementia, improves the quality of life, and reduces the level of deterioration in executive functions through a magnitude of changes experienced in the brain.

A significant amount of data suggests that exercise reduces the risk of various neurological diseases and protects the brain from the negative effects of aging by enhancing neurogenesis and brain plasticity (Basso & Suzuki, 2017). The area that underwent the most improvement was the PFC where exercise induced benefits were found in attention and other executive functions (Basso & Suzuki, 2017). Exercise enhances attention and WM, due to increased cerebral blood flow (CBF) to the PFC and DLPFC (Boere et al., 2023).

The neurological benefits of exercise in human studies include increased GMV in frontal and HIPP regions, increased levels of BDNF and blood flow, increased academic achievement in children, improved learning and memory, prevention of cognitive decline and reduced risk of developing dementia, and the modification of the neural communication network (Gelfo et al., 2018; Mandolesi et al., 2018).

Mahindru et al. (2023) also reported that regular exercise improves the functioning of hormone regulation in the HPA axis by lowering cortisol secretion and restoring the balance of leptin and ghrelin. Emotions and memory are controlled by the HPA axis and are crucial elements in the limbic system (Shaik et al., 2020). Hallam et al. (2018) explained attention, focus, cognition, decision-making, language fluency, and memory improved for up to two hours following exercise. Regular exercise lowers systematic inflammation and increases plasma BDNF, and may reduce amyloid-β toxicity linked to AD progression (Mahindru et al., 2023). Mahindru et al. (2023) also emphasized exercise causes the brain to produce endogenous opioid peptides or endorphins to reduce pain and increase mood.

In animal studies, Gelfo et al. (2018) reported neurological improvements such as increased neurogenesis, synaptogenesis, and gliogenesis in the HIPP and neocortex. Other improvements included angiogenesis in the HIPP, neocortex, and cerebellum, modulation in neurotransmission systems (serotonin, noradrenalin, acetylcholine), increased neurotrophic factors (BDNF and IGF-1), and improved spacial memory performance. Basso and Suzuki (2017) acknowledged that while animal models have primarily focused on the effects of exercise on hippocampal neurogenesis and hippocampal-dependent learning and memory as a main effect of long-term exercise, human studies have only begun to identify the neuroanatomical systems found in long-term increases in exercise.

Boere et al. (2023) reported several studies where increased levels of dopamine, epinephrine, and norepinephrine were found in the PFC post-exercise. Exercise positively modulates the mesolimbic reward pathway which transports dopamine from the ventral

tegmental area (VTA) to the amygdala and nucleus accumbens (Tyler et al., 2023). The striatum encompasses the nucleus accumbens and modulates reward and desire (Tyler et al., 2023). Levels of striatal dopamine depletion and associated motor deficits were observed in Parkinson's Disease patients (Marques et al., 2021).

Marques et al. (2021) analyzed fifteen articles to investigate the potential bidirectional effects of exercise on dopamine in young adulthood to old age. This systematic review found dopamine to be a key neurotransmitter in the support of cognitive control in the neural system. Modulated by exercise, dopamine has a well-established role in regulating motor neurons, spatial memory function, and is crucial in maintaining chemical balance in the CNS (Marques et al., 2021). Although the underlying mechanisms are still being debated, exercise increases dopamine receptor availability and may reduce the severity of anxiety, depression, and other mental-related issues (Marques et al., 2021).

While exercise is recommended to combat mental illness and preserve mental wellness, the amount of time required to experience these benefits has remained controversial (Mahindru et al., 2023). According to Lee, et al. (2022), the guidelines set forth by the 2018 physical guidelines for Americans recommended moderate exercise of at least 2.5 to 5 hours/week or 1.25 to 2.25 hours/week of vigorous exercise or a combination of both. However, it remains unclear what levels are associated with lower mortality.

A study by Chaire et al. (2020) measured the theta and alpha power in visual WM and attention tasks before and following a 4-month physical exercise training in 43 sedentary young adults. Theta-band activity, measured by neural oscillations during an

electroencephalogram (EEG) has been implicated in WM processes and is thought to be, in part, related to HIPP activity. Alpha-band activity has been associated with thalamocortical and corticocortical networks related to attention, alertness, and memory performance. When compared to the preintervention baseline, the exercise group in Chaire et al. (2020) experienced increased frontal alpha power, correlating positively with changes in physical fitness.

Cognitive Effects of Exercise

Given exercise's accessibility, ease of use, and cost-effectiveness, Tyler et al. (2023), analyzed a form of exercise, high intensity interval training (HIIT), on the treatment of substance use disorders (SUDs). HIIT was defined by the American College of Sports Medicine as an anaerobic activity that alternates short bouts of low intensity with short bouts of high intensity (greater than 65% max capacity; Tyler et al., 2023). HIIT has been proven to be an effective exercise due to its improvements in VO2 max, reduction of fasting glucose levels and insulin resistance, and significant enhancement of WM capacity when compared to moderate intensity aerobic exercise (MIAE; Tyler et al., 2023).

When combined with IF, exercise increases muscle mass and quality, decreases circulating lipids and fat mass, decreases glucose levels, increases insulin sensitivity, and reduces fatty liver and appetite (Parr et al., 2020). Zhidong et al. (2021) conducted a systematic and meta-analyctic review to examine the effects of physical exercise on WM in older adults. Of the twenty-eight published studies, it was determined physical fitness had a significant effect on WM in older adults and moderated by frequency, type,

duration, intensity. While exercise exhibits positive effects on overall health, studies focusing on IF and exercise on WM in MT are lacking.

Estrogen, specifically estradiol (E2) or 17β estradiol, play a leading role in the proper functioning of cognitive behavior and tasks in women during reproductive years. During the MT, the loss of estrogen in neural regions inhibits proper functioning of cognitive conduct such as WM. This decrease in estrogen disrupts the neurotransmitters' ability to regulate proper cell function and to protect against amyloid-β production. When estrogen levels decrease during the MT, women are at a significantly higher risk of developing AD and other severe neurological disorders, burdening the patient, families, and the healthcare system (Yang et al., 2023). IF aligned with circadian rhythms are cost-efficient and simple regimens used to increase cognitive function and to decrease biomarkers that lead to cardiovascular disease, improve BMI, weight loss, decrease blood pressure, and a plethora of additional health benefits (Mosconi et al., 2021; Morgan et al., 2018; Queiroz et al., 2021). Regular exercise increases HIPP size, protects neuroplasticity and brain neurogenesis, and significantly reduces the risk of detrimental diseases and premature death (Bagit et al., 2020; Chaire et al., 2020; Mandolesi et al., 2018). Therefore, the implementation of early interventions such as IF and exercise during the MT to improve WM potentially halts the production of amyloid-β and decreases the risk of AD and other detrimental neurological conditions (Adafer et al., 2020; Bagit et al., 2020; Chaire et al., 2020; Mosconi et al., 2021; Morgan et al., 2018). Engaging in healthy behaviors such as IF and exercise are easy, cost-effective ways to improve overall brain function, thereby increasing WM during the MT.

Biblical Foundations of the Study

The Bible encourages us to live a healthy lifestyle. Our bodies are the temple of the Holy Spirit and He expects us to treat them with the utmost care. 1 Corinthians 6:19 explains, “What? know ye not that your body is the temple of the Holy Ghost *which is* in you, which ye have of God, and ye are not your own?” (*King James Bible*, 1769/2017).

The Bible provides numerous examples of fasting. There are varying reasons to fast, and scripture supports those who choose to fast. Various verses provide guides for spiritual strength, time to worship, and time to focus on God. “So we fasted and implored our God for this, and he listened to our entreaty” (*English Standard Version Bible*, 2001/2023). During challenging fasts, the Bible provides encouragement, a reminder of our dependence on God, and His guidance. Varying scriptures offer types, lengths, and dietary considerations of fasting options. In Deuteronomy 9:9-18, Moses fasted for 40 days on his way to receiving the commandments of God written on stone tablets. “When I was gone up into the mount to receive the tables of stone, even the tables of the covenant which the LORD made with you, then I abode in the mount forty days and forty nights, I neither did eat bread nor drink water” (*King James Bible*, 1769/2017). David and Bathsheba’s young son became ill in 2 Samuel 12:15-20 and David fasted for seven days until his child’s death, “David therefore besought God for the child; and David fasted, and went in, and lay all night upon the earth” (*King James Bible*, 1769/2017). Elijah fasted for 40 days while escaping Queen Jezebel. “And he came thither unto a cave, and lodged there; and, behold, the word of the LORD came to him, and he said unto him, What doest thou here, Elijah?” (*King James Bible*, 1769/2017).

Another popular fast found in the Bible is The Daniel fast. The Daniel fast resembles the modern-day Vegan diet which focuses primarily on vegetables and water

and limits “royal foods” such as meat and wine (“Daniel Fast,” 2023). Abstaining from certain food or drink requires self-discipline and a connection to God through faith and gratitude. Scripture provides the support to worship, to pray, and to focus our attention on God during a fast.

Optimal nutrition is crucial for quality of life and proper brain functioning. Essential vitamins and nutrients are needed to carry out the functions He has put forth for us. God wants us to live the best life possible and through the Bible, He guides us towards optimal health. “Take thou also unto thee wheat, and barley, and beans, and lentils, and millet, and fitches, and put them in one vessel, and make thee bread thereof, according to the number of the days that thou shalt lie upon thy side, three hundred and ninety days shalt thou eat thereof” (Ezekiel 4:9, *King James Bible*, 1769/2017). Although training for godliness is most important, 1 Timothy 4:8 is a reminder that physical training is important as well, “For bodily exercise profiteth little: but godliness is profitable unto all things, having promise of the life that now is, and of that which is to come” (*King James Bible*, 1769/2017).

Combining spiritual growth with healthy activities such as eating nutritiously and exercising regularly, illustrates the abilities for which He has created to ensure a long and healthy existence. Representing, supporting, and glorifying that which He has given us requires proper maintenance and the strength to glorify God. Isaiah 58:6 reminds us of our power invoked by fasting, “Is not this the fast that I have chosen? to loose the bands of wickedness, to undo the heavy burdens, and to let the oppressed go free, and that ye break every yoke?” (*King James Bible*, 1769/2017).

Summary

Throughout this literature review, it was shown that the decline of estrogen levels experienced during the MT negatively impact WM (Hara et al., 2018). E2 decline has also been linked to advanced neuropsychiatric disorders such as AD, depression, and schizophrenia (Bortz et al., 2022; Denley et al., 2018). Given the positive effects of IF and exercise on biomarkers of disease, weight, and general cognitive functioning as evidenced in Anton et al. (2019), Bagit et al. (2021), and Currenti et al. (2021), it was important to conduct this RCT to address a gap in the literature by investigating the effects of an 8/16 IF regimen on WM during the MT with a covariate of exercise. In conjunction with scripture, this review provided supportive measures to improve health during the MT. Current research and a biblical perspective provides for a potential treatment for millions of women experiencing a decrease in cognitive functioning during the MT. Chapter three describes research methodology, design, procedures, and recruitment.

CHAPTER 3: RESEARCH METHOD

Overview

Chapter two consisted of a literature review which evidenced a gap in research that was filled by conducting this study. This chapter discusses how this study investigated the effects of an 8/16 intermittent fasting (IF) regimen on working memory (WM) during the menopause transition (MT) with a covariate of exercise. In this chapter, the methodology for this experimental study is provided in detail and will begin by stating the research questions and hypotheses. The research design and study procedures are included, along with the recruitment method utilized to obtain participants in the studied population and the required inclusion/exclusion criteria. A detailed description of supporting material and instruments used to measure variables are included. Finally, a comprehensive explanation of the assumptions and limitations are provided.

Research Questions and Hypotheses

Research Questions

RQ1: What mean differences are there between perimenopausal women who engage in an 8/16 intermittent fasting regimen for two consecutive weeks in Working Memory Questionnaire posttest scores with a covariate adjustment of exercise when compared to a control group?

RQ2: What is the relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week?

