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Examining the Relationship Between Yoga Participation and Health. You Down, Dog?

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EXAMINING THE RELATIONSHIP BETWEEN YOGA PARTICIPATION AND HEALTH. YOU DOWN, DOG?

by

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ABSTRACT

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The prevalence of debilitating chronic diseases, such as cardiovascular disease (CVD) and Alzheimer's disease, are increasing in the United States. Inflammation, mitochondrial dysfunction, stress and depression are common pathologies associated with these chronic diseases. Many individuals engage in yoga because they believe it will improve their health. However, research examining the impact of yoga on markers of health associated with chronic diseases is limited and often reports conflicting results. Therefore, the purpose of this dissertation is to examine the relationship between yoga and inflammation, protein content of oxidative phosphorylation complexes, stress and depression, which may support the use of lifestyle interventions to promote health and wellbeing. The overall hypothesis of this dissertation is that yoga will be associated with improved markers of health; this will be tested through two separate studies. Study 1: Yoga and Health: A Cross Sectional Study used a cross-sectional study design to compare markers of health that are common pathologies for multiple, prevalent diseases between yoga participants and individuals who do not engage in yoga. Results support that yoga participants who engaged in yoga at least two times a week for the last six months have significantly improved perceived stress and symptoms of depression compared to non-yoga participants. Differences based on clinical cutoffs were also observed in a measure of systemic inflammation (erythrocyte sedimentation rate [ESR]). However, no differences were observed in C-reactive protein (CRP), tumor necrosis factor alpha (TNF-α), nor adiponectin. Additionally, the Complex V protein content was not different between the groups,

but this may be due to the age difference of the groups rather than differences in their yoga participation. Study 2: Adherence to and Changes in Physiologic and Psychologic Health during an 8-week Yoga Intervention: A Pilot Study was conducted to evaluate the feasibility and explore the impact of an 8-week yoga intervention on perceived stress, symptoms of depression, inflammation, and protein content of oxidative phosphorylation complexes to provide insight on the relationship between yoga and the pathology of CVD. While the majority (67%) of participants adhered to the protocol, our feasibility cutoff of ≥ 85%, created a priori, was not attained. Participants who completed the study (n = 8; 89%) observed reductions in levels of perceived stress (13.9%), depression symptoms (27%) and systemic inflammation (34%), and CRP (10%). An increase of 21% was observed in adiponectin. Contrary to the hypothesis TNF-α increased by 11% and there was a minimal change in the protein content of Complex V. **Overall conclusion**. Collectively, the findings from both studies support that participation in yoga can improve levels of perceived stress and symptoms of depression. Further, differences based on clinical cutoffs in the cross-sectional study and exploratory analyses from the pilot study show promising findings regarding the relationship between yoga and systemic inflammation. However, this work was not able to demonstrate a clear relationship between participation in yoga and inflammatory markers of CRP, TNF-α, adiponectin, nor mitochondrial protein content. These studies are the first to directly measure changes within the mitochondria in relation to yoga participation. Additionally, results support that yoga may be recommended as a lifestyle intervention to improve mental health outcomes and, with further research, possibly be used for physiologic variables.

TABLE OF CONTENTS

LIST OF FIGURES

Chapter

LIST OF TABLES

Chapter

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Chapter 1: Introduction & Review of Literature

Prevalence of inflammation, mitochondrial function, and mental health concerns

Costs associated with healthcare result in an estimated $2.9 trillion dollars, almost 20%, of the United States economy (Mathur, Srivastava, & Mehta, 2015). The most prevalent chronic diseases (e.g. cardiovascular disease [CVD] or Type 2 diabetes) are multifaceted and incur a large burden on the healthcare system through financial costs and being leading causes of death (Centers for Disease Control and Prevention, 2016). The cost of CVD and Type 2 diabetes, specifically, corresponds to a financial burden on the United States economy of $200 and $327 billion dollars per year, respectively, (American Diabetes Association, 2017; Centers for Disease Control and Prevention, 2016). While distinct from each other, cardiovascular disease and Type 2 diabetes share multiple pathologies that preempt disease onset. Inflammation, mitochondrial dysfunction, and mental health (i.e. chronic stress and depression) are common pathologies/conditions associated with these chronic diseases (Ballinger, 2005; Libby, 2007; Marín-García, & Goldenthal, 2002; Marsollier, Ferré, & Foufelle, 2011; Pearson, et al. 2003). These individual conditions (inflammation, mitochondrial dysfunction, and mental health) have detrimental impacts on health by themselves, but, further, work synergistically and put individuals at even greater health risks (Dowlati et al., 2010; Fattal, Link, Quinn, Cohen, & Franco, 2007; Gardner & Boles, 2011; Kaplan, Rucklidge, Romijn, & McLeod, 2015; Luft, 1994). Research working to improve these markers of health support that these conditions are modifiable through behavioral lifestyle changes, such as physical activity.

Inflammation

Inflammation within the body is a normal process that occurs due to an immune response subsequent an infection, illness, or injury and is typically limited in duration. However, some conditions or illnesses, such as obesity or stress, result in high levels of inflammatory markers being maintained for a long period of time; this leads to chronic inflammation (Berg &

Scherer, 2005; Sarvottam & Yadav, 2014). Chronic inflammation underlies and furthers the progression of many disease conditions, including: cardiovascular disease, metabolic syndrome, neurodegeneration, and cancers (Coussens & Werb, 2002; Libby, 2007; Marsollier, Ferré, & Foufelle, 2011; Perry, Cunningham, & Holmes, 2007; von Hundelshausen & Weber, 2007).

There are multiple types of markers of inflammation, including pro-inflammatory, anti-inflammatory, and mediating markers. Pro-inflammatory markers promote or result in increased inflammation and lead to worsened disease states. Anti-inflammatory markers are associated with reduced inflammation, thus improving health. Finally, inflammatory mediators are activated by changes in health or disease homeostasis within the body and can activate pro or anti-inflammatory pathologies leading to worsened or improved health conditions, depending on the specific mediator. Common pro-inflammatory markers include: C-reactive protein (CRP), Interferon gamma (IFN-γ), Interleukin (IL)-6, IL-8, IL-12, Tumor necrosis factor – alpha (TNF-α), (Brenner, et al., 2014). Common anti-inflammatory markers include: adiponectin, IL-4, IL-10, (Brenner, et al., 2014)

While each marker of inflammation interacts with diseases differently, they are a part of a response that ultimately has associations with the development of chronic diseases. There are a variety of conditions (e.g. obesity or stress) that, through a cascade of events, result in an increase of pro-inflammatory markers and reductions in anti-inflammatory markers. While each inflammatory marker has its own stimuli and effects on the body, there is strong evidence of chronic inflammation and its association with disease. This dissertation will be focusing on three specific markers of inflammation: CRP, TNF-α, and adiponectin (Table 1). C-reactive protein, and TNF-α are two pro-inflammatory markers of considerable interest in chronic inflammatory processes that are positively associated with severe chronic diseases. Conversely, adiponectin is an anti-inflammatory marker and is inversely related to chronic diseases. C-reactive protein is produced in the presence of inflammatory diseases, with a role to assist in identifying

inflammatory markers (Berg & Scherer, 2005; Brenner et al., 2014). C-reactive protein does not contribute to increased inflammation in the body but is a pro-inflammatory marker for systemic inflammation (Brenner, et al., 2014). High levels of inflammation stimulate an increased production of CRP and therefore, high levels of CRP are associated with cardiovascular disease and its comorbidities (Du Clos, 2000; Yeh, Anderson, Pasceri, & Willerson, 2001). Tumor Necrosis Factor – alpha is another pro-inflammatory marker that is associated with chronic diseases, such as Type 2 diabetes, and comorbidities of cardiovascular disease, including: obesity, hypertension, and dyslipidemia (Popa, Netea, Van Riel, Van Der Meer, & Stalenhoef, 2007). Tumor Necrosis Factor – alpha is considered a pro-inflammatory mediator, produced by a variety of cell types including: macrophages, T-cells, monocytes, and adipocytes. Its association with chronic diseases is related to processes of insulin resistance and lipid metabolism (Popa et al., 2007).

In contrast to pro-inflammatory markers, adiponectin, an anti-inflammatory marker, has a beneficial role within the body and is considered as a protective risk factor for disease conditions, including: atherosclerosis, dyslipidemia, myocardial infarctions and Type 2 diabetes, (Giannessi, Maltinti, & Del Ry, 2007; Goldstein & Scalia, 2004; Matsuzawa, Funahashi, Kihara, & Shimomura, 2004; Oh, Ciaraldi, & Henry, 2007). Adiponectin likely has both mediating and direct effects on the vasculature, and metabolism of glucose and lipids and, in these ways, has cardioprotective properties that promote health (Giannessi et al., 2007; Matsuzawa et al., 2004; Oh, Ciaraldi, & Henry, 2007). Across multiple markers of pro and anti-inflammation, a relationship is observed that supports the mediating effects of prolonged inflammation on chronic diseases and their pathologies.