Hypotheses

*Ho*1: There will be no significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ho*2: There will be no significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

*Ha*1: There will be significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ha*2: There will be significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

Research Design

The randomized controlled trial (RCT) is the most rigorous method used to determine whether a cause-effect relationship exists between a treatment and an outcome. The RCT also evaluates the effectiveness and safety of an intervention aimed to decrease the risk of cognitive decline. This randomized experiment was the most appropriate interventional study design because it provided a deeper understanding of how IF, while controlling for a covariate of exercise, effects WM among the perimenopausal population. This design took a homogenous group of participants and randomized them into two separate groups, the experiment group and the control group. The design measured all participants Working Memory Questionnaire (WMQ) scores before and after the trial while participants self-reported the average number of hours per week they engaged in any type of exercise.

This methodology was used to understand the impact of an 8/16 IF regimen with a covariate of exercise had on WM and determined whether findings supported the hypotheses. This approach explored the impact of an 8/16 IF treatment on WM during the MT as a potential early intervention to decrease cognitive decline during the MT while controlling for the effects of exercise.

Participants

Convenience sampling was used to recruit participants from social media (Instagram, Facebook, LinkedIn, blogs), physicians' offices in Northeastern North Carolina, students from Liberty University's School of Behavioral Sciences, and by word of mouth. The recruitment flyer (Appendix A), social media post (Appendix B), and Liberty University's letter (Appendix C) highlighted the study's methodology and eligibility requirements. Interested participants scanned the QR code or visited the link provided on the recruitment tools to complete the pre-study survey.

A formal a priori power analysis was conducted using G*Power 3.1 (Faul et al., 2007). The analysis indicated that a sample of thirty-four total participants would allow 80% power to detect a medium effect size (f = .50, α = .05).

All participants were required to meet the following inclusion criteria for enrollment: (a) at least 18 years old, (b) a perimenopausal woman, and (c) experiencing the loss of a period for no more than ten consecutive months but more than two months.

Exclusion criteria included: (a) currently adhering to an average daily IF window of 8 hours or less, (b) adhering to any IF schedule within the last two weeks, (c) taking medications affecting glucose levels or other medications that interfere with cognitive functioning, (c) having a past or present health condition that could affect cognitive

function such as neurocognitive disorders (e.g., traumatic brain injury), or neurological diseases (e.g., Multiple Sclerosis, Stroke, Lyme Disease), (d) no chronic metabolic illnesses (e.g., diabetes, high blood pressure, or any other illness) that would impair the ability to follow an 8/16 IF regimen, (e) being diagnosed with psychiatric condition of major depressive disorder, bipolar disorder, psychotic disorder, eating disorder, substance abuse or any other psychiatric diagnosis, (f) any other restriction that would preclude an individual from adhering to the study's requirements, and (g) any dietary restrictions.

Study Procedures

Interested potential participants scanned a QR code or visited the link provided on the recruitment flyer (Appendix A), social media post (Appendix B), or Liberty University's School of Behavioral Sciences Letter (Appendix C) that took them to the pre-study survey on SurveyMonkey ™. Participants first answered eligibility questions (Appendix D) and then read and signed the informed consent form (Appendix E). If they consented to the study, they typed their name and date into the online form and automatically proceeded to the demographic questionnaire (Appendix F) and WMQ (Appendix G). Once the pre-study survey was complete, the primary researcher (PR) assigned participants a corresponding number. The numbers, along with correlating names and data were stored in a document saved on a password protected computer, accessible only by the PR. The PR randomly assigned each participant to either the experimental group or control group using an online random group generator (Random Number Generator Picker Wheel©, 2023). The PR sent participants instructions according to their group assignment (experiment or control; Appendix H or I). The instructions included contact information for the PR if questions or concerns arose during

the trial. The instructions also provided participants with the QR code and link to the post-study WMQ on SurveyMonkey ™. After two weeks, the PR sent a reminder to each participant who did not complete the post-study.

Instrumentation and Measurement

Recruitment Flyer (Appendix A)

The recruitment flyer explained the study's purpose and eligibility requirements. A brief explanation of the study's methodology was included on the flyer. Interested participants scanned the QR code or visited the link provided on the flyer to complete the informed consent form, eligibility questionnaire, demographic questionnaire, and WMQ.

Social Media Recruitment Post (Appendix B)

The social media recruitment post was used to recruit participants from social media websites. The post explained the study's purpose and eligibility requirements. A brief explanation of the study's methodology was included in the post. Interested participants scanned the QR code or visited the link provided on the post to complete the informed consent form, eligibility questionnaire, demographic questionnaire, and WMQ.

Liberty University's School of Behavioral Sciences Letter (Appendix C)

The Liberty University letter was used to recruit participants from Liberty University's School of Behavioral Sciences. The letter was posted on Liberty University's website and explained the study's purpose and eligibility requirements. A brief explanation of the study's methodology was also included. Interested participants scanned the QR code or visited the link provided in the letter to complete the informed consent form, eligibility questionnaire, demographic questionnaire, and WMQ.

Eligibility Questionnaire (Appendix D)

Participants who scanned the QR code obtained access to eligibility questions on SurveyMonkey ™. Participants were asked questions according to the inclusion/exclusion criteria. The online survey took two minutes to complete.

Informed Consent (Appendix E)

Eligible participants read the informed consent form that included key information about the research study, risks/benefits, and contact information. Participants who provided informed consent typed their name and the date on the form. This portion took approximately five minutes to complete.

Demographic Questionnaire (Appendix F)

After participants typed their name and the date on the informed consent form, they automatically proceeded to demographic questions. Participants provided personal contact information and answered demographic questions such as age, average hours of exercise per week, race, work status, and marital status. This portion took three minutes to complete.

Working Memory Questionnaire (Vallat-Azouvi et al., 2021; Appendix G)

After completing the demographic questions, participants automatically continued to the initial SurveyMonkey ™ survey to complete the self-administered test of WM both pre- and post-trial. This portion took five minutes to complete. The purpose of the WMQ was to identify subjective cognitive deficiencies in multiple cultures and languages (Vallat-Azouvi et al., 2012). According to Vallat-Azouvi et al. (2012), the WMQ is an open-source assessment that does not require extensive training to administer and assesses participants' perception of three domains of WM: short-term storage, attention, and executive control. The first domain, short-term storage corresponds to the ability to

maintain information in short-term memory for a brief period, mental calculation, or written text comprehension. The second area is attention and addresses distractibility, mental slowness, mental fatigue, or dual-task processing. The third and last domain relates to executive aspects of WM such as decision making, planning, or shifting. Each domain includes 10 questions each presented in random order to avoid response bias. Participants respond to 30 questions in random order to avoid response bias by rating them on a 5-point Likert-type scale. The response options range from 0 to 4, where 0 indicates no problem at all and 4 indicates very severe problems. The maximum score for each domain was 40 with a total score of 120 where higher scores corresponded to more difficulties/complaints (Vallat-Azouvi et al., 2012). Vallat-Azouvi et al. (2012) found the WMQ to have good validity, the ability to distinguish between patients with a traumatic brain injury and healthy patients and also to recognize central executive dysfunction in WM in everyday life and monitor improvement. Vallat-Azouvi et al. (2012) also found a Cronbach's alpha of .89, indicating good reliability. The WMQ was downloaded and provided as an appendix for public use by authors Armand Trousseau and Philippe Azouvi on May 2, 2012 (Vallat-Azouvi et al., 2012; Appendix J).

Participant Instructions – Experimental & Control Group (Appendix H & I)

The PR randomly assigned each participant to either the IF or control group using an online random group generator (bravowheel.com/tools/random-number-generator/). The PR sent participants instructions according to their group assignment. The instructions included contact information for the PR if they had any questions or concerns during the trial. The instructions also provided participants with the QR code and link to the final survey on SurveyMonkey ™.

Operationalization of Variables

Intermittent Fasting – Operationally defined as "eating windows" and had 2 levels: 1) an experimental group who followed 16 hours of abstinence from food intake intervened with 8 hours of normal meal consumption, and 2) a control group who has no restriction on when they ate or fasted.

Working Memory – Working memory was assessed using scores on the WMQ, an interval level variable, measured on a Likert-type scale with score totals ranging between 0 – 120 where higher scores indicated more difficulties/complaints (Vallat-Azouvi et al., 2012).

Exercise - Exercise was operationally defined as the average hours per week participants engaged in exercise. Participants reported the number of hours per week on the pre-study survey.

Data Analysis

This study utilized an experimental design. All data were analyzed by extracting the data from SurveyMonkey™ to SPSS Statistics®. Prior to and following the two-week intervention, participants completed the WMQ via SurveyMonkey ™. As data were collected, they were reviewed, and any questions and/or concerns were immediately addressed. Descriptive statistics for the demographic were calculated to describe the participant sample.

The ANCOVA was used to test the first null hypothesis of this research study: There will be no significant mean differences in WMQ posttest scores across groups with a covariate adjustment of hours per week of exercise. A Pearson's correlation was used to determine the results of the second hypothesis of this study: There will be no significant

relationship between Working Memory Questionnaire (WMQ) posttest scores and hours of exercise per week.

Delimitations, Assumptions, and Limitations

A delimitation of this study was that it only addressed participants in the MT and did not explore the effects of an 8/16 IF regimen on WM with a covariate of exercise in individuals leading up to the MT or post-menopause. This study did not seek to produce an exhaustive exploration of all factors that may affect a perimenopausal women's WM. Instead, this research focused on how IF impacts WM during the MT while controlling for the effects of exercise. An additional delimitation of this study was the limited scope focusing on WM. Memory is orchestrated by various brain regions and includes several types of memory such as recall memory, visual memory, episodic memory, associative memory, WM, and others (Mosconi et al., 2021; Seitz et al., 2019; Zhang et al., 2022). This research study focused only on an 8/16 IF regimen with a covariate of exercise on WM during the MT.

An assumption was the timeframe participants were absent a period. Participants were not required to report the number of months without a menstrual cycle however, they were required to have experienced the loss of a period for more than two consecutive months but no more than ten consecutive months. Participants may have lost track of the months or reported inaccurate numbers. A second assumption was that the data gathered through the self-administered surveys were accurate and complete. To mitigate this risk, the researcher analyzed the data for potential errors and required

participants to complete each questionnaire in its entirety before progressing through the remainder of the survey.

The first potential limitation was the intervention length or length of the trial. Some research evidences the effects of an IF regimen within a few days, whereas some participants, due to a plethora of circumstances, may not experience any changes in a short timeframe. A second potential limitation is that exercise is a congruent limitation in that participants may have over or underestimated the number of hours they engage in exercise. Participants may have also experienced response bias and social desirability, leading them to over-report or under-report average hours of exercise per week, based on their favorability perspective. They may have believed that overestimating the number of hours would appear favorable and present themselves as more suitable to gain PR or other participants approval. A third limitation was the varying MT stages. The stages are dependent on how long participants were in the MT, due to the average length of the transition varying from person to person. Absent of blood work to determine hormone levels, each participant's MT stage remained unknown. A fourth limitation was the participants adherence to IF. Participants who completed the study were required to follow an 8/16 IF regimen. However, their compliance may be inaccurate or miscalculated.

Summary

The aim of chapter 3 was to discuss how this RCT investigated the effects of an 8/16 IF regimen on WM during the MT with a covariate of exercise. The methodology for this experiment was discussed in detail and research questions and hypotheses were provided. The research design analyzed IF effects on WM with a covariate of exercise.

Thirty-four participants were recruited from physicians' offices in Northeastern North Carolina, social media (Instagram, Facebook, LinkedIn, and blogs), Liberty University's School of Behavioral Sciences, and by word of mouth. Qualified participants were randomized to one of two groups using an online randomizer: (1) control group or (2) experimental group. A list of inclusion/exclusion criteria was specifically addressed. Data analysis was conducted in SPSS. The inferential test used to address the first research question was the ANCOVA and a Pearson's correlation was used to address the second.

Also in this chapter, a complete and detailed description of all supporting material and instruments used to measure variables was also included. Finally, a comprehensive explanation of the assumptions and limitations were examined, and potential mitigating considerations were provided.

CHAPTER 4: RESULTS

Overview

This quantitative, randomized controlled trial (RCT) evaluated the effects of an 8/16 intermittent fasting (IF) regimen on working memory (WM) during the menopause transition (MT) with a covariate of exercise. A literature review revealed a gap in research examining treatment options for WM during the MT. This chapter provides a summary of research components, questions, and hypotheses. This chapter also demonstrates the sample demographic, statistical measurements, data analysis, findings, and summary of results.

Participants were recruited from physicians' offices in Northeast North Carolina, social media (Instagram, Facebook, LinkedIn, and blogs), Liberty University's School of Behavioral Sciences, and by word of mouth. The recruitment flyer, social media recruitment post, and letter highlighted the methodology, risks, and benefits associated with this study. Participants scanned the QR code or followed the link provided and were directed to a survey on SurveyMonkey ™.

The research design utilized in this study was a two-group, posttest randomized experimental design with a covariate. This RCT study examined the effects of an 8/16 IF regimen on Working Memory Questionnaire (WMQ) posttest scores among the perimenopausal population with a covariate of hours of exercise per week. This design compared WMQ posttest scores adjusted by the covariate of exercise in perimenopausal women receiving one of two treatment conditions. This study involved randomizing eligible participants to either an experimental group who engaged in two weeks of an

8/16 IF regimen or a control group who did not follow the fasting regimen. Both groups ad libitum without dietary restrictions.

The effects of intermittent fasting on WMQ posttest scores were analyzed using an ANCOVA with hours of exercise as the covariate. The null hypothesis that there would be no significant mean differences in WMQ posttest scores across the perimenopausal population with a covariate adjustment of exercise was tested. The purpose of the ANCOVA was to remove the effects of exercise on WMQ posttest scores which allowed for a more accurate assessment of the effects of intermittent fasting. Using exercise to reduce the residual error, the analysis more effectively detected differences between the experimental and control groups and provided greater precision when determining mean WMQ posttest score differences between the two groups (effect sizes).

Research Questions and Hypotheses

Research Questions

RQ1: What mean differences are there between perimenopausal women who engage in an 8/16 intermittent fasting regimen for two consecutive weeks in Working Memory Questionnaire posttest scores with a covariate adjustment of exercise when compared to a control group?

RQ2: What is the relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week?

Hypotheses

*Ho*1: There will be no significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ha*1: There will be significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ho*2: There will be no significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

*Ha*2: There will be a significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

Study Procedures

Interested potential participants scanned a QR code or visited the link provided on the recruitment flyer (Appendix A), social media post (Appendix B), or Liberty University's School of Behavioral Sciences Letter (Appendix C) that took them to the pre-study survey on SurveyMonkey ™. Participants first answered eligibility questions (Appendix D) and then read and signed the informed consent form (Appendix E). If they consented to the study, they typed their name and date into the online form and automatically proceeded to the demographic questionnaire (Appendix F) and subsequently the WMQ (Appendix G). Once the pre-study survey was completed, the primary researcher (PR) assigned participants a corresponding number. The numbers, along with correlating names and data were stored in a document saved on a password protected computer, accessible only by the PR. The PR randomly assigned each participant to either an experimental group or a control group using an online random group generator (Random Number Generator Picker Wheel©, 2023). The PR sent participants instructions according to their group assignment (experimental or control; Appendix H or I). The instructions included contact information for the PR if they had

any questions or concerns during the trial. The instructions also provided participants with the QR code and link to the post-study WMQ on SurveyMonkey ™. At the end of the two weeks, the PR sent a reminder to each participant who did not complete the post-study WMQ.

Descriptive Results

A total of 34 participants was sufficient, according to a priori power analysis, to allow 80% to detect a medium effect size (f = .25, α = .05). Fifty-seven potential participants initiated completion toward the pre-study survey. Nine pre-study surveys were incomplete, fourteen were disqualified, and six did not complete the post-study survey. Thirty-four participants fully completed the intervention (control group (n = 17) and experimental group (n = 17)).

After participants completed the consent portion of the pre-study survey, demographic data was collected from the sample to include hormonal birth control and HRT usage, race/ethnicity, employment status, relationship status, and education level. Table 1 shows the frequency of hormonal birth control usage among the sample population of perimenopausal women. The percentage of participants reporting the usage of hormonal birth control was 8.8%.

Table 1

Hormonal Birth Control Use

	Frequency	Percent
Yes	3	8.8%
No	31	91.2%

Table 2 shows the frequency of hormone replacement therapy (HRT) usage among the sample. The percentage of participants reporting the usage of HRT was 35.3%.

Table 2

Hormonal Replacement Therapy (HRT) Use

	Frequency	Percent
Yes	12	35.3%
No	22	64.7%

Participants were given the choice of American Indian or Alaskan Native, Asian/Pacific Islander, Black or African American, Hispanic, White/Caucasian, or Multiple ethnicity/Other for identifying with a race. Table 1 displays 11.8% of the sample identified as Black or African American, and nearly 88.2% identified as White.

Table 3

Race/Ethnicity of Participants

	Frequency	Percent
American Indian or Alaskan Native	0	0.0%
Asian/Pacific Islander	0	0.0%
Black or African American	4	11.8%
Hispanic	0	0.0%
White/Caucasian	30	88.2%
Multiple ethnicity/Other	0	0.0%

Employment status was another demographic gathered. For this question, participants identified with one of the following options: employed/working full-time, employed/working part-time, not employed/looking for work, not employed/not looking for work, retired, and disabled/not able to work. Participants employed, working full-time were represented at 73.5%, not employed, not looking for work were 14.7% of the population, and 11.8% reported as retired.

Table 4

Employment Status of Participants

	Frequency	Percent
Employed, working full-time	25	73.5%
Employed, working part-time	0	0.0%
Not employed, looking for work	0	0.0%
Not employed, not looking for work	5	14.7%
Retired	4	11.8%
Disabled, not able to work	0	0.0%

Another demographic gathered from participants was relationship status. For this question, participants identified with one of the following options: married, widowed, divorced, separated, cohabitating with a significant other or in a domestic partnership, single/never married, or prefer not to answer. The percentage of participants who reported as married was 76.5%, divorced 14.7%, and single 8.8%.

Table 5

Relationship Status of Participants

	Frequency	Percent
Married	26	76.5%
Widowed	0	0.0%
Divorced	5	14.7%
Separated	0	0.0%
Cohabitating	0	0.0%
Single	3	8.8%
No answer	0	0.0%

Education level was the last demographic gathered. For this question, participants identified with one of the following options: less than high school diploma, high school diploma (or GED), some college but no degree, associate's degree, bachelor's degree, master's degree, or Doctorate or professional degree. Of the 34 participants who completed the study, 2.9% reported obtaining a high school diploma (or GED), 5.9% had some college, but not degree, 5.9% obtained an associate's degree, 41.2% a bachelor's

degree, 26. 5% master's degree, and the remaining 17.6% reported having a doctorate or professional degree.

Table 6

Education Level of Participants

	Frequency	Percent
Less than high school diploma	0	0.0%
High school diploma (or GED)	1	2.9%
Some college, but no degree	2	5.9%
Associate's degree	2	5.9%
Bachelor's degree	14	41.2%
Master's degree	9	26.5%
Doctorate or professional degree	6	17.6%

Study Findings

An ANCOVA was used to determine mean differences in WMQ posttest scores between the control group and experimental group while controlling for the covariate of exercise to determine the effects of 8/16 IF on WM for the perimenopausal population.

The ANCOVA was the statistical method used to incorporate both analysis of variance and regression analysis. The purpose of the ANCOVA was to increase the sensitivity of the main effects and interactions by adjusting for the relationship between WM and number of hours of exercise per week. Because individual differences in exercise can significantly impact WMQ posttest scores, incorporating exercise as a covariate adjustment allowed for a more accurate understanding of whether participant WMQ posttest scores were due to the IF regimen or preexisting level of exercise. The introduction of exercise as a covariate represented a variable that, although was not controlled for in this study nor was it of primary interest, could have influenced WMQ posttest scores. To account for the covariate, the means of WMQ posttest scores were adjusted to what they would be if all participants engaged in the same number of hours of exercise per week. The purpose was to determine the outcome of posttest scores if the number of hours of exercise participants engaged in per week were equal. Therefore, using exercise to reduce the error, the ANCOVA method was able to more efficiently detect differences between groups (power) and provide increased precision when estimating mean WMQ posttest score differences between the groups (effect sizes).

To maintain data integrity, data were screened to ensure proper entry, extraction, and importation into SPSS. Data screening was also conducted to locate and address any

missing data, uncover, and account for potential outliers in WMQ posttest scores and hours of exercise per week, and to assess for univariate underlying assumptions.

The ANCOVA underlying assumptions are normality, homogeneity of variance, independence, and homogeneity of regression (slope; Martin & Bridgmon, 2012). Regression analysis was performed to ensure all of the following ANCOVA assumptions were met: 1.) The independent variable was a categorical variable because participants were randomly assigned to either an experimental or control group, 2.) The WMQ scores were measured on a Likert-type scale with corresponding numerical answers on a scale of 0 to 4 where 0 = Not at all, 1 = A little, 2 = Moderately, 3 = A lot, and 4 = Extremely. Therefore, the scores were considered continuous and the intervals between answers were presumed equal, and 3.) The observations were independent because participants were randomized into two conditions.

Normality and homogeneity of variance by group were evaluated by examining histograms, skewness, kurtosis, the Shapiro-Wilk statistic, normal Q-Q plots, and Levene statistics. The highest and lowest positive scores for the covariate exercise and WMQ posttest scores are identified in Table 7. It was determined that no participant WMQ posttest scores represented univariate outliers on either the covariate of exercise or WMQ posttest scores.

Table 7

Highest ± z- Scores for the Covariate Exercise and WMQ Posttest Scores

Highest +z	**Outlier? ≥ ± 3.29**	**Highest - z**	**Outlier? ≥ ± 3.29**
CovEx 2.161	No	-1.857	No
WMQPost 2.150	No	-2.478	No

The output of skewness, kurtosis, and standard errors for the covariate exercise and WMQ posttest scores by group are presented in Table 8. Since the skewness z-scores values are less than ± 3.29, it was concluded that the distributions were not significantly skewed (see Table 9).

Table 8

Descriptive Statistics for Exercise Hours and WMQ Posttest Scores (n=34)

Exercise Hours per week								
	Mean	95%CI	SD	Min	Max	IQR	Skew	Kurt
Control	4.71	3.74-7.67	1.88	1.5	8.5	3	.163	-.346
Exp	4.77	3.92-5.61	1.65	3	8	2.75	.804	-.271
WMQ Posttest Scores								
	Mean	95%CI	SD	Min	Max	IQR	Skew	Kurt
Control	32	28.79-35.21	6.24	21	47	8.5	.589	.923
Exp	25.76	20.97-30.56	9.32	8	41	13.5	-.25	-.472

Table 9

Skewness z-Scores by Group

Variable/Condition	**Skewness Z (Stat./Std.Error = z)**	**Sig. (> ± 3.29)**
Covariate exercise		
Control	.163/ .55 = .296	No
Experimental	.804/ .55 = 1.462	No
WMQ posttest		
Control	.589/ .55 = 1.071	No
Experimental	- .25/ .55 = - .455	No

The kurtosis z-scores were also all within acceptable standards of being normally distributed (< ± 3.29; see Table 10).

Table 10

Kurtosis z-Scores by Group

Variable/Condition	Kurtosis Z (Stat./Std.Error = z)	Kurtosis Direction	Sig. (> ± 3.29)
Covariate exercise			
Control	- .346/ 1.063 = - .326	Platykurtic	No
Experimental	- .271/ 1.063 = - .255	Platykurtic	No
WMQ posttest			
Control	.923/ 1.063 = .868	Leptokurtic	No
Experimental	- .472/ 1.063 = - .444	Platykurtic	No

The Shapiro-Wilk (S-W) statistic was used to establish that the sample distribution used did not deviate significantly from normal (see Table 11). It was determined that the significant S-W statistical probability levels were all larger than the set alpha level of .05, it was concluded that the group distributions on both the covariate exercise hours and WMQ posttest scores did not deviate significantly from normal.

Furthermore, Q-Q plots for each distribution are shown below (see Figure 3 and Figure 4). The majority of points of all distributions for both groups fall on or near the line. Therefore, the Q-Q plots support the normality of the distributions.