Table 1.1. Inflammatory Markers and Associated Diseases

Inflammatory Marker	Marker for anti / pro-inflammation	Associated Diseases
Adiponectin	Anti-inflammatory	Alzheimer's disease Atherosclerosis Dyslipidemia Myocardial infarctions Type 2 diabetes
C-Reactive Protein	Pro-inflammatory	Cardiovascular disease Type 2 diabetes Lung Cancer Breast Cancer
Tumor Necrosis Factor – Alpha	Pro-inflammatory mediator	Dyslipidemia Lung cancer Hypertension non-Hodgkin's lymphoma Type 2 diabetes

(Brenner et at., 2014; Oh, Ciaraldi, & Henry, 2007; Popa et al., 2007).

Mitochondrial Function and Dysfunction

Mitochondria are commonly referred to as the "powerhouse" of the cell because of their essential role in adenosine triphosphate (ATP), or energy, production (Powers & Howley, 2007). The production of ATP involves the breakdown of fuel substrates (e.g. glucose); the final two processes of ATP production, aerobic glycolysis (Krebs cycle and oxidative phosphorylation), occur within the mitochondria, hence why mitochondria are attributed to ATP production. In oxidative phosphorylation, the final process of ATP production, electrons move down a gradient through five different complexes (complex I [NADH reductase], II [succinate dehydrogenase], III [cytochrome reductase], complex IV [cytochrome C oxidase], complex V [ATP synthase]) and are accepted by oxygen to produce ATP (Powers & Howley, 2007). The mitochondria are also responsible for processes such as apoptosis, cholesterol synthesis, and signaling for reactive oxygen species (ROS) (Butow & Avadhani, 2004; Hamanaka & Chandel, 2010; Murphy, 2009). The production of ATP produces low levels of ROS which are easily managed by the body. However, high levels of ROS, which can be produced by prolonged environmental stress or by changes in mitochondrial functioning, can damage cells and are associated with systemic

inflammation, this process is commonly referred to as oxidative stress (Gardner & Boles, 2011; Hedge, Adhikari, Shetty, Manjrekar, & D'Souza, 2013; Medina-Gómez, 2012).

Due to these crucial roles within the body, functioning mitochondria are vital to health, and mitochondrial dysfunction may result in multiple health concerns. The significance of mitochondrial dysfunction was stated in 1994 by Luft, when he was able to link mitochondrial dysfunction to over 100 diseases and to the body's aging process (Luft, 1994). Notable disease states that mitochondrial dysfunction is associated with include: Alzheimer's disease, Type 2 diabetes, cardiovascular disease, and some cancers (Balaban, Nemoto, & Finkel, 2005; Hauptmann et al., 2006; H. Lee et al., 2005; Ren, Pulakat, Whaley-Connell, & Sowers, 2010; Widlansky et al., 2010; Wu et al., 2007).

Mitochondrial dysfunction commonly arises due to mutations in either nuclear or mitochondrial DNA, reduced enzyme functioning, or deficiencies of electron transport chain cofactors (e.g. CoQ10, carnitine, or B-vitamins) (Gardner & Boles, 2011; Luft 1994). Additionally, there is an observed relationship between protein content of oxidative phosphorylation complexes and the enzyme activity of those complexes. This is evident in the mitochondrial functioning of different tissues due to differences in their metabolic demands (e.g. liver, heart, or kidneys) (Johnson, Harris, Blair, & Balaban, 2007), in the aging process (Larsen, Hey-Mogensen, Rabøl, Stride, Helge, & Dela, 2012; No et al., 2018) and in diseases such as heart disease and Luft (mitochondrial) disease (Luft, 1994; No et al., 2018). Mitochondrial dysfunction can result in increased oxidative stress and promotion of systemic inflammation, and ultimately lead to a higher susceptibility of disease pathologies associated with these conditions (Gardner & Boles, 2011; Medina-Gómez, 2012). Thus, the functioning of mitochondria is essential to health within the body.

Depression

Major depression is a psychological disorder that is defined by changes in mood, loss of interest/pleasure, and additional cognitive or physical symptoms over a two-week period (American Psychiatic Association, 2013). The term depression can cover a wide range of symptoms and levels of severity within the symptoms; these can range from a lack of interest in common activities to thoughts of death and/or suicide (Kazdin, 2000). Depression is a common condition in the United States with almost 7% of all adults experiencing at least one major depressive episode within the last year. Higher prevalence rates are found in younger age groups, with individuals18-25 years old having a 10.9% prevalence rate followed by individuals 26-49 years old at a prevalence of 7.4% (Quality, 2017).

Altered levels of monoamines (e.g. serotonin) were originally thought to cause depression (Coppen, 1967). Current research supports a more complex pathology, potentially involving mitochondrial dysfunction and/or inflammation (Gardner & Boles, 2011). Depression, in addition to impacting an individual's mental state, is commonly associated with a lower quality of life, fatigue, and stress (Cramer, Lauche, Langhorst, & Dobos, 2013). Further, in the age groups with the highest prevalence rates, depression is found to be the leading cause of disability (Quality, 2017). Due to the high prevalence rates of depression, its strong relationship with suicide (a leading cause of death in the United states; Kessing, 2004), and association with poor health (Gaynes, Burns, Tweed, & Erickson, 2002; Moussavi et al., 2007) depression has become a pressing matter for society and its health.

Stress

Stress is a condition in which there is a physiologic and/or psychologic response to demands placed on an individual from their surrounding environment or situation (Butler, 1993). Low levels of stress that elicit a positive response is commonly called 'eustress' and can be beneficial for individuals (Le Fevre, Matheny, & Kolt, 2003). However, higher levels of stress are considered to be unhealthy; in this vein, over half of the United States population self-reports

moderate to high levels of stress (Wiegner, Hange, Björkelund, & Ahlborg, 2015). Furthermore, higher levels of stress and prevalence rates are reported in specific sub-groups of the population, such as college students and caregivers (Anderson et al., 2012; Brougham, Zail, Mendoza, & Miller, 2009).

Psychologic stress not only has a negative impact on psychologic health, but it can also negatively impact physiologic processes (Brotman, Golden, & Wittstein, 2007; Cohen, Janicki-Deverts, & Miller, 2007; Hammen, 2005). Stress creates disruption in multiple physiologic processes/pathologies; but two of the first systems to be impacted by stress are the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS) (Brotman et al., 2007; Ross & Thomas, 2010). From here, the stress extends throughout the body, impacting key physiologic functions (e.g. nor/epinephrine, cortisol, heart rate, blood pressure, fuel utilization, etc) and may result in changes such as increased pro-inflammatory markers (e.g. IL-6, TNF-α) (Juster, McEwen, & Lupien, 2009), reduced immune function (Rojas, Padgett, Sheridan, & Marucha, 2002), increased risk for metabolic syndrome (Chandola, Brunner, & Marmot, 2006), and exacerbation of the cardiovascular disease or events (Kivimäki et al., 2002). Ultimately psychologic stress can lead to an increase in susceptibility of illness or diseases (Brotman et al., 2007) through the physiologic response it elicits and, thus, is related to 80% of all diseases and illnesses (e.g. cold, cardiovascular disease, and cancer) (Chong, Tsunaka, & Chan, 2011; Cohen, Tyrrell, & Smith, 1993). Therefore, methods to reduce stress levels are essential because of the strong consequences that stress has on health.

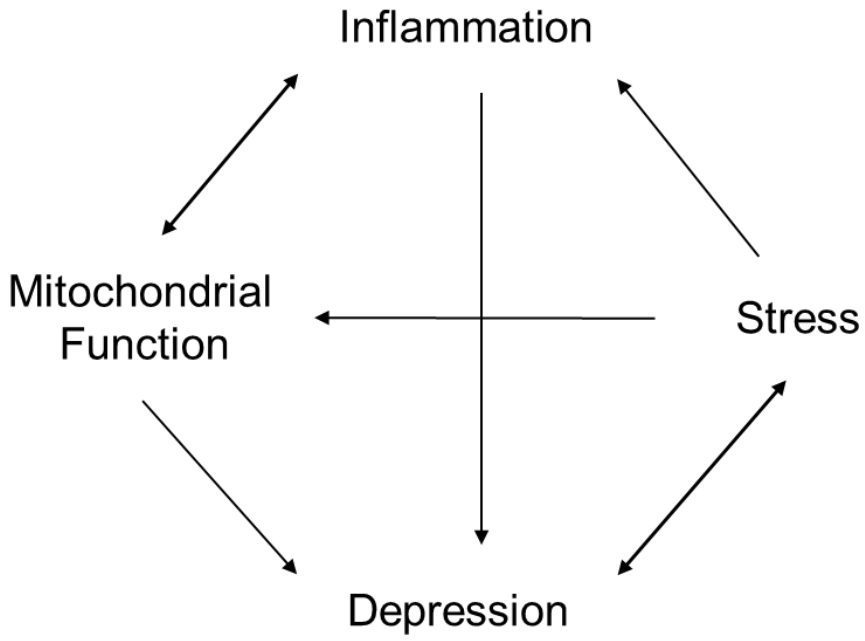
Because of the multiple ways that stress can impact the body both psychologically and physiologically, there are many potential markers of stress that involve subjective, self-reported measures or objective biomarkers. Perceived stress or reporting of stressful life events are common measures of subjective stress (Cohen, Kamarck, & Mermelstein, 1983; Cohen, Tyrrell, & Smith, 1993). Examples of physiologic markers that reflect psychologic stress include: cortisol

levels, epinephrine, IL-6, TNF-α, heart rate variability, and blood pressure, among many others (Juster, McEwen, & Lupien, 2009).