Table 11

Shapiro-Wilk Statistics by Group

Tests of Normality						
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
Group	**Statistic**	***df***	**Sig.**	**Statistic**	***df***	**Sig.**
Covariate exercise						
Control	.112	17	.200*	.979	17	.950
Intervention	.208	17	.049	.884	17	.037
Post-intervention WMQ scores						
Control	.147	17	.200*	.964	17	.708
Intervention	.157	17	.200*	.972	17	.854

* This is a lower bound of the true significance. a. Lilliefors Significance Correction

Figure 3

Normal Q-Q Plots of Covariate Exercise for Control Group

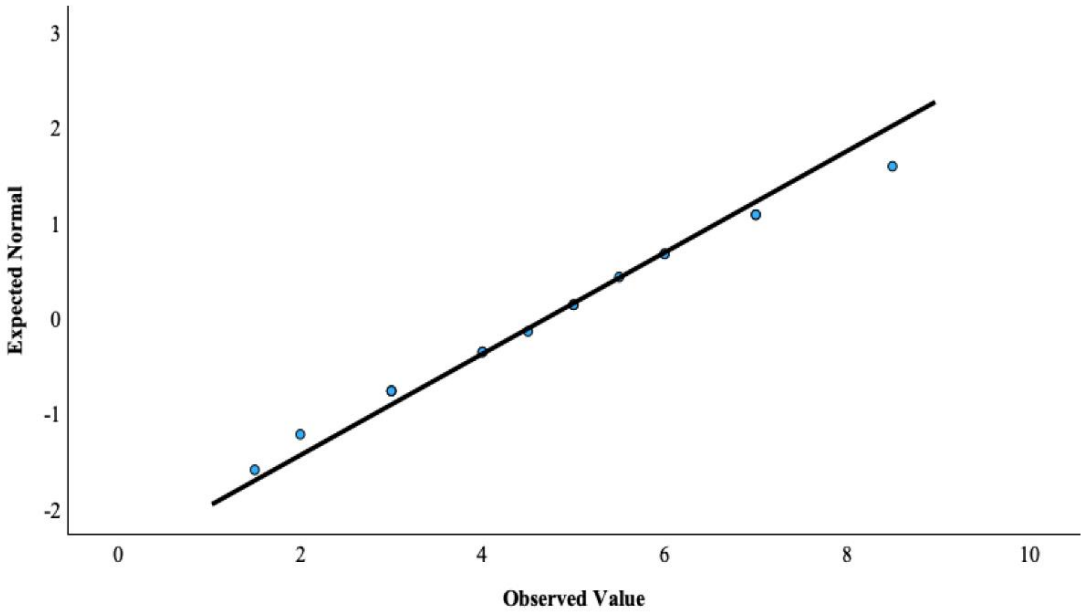


Figure 4

Normal Q-Q Plots of Covariate Exercise for Experimental Group

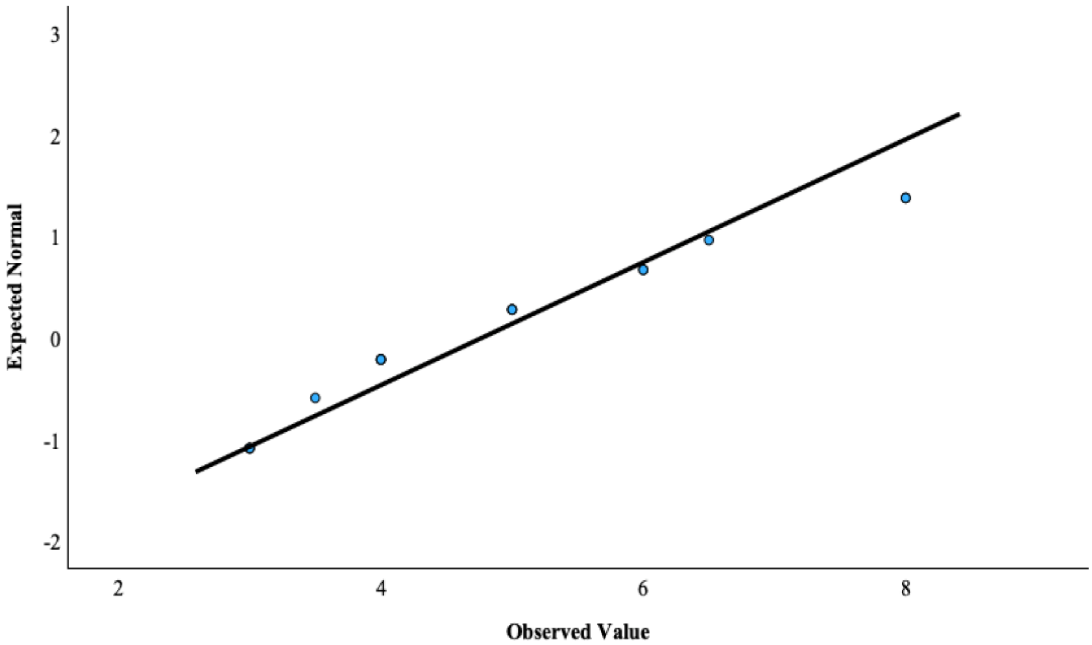


Figure 5

Normal Q-Q Plots of WMQ Posttest Scores for Control Group

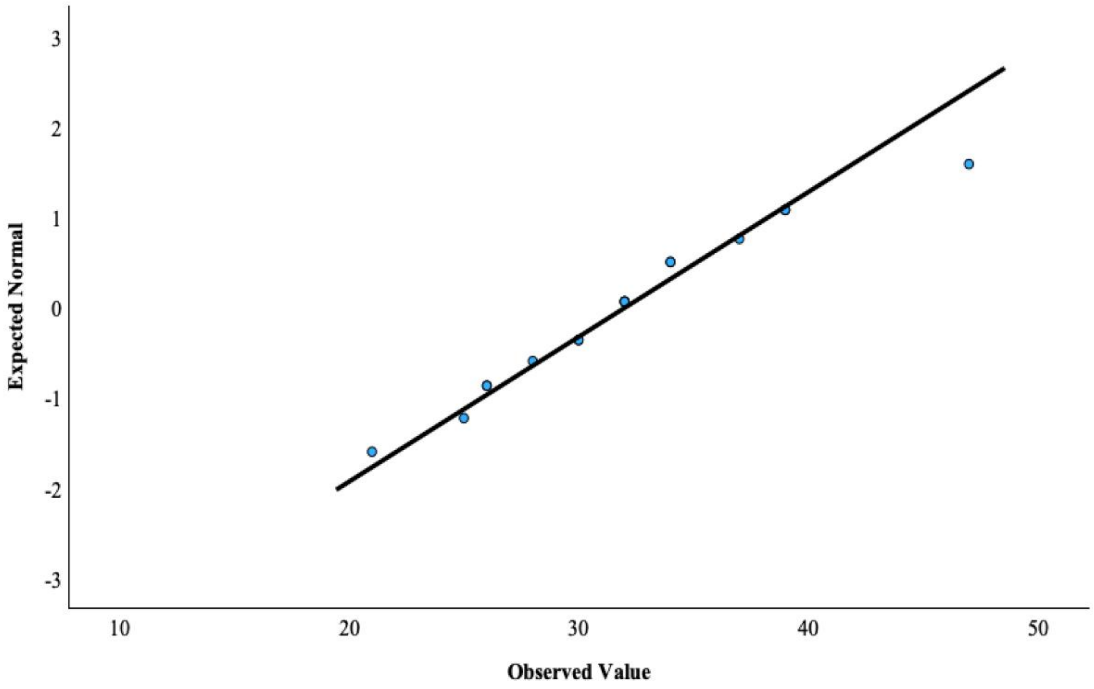
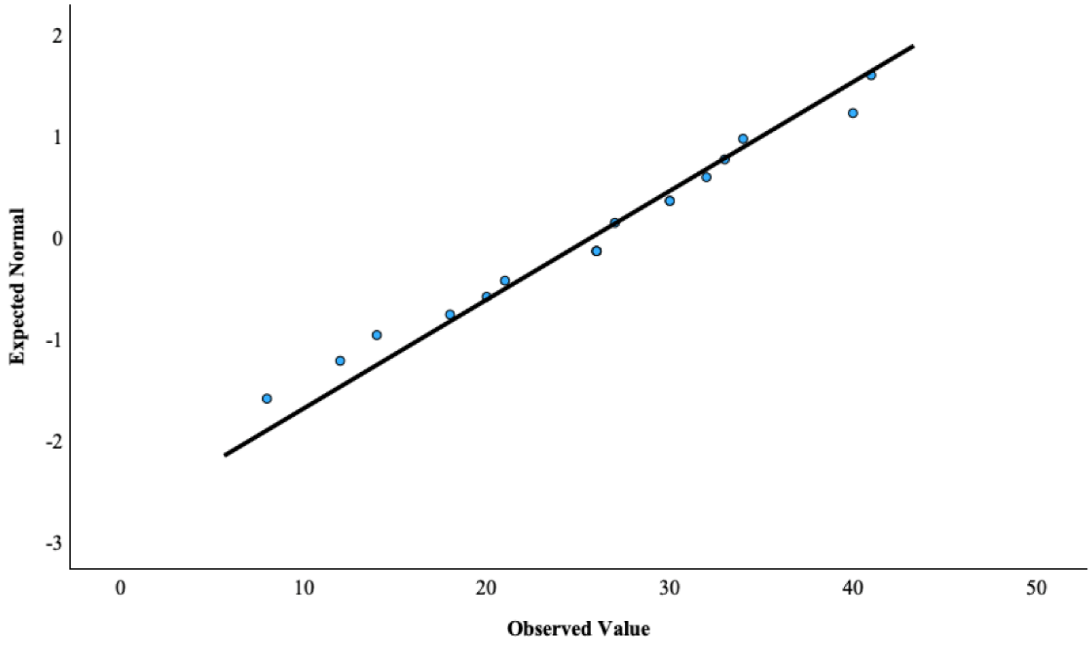


Figure 6

Normal Q-Q Plots of WMQ Posttest Scores for Experimental Group



The normality of the distributions was supported by the integrated results of the data analysis of univariate outliers, skewness z-scores, kurtosis z-scores, S-W statistics, and the Q-Q plots.

Homogeneity of Variance

In this study, it was expected that the treatment condition would affect the means of the covariate exercise and the WMQ posttest scores but not the variances of the groups, leaving the two groups relatively constant. Both groups had the same number of participants, equating to a group size ratio of 1; below a group size ratio of 4 therefore, the guideline is *F*max = 10 (Tabachnick & Fidell, 2007). The control group had the highest variance on covariate exercise of 3.53 and the experimental group had the lowest of 2.722 (see Table 8). The *F*max = 3.53/2.722 = 1.297, and the ratio is well below 10. For the WMQ posttest scores, the control group had the lowest variance of 38.875 and the experimental group had the highest of 86.941. The *F*max = 38.875/86.941 = .45 and was also well below 10. The low variance ratios support homogeneity of variance across the two groups on both variables. The Levene's test also confirms this finding.

Equality of the variances between the groups was tested using Levene's test of homogeneity of variance. The null hypothesis was not rejected that the error variances are equal since the probability values (Sig.) based on the mean (Covariate exercise = .667 and WMQ posttest scores = .111) are greater than .05. The evidence from the variance ratios and Levene's statistic supports the underlying assumptions of homogeneity of variance.

Table 12

Test of Homogeneity of Variance for Covariate Exercise and WMQ Posttest Scores

		Levene's Statistic	df1	df2	Sig.
Covariate exercise	Based on Mean	.188	1	32	.667
	Based on Median	.183	1	32	.672
	Based on Median and with adjusted df	.183	1	31.786	.672
	Based on trimmed mean	.204	1	32	.654
WMQ Posttest scores	Based on Mean	2.683	1	32	.111
	Based on Median	2.493	1	32	.124
	Based on Median and with adjusted df	2.493	1	29.466	.125
	Based on trimmed mean	2.512	1	32	.123

Independence

To assess the independence of observations, the following graph displays the responses of participants on the WMQ posttest by group based on the same order they were obtained. The matrix scatterplot in Figure 7 displays the control group scores compared to the experimental group. The scores are in the order they were obtained and are paired as circles in each graph and because the points scatter in many directions, it was concluded that the assumption of independence was met.

Figure 7

Matrix Scatter Plot to Assess Independence

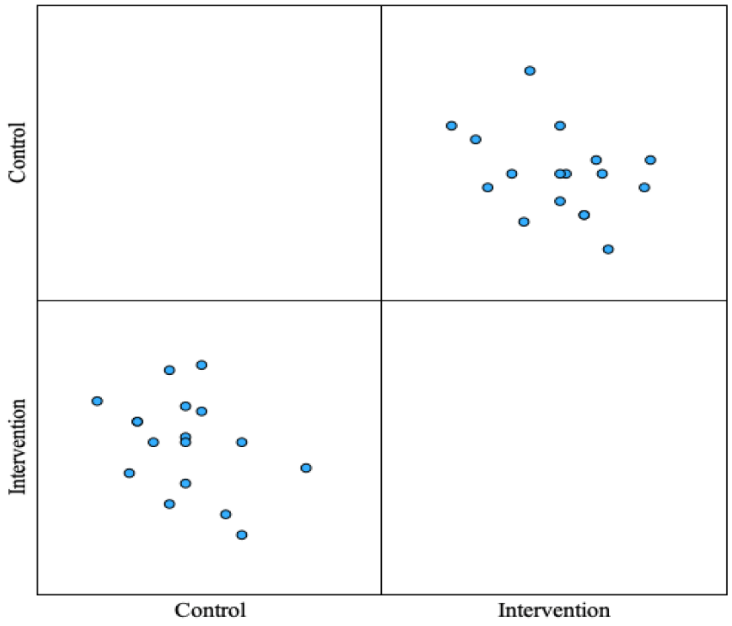


Table 13

ANCOVA Results for 8/16 IF Group vs. Control with Covariate of Exercise

ANCOVA

Source	Type III Sum of Squares	*df*	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[b]
Group	1.261	1	1.261	.019	.891	.001	.019	.052
exercise	25.429	1	25.429	.388	.538	.013	.388	.093
Grp * exe	28.153	1	28.153	.430	.517	.014	.430	.097
Error	1965.614	30	65.520					
Total	30706.000	34						

a. R Squared = .161 (Adjusted R Squared = .077)
b. Computed using a = .05

It was demonstrated that the posttest score distributions on the WMQ for both the control group and experimental group did not deviate from normality, both measures of homogeneity of variance supported the assumption of equality, scatter plots displayed independence, homogeneity of regression (slope) was not significant and the ANCOVA

statistic was then used to test the omnibus null hypothesis of this research study that there would be no significant mean differences in WMQ posttest scores across groups (control and experimental) with a covariate adjustment of hours of exercise per week.

ANCOVA Results

The ANCOVA was run to determine the effects of an 8/16 IF regimen on WMQ posttest scores in the perimenopausal population after controlling for hours of exercise per week. The ANCOVA results shown in Table 13 were used to answer the following omnibus null hypothesis of this research study:

> *Ho*1: There will be no significant mean differences in Working Memory Questionnaire (WMQ) posttest scores across groups (control and experimental) with a covariate adjustment of hours of exercise per week.
>
> *Ha*1: There will be significant mean differences in Working Memory Questionnaire (WMQ) posttest scores across groups (control and experimental) with a covariate adjustment of hours of exercise per week.

The criterion selected to make a decision about rejecting the null hypothesis was $\alpha = .05$. The significant statistical probability of .891 is more than $\alpha = .05$, therefore the null hypothesis was not rejected ($p > .05$). The omnibus null hypothesis was tested, and there was not a significant difference in WMQ scores among participants in the control group when compared to an experimental group with exercise used as a covariate, F (1, 30) = .019, $p > .891$. The covariate of exercise was also not significant ($p = .538$), indicating the groups did not differ in the average hours of exercise per week.

The purpose of the ANCOVA was to control for the effects of hours of exercise per week. In other words, what would the mean difference in WMQ posttest scores be if

the participants in both the control group and experimental group had not differed on the covariate of exercise. The ANCOVA statistic partials out the covariate effects on WMQ scores on the means produced by the control and experimental groups. These adjusted means were then tested for significant differences. The adjusted (estimated) means are presented in Table 14. The estimated (adjusted) WMQ posttest scores mean for the control group was *M* = 32.001, and before the mean was adjusted for the covariate of exercise it was *M* = 32 (see Table 8). The estimated WMQ posttest scores mean for the experimental group was *M* = 25.795, compared to the unadjusted means of *M* = 25.76 (see Table 8). The plot of the two estimated marginal means is depicted in Figure 8. The visible lower adjusted mean representing WMQ posttest scores for participants who received the experimental compared to the control group. The difference was not significant.

Table 14

Estimated Marginal Means

Estimates

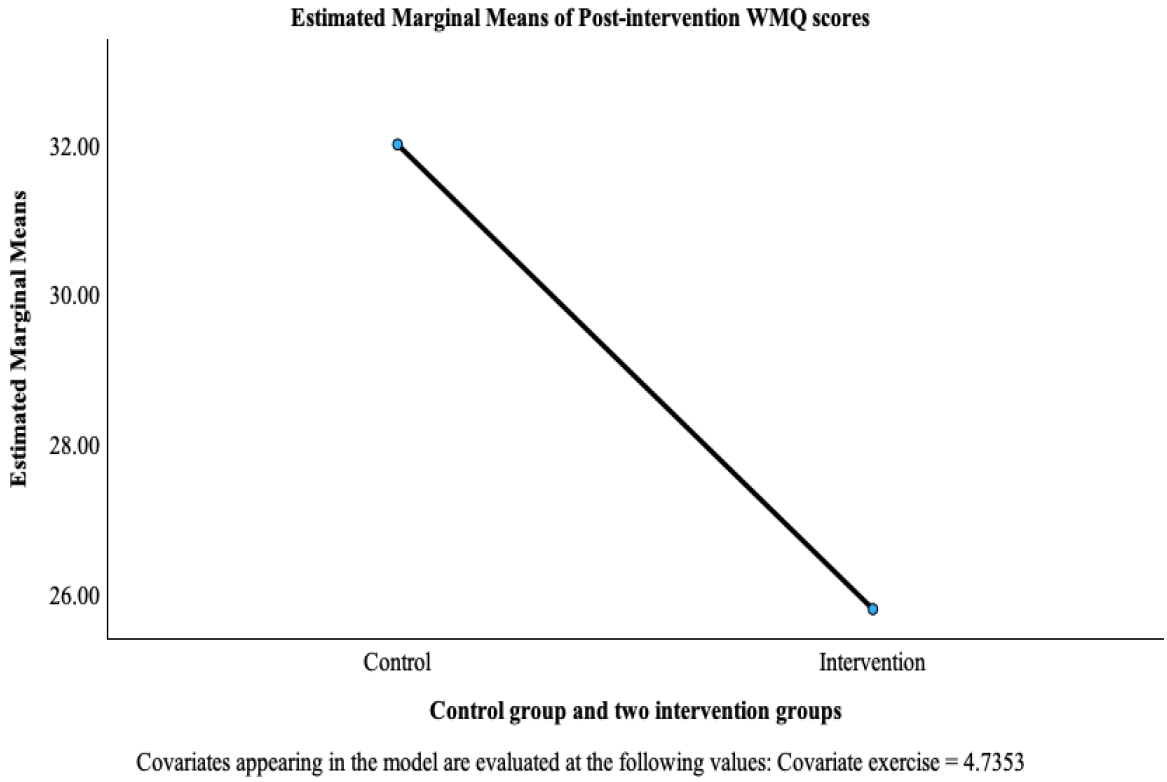
Dependent Variable: WMQ Posttest Scores

			99% Confidence Interval	
Group	**Mean**	**Std. Error**	**Lower Bound**	**Upper Bound**
Control	32.001[a]	1.963	27.991	36.011
Experimental	25.795[a]	1.964	21.785	29.805

a. Covariates appearing in the model are evaluated at the following values: Covariate exercise = 4.7353

Figure 8

Profile Plot



Post Hoc Testing

The post hoc effect size was $\eta^2 = .097$, which was significantly smaller than the criterion of .80. The probability is .99 that this interval (11.876) – (.534) will include the true mean difference between the population means of WMQ posttest scores between the control group and experimental group adjusted for exercise.

Pearson's *r*

A Pearson's r was used to answer the second research question:

RQ2: What is the relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week?

Testing Assumptions

Testing assumptions for the Pearson's correlation test were examined to make sure the following assumptions by Laerd Statistics (2017) were met for the analysis:

1. Both are continuous variables.
2. Two variables must be paired.
3. Data must have no outliers.
4. Data is from a random or representative sample.
5. A linear relationship is expected between the two variables.

The first assumption was met because Likert-style ratings are considered continuous data when they are totaled and have at least 4 points (Carifio & Perla, 2008). The second assumption was met because WMQ posttest scores and number of hours of exercise per week are paired. The third, fourth, and fifth assumptions were met because the data had no outliers, the data were from a representative sample of the perimenopausal population, and a linear relationship was expected between WMQ posttest scores and number of hours of exercise per week.

Testing assumptions for the Kruskal-Wallis test was examined to ensure the following assumptions were met for the analysis:

1. Samples are random samples, or allocation to treatment group is random.
2. The two samples are mutually independent.
3. The measurement scale is at least ordinal, and the variable is continuous.

The first assumption was met because the allocation to treatment group was randomized. The second assumption was met because the members of each group were randomly assigned and had no further contact with each other. The third assumption was

met because the variables were continuous and the WMQ posttest scores reported interval data.

The null hypothesis was that there would not be a significant relationship between scores on the working memory questionnaire (WMQ) posttest scores and number of hours of exercise per week. An evaluation of this relationship was conducted using Pearson correlations in SPSS. The Pearson correlation was not statistically significant between WMQ posttest scores and number of hours of exercise per week (r = -.097, n = 34, p = .585). Table 15 shows the Pearson correlation between WMQ posttest scores and hours of exercise per week.

Table 15

Correlations of WMQ Posttest Scores with Exercise

		Exercise	**Sig. (2-tailed)**
WMQ Posttest Scores	Pearson Correlation	- .097	.585

Summary

This section concludes Chapter 4. This quantitative RCT aimed to evaluate the effects of an 8/16 IF regimen on WM in perimenopausal women with a covariate of number of hours of exercise per week. A literature review revealed a gap in research examining treatment options for WM during the MT. This chapter provides a summary of research components, questions, and hypotheses. This chapter demonstrated the sample demographics, statistical measurements, data analysis, findings, and summary of results.

An ANCOVA determined the effects of an 8/16 IF regimen on WM in the perimenopausal population after controlling for number of hours of exercise per week. The ANCOVA results shown in Table 13 were used to answer the following omnibus null hypothesis of this research study: There will be no significant mean differences in

Working Memory Questionnaire (WMQ) posttest scores across groups (control and experimental) with a covariate adjustment of number of hours per week of exercise. The criterion selected to make a decision about rejecting the null hypothesis was $a = .05$. The null hypothesis failed to be rejected ($p < .05$). The omnibus null hypothesis was tested, and there was not a significant difference in WMQ scores among participants in the control group when compared to an experimental group with exercise used as a covariate. A Pearson's r was used to answer the second research question: What is the relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week? The Pearson correlation established there was no significant relationship.

CHAPTER 5: DISCUSSION

Overview

This experimental, quantitative study examined the effects of 8/16 intermittent fasting (IF) on working memory (WM) with a covariate of exercise among the perimenopausal population. Concentration on this topic began with a literature review describing the increased risk for cognitive decline resulting from fluctuation and eventual decrease in circulating estrogen during the menopause transition (MT). The literature presented an extensive gap between WM deficits in perimenopausal women and cost-effective treatments to mitigate the risk. This chapter provides a summary of the findings, discussion of the findings, implications, and limitations. This chapter will commence with recommendations for future research and a summarization of this study's findings. Some theory of constructs and biblical foundations discussed in Chapter 2 will also be reviewed in this chapter and compared to the findings of this research study.