Associations between Inflammation, Mitochondrial Dysfunction, & Mental Health

As Libby (2007) stated in their paper examining the impact of inflammation on chronic diseases, “many…diseases have more mechanisms in common than usually recognized or acknowledged” (p. S141). This concept applies not only to inflammatory mechanisms but can encompass additional pathologies such as mitochondrial dysfunction and mental health. Research is beginning to examine the relationships between these conditions and their implications in chronic diseases. While research has shown associations between these pathologies (Dowlati et al., 2010; Fattal et al., 2007; Gardner & Boles, 2011; Kaplan et al., 2015), the exact nature of each relationship is unknown (Figure 1). Research supports that mental health concerns (e.g. depression and stress) can impact physiologic pathways, including both inflammation and mitochondrial dysfunction.

Figure 1.1. Relationships between inflammation, mitochondrial dysfunction, stress & depression.



Depression & Inflammation

The relationship between inflammation and depression was first suggested in the 1990s (Maes et al., 1990-1991; Maes, Smith, & Scharpe, 1995). Specific inflammatory markers that are associated with depression include: CRP, IL-6, and TNF-α (Gimeno et al., 2009; Hickie & Lloyd, 1995; Howren, Lamkin, & Suls, 2009; McEwen, 2006; Penninx, 2003). Briefly, the proposed relationship is that inflammation limits the ability of tryptophan, an amino acid of serotonin, to perform its function, which therefore limits the availability and abilities of serotonin (Dowlati et al., 2010). However, this pathology assumes the serotonin hypothesis for depression, which is currently under further consideration (Gardner & Boles, 2011).

Depression & Mitochondrial Function

Studies have observed that individuals with mitochondrial dysfunction have a higher likelihood of having depression (Fattal et al., 2007). In a study of individuals with a mitochondrial disorder, 54% of the participants were diagnosed with depression (Fattal et al., 2007). Further, in a post-mortem study that examined individuals with major depression and healthy controls,

the individuals with major depression had over thirty percent higher levels of oxidative stress, which was attributed to mitochondrial dysfunction (Wang, Shao, Sun, & Young, 2009). One suggestion of the relationship between the conditions is that depression may be a non-specific symptom of mitochondrial dysfunction (Gardner & Boles, 2011).

Stress & Mitochondrial Function

A relationship between psychologic stress and mitochondrial function and dysfunction is supported in both rodent and human research, with higher levels of stress corresponding to enhanced markers of mitochondrial dysfunction (Picard, McEwen, Epel & Sandi, 2018; Picard & McEwen, 2018; Sivoňová, et al., 2004). Research in rodents supports that prolonged psychological stress can impact the structure of the mitochondria, leading to swelling of the mitochondria in cardiac and brain tissue (Gak et al., 2015; Gesi et al., 2002; Gong, Chai, Ding, Sun, & Hu, 2011; Picard & McEwen, 2018; Soldani et al., 1997), and decrease the ability of the mitochondria to properly function (Picard & McEwen, 2018). Stress can also reduce the amount of oxygen that is delivered within the body (Picard, McEwen, Epel, & Sandi, 2018). With reduced levels of oxygen, the mitochondria cannot effectively create energy through aerobic glycolysis because oxygen is necessary in the final step to accept electrons (Picard et al., 2018). Changes in the function of mitochondria and lowered levels of delivered oxygen result in changes to energy production, both overstimulating in the short term and reducing capacity after extended periods. Additionally, as mitochondria are essential to energy/metabolism and health, altered states within the structure and function of the mitochondria over time may lead to changes in metabolism and health or disease status of stressed individuals.

Inflammation & Mitochondrial Function

Adding additional complexity in disease states, inflammation and mitochondrial function appear to be bidirectionally associated with each other and, therefore, add uncertainty in the causation of their relationships with depression. Reactive oxidative species (ROS) are produced during normal ATP production within the mitochondria (Murphy, 2009). Mitochondrial

dysfunction can lead to an overproduction of ROS. This overproduction leads to high concentrations of ROS and can result in cell injury or death, and ultimately promotes increases in inflammation due to cytokine production to reduce injuries to cells. However, cytokines may also interact with the mitochondria and lead to increased ROS production. For example, reflective of inflammation, TNF-α can inhibit substrates in mitochondrial oxidation, suppressing the ability for ATP production, and can result in increased concentrations of ROS.

Inflammation & Stress

Psychological stress, with its impacts on the body is associated with elevated markers of inflammation (e.g. TNF-α and CRP) (Glaser & Kiecolt-Glaser, 2005; Juster et al., 2009). This is likely due to chronic stress activating the sympathetic nervous system (SNS) and/or the hypothalamic-pituitary-adrenal (HPA) axis. The activation of the SNS/HPA axis for prolonged periods of time leads to physiologic events resulting in an increase in cytokines, leading to higher levels of inflammation within the body (Cohen et al., 2007; Gu, Tang & Yang, 2012; Miller, Cohen & Ritchey, 2002).

Depression & Stress

Depression and stress can impact each other, and thus are bidirectionally associated with each other. For example, an individual diagnosed with depression may have an increase in stress due to their diagnosis or handling their symptoms of depression. Additionally, an individual going through a stressful life event (e.g. losing a job) or in a stressful environment (e.g. medical school) is more likely to observe an increase in their symptoms of depression and/or be diagnosed with depression (Hammen, 2005; Mazure, 1998). This bidirectional relationship, where each variable can influence/cause the other, creates difficulty in establishing a cause-effect relationship (Cohen et al., 2007; Hammen, 2005).

Stress and depression are common conditions in society with known prevalence rates (Quality, 2017; Wiegner et al., 2015). However, no prevalence rates exist for inflammation and mitochondrial dysfunction within the population, but these conditions are known to be

associated with some of the most prevalent diseases in the United States population (e.g. cardiovascular disease, Alzheimer's, diabetes, etc). Due to the relationships between each of these four conditions, they work synergistically and place impacted individuals at a higher risk for developing chronic, debilitating diseases (Dowlati et al., 2010; Fattal et al., 2007; Gardner & Boles, 2011; Kaplan et al., 2015). Collectively these conditions are associated with six of the ten leading cause of death in the United States (Nichos, 2017; Xu et al., 2018); thus, strategies to prevent and/or reduce the prevalence of these conditions should be a priority.

Physical Activity for Health

Research supports that physical activity can improve each of the aforementioned conditions and has additional implications for disease progression. Research supporting the concept that physical activity is related to health was first realized in the 1950s with the London bus study (Morris, Heady, Raffle, Roberts, & Parks, 1953). The study observed that bus conductors, with jobs that required walking through the bus to collect tickets/payments, had a lower risk of heart disease compared to bus drivers, who's job involved no physical activity (Morris, Heady, Raffle, Roberts, & Parks, 1953). Additional research was conducted to eliminate the potential cofounding variables of emotional stress and job strain and the study results were supported by examining additional jobs including sedentary secretaries and active postal workers (Morris el al., 1953; Paffenbarger, Blair, & Lee, 2001). Since this first study encouraging the benefits of physical activity, new fields of study have developed further examining the relationships between physical activity, physical fitness, and health/disease conditions. Physical activity is currently supported as a mechanism to prevent, delay, or maintain a variety of health conditions, such as CVD, CVD comorbidities, and Type 2 diabetes (Diabetes Prevetion Program Group, 2002; Lakka & Laaksonen, 2007; Paffenbarger Jr, Wing, Hyde, & Jung, 1983; Wannamethee & Shaper, 2001). With the strong basis regarding the relationship between physical activity and chronic diseases, research has shifted to understand how these changes

occur by examining the effects of physical activity on pathologies of common diseases, including: inflammation, mitochondrial function and mental health.

Physical Activity for Inflammation

Research supports that there is a relationship between physical activity and anti-inflammatory effects within the body, with the most favorable outcomes observed due to more frequent exercise (i.e. 22 times a month) or higher intensity exercises (i.e. moderate or high intensity), but not to points of excess (Beavers, & Nicklas, 2010). The benefits to inflammation levels from physical activity appear to come from both reducing pro-inflammatory markers (e.g. CRP and TNF-α) and through increasing anti-inflammatory markers (e.g. adiponectin). There are currently a variety of mechanisms under investigation to explain the relationship between physical activity and inflammation, including reductions in adipose tissue or body mass index (BMI) and changes within the muscle.

One of the most commonly cited and best understood mechanisms regarding how chronic exercise can elicit adaptations in levels of inflammation are through reducing body weight, BMI, or fat mass (i.e. adipose tissue). Adipose tissue, an endocrine organ, produces, releases, and regulates many markers of inflammation (e.g. adiponectin, IL-6 and TNF-α) (Beavers et al., 2010; Coelho, Oliveira, & Fernandes, 2013; Fonseca-Alaniz, Takada, Alonso-Vale, Lima, 2007; Nimmo, Leggate, Viana, & King, 2013). The production of cytokines such as IL-6 and TNF-α, both increase the level of inflammation by themselves, but also stimulate pro-inflammatory processes, such as hepatic CRP production (Beavers et al., 2010; Coelho, 2013) Flynn, McFarlin, & Karkofski, 2007; Kasapis & Thompson, 2005). Thus, by reducing adipose tissue the amount of pro-inflammatory cytokines would also be reduced (Beavers et al., 2010; Ford, 2002). Additionally, adiponectin, a protein hormone with anti-inflammatory properties, is inversely related to fat mass (Flynn et al., 2007; Simpson & Singh, 2008). While the reduction of BMI or fat mass are proposed mechanisms through which physical activity can improve inflammation within the body, some research supports that physical activity can improve

inflammation even when controlling for BMI or body fat (Beavers et al., 2010; Flynn et al., 2007; Ford, 2002).