Summary of Findings

The purpose of this randomized controlled trial (RCT) was to assess if 8/16 IF effects WM during the MT while controlling for the additive effects of exercise. This study design was used to collect self-reported survey data from perimenopausal women who have experienced the loss of a period for a minimum of two months but no more than ten months. The data collected from thirty-four participants was analyzed using an ANCOVA and Pearson's correlation to answer the following research questions and hypotheses:

Research Questions

RQ1: What mean differences are there between perimenopausal women who engage in an 8/16 intermittent fasting regimen for two consecutive weeks in Working Memory Questionnaire posttest scores with a covariate adjustment of exercise when compared to a control group?

RQ2: What is the relationship between Working Memory Questionnaire posttest scores and average hours of exercise per week?

Hypotheses

*Ho*1: There will be no significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ho*2: There will be no significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

*Ha*1: There will be significant mean differences in the Working Memory Questionnaire posttest scores across groups with a covariate adjustment of average hours per week of exercise.

*Ha*2: There will be significant relationship between the Working Memory Questionnaire posttest scores and average hours of exercise per week.

Discussion of Findings

The findings from this research study contribute to the limited literature on the perimenopausal population by providing empirical evidence that there were no significant mean differences in WMQ posttest scores across groups (control and experimental) with a covariate adjustment of hours of exercise per week. Additional findings from this study

contribute to the literature by providing empirical evidence that established there was no significant relationship between WMQ posttest scores and hours of exercise per week (r = - .097, n = 34, p < .585).

Due to the limited data on this specific topic, there were no similar prior research studies conducted to compare findings. However, future research studies that include a larger number of participants, and a longer duration of intervention may address the limitations encountered.

Implications

Theoretical Implications

The theoretical framework for this study stemmed from the Capability, Opportunity, Motivation, and Behavior (COM-B) model used to design behavior change interventions (Khalilollahi et al., 2023; Yap et al., 2023). The COM-B model provided a comprehensive framework for understanding the motivations and barriers to promulgating change in dietary behaviors through the interaction of three components: capability, opportunity, and motivation (see Figure 1; Khalilollahi et al., 2023; Yap et al., 2023). In other words, individuals must have the ability to carry out a new behavior psychologically or physically, an opportunity driven by external social and physical influences, and both the reflective and automatic motivations to engage in new behavior (Khalilollahi et al., 2023; Yap et al., 2023). This study provided participants with the opportunity to change their behavior and to improve their health. They were required to have both the physical and psychological skills to engage in 8/16 IF and were motivated to improve their WM during the MT.

Biblical Implications

The biblical foundations of this study were supported by scripture. During fasts, we may be reminded by scripture of our dependence on God (2 Samuel 12:15-20, *King James Bible*, 1769/2017). Through the Bible, He provides guidance to support the behaviors necessary to make important dietary and physical changes for improved health. For example, 1 Corinthians 15:58 states, "Therefore, my beloved brethren, be ye steadfast, unmoveable, always abounding in the work of the Lord, forasmuch as ye know that your labour is not in vain in the Lord" (*King James Bible*, 1769/2017).

Both the theoretical and biblical foundations can be used to impact the scientific community, in psychological practice/consulting, and/or in the church or other organizations by implementing ways to improve health, the motivation to seek changes, and to better understand the perimenopausal population.

Limitations

The first limitation uncovered during this study was that participants were presumably at various MT stages; therefore, their levels of circulating estrogen varied and may have affected the results. The MT stage was dependent on how long the participant had been in the transition. The MT can last greater than or less than the average length of approximately 8 years. Each participant's MT stage remains unknown because of the absence of blood work to determine hormone levels. For example, a woman who is in the beginning of the MT may have more circulating estrogen levels than a woman near the end of the transition. The limited number of participants in this study may have also impacted the results.

Secondly, due to the limitation of social desirability/limitation of self-reported measures, participants may have over-reported good behavior (exercise, 8/16 IF

adherence, etc.) and underestimated answers on the WMQ. Participants may have over- or underestimated eating windows, leading to inaccurate results. Specific guidelines regarding the time of day of the 8/16 IF windows (early versus late) were not provided which may have negated additional confounding factors. Participants experiencing difficulty adhering to 8/16 IF may have been a cause for attrition.

Another limitation was that participants may have over- or underestimated the number of hours of their exercise, leading to inaccurate reporting. Participants experiencing response bias and social desirability, may have led them to over-report or under-report exercise, based on their favorability perspective. They may have believed that overestimating their exercise would appear favorable and therefore presented themselves more suitable to gain the approval of the PR or other participants. Additionally, exercise intensity and aerobic vs non-aerobic exercise were also not measured. For example, participants who engaged in more intense workouts may have experienced greater benefits in WM improvements than participants who engaged in less intensive or less vigorous exercise programs. This study was also limited in that the types of exercise participants engaged in were not measured (i.e., running, weightlifting, yoga, etc.).

Other limitations included caloric intake and intervention length, and the measurement of other potential confounding variables. Caloric intake was not monitored during this study, therefore the number and types (carbohydrates, fats, protein) of calories consumed by participants were not taken into consideration, potentially affecting the results. This research study implemented an 8/16 IF regimen for two consecutive weeks. This short duration may have impacted the study’s significance. Some research has

shown the effects of IF to be evident within a few days, whereas some participants, due to environmental or socioeconomical factors, may not have experienced any changes in two weeks. This study also did not account for other potential confounding factors/variables such as levels of stress, lack of sleep, or time of year.

After participants completed the pre-study survey, no specified time was required for participants to begin the intervention, which was an additional limitation of this study. For example, some participants assigned to the experimental group began the two-week trial the day after they completed the pre-study survey, whereas others began the intervention more than one day after the completion of the pre-study survey. Therefore, the timeframe between pre-study and post-study WMQ scores were not all exactly two weeks apart.

Lastly, participants prior eating window may have affected any changes in participants WMQ scores. For example, participants who previously and unknowingly engaged in eating windows greater than 14 hours per day may have experienced greater WM improvements as opposed to participants who had eating windows less than 14 hours.

Recommendations for Future Research

Through a literature review, this study provided a sufficient starting point to examine possible interventions to reduce cognitive decline that begins during the MT, due to the fluctuation and loss of circulating estrogen levels. Both IF and exercise were proven to be cost-effective, lifestyle changes that support long-term brain health (Anton et al., 2019; Santos-Baez et al., 2022). Recommendations for future research that

emerged from the current study findings are discussed below. This study was limited to a number of areas that are important for future research considerations.

Areas to explore for future research studies include the implementation blood tests to determine hormone levels, indicating each participants MT state. This knowledge may presumably indicate whether IF and/or exercise impact WM at varying stages. The increase in the number of participants in future research studies may provide an expanded population to determine if the variables of focus in this research improve WM. Requiring participants to document eating windows may reduce the over- or underestimation of eating windows. Implementing specific guidelines regarding the IF windows (early versus late) may negate this additional confounding factor. Measuring exercise intensity and aerobic vs non-aerobic exercise through the use of a verified measurement tool may provide insight into the differences between those who engage in more intense workouts versus participants who engage in less intensive or less vigorous exercise programs. The types of exercise (i.e., running, weight lifting, yoga, etc.) participants engaged in were also not measured and future research might add this measurement.

Other considerations for future studies include monitoring and/or limiting caloric intake, increasing the duration of the intervention, requesting participants age, and measuring types of calories (carbohydrates, fats, protein). Monitoring other factors such as levels of stress, lack of sleep, or time of year may prove beneficial in providing insight into the potential changes in WM caused by IF and/or exercise. Requiring participants to complete the pre-study survey within 24-28 hours after the pre-study survey completion may be beneficial to negate this limitation. Lastly, requiring participants to provide prior eating windows (early vs. late) may be valuable.

Summary

This research study investigated the effects of 8/16 IF on WM with a covariate of exercise among the perimenopausal population. Concentration on this topic began with a literature review uncovering a gap in the research between WM deficits in perimenopausal women and cost-effective treatments to reduce this risk. The findings from this RCT contributed to the literature by providing that there were no significant mean differences in WMQ posttest scores across groups (control and experimental) of perimenopausal women with a covariate adjustment of hours of exercise per week. Additional findings provided empirical evidence that established there was no significant relationship between WMQ posttest scores and hours of exercise per week.

This chapter provided a summary of the findings, discussion, implications, limitations, and recommendations for future research. This chapter commenced by providing the theory of constructs and biblical foundations found in this study. Recommendations for future research include implementing controls of other possible confounding factors such as testing blood to monitor hormone levels, increasing the number of participants, and recording caloric intake and exercise levels. The results of this study contribute to the literature by demonstrating the effects of an 8/16 IF regimen on WM during the MT.

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APPENDIX A: RECRUITMENT FLYER

Research Participants Needed

The Effects of Intermittent Fasting and Exercise on Working Memory During the Menopause Transition

Are you in perimenopause?

Karen Veltri, a PhD Candidate from Liberty University is seeking perimenopausal women who have experienced the loss of a period for at least 2 months but no more than 10 months to participate in a research study to examine the effects of intermittent fasting and exercise on working memory during the menopause transition.

What is required?

1. Complete pre-survey that includes a demographic and working memory questionnaire after confirming eligibility and signing consent (5 minutes).
2. Follow the instructions for the group to which you are randomly assigned. In the intermittent fasting regimen, you will consume all of your dietary intake, with the exception of water & black coffee, within an 8-hour consecutive timeframe for 2 weeks and refrain from any dietary intake for the remaining 16 hours of the day. In the control group, you will consume dietary intake as normal.
3. Complete a post-survey that includes the working memory questionnaire (5 minutes).

A consent document will be provided once eligibility is confirmed.

To confirm your eligibility, read and sign the consent form, and complete the pre-survey, please scan the QR code or go to https://www.surveymonkey.com/r/NCCZRZZ.

APPENDIX B: SOCIAL MEDIA RECRUITMENT

ATTENTION PERIMENOPAUSAL WOMEN: I am conducting research as part of the requirements for a Doctor of Philosophy at Liberty University. The purpose of my research is to better understand the effects of intermittent fasting and exercise on working memory during the menopause transition. To participate, you must be at least 18 years old and a perimenopausal woman experiencing the loss of your period for at least 2 months but no more than 10 months. You will be asked to take an online, confidential survey, which should take approximately 5 minutes after consent is signed. Participants will then be randomly assigned to one of the following: 1.) an experimental group where you will follow an intermittent fasting regimen for 2 weeks and consume all of your dietary intake within an 8-hour consecutive timeframe and refrain from any dietary intake for the remaining 16 hours of the day, or 2.) a control group where you will consume dietary intake as normal. You will be asked to complete a 5-minute post-survey at the conclusion of the 2 weeks. If you are interested, please scan the QR code below or click the link provided at the end of this post. A consent document will be provided once eligibility is confirmed.

If you meet the study criteria and would like to participate, please scan the QR code or go to https://www.surveymonkey.com/r/NCCZRZZ.

APPENDIX C: LIBERTY UNIVERSITY RECRUITMENT LETTER

Dear Potential Participants,

As a graduate student in the School of Behavioral Sciences at Liberty University, I am conducting research as part of the requirements for a doctoral degree. The purpose of my research is to better understand the effects of intermittent fasting and exercise on working memory during the menopause transition.

To participate, you must be at least 18 years old and a perimenopausal woman experiencing the loss of your period for at least 2 months but no more than 10 months. You will be asked to take an online, confidential survey, which should take approximately 5 minutes after consent is signed. Participants will then be randomly assigned to one of the following: 1.) an experimental group where you will follow an intermittent fasting regimen for 2 weeks and consume all of your dietary intake within an 8-hour consecutive timeframe and refrain from any dietary intake for the remaining 16 hours of the day, or 2.) a control group where you will consume dietary intake as normal. You will be asked to complete a 5-minute post-survey at the conclusion of the 2 weeks.

If you are interested, please scan the QR code below or click the link provided at the end of this post. A consent document will be provided once eligibility is confirmed.

If you meet the study criteria and would like to participate, please scan the QR code or go to https://www.surveymonkey.com/r/NCCZRZZ.