Therefore, additional mechanisms, beyond fat mass, are currently being explored and are not yet well understood. Some of the likely other pathways for improved inflammation from physical activity are explained through local changes within muscles. During exercise there is an increase in calcium content within muscle cells (myokines), that stimulate production of IL-6, which, in this instance, has anti-inflammatory properties (Nimmo et al., 2013). This increase in IL-6 results in multiple actions that may improve inflammation including: stimulating antagonistic receptors which reducing the level of TNF-α released and eliciting increases in IL-10, an anti-inflammatory cytokine (Nimmo et al., 2013; Smith, Dykes, Douglas, Krishnaswamy, & Berk, 1999; Timmerman, Flynn, Coen, Markofski, & Pence, 2008). Many other thoughts on possible mechanisms for how physical activity improves inflammation exist, but many have not been rigorously explored (Flynn et al., 2007) (e.g. exercise stimulating cortisol, adrenaline, T-cells, toll-like receptors (TLR4), or heat shock proteins), all of which may have anti-inflammatory effects (Beavers et al., 2010; Flynn et al., 2007; Nimmo et al., 2013).

Finally, physical activity can improve inflammation through increasing adiponectin. Cross sectional studies support that higher levels of physical activity can elicit increases in adiponectin (Simpson & Singh, 2008). Results from randomized controlled trials are not as conclusive supporting the relationship between adiponectin and physical activity but have found improvements in adiponectin by 38% after exercise interventions lasting between one and 12 months (Simpson & Singh, 2008). While complete understanding for the pathology is evasive, increased levels of adiponectin are of value because it can have inhibitory effects on TNF-α and thus indirectly decrease CRP (Flynn et al., 2007; Simpson & Singh, 2008). Adiponectin also impacts the production of nitric oxide, which can have protective effects against ROS (Beavers et al., 2010) and reduce CRP (Kasapis & Thompson, 2005).

Physical Activity for Mitochondrial Function

Research supports that physical activity can increase mitochondrial content and size; these changes reflect alterations in metabolic capacity of the mitochondria (MacInnis & Gibala, 2017). Engaging in physical activity increases the demand for energy throughout the body, which increases the energy demand at the cellular level and creates opportunities for signaling which results in mitochondrial biogenesis (Picard, Wallace, & Burelle, 2016; Weibel & Hoppeler, 2005). Exact processes have yet to be defined, but research has demonstrated evidence of factors that likely play an important role in mitochondrial biogenesis, including: peroxisome proliferator-activated receptor gamma coactivator 1alpha (PGC-1α), nuclear respiratory factors (NRF) 1 and 2, phosphorylation of AMP-dependent protein kinase (AMPK), and p38 MAPK, calcium signaling (Norrbom et al., 2004). During physical activity, an increase in activation is observed in each of these factors (phosphorylation of AMPK, p38y MAPK, citrate synthase, and PGC-1α mRNA expression) (Gibala et al., 2009; Lira, Benton, Yan, & Bonen, 2010; Metcalfe et al., 2015; Norrbom et al., 2004). Briefly, once exercise begins, there is an increase in calcium signaling, to allow for contractile activity of the muscle. This signaling then activates calcium dependent protein kinases which activate p38y MAPK. PGC-1α is then up regulated during exercise by the activation p38y MAPK. PGC-1α is a coactivator and has the ability to affect factors in transcription of DNA (Norrbom et al., 2004). Once activated, PGC-1α then activates NRF 1 and 2, which directly affect the transcription and replication of DNA (Norrbom et al., 2004) and mitochondrial biogenesis (Lira et al., 2010). Continued or regular physical activity promote continued mitochondrial biogenesis and lead to repeated activation of these mechanisms, leading to an increase in mitochondrial density.

The majority of research in this area examines the impact of physical activity and exercise on mitochondria in the skeletal muscle (Holloszy & Coyle, 1984; Jacobs et al., 2013; Vincent et al., 2015). Adaptations to skeletal muscle mitochondria can occur quickly, seeing increased mitochondrial content within two weeks (Hedges et al., 2019). Research has also observed an increase of ~30% in mitochondrial content after only seven training sessions of

high-intensity interval training (MacInnis et al., 2017). Most studies show that these large improvements over short periods of time employ exercise training plans that involve vigorous intensity physical activity or large volumes of moderate intensity physical activity (MacInnis & Gibala, 2017).

However, the methods to conduct research examining the changes in skeletal muscle mitochondria require muscle biopsies which are invasive for participants. Thus, recent research has turned to focus on assessing mitochondria within the blood stream, and research in this area continues to grow. Due to the differences in tissue of the mitochondria in blood and muscle, there are inherent differences in how the mitochondria in each environment will react to physical activity. Despite these differences, correlations are evident between physical activity and mitochondria found within peripheral blood mononuclear cells (PBMCs) in the blood (Tyrrell et al., 2014). However, studies do not observe adaptations as quickly in circulating mitochondria in the blood compared to skeletal muscle (Hedges et al., 2019) as changes in mitochondrial protein expression may take at least eight weeks to observe in PBMCs (Busquets-Cortés et al., 2017). Therefore, longer training periods may be needed to observe mitochondrial changes in PBMCs.

Physical Activity for Mental Health

Research supports that there is an association between physical activity and mental health, however this relationship is complex and not well described (Scully, Kremer, Meade, Graham, & Dudgeon, 1998). Cross sectional studies observe that that individuals who engage in more sedentary behavior have a higher likelihood of being depressed (Martinsen, 1990), while those who are more active are likely to have fewer days with poor mental health (Chekroud et al., 2018). Longitudinal studies expand on this and have supported that those who are more active, have lower odds of being diagnosed with depression (Farmer et al., 1998). Still, the complex relationship between physical activity and mental health exist because sedentary behavior may be a symptom of, as well as a contributor to, poor mental health, while in contrast

regular engagement in physical activity may be a symptom of and contribute to mental wellbeing (Chekroud et al., 2018). Similar to mitochondrial function and inflammation, there are many suggested mechanisms for how exercise may improve mental health (i.e. stress and depression), but within mental health there are both psychologic and physiologic pathways to be considered. Additionally, many of these proposed relationships have yet to be rigorously tested and understood through research.

Exercise may improve stress and depression through psychologic mechanisms such as gaining confidence or achieving a challenge/new skill (exercise). The pathways are defined through the theories of self-efficacy and mastery (Bandura, 1977; Paluska & Schwenk, 2000). These theories support the idea that through engaging in regular exercise, confidence and/or successful feeling related to the exercise task will be developed and may crossover into other aspects of life, thus improving mental wellbeing (Greist et al., 1979; Marcus, Selby, Niaura, & Rossi, 1992; North, McCullagh, & Tran, 1990).

As discussed in previous sections, exercise elicits both acute physiologic changes and chronic adaptations within the body. There is support that some of these physiologic changes from exercise can improve stress and depression, such as increasing monoamines or endorphins. One suggested mechanism is that exercise elicits an increase in monoamines (e.g. dopamine, norepinephrine, serotonin) and thus improves mental health through the relationships between monoamines and depression or sleep disorders (Dunn & Dishman, 1991; Paluska & Schwenk, 2000; Ransford, 1982). Another concept is that exercise increases endorphins, which may reduce pain and encourage a positive mental state in an individual (Moore, 1982; Morgan, 1985; Nicoloff & Schwenk, 1995; Paluska & Schwenk, 2000). Taken together, research has yet to fully explain the mechanisms of action within the relationship between physical activity and mental health but does support a positive association.

Research supports that engaging in physical activity can improve, prevent, or delay inflammation, mitochondrial dysfunction, and mental health and thus improve chronic diseases outcomes (Apabhai et al., 2011; AL. Dunn, Trivedi, & O'Neal, 2001; Kasapis & Thompson, 2005; Ströhle, 2009). The majority of these studies use aerobic activities (e.g. walking, running, or cycling) as their physical activity modality. Studies examining other types of activities, such as yoga, are limited in number.

Yoga and Health

Yoga is a form of physical activity that also includes meditative and spiritual components. Yoga started in Eastern cultures but grew in popularity among western cultures around the 1970s (Burley, 2000). Current estimates state that over 20 million adults in the U.S. practice yoga and it has been a top 10 fitness trend for the last 5 years (Birdee et al., 2008; Clarke, Black, Stussman, Barnes, & Nahin, 2015; Thompson, 2013, 2014, 2015, 2016, 2017, 2018). It is important to note that many different styles of yoga are incorporated into 'yoga' as an umbrella term. Yoga styles commonly vary by poses and/or sequences included in the class and the duration of how long the poses are held. For example, flow-style yoga (e.g. hatha or vinyasa yoga) moves through poses quickly, only holding a pose for a few breaths. Iyengar yoga focuses on body alignment and holds poses for ~60 seconds. Finally, restorative (yin) yoga has a focus on grounding or relaxation, and commonly holds poses for ≥ 5 minutes.

Most individuals who practice yoga believe that their health will be improved in a variety of ways through their yoga practice (Birdee et al., 2008; Clarke et al., 2015; Collins, 1998; Ross, Friedmann, Bevans, & Thomas, 2012). While popular press has promoted the health benefits of yoga, there is a paucity of research conducted that supports this notion. Overall, research has supported that yoga may improve perceived health status, back pain (Cramer, Lauche, Haller, & Dobos, 2013), and levels of stress (Cowan & Adams, 2005; Harner, Hanlon, & Garfinkel, 2010; Michalsen et al., 2005; Michalsen et al., 2012; Pascoe, Thompson, & Ski, 2017). However, there

is a paucity of research examining the impact of yoga on other areas of health (e.g. depression, diabetes, neurodegenerative diseases, etc).

Yoga as a Means to Improve Inflammation, Mitochondrial Function and Mental Health

While the belief that yoga can improve a wide variety of health outcomes, there is a paucity of research conducted to support this belief. As physical activity can improve health outcomes, the physical postures performed during yoga (asanas) may elicit health benefits associated with yoga. However, yoga is a 'mind-body' activity and also involves breathwork and meditation components which may further contribute to the purported health benefits (Collins, 1998; Garfinkel & Schumacher Jr, 2000). While many believe that yoga can improve a wide variety of health outcomes, there is a paucity of research conducted to support this belief or understand the mechanisms of how yoga elicits health benefits.

Inflammatory Markers

There is limited and conflicting support for yoga's impact on markers of inflammation. Research documenting the most promise for yoga's impact on pro-inflammatory markers are in patients with elevated levels of inflammation due to diagnosed cardiovascular disease (Pullen et al., 2008; Yadav, Magan, Mehta, Sharma, & Mahapatra, 2012) or who are in cancer remission (Bower et al., 2014; Kiecolt-Glaser et al., 2014; Parma et al., 2015). Studies assessing individuals who did not have a diagnosed chronic illness reported conflicting results for yoga's impact on pro-inflammatory markers including CRP and TNF-α (Azami, Reza, Ahmadi, Hossein, & Qavam, 2019; Cho, Moon, & Kim, 2015; Harkess, Ryan, Delfabbro, & Cohen-Woods, 2016; Shete, Kulkarni, & Thakur, 2012; Shete, Verma, Kulkarni, & Bhogal, 2017; Wolff, Memon, Chalmers, Sundquist, & Midlöv, 2015); with over half (4 of 6) of these studies reporting no change in inflammatory markers after a yoga intervention (Azami et al., 2019; Cho et al., 2015; Harkess et al., 2016; Wolff et al., 2015). Some of the varied results may be due to sex differences in variables of interest or low doses/frequency in yoga. The studies that observed

positive results on inflammation included only male participants and the intervention involved engaging in yoga six or seven times a week (Shete et al., 2012; Shete et al., 2017). However, studies that resulted in less favorable changes had participants engage in only one or two yoga classes each week (Azami et al., 2019; Cho et al., 2015; Harkess et al., 2016; Wolff et al., 2015). Gaps remain in the research regarding if both men and women can improve inflammatory status through yoga, and the dose/frequency of yoga that is required for improvements in pro-inflammatory markers.

In the three studies conducted examining yoga's effects on markers of anti-inflammation, research supports that yoga can increase adiponectin by ~24% (Kiecolt-Glaser et al., 2012; Lee, Kim, & Kim, 2012; Sarvottam, Magan, Yadav, Mehta, & Mahapatra, 2013). Kiecolt-Glaser et al., matched and compared women who were novice yoga participants to women who had been practicing yoga two times a week for two or more years. Women practicing yoga for two or more years were found to have 28% higher adiponectin levels compared to novice participants (Kiecolt-Glaser et al., 2012). Lee et al. (2012) then expanded on this cross-sectional study by implementing a yoga intervention with three classes a week for 16-weeks to examine if changes in adiponectin could be observed in obese women compared to a control group. Results supported that obese participants in the yoga intervention improved adiponectin levels by 23%, while the control group had lower adiponectin levels after the four months (Lee et al., 2012). The third study examined the effects of a daily yoga intervention for 10 days in overweight/obese men and found a significant increase in adiponectin by 27% from baseline (Sarvottam et al., 2013). While this is exciting research, more work is necessary to understand how yoga may impact adiponectin because each of the studies assessed the relationship between adiponectin and yoga differently and in different populations, through examining years practiced, sex, and weight status. Kiecolt-Glaser (2013) examined the impact of years practicing yoga on adiponectin levels in women. Lee et al. (2012) and Sarvottam et al. (2013) both

considered the impact of yoga in obese individuals, but their research is separated by sex differences. Future work should consider the amount of time or dose of yoga necessary to observe changes in adiponectin. While changes were observed in a 10-day period after daily engagement, it is not known how quickly improvements may be observed if an individual only engages in yoga two or three times a week. The impact of how weight mediates the changes in adiponectin from yoga should also be further examined as overweight/obesity is commonly associated with lower levels of adiponectin. Finally, future work should also examine if increasing levels of adiponectin are accompanied with equivalent changes in pro-inflammatory markers.

Mitochondrial Function

There is very limited research regarding yoga's impact on mitochondrial function as no study has directly measured changes, structural or functional, within the mitochondria as an outcome after a yoga intervention. Through the breathwork and the physical activity components, yoga may improve oxygen delivery to mitochondria and the ability to improve mitochondrial functioning. Five studies have examined yoga's influence on oxidative stress and used this as an indirect marker for mitochondrial function (Gordon et al., 2008; Hedge et al., 2011; Hegde, Adhikari, Shetty, Manjrekar, & D'Souza, 2013; Patil, Dhanakshirur, Aithala, Naregal, & Das, 2014; Singh et al., 2001). These studies observed positive impacts from yoga on oxidative stress with decreases in malondialdehyde, a marker of oxidative stress, by ~20% after yoga interventions (Gordon et al., 2008; Hedge et al., 2011; Hegde et al., 2013; Patil et al., 2014). Research examining other markers of oxidative stress (i.e. phospholipase A2, protein oxidation) report inconsistent findings on the impact of yoga on these markers and on antioxidants (i.e. superoxide dismutase; glutathione, and vitamins C and E) (Hedge et al., 2011; Hegde et al., 2013; Patil et al., 2014). The apparent lack of studies and outcome variables in

this area of research lead to a gap in knowledge regarding the impact of yoga within the mitochondria and mitochondrial function.

Depression

There are promising results for the impact of yoga in populations with high levels of depression (Gatantino et al., 2004; Harner, Hanlon, & Garfinkel, 2010; Javnbakht, Kenari, & Ghasemi, 2009; Krishnamurthy & Telles, 2007; Michalsen et al., 2005; Shapiro et al., 2007; Woolery, Myers, Sternlieb, & Zeltzer, 2004). The studies including participants with depression consistently included engaging in yoga two times each week for 5 - 12 weeks (Gatantino et al., 2004; Harner et al., 2010; Javnbakht et al., 2009; Michalsen et al., 2005; Shapiro et al., 2007; Woolery et al., 2004). There was a total of 102 participants who engaged in yoga interventions and observed an average reduction of 46% in their depression scores (Harner et al., 2010; Javnbakht et al., 2009; Michalsen et al., 2005; Shapiro et al., 2007; Woolery et al., 2004). Iyengar yoga was most often used in these studies with four of the eight studies employing it for their intervention (Harner et al., 2010; Michalsen et al., 2005; Shapiro et al., 2007; Woolery et al., 2004).

Studies examining reductions in symptoms of depression in persons not diagnosed with depression have found mixed results for the impact of yoga on depression scores (Daukantaitė, Tellhed, Maddux, Svensson, & Melander, 2018; Rocha et al., 2012; Simard & Henry, 2009). Medical students are in an environment that may elicit poor mental health status due to the high stress of schooling. Thus, Simard and Henry (2009) examined the impact of a semester long hatha yoga intervention on depression scores in medical students. Over the course of the 16-week intervention, no changes were observed in depression scores at midpoint or post intervention testing (Simard & Henry, 2009). While stress levels were reported to be within a moderate range, the actual scores were not reported and thus baseline compared to post intervention values cannot be interpreted. Military members are another group that are in high

stress environments and may be at a higher risk for depression. Rocha et al. (2012) observed that implementing two yoga classes a week into the schedule of military men, on top of required physical exercise, significantly improved depression scores after 6 months (Rocha et al., 2012). In contrast to studying populations in structured, high stress environments, Daukantaitė et al. (2018) examined three groups of participants from the general popuation after five weeks of 1) yin yoga (2 times per week) 2) a yoga and mindfulness intervention or 3) a control group. Participants of the yin yoga saw minor improvements in depression scores, but these were not signifcant compared to baseline or compared to the other groups (Daukantaitė et al., 2018). Finally, Oka et al. (2019) examined the impact of an eight-week seated isometric yoga intervention in indiviudal with chronic fatigue syndrome. While handling their diagnosis may have been stressful, the participants were not in otherwise-stressful environments; no changes were observed in their depression scores (Oka, Tanahashi, Lkhagvasuren, & Yamada, 2019). While all of these studies had participants engage in yoga twice each week for multiple weeks, due to the small amount of studies conducted it cannot be determined why the results are varied. Some reasons may be that different yoga styles were used in the interventions (i.e. hatha yoga and yin yoga). Another reason may be that the participants with moderate to lower symptoms of depression may not observe significant changes as individuals with higher symptoms of depression because they have less room to improve upon. However it is interesting to note that one study conducted in these healthy participants did find significant, positive results (Rocha et al., 2012). Further research should be conducted to assess what styles of yoga can elicit positive changes in depression and if populations who are at-risk for depression can also achieve mental health benefits from yoga. Additionally, research should work to understand the mechanism(s) of how yoga elicits changes in depression (Kinser, Goehler, & Taylor, 2012).