Sincerely,

Karen Veltri
LU Graduate Student

APPENDIX D: ELIGIBILITY QUESTIONNAIRE

1. Are you at least 18 years old?
   Yes or No

2. Are you a perimenopausal woman?
   Yes or No

3. Have you experienced the loss of a period for more than 2 consecutive months but no more than 10 consecutive months?
   Yes or No

4. Do you currently have an average daily intermittent fasting window of 8 hours or less?
   Yes or No

5. Have you previously adhered to an intermittent fasting schedule within the last 2 weeks?
   Yes or No

6. Are you taking any medications affecting glucose levels or other medications that interfere with cognitive functioning?
   Yes or No

7. Do you currently have or have had a health condition that could affect cognitive function such as neurodevelopmental disorders (e.g., intellectual disabilities), neurocognitive disorders (e.g., traumatic brain injury), or neurological diseases (e.g., Multiple Sclerosis, Stroke, Lyme Disease)?
   Yes or No

8. Have you been diagnosed with any chronic metabolic illnesses (e.g., diabetes, high blood pressure, or any other illness inconducive to successful and safe implementation of intermittent fasting)?
   Yes or No

9. Have you been diagnosed with a psychiatric diagnosis of major depressive disorder, bipolar disorder, psychotic disorder, eating disorder, substance abuse or any other psychiatric diagnosis?
   Yes or No

10. Do you have any other restriction that would preclude you from adhering to this study's requirements?
    Yes or No

11. Do you have any dietary restrictions?
    Yes or No

APPENDIX E: INFORMED CONSENT

Title of the Project: The Effects of Intermittent Fasting and Exercise on Working Memory During the Menopause Transition: A Randomized Controlled Trial

Principal Investigator: Karen Veltri, Doctoral Candidate, Psychology Department, Liberty University

Consent

You are invited to participate in a research study. To participate, you must be at least 18 years old, a perimenopausal women experiencing the loss of a period for between 2 and 10 months, and meet the following conditions:

- Have not engaged in intermittent fasting within the last 2 weeks
- Not taking medications affecting glucose levels or cognitive functioning
- No past or present health condition affecting cognitive functioning
- No chronic metabolic illnesses
- No psychosis diagnoses

Things you should know:

- The purpose of the study is to explore techniques women may use to overcome deficits in working memory during perimenopause. If you choose to participate, you will be asked to either consume all of your dietary intake within an 8-hour consecutive timeframe for 2 weeks and refrain from any dietary intake for the remaining 16 hours of the day, or you will be assigned to a control group where you will consume dietary intake as normal. Participants in both groups will be asked to take pre- and post-surveys, which will take approximately 5 minutes each. This study will take approximately one month.
- The expected risks from participating in this study are minimal, which means they are equal to the risks you would encounter in everyday life. It may be possible to have adverse reactions to an intermittent fasting routine. Participants must contact the researcher if you experience adverse reactions.
- Taking part in this research project is voluntary. You do not have to participate, and you can stop at any time.

Please take time to read this entire form and ask questions before deciding whether to take part in this research.

What is the study about and why is it being done?

The purpose of the study is to explore techniques women may use to overcome deficits in working memory during perimenopause.

What will happen if you take part in this study?

If you agree to be in this study, I will ask you to do the following:

1. Complete pre-survey that includes a demographic and working memory questionnaire after confirming eligibility and signing consent (5 minutes).
2. Follow the instructions for the group to which you are randomly assigned. In the intermittent fasting regimen, you will consume all of your dietary intake, with the exception of water & black coffee, within an 8-hour consecutive timeframe for 2 weeks and refrain from any dietary intake for the remaining 16 hours of the day. In the control group, you will consume dietary intake as normal.
3. Complete a post-survey that includes the working memory questionnaire (5 minutes).

How could you or others benefit from this study?

The direct benefits participants should expect from participating in this study include an increase in working memory functioning.

Benefits to society include gaining alternate techniques to increase working memory during perimenopause.

What risks might you experience from being in this study?

The expected risks from participating in this study are minimal, which means they are equal to the risks you would encounter in everyday life. The risks involved in this study may include adverse reactions to an intermittent fasting routine. To mitigate any potential risks, the researcher will check in with participants who are intermittent fasting each week via email and participants will be required to stop intermittent fasting if adverse effects are experienced. Participants must contact the researcher if they experience adverse reactions.

How will personal information be protected?

The records of this study will be kept private. Published reports will not include any information that will make it possible to identify a subject. Research records will be stored securely, and only the primary researcher will have access to the records.

- Participant responses will be kept confidential by replacing names with numbers.
- Data will be stored on a password-locked laptop and only accessible by the primary researcher. After three years, all electronic records will be deleted, and all hardcopy records will be shredded.

Is study participation voluntary?

Participation in this study is voluntary. Your decision whether to participate will not affect your current or future relations with Liberty University. If you decide to

participate, you are free to not answer any question or withdraw at any time prior to submitting the surveys without affecting those relationships.

What should you do if you decide to withdraw from the study?

If you choose to withdraw from the study, please contact the researcher at the email address in the next paragraph. Should you choose to withdraw at any time, data collected from you will be destroyed immediately and not included in this study.

Whom do you contact if you have questions or concerns about the study?

The researcher conducting this study is Karen Veltri. You may ask any questions you have now. If you have questions later, **you are encouraged** to contact her at [redacted]. You may also contact the researcher's faculty sponsor, Dr. Patrick Slowinski at [redacted].

Whom do you contact if you have questions about your rights as a research participant?

If you have any questions or concerns regarding this study and would like to talk to someone other than the researcher, **you are encouraged** to contact the IRB. Our physical address is Institutional Review Board, 1971 University Blvd., Green Hall Ste. 2845, Lynchburg, VA, 24515; our phone number is 434-592-5530, and our email address is irb@liberty.edu.

Disclaimer: The Institutional Review Board (IRB) is tasked with ensuring that human subjects research will be conducted in an ethical manner as defined and required by federal regulations. The topics covered and viewpoints expressed or alluded to by student and faculty researchers are those of the researchers and do not necessarily reflect the official policies or positions of Liberty University.

Your Consent

By signing this document, you agree to participate in this study. Make sure you understand what the study is about before you sign. Please contact the researcher at [redacted] have any questions before consenting. You can print a copy of this document for your records. If you have any questions about the study after you sign this document, you can contact the researcher using the information provided above.

I have read and understood the above information. I have asked questions and I have received answers. I consent to participate in the study.

Please type your name and the date in the text box below:

[redacted]

APPENDIX F: DEMOGRAPHIC QUESTIONNAIRE

1. What is your first and last name? _____
2. What is your email address? _____
3. What is your cellular telephone number? _____
4. Are you currently using any form of hormonal birth control?
   Yes or No
5. Are you currently using any form of hormone replacement therapy (HRT)?
   Yes or No
6. How many hours per week do you exercise?

7. What is your race?
   a.) White
   b.) Black or African American
   c.) American Indian or Alaska Native
   d.) Asian
   e.) Native Hawaiian or Pacific Islander
   f.) Other
8. What is your work status?
   a.) Full Time (40 or more hours per week)
   b.) Part Time (up to 39 hours per week)
   c.) Retired
   d.) Unemployed
   e.) Homemaker
   f.) Self-employed
   g.) Unable to work
9. What is your marital status?
   a.) Single (never married)
   b.) Married, or in a domestic partnership
   c.) Widowed
   d.) Divorced
   e.) Separated
10. What is your education level?
    a.) Less than high school diploma
    b.) High school diploma or equivalent (GED)
    c.) Some college, no degree

d.) Associate degree (AA, AS)
e.) Bachelor's degree (BA, BS)
f.) Master's degree (MA, MS, Med)
g.) Doctorate or professional degree (PhD, MD, DDS, etc.)

APPENDIX G: WORKING MEMORY QUESTIONNAIRE (Vallat-Azouvi et al., 2012)

Name: _____

1. Do you feel that you tire quickly during the day?
   Not At All A Little Moderately A Lot Extremely Not Relevant

2. Do you find it difficult to carry out a project such as choosing and organizing your holidays?
   Not At All A Little Moderately A Lot Extremely Not Relevant

3. Do you have problems with remembering sequences of numbers, for example, when you have to note down a telephone number?
   Not At All A Little Moderately A Lot Extremely Not Relevant

4. Do you need to make an effort to concentrate in order to follow a conversation in which you are participating with many other people?
   Not At All A Little Moderately A Lot Extremely Not Relevant

5. Do you find it difficult to remember the name of a person who has just been introduced to you?
   Not At All A Little Moderately A Lot Extremely Not Relevant

6. When you shop, do you often spend more than the budget you set for yourself?
   Not At All A Little Moderately A Lot Extremely Not Relevant

7. Do you have difficulty remembering what you have read?
   Not At All A Little Moderately A Lot Extremely Not Relevant

8. When you are interrupted during an activity by a loud noise (door slam, car horn) do you have difficulty in getting back to the activity?
   Not At All A Little Moderately A Lot Extremely Not Relevant

9. Do you find it difficult to carry out an activity with chronological steps (cooking, sewing, DIY)?
   Not At All A Little Moderately A Lot Extremely Not Relevant

10. Do nearby conversations disturb you during a conversation with another person?
    Not At All A Little Moderately A Lot Extremely Not Relevant

11. Do you need to re-read a sentence several times to understand a simple text?
    Not At All A Little Moderately A Lot Extremely Not Relevant

12. Do you have difficulty in organizing your time with regard to appointments and your daily activities?
    Not At All A Little Moderately A Lot Extremely Not Relevant

13. Do you find it difficult to do two (or several) things at the same time such as:
    - DIY and listening to the radio at the same time?
    - Cooking and listening to the radio at the same time?
    Not At All A Little Moderately A Lot Extremely Not Relevant

14. When you are carrying out an activity, if you realize that you are making a mistake, do you find it difficult to change strategy?
    Not At All A Little Moderately A Lot Extremely Not Relevant

15. Do you have difficulty understanding what you read?
    Not At All A Little Moderately A Lot Extremely Not Relevant

16. Do you feel that fatigue excessively reduces your concentration?
    Not At All A Little Moderately A Lot Extremely Not Relevant

17. When you pay cash for an item, do you have difficulty in realizing if you have been given the correct change?
    Not At All A Little Moderately A Lot Extremely Not Relevant

18. Do you find it difficult to follow the different steps of a user's guide (putting kit furniture together, installing a new electrical device)?
    Not At All A Little Moderately A Lot Extremely Not Relevant

19. Do you find it difficult to carry out an activity in the presence of background noise (traffic, radio or television)?
    Not At All A Little Moderately A Lot Extremely Not Relevant

20. Are you particularly disturbed if an unexpected event interrupts your day or what you are in the process of doing?
    Not At All A Little Moderately A Lot Extremely Not Relevant

21. If a character in a text is designated in different ways (he, him), do you have difficulty in understanding the story?
    Not At All A Little Moderately A Lot Extremely Not Relevant

22. Do you feel embarrassed when you have a conversation with an unfamiliar person?
    Not At All A Little Moderately A Lot Extremely Not Relevant

23. Do you find that you hesitate for a long time before buying even a common item?
    Not At All A Little Moderately A Lot Extremely Not Relevant

24. Do you feel that you are very slow to carry out your usual activities?
    Not At All A Little Moderately A Lot Extremely Not Relevant

25. Do you have to look at a written phone number many times before dialing a number that you don't know off by heart?
    Not At All A Little Moderately A Lot Extremely Not Relevant

26. Do you have difficulty in managing your paperwork, sending social security papers, paying bills, etc.?
    Not At All A Little Moderately A Lot Extremely Not Relevant

27. If somebody speaks quickly to you, do you find it difficult to remember what you were told or asked?
    Not At All A Little Moderately A Lot Extremely Not Relevant

28. Do you find that you tire quickly during an activity which demands a lot of attention (for example, reading)?
    Not At All A Little Moderately A Lot Extremely Not Relevant

29. After doing your shopping, are you surprised to find that you have bought many useless items?
    Not At All A Little Moderately A Lot Extremely Not Relevant

30. Do you find it difficult to participate in a conversation with several people at once?
    Not At All A Little Moderately A Lot Extremely Not Relevant

APPENDIX H: PARTICIPANT INSTRUCTIONS – EXPERIMENTAL GROUP

Thank you for participating in this research study to explore techniques women may use to overcome deficits in working memory during perimenopause.