Stress

Research supports that yoga can improve stress. The majority (~80%) of the studies conducted in this area examine populations with high levels of stress or in settings that elicit stress (Daukantaitė et al., 2018; Granath, Ingvarsson, von Thiele, & Lundberg, 2006; Harner et al., 2010; Hartfiel et al., 2012; Kinser, Bourguignon, Whaley, Hauenstein, & Taylor, 2012; Michalsen et al., 2005; Michalsen et al., 2012; Simard & Henry, 2009). However, studies involving individuals in lower stress environments also observed improved stress after engaging in yoga (Daukantaitė et al., 2018; Granath et al., 2006; Hartfiel et al., 2012; West, Otte, Geher, Johnson, & Mohr, 2004). Interventions commonly have participants engage in yoga one or two times each week and have shown that multiple styles of yoga can improve stress, including: kundalini, hatha, DRU, iyengar, and gentle yoga. With these positive results in yoga interventions, research should work to include more rigorous methodology, including adding control groups, examine physiologic markers of stress in addition to self-reported stress, assess how long the effects of yoga last for reducing stress, and incorporate demographic factors that may put an individual at a higher risk for stress or depression (e.g. age, sex, and weight status).

In conclusion, yoga has the potential to impact both physiologic and psychologic health variables. Current research supports that yoga can improve stress and can improve depression in individuals with higher levels of depression. However, there are inconclusive findings regarding yoga's impact on inflammation, depression scores in individuals at-risk for depression; and there is no research directly examining the impact of yoga on mitochondria. Further, no research has examined if yoga influences inflammation, mitochondrial function, and mental health to similar extents. New research examining the impacts of yoga on these disease conditions will lead to a more complete understanding of yoga's role in health.

Hypothesis and Specific Aims

Inflammation, mitochondrial dysfunction and poor mental health are common ailments in society, and each of these conditions are associated with each other, putting an impacted individual at a greater risk for developing multiple, chronic diseases. Most individuals who practice yoga report engaging in yoga to improve their health. However, there is a paucity in the literature regarding the relationship between yoga and health; initial studies support that yoga may improve markers of health, but the research is conflicting and there are inconsistencies in protocols and variables of interest. Findings are inconclusive regarding the impact of yoga on: markers of inflammation, depression in individuals at-risk for depression; and there is no research examining the impact of yoga directly on the mitochondria. Based on these data, I propose to examine the relationship between yoga and mental health, inflammation, and mitochondrial protein content, which will support the use of yoga in lifestyle interventions to promote health and wellbeing. The overall hypothesis of this dissertation is that yoga will be associated with improved markers of health; this will be tested through two separate studies.

Study 1 Objective: Examine if a relationship between yoga and markers of health exist by comparing current yoga participants to non-yoga participants. The hypothesis for this study is that current yoga participants will have improved markers of inflammation, mitochondrial protein content, and mental health compared to individuals who do not practice yoga.

Aim 1: Examine if there is a difference between yoga participants and non-yoga controls on markers of inflammation (c-reactive protein [CRP], erythrocyte sedimentation rate (ESR), Tumor necrosis factor alpha (TNF-α) and Adiponectin), protein content of oxidative phosphorylation (oxphos) complexes within the mitochondria, and mental health (Beck Depression Inventory -II [BDI-II], Perceived Stress Scale [PSS]).

Exploratory aim: Within the yoga participants, examine if the self-reported frequency or years of practice has an impact on inflammatory, oxphos protein content, and mental health markers.

Study 2 Objective: Examine the feasibility of a yoga intervention and explore the impact of yoga on markers of health. The hypotheses for this study are that the intervention will be feasible and that markers of health will be improved. These hypotheses will be tested by the following aims:

Aim 1: Evaluate the feasibility of implementing an 8-week yoga intervention on a college campus.

Aim 2: The second aim of this study is to explore the impact of yoga on markers of health including: stress, depression, inflammation, and oxidative phosphorylation protein content in mitochondria.

Chapter 2: Study 1
Yoga and Health: A Cross Sectional Study

Abstract

Background: The prevalence of chronic diseases is increasing within the United States. Behavioral approaches, such as engaging in physical activity, to prevent and/or treat chronic diseases are encouraged. Yoga is an ideal activity to help reduce disease risk due to its popularity and ability to be modified for different populations. However, research examining the relationship between yoga and health outcomes is limited, inconsistent in methodology, leading to conflicting or non-significant results. Purpose: To compare markers of health commonly associated with the pathology of prevalent chronic diseases between yoga participants and individuals who do not engage in yoga. Methods: Participants between the ages of 18-60 years were categorized into one of two groups: 1) “Yoga” engaging in yoga at least two times per week for the last six months, or 2) “Non-yoga” engaging in <150 minutes/week of physical activity and not engaging in yoga. Data were collected on perceived stress, symptoms of depression, pro and anti-inflammatory markers (erythrocyte sedimentation rate [ESR], c-reactive protein [CRP], tumor necrosis factor alpha [TNF-α] and adiponectin) and protein content within each complex of the electron transport chain, responsible for oxidative phosphorylation. Results: Yoga and non-yoga participants differed in their age (39.3 vs. 28.9 years, respectively) and exercise vital sign (EVS) (337 vs 66 minutes/week). The difference in EVS was expected as the inclusion criteria for the non-yoga group included participants being inactive. Scores from both the perceived stress scale and Beck Depression Inventory-II were significantly different between the yoga and non-yoga groups (perceived stress scores 8.0 vs. 17.5, respectively, $p < 0.05$; BDI scores 1.0 vs. 5.5, respectively, $p < 0.05$). However, there were no statistical differences between groups for any of the inflammatory markers nor in the protein content of Complex V. The median ESR values of the groups observed a difference based on clinical cutoffs, with yoga participants being categorized as normal and non-yoga participants

being categorized within a higher-risk group. Conclusion: This research supports that yoga participation is associated with lower levels of perceived stress and symptoms of depression, but does not support a relationship with markers of inflammation (i.e. CRP, TNF-α, ESR adiponectin).

Introduction

The prevalence of debilitating chronic diseases, such as cardiovascular disease (CVD), Type 2 Diabetes, and Alzheimer's disease, are increasing. It is estimated that over 28 million adults are presently diagnosed with CVD and it continues to be a leading cause of death for individuals in the United States (U.S.) (Murphy, Xu, Kochanek, & Arias, 2019). Similarly, approximately 21 million adults are diagnosed with Type 2 Diabetes (Bullard, et al., 2018) and it is expected that an additional 33% (84.1 million) of the U.S. adult population is pre-diabetic (Centers for Disease Control and Prevention, 2017). These high prevalence rates make it no surprise that Type 2 Diabetes is also a leading cause of death, relating to ~3% of all deaths in the United states (Murphy, Xu, Kochanek, & Arias, 2019). Finally, 5.5 million U.S. adults are currently diagnosed and living with Alzheimer's disease (AD). Furthermore, AD contributed to over 120,000 deaths in 2017 ("2019 Alzheimer's Disease Facts and Figures," 2019; Association, 2019). These chronic diseases are multifaceted in their pathologies and comorbidities. While pharmacological approaches are commonly used to treat these conditions, only 41% of patients believe their treatment as adequate (Kessler et al., 2003). Additionally, most medications work to treat a disease after the onset rather than help with prevention and are commonly associated with a myriad of serious side effects. In comparison, behavioral approaches are effective at managing these chronic diseases with limited side effects. Thus, behavioral approaches in conjunction with pharmacological treatments may prevent or improve chronic diseases more effectively than just pharmacological interventions (Diabetes Prevention Program Group, 2002).

Physical activity is a behavioral approach with a primary focus for the prevention and/or treatment of many chronic diseases. The relationship between physical activity and health was first studied in the early 1950s in Jeremy Morris's London bus study. The study compared bus drivers, who had less active jobs, with conductors, whose jobs were more physically active, and found that those with the more active jobs had lower prevalence rates of coronary heart disease (Morris, Heady, Raffle, Roberts, & Parks, 1953). Since this first study, longitudinal research and

randomized controlled trials continue to support the notion that physical activity can decrease the risk of developing, or be a treatment modality for chronic diseases (Diabetes Prevention Program Group, 2002; Hu et al., 1999; Lee & Skerrett, 2001; Paffenbarger Jr, Wing, Hyde, & Jung, 1983; Paffenbarger Jr, Hyde, Wing, & Hsieh, 1986; Paffenbarger, Blair, & Lee, 2001). Despite this evidence and the development of physical activity guidelines, many adults in the United States are not engaging in levels of recommended physical (i.e. ≥150 minutes/ week of moderate to vigorous physical activity) (Carlson, Fulton, Schoenborn, & Loustalot, 2010; "Trends in meeting the 2008 Physical Activity Guidelines, 2008-2017," 2018). Therefore, researchers continue to explore different types of physical activity that improve health, would appeal to and are feasible for the general public to perform.

Yoga is a type of physical activity that has become increasingly popular over the last decade and continues to be a top fitness trend (Thompson, 2013, 2014, 2015, 2016, 2017, 2018). Furthermore, the majority of individuals who participate in yoga report doing so to improve their health (Penman, Coehen, Stevens, & Jackson, 2012; Quilty, Saper, Goldstein, & Khalsa, 2013; Ross, Friedmann, Bevans, & Thomas, 2012). Yoga is easily adaptable to fit the needs of participants and can be administered to large groups. Thus, yoga may be a viable option to improve physical activity levels and general health for people of all ages and levels of fitness and/or abilities. However, limited research exists supporting the ability of yoga to improve objectively measured markers of health. Thus, empirical and conclusive evidence is often lacking regarding the potential influence of yoga on health outcomes.

Current studies examining the health impacts of yoga are limited and lack rigorous methodology. Furthermore, interventions commonly implement inconsistent doses of yoga, use different yoga styles, or have decreased generalizability as they include small sample sizes or are performed in a specific population of individuals (e.g. individuals diagnosed with cardiovascular disease or who are in cancer remission; Bower et al., 2014; Elwy et al., 2014; Kiecolt-Glaser et al., 2014; Parma et al., 2015; Pullen et al., 2008; Yadav, Magan, Mehta,

Sharma, & Mahapatra, 2012). This has led to conflicting or non-significant results regarding the impact of yoga on objective markers of health (Cramer, Anheyer, Lauche, & Dobos, 2017; Field, 2011; Pilkington, 2013). For yoga to be accepted as a preventative or treatment modality, it is imperative to understand the associations between yoga and health and to document the impact of yoga on accepted markers of health..

In the limited research that exists, health benefits in yoga participants compared to the general population are evident. Forseth, et al. (2019) used a nationally representative database, and divided participants into one of three groups 1) yoga participants 2) participants who were physically active but did not engage in yoga and 3) participants who were not active (0 minutes of physical activity). Yoga participants had health benefits compared to non-yoga active participants, including lower waist circumferences, lower blood glucose, and higher high-density lipoprotein (HDL) cholesterol. Yoga participants were also found to have improved body mass index, waist circumference, and triglyceride values compared to participants who were not active. Yoga participants did not differ from their comparison groups on health markers including: blood pressure, fasting insulin, homeostatic model assessment of insulin resistance, low density lipoprotein cholesterol, or C-reactive protein (CRP) (Forseth Boyer, Miller, & Fitzhugh, 2019). Loprinzi, (2015) also examined the possible benefits of yoga in the samenationally representative database but found that yoga was not associated with a reduced risk in all-cause mortality (Loprinzi, 2015). Finally, in a smaller cross-sectional study, expert yoga participants, with two years of yoga experience, were found to have higher leptin values compared to participants who were new to yoga but found no differences in adiponectin levels between groups (Kiecolt-Glaser et al., 2012). Together, these cross-sectional studies support that yoga may be a method to improve some markers of health but may not improve all health variables nor risk of all cause mortality. While these three studies cover multiple markers of health, the outcome variables included are by no means inclusive of all markers of health or pathologies associated with chronic diseases; further, these studies have not been replicated.

Therefore, the purpose of this study is to compare markers of health that are commonly associated with pathologies for multiple, prevalent chronic diseases (e.g. cardiovascular disease and Alzheimer's disease) between yoga participants and individuals who do not engage in yoga. It is hypothesized that the yoga participants will have improved health, as measured by perceived levels of stress, symptoms of depression, markers of inflammation, and oxidative phosphorylation (oxphos) protein content in the mitochondria. As an exploratory aim, associations between participation in yoga (i.e. weekly frequency, total minutes of weekly yoga practice, and duration of practice [in years]) and markers of health will be explored. This study will provide a better understanding of whether a relationship exists between yoga participation and health variables related to prevalent and debilitating diseases.

Methods

Participants. Men and women between the age of 18-60 were recruited to be participants in one of two study groups, Yoga or Non-yoga. The yoga group included individuals who self-reported engaging in yoga at least twice a week for the last six months. The second group included individuals who self-reported being inactive, defined as achieving less than 150 minutes of moderate to vigorous physical activity each week, for the past six months. Exclusion criteria for participation included smoking, taking prescription blood thinners, and women who were pregnant.. Prior to participation in the research, participants provided informed consent to be involved in the study. The institutional review board at the University of Wisconsin – Milwaukee approved study procedures.

Overview. For this descriptive cross-sectional study, participants visited the lab one time for data collection. Participants were encouraged to visit the lab in the morning after an overnight fast. Information regarding demographics, health history, health behaviors (physical activity, diet, and sleep), and mental health was collected via paper surveys. Participants in the yoga group also provided information about their yoga practice including the style of yoga they usually engaged in, the length of their practice (in months), the average frequency per week,

and the primary reason they engaged in yoga. Once the surveys were completed, a small blood sample (~12 mL) was drawn from participants.

Measures

Exercise Vital Sign is a three-question tool that provides information on an individual's physical activity habits. The average total amount of minutes per week of moderate to vigorous physical activity can be calculated from the brief questionnaire (Coleman et al., 2012). This instrument is highly reliable (interclass correlation = 0.98) and is valid compared to accelerometry data (Quiles, McCullough, & Piao, 2019).

Automated- Self Administered 24 Hour Dietary Assessment Tool (ASA24) is a self-reported measure providing information on the food and portion sizes consumed during the previous 24 hours (Subar et al., 2012). Results are used to calculate the Healthy Eating Index (HEI) which provides information on the diet quality of an individual (Freedman, Guenther, Krebs-Smith, Dodd, & Midthune, 2010; Tooze et al., 2006; Zhang et al., 2011). The ASA24 provides comparable data to other nutrition intake standards (Kirkpatrick et al, 2014; Thompson et al, 2015).

Pittsburgh Sleep Quality Index (PSQI) is a self-report instrument that involves nine questions providing information on sleep quality over the past month (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). A global sum score of ≥ 5 is classified as the participant having 'poor' sleep, with lower global sum scores representing better sleep quality. This index has an adequate Cronbach's α in younger adults of 0.702 (Vargas, Flores, & Robles, 2014) and in older adults of 0.83 (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989)

Psychologic Health Measures. Psychologic health was assessed based on two measures; perceived stress and symptoms of depression. The *Perceived Stress Scale* is a 10-question self-report instrument that assesses an individual's perceived stress from the past month and classifies the stress into one of three levels: low stress (scores 0-13), moderate stress (scores 14-26), or high stress (scores 27- 40) (Cohen, Kamarck, & Mermelstein, 1994).

This survey has been found to have an internal consistency (Cronbach's α) in adults of 0.78 (Cohen & Williamson, 1988). Results were scored and classified using standard protocol (Cohen et al., 1994). The *Beck Depression Inventory-II* is a 21-question self-reported instrument that assesses symptoms and intensity of depression from the previous two weeks and classifies an individual's responses into one of six levels: normal mood swings (score 0-10), mild mood disturbance (score 11-16), borderline clinical depression (score 18-20), moderate depression (score 21-30), severe depression (score 31-40), or extreme depression (score >40) (Beck, Steer, Ball, & Ranieri, 1996; Beck, Steer, & Brown, 1996; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). The BDI-II is a reliable and validated tool for assessing depression both in research and in clinical practices (Beck et al., 1961); with a high Cronbach's α in non-clinical adults ranging between 0.79-0.93 (Beck & Steer, 1993). Results were scored using standard protocol (Beck, Steer, & Brown, 1996).

Blood samples. Blood (~12mL total) was collected from participants to analyze inflammatory markers and oxphos protein content; the blood was collected in two separate tubes, an EDTA, anti-coagulated tube for whole blood analyses and a coagulated tube to allow for serum separation. Inflammation in the body was measured by Erythrocyte sedimentation rate (ESR), CRP, and tumor necrosis factor – alpha (TNF-α); adiponectin, an anti-inflammatory marker, was also analyzed. Blood collected in EDTA tubes was used for ESR and oxphos protein content analyses. Erythrocyte sedimentation rate is a measure of non-descriptive inflammation within the body and was measured via the Westergren method (Jou et al., 2011). C-reactive protein, TNF-α, and adiponectin were assessed in serum samples from blood collected in vacutainers without an anticoagulant or preservative. The serum was separated from blood by centrifugation at 1,000 rpm for 10 minutes and frozen at -80°C until analysis. Quantikine kit enzyme-linked immunosorbent assays (ELISAs) from R&D Systems Inc. (Minneapolis, MN) were used to test the serum samples according to manufacturer's instructions. Limits of detection for CRP ranged 0.8-50 ng/mL, for TNF- α ranged 4.0-1,000

pg/mL and for adiponectin ranged between 3.9-250 ng/mL. *Oxphos Protein Content* was used as a marker of mitochondrial function, because impaired or reduced protein assembly within the mitochondria can lead to mitochondrial dysfunction (Anderson et al., 2009; Antoun et al., 2016; Hedges et al., 2019). Peripheral blood mononuclear cells (PBMCs) were separated from the whole blood sample using Ficoll-Plaque PLUS reagent (GE Healthcare, Chalfont St Giles, UK). Briefly, phosphate-buffered saline (PBS) and ficoll were added to ~5mL of blood in a 1:1:1 ratio. This mixture was centrifuged at 1950 rpm at 8 °C for 20 minutes, with no brake. The PBMC layer was then washed with PBS two times and stored at -80°C until analyzed. Protein was isolated from PBMCs with lysing RIPA buffer (EMD Millipore, Temecula, CA) containing complete mini protease inhibitor cocktail tablet (Roche, Basel, Switzerland) and PhosSTOP phosphatase inhibitor (Roche). Western blots on 10ug of PBMC protein were performed by Dr. Michael Lawlor's lab at the Medical College of Wisconsin. Transferred proteins were probed with an antibody against complexes I-V of the oxidative phosphorylation pathway (ab110412; Abcam) and subsequently a horseradish peroxidase conjugated α-mouse secondary (715-035-150; Jackson Labs). Western blots were visualized using enhanced luminol based chemiluminescent substrate (RPN2236; GE Life Sciences) and compared to a molecular weight ladder (Precision Plus Protein Dual Color Standards #1610374, Bio-Rad Laboratories Inc, Des Plaines, IL, USA) to estimate molecular weight. Western blot procedures followed previous protocols from the Lawlor Lab (Lawlor et al., 2014; Siebers et al., 2018). Quantification of protein levels normalized to Vinculin (Cell Signaling #18799) was performed with Image Lab Software (Bio-Rad Laboratories Inc.).