1. Complete pre-survey that includes a demographic and working memory questionnaire after confirming eligibility and signing consent (5 minutes).
2. Follow the instructions for the intermittent fasting regimen. You will consume all of your dietary intake, with the exception of water & black coffee, within an 8-hour consecutive timeframe for 2 weeks and refrain from any dietary intake for the remaining 16 hours of the day.
3. Complete a post-survey that includes the working memory questionnaire (5 minutes).

Please contact me if you have any questions or concerns at [redacted] and thank you for your time!

Final Online Survey QR Code and Link –

https://www.surveymonkey.com/r/NCQ8HTF

APPENDIX I: PARTICIPANT INSTRUCTIONS – CONTROL GROUP

Thank you for participating in this research study to explore a technique women may use to overcome deficits in working memory during perimenopause.

1. Complete pre-survey that includes a demographic and working memory questionnaire after confirming eligibility and signing consent (5 minutes).
2. Follow the instructions for the control group. You will consume dietary intake as normal.
3. Complete a post-survey that includes the working memory questionnaire (5 minutes).

Please contact me if you have any questions or concerns at [redacted] and thank you for your time!

Final Online Survey QR Code and Link –

https://www.surveymonkey.com/r/NCQ8HTF

APPENDIX J: EZZATI EMAIL APPROVAL

From: "Veltri, Karen Marie" <[redacted]
Subject: Re: [External] Re: Permission to Utilize Figure in Dissertation
Date: February 21, 2024 at 1:50:15 PM EST
To: Armin Ezzati <arminez@ksu.edu>

Hi Armin,

Thank you very much for your permission to utilize the Figure for purposes of my dissertation research study. I will ensure the proper citation and thank you again for your consideration, kindness, and permission.

Kindly,
Karen

From: Armin Ezzati <arminez@ksu.edu>
Sent: Wednesday, February 21, 2024 1:25 PM
To: Veltri, Karen Marie <[redacted] Victoria.m.pak@emory.edu <Victoria.m.pak@emory.edu>
Subject: [External] Re: Permission to Utilize Figure in Dissertation

You don't often get email from arminez@ksu.edu. Learn why this is important

[EXTERNAL EMAIL: Do not click any links or open attachments unless you know the sender and trust the content.]

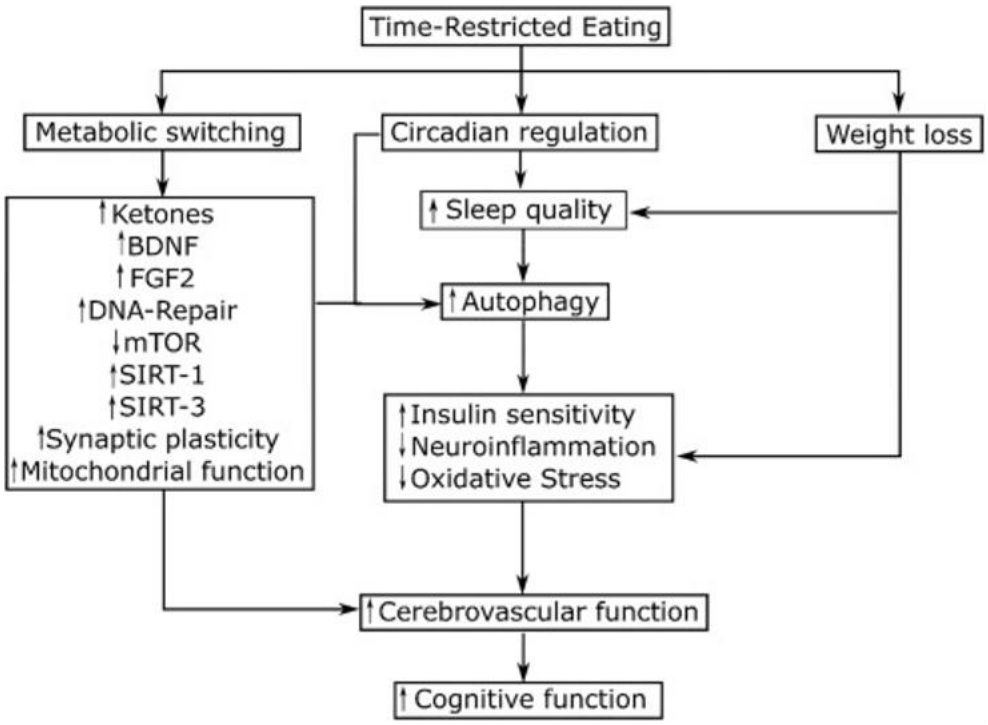
Dear Karen,
I am happy to grant you permission to use the Figure for your dissertation. Please ensure that appropriate citation is provided to acknowledge the source of the Figure within your dissertation.
Best,
Armin

From: Veltri, Karen Marie [redacted]>Sent: Wednesday, February 21, 2024 9:55 AMTo: Armin Ezzati <arminez@ksu.edu>; Victoria.m.pak@emory.edu <Victoria.m.pak@emory.edu>Subject: Permission to Utilize Figure in Dissertation

This email originated from outside of K-State.

Hello,

I am respectfully requesting permission to utilize the Figure below, found in one of your research studies provided below for purposes of my dissertation at Liberty University:



Ezzati, A., & Pak, V. M. (2023). The effects of time-restricted eating on sleep, cognitive decline, and Alzheimer's disease. Experimental Gerontology, 171, 112033. https://doi.org/10.1016/j.exger.2022.112033

Please let me know if you have any questions or concerns and whether I have your permission to use this figure.

Graciously,
Karen Veltri

APPENDIX K: KHALILOLLAHI EMAIL APPROVAL (Khalilollahi et al., 2023)

From: "Veltri, Karen Marie" <[redacted]
Subject: Re: [External] Re: Permission Request to Utilize COM-B Model in Dissertation
Date: February 21, 2024 at 1:49:12 PM EST
To: "Khalilollahi, Avin" <a.khalilollahi@tue.nl>

Hi Avin, (Khalilollahi et al., 2023)

Thank you very much for your permission to utilize the COM-B Model Figure for purposes of my dissertation research study. The proposed study seeks to examine the effects of Time-Restricted Eating (TRE) on Working Memory (WM) during the Menopause Transition (MT), while controlling for the relative effects of Physical Activity (PA). The COM-B Model Figure supports the theoretical framework of this study and the capability, opportunity, motivation, and behaviors required to engage in a new intervention.

I will also ensure the proper citation for the COM-B Model Figure and thank you again for your consideration, kindness, and permission.

Kindly,
Karen
From: Khalilollahi, Avin <a.khalilollahi@tue.nl>
Sent: Wednesday, February 21, 2024 12:37 PM
To: Veltri, Karen Marie <[redacted]
Subject: [External] Re: Permission Request to Utilize COM-B Model in Dissertation

You don't often get email from a.khalilollahi@tue.nl. Learn why this is important

[EXTERNAL EMAIL: Do not click any links or open attachments unless you know the sender and trust the content.]

Dear Karen,

Thank you for reaching out regarding your dissertation research. I'm pleased to grant you permission to utilize the COM-B Model Figure from our study cited in Children's Geographies. Your interest in incorporating our research into your work is appreciated.

I'm also curious about your field of research. Could you kindly provide more insight into your area of study and how our model figure fits into your dissertation?

Could you please provide me with your LinkedIn or ResearchGate profile? I would like to learn more about your research interests and keep in touch as you progress with your dissertation.

If you have any further questions or require additional information, please don't hesitate to ask. I wish you the best with your dissertation research.

Kind regards,
Avin

Sent from Outlook for iOS
From: Veltri, Karen Marie <[redacted]
Sent: Wednesday, February 21, 2024 3:48:32 PM
To: Khalilollahi, Avin <a.khalilollahi@tue.nl>
Subject: Permission Request to Utilize COM-B Model in Dissertation

You don't often get email from [redacted]. Learn why this is important

Hello,

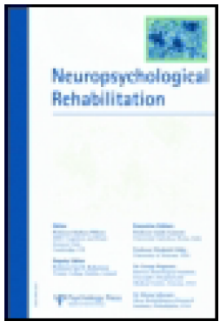
I am respectfully requesting permission to utilize the COM-B Model Figure found in the following study for purposes of my dissertation at Liberty University:

Khalilollahi, A., Kasraian, D., Kemperman, A. A., & van Wesemael, P. (2023). Application of the COM-B model to the correlates of children's outdoor playing and the potential role of digital interventions: a systematic literature review. Children's Geographies, 21(3), 442-458. https://doi.org/10.1080/14733285.2022.2075692

Please let me know if you have any questions or concerns and whether I have your permission to use this figure.

Graciously,
Karen Veltri

APPENDIX L: WORKING MEMORY QUESTIONNAIRE PUBLIC USE



Neuropsychological Rehabilitation: An International Journal

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/pnrh20

The Working Memory Questionnaire: A scale to assess everyday life problems related to deficits of working memory in brain injured patients

Claire Vallat-Azouvi [a b], Pascale Pradat-Diehl [b c] & Philippe Azouvi [b d e]

[a] UGECAM-antenne UEROS, Raymond Poincare hospital, Garches, France

APPENDIX M: LIBERTY UNIVERSITY PERMISSION EMAIL

From: Knapp, Kenyon Christian (School of Behavioral Sciences Admin)
[redacted]
Sent: Thursday, June 20, 2024 2:21:34 PM
To: Veltri, Karen Marie [redacted]
Cc: Slowinski, Patrick Thomas (Psychology) <[redacted]>; Piferi, Rachel L (Psychology) <[redacted]>
Subject: RE: Participant Recruitment

Dear Ms. Veltri,

Your research with School of Behavioral Sciences students is approved, contingent on your also receiving IRB approval from Liberty University. Thanks.

Kenyon Knapp, Ph.D., LPC
Dean
School of Behavioral Sciences
Health Professions
[redacted]

LIBERTY
UNIVERSITY
Liberty University | Training Champions for Christ since 1971

From: Veltri, Karen Marie <[redacted]>
Sent: Thursday, June 20, 2024 2:15 PM
To: Knapp, Kenyon Christian (School of Behavioral Sciences Admin)
[redacted]
Cc: Slowinski, Patrick Thomas (Psychology) <[redacted]>
Subject: Participant Recruitment

Dr. Knapp,

I am a doctoral student seeking to examine the effects of intermittent fasting and exercise on working memory in the perimenopause population and am respectfully requesting the permission to recruit participants from Liberty University's School of Behavioral Sciences.

Blessings,
Karen

APPENDIX N: IRB APPROVAL

LIBERTY UNIVERSITY.
INSTITUTIONAL REVIEW BOARD

July 9, 2024

Karen Veltri
Patrick Slowinski

Re: IRB Approval - IRB-FY23-24-1624 The Effects of Intermittent Fasting and Exercise on Working Memory During the Menopause Transition: A Randomized Controlled Trial

Dear Karen Veltri, Patrick Slowinski,

We are pleased to inform you that your study has been approved by the Liberty University Institutional Review Board (IRB). This approval is extended to you for one year from the following date: July 9, 2024. If you need to make changes to the methodology as it pertains to human subjects, you must submit a modification to the IRB. Modifications can be completed through your Cayuse IRB account.

Your study falls under the expedited review category (45 CFR 46.110), which is applicable to specific, minimal risk studies and minor changes to approved studies for the following reason(s):

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

For a PDF of your approval letter, click on your study number in the My Studies card on your Cayuse dashboard. Next, click the Submissions bar beside the Study Details bar on the Study Details page. Finally, click Initial under Submission Type and choose the Letters tab toward the bottom of the Submission Details page. Your stamped consent form(s) and final versions of your study documents can be found on the same page under the Attachments tab. Your stamped consent form(s) should be copied and used to gain the consent of your research participants. If you plan to provide your consent information electronically, the contents of the attached consent document(s) should be made available without alteration.

Thank you for your cooperation with the IRB, and we wish you well with your research project.

Sincerely,

G. Michele Baker, PhD, CIP
Administrative Chair
Research Ethics Office