Statistical analyses

Descriptive statistics (mean and standard deviation) were used to describe the two study groups. Outcome variables were checked for normality. The data for PSS, BDI-II, ESR, CRP, adiponectin, and oxphos protein content were not normally distributed and therefore Mann-Whitney tests were used to compare these markers of health between the two groups, to test

the primary purpose of this paper. The data for TNF-α had a normal distribution and therefore an independent sample t-test was performed to compare groups. The second aim, examining if characteristics of yoga participation are related to markers of health, was tested through Spearman's rho correlations. Significance was set *a priori* at $p \leq 0.05$ and all statistical analysis were performed using SPSS (version 25; IBM, Chicago, IL).

Results

A total of 37 individuals expressed interest in and were eligible for the study. Seven of the individuals did not come in for testing due to declining to participate (n = 3) or scheduling conflicts (n = 4). The study included a total 30 participants: 15 in the yoga group and 15 in the non-yoga group. One participant in the non-yoga group was not able to provide enough blood for the testing and was excluded from all blood analyses. Additionally, one participant in the yoga group was not able to provide enough blood for the serum samples and was therefore excluded from the CRP, TNF-α and adiponectin analyses, but enough blood was collected for the participant to be included in the ESR and oxphos analyses. Demographic and descriptive information of participants in the yoga and non-yoga group are shown in Table 2.1. Groups were significantly different based on age and their exercise vital sign (Table 2.1). Participants in the yoga group, engaged in yoga 3.5 ± 1.5 times per week and had been practicing yoga for an average of 6.6 years (range 1 – 24 years). The most common styles of yoga practiced in this study sample included vinyasa (n = 7; 47%), power (n = 3; 20%), and hot yoga (n = 2; 13%).

Table 2.1. Participant demographic and descriptive information

Demographic Variable	Yoga participants n = 15	Non-Yoga participants n = 15
Age (years)*	39.3 (15.5)	28.9 (8.6)
Female : Male	14:1	12:3
Height (m)	1.67 (0.04)	1.64 (0.1)
Weight (kg)	68.7 (11.7)	70.7 (13.2)
BMI (kg/m^2)	24.6 (4.2)	26.1 (3.9)
Heart rate (bpm)	66.0 (15.0)	74.3 (17.8)
Healthy Eating Index	53.7 (8.8)	50.4 (8.3)
Alcohol (drinks/week)	3.1 (2.9)	2.9 (4.8)
Pittsburgh Sleep Quality Index	5.8 (3.2)	8.2 (3.6)
Exercise Vital Sign (min/week)*	337.8 (172.3)	66.8 (64.6)
Yoga participation (min/week)	208.0 (89.6)	-

Note: BMI body mass index; * $p < 0.05$; Mean (standard deviation)

Scores from both the PSS and BDI-II were significantly different between the yoga and non-yoga group ($U = 36.00$, $p < 0.01$; and $U = 45.50$, $p < 0.01$, respectively; Table 2.2). The majority of all participants (93%) were classified within the same BDI-II score category, normal or mild mood disturbance; thus, while there is a statistical difference in the scores, there is not a clinical difference between the groups. More variability was evident between groups based on their PSS scores, with the majority (n = 9, 60%) of the non-yoga group were classified into the moderate stress category, while only a few yoga participants (n = 4, 27%) were classified into the moderate stress category.

There were no significant differences between groups for any of the inflammatory markers (Table 2.2). The ESR values were not statistically different between the yoga and non-yoga group ($U = 80.50$; $p = 0.28$; Table 2.2). CRP values were not significantly different between groups ($U = 78.00$; $p = 0.24$; Table 2.2). Additionally, the TNF-α and adiponectin values were not significantly different between the groups ($p = 0.49$ and $U = 73.00$; $p = 0.16$, respectively; Table 2.2).

Table 2.2. Psychologic and Physiologic Variables between Yoga and Non-Yoga Participants

Health Variable	Yoga participants		Non-Yoga participants		Effect size
	Median [min, max]	Sum of ranks	Median [min, max]	Sum of ranks	
Perceived Stress Scale*	8.0 [1.0, 19.5]	156.0	17.5 [8.0, 29.0]	309.0	1.39
Beck Depression Inventory*	1.0 [0.0, 9.0]	165.5	5.5 [0.0, 30.0]	299.5	1.22
ESR (mm)	11.0 [4.0, 50.0]	200.0	21.5 [5.0, 47.0]	234.0	0.54
CRP (ug/mL)	0.9 [.1, 17.7]	198.0	1.9 [0.2, 156.5]	237.0	0.45
TNF-α (pg/mL)	10.6 [9.0, 12.7]	-	9.8 [8.61-12.68]	-	0.45
Adiponectin (ug/mL)	10.7 [6.7, 43.9]	257.0	10.0 [1.2, 26.9]	178.0	0.54

Note: * $p < 0.05$; Median [minimum, maximum].. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; TNF-α: Tumor Necrosis Factor – alpha; Effect size based on Cohen's d.

Complex V of the oxphos complexes was the only complex visible and able to be quantified from the western blots. There was no significant difference between the yoga (0.61 ± 1.11) and non-yoga (1.43 ± 1.45) groups on the protein content of Complex V ($p = 0.06$). The absence of a significant difference based on engagement in physical activity and yoga was surprising, but there are many other variables that can affect aspects of mitochondrial functioning. Research supports that age can impact mitochondrial protein content and functioning (Jonckheere, Smeitink, & Rodenburg, 2012; Xiao et al., 1998; Yaniv, Juhaszova, & Sollott, 2013) and there was a significant difference in age between the groups of this study. Thus, a non-linear regression was conducted, based on a visual analysis of the data's relationship, to analyze if there was a relationship between age of the participants and their complex V protein content. The regression showed a significant compound relationship between age and protein content within the whole study population ($R^2 = 0.19$, $p < 0.05$).

To test the second aim of the paper, correlations were performed between markers of health and total minutes per week of yoga, frequency per week, and years of yoga practice. Scatter plots were first created for each marker of health and each yoga participation characteristic to visualize if a linear relationship existed. From the scatter plot results, spearman's rho correlations were conducted for both minutes per week of yoga participation and frequency of yoga classes per week regarding PSS and BDI-II scores, TNF-α, and adiponectin. Additionally, the relationship between adiponectin and years of practice was examined. No significant associations were found between any marker of health nor characteristics of yoga participation.

Discussion

While yoga has become a popular activity in the last decade, both for the general population and for interventional use in research, there is limited and conflicting data supporting the relationship between yoga and health outcomes (Field, 2016). This study found that yoga participants had lower perceptions of their stress and symptoms of depression, but similar levels

of pro and anti-inflammatory markers compared to their non-yoga counter parts. Lower levels of proteins were also found in the oxphos Complex V in the yoga participants compared to their non-yoga counterparts. Each of the variables of health examined were selected because they are common mechanisms of pathology for many prevalent chronic diseases (Ballinger, 2005; Libby, 2007; Marsollier, Ferré, & Foufelle, 2011; Pearson et al., 2003). Results presented here provide support that yoga may positively impact psychologic health, but do not support a relationship with physiologic markers of health.

Study participants were primarily Caucasian females with an average age of 40-50 years. These demographics are similar to previous cross-sectional studies examining yoga participants(Birdee et al., 2008; Forseth et al., 2019; Ross, Friedmann, Bevans, & Thomas, 2012). The sample within this study participated in yoga an average of 3.5 ± 1.5 times per week. This was slightly higher than previously reported in Iyengar yoga participants who reported engaging in yoga 1.5 ± 1.0 times per week (Ross et al., 2012). Participants of both studies did report engaging in yoga for an extended length of time with similar ranges of 0-25 years of practice (Ross et al., 2012). It is also interesting to note that within the sample from the present study, only two of the yoga participants (13%) used yoga as their sole form of exercise. In contrast, 13 yoga participants reported engaging in other forms of exercise in addition to yoga, commonly referencing light resistance training and cycling as their other activities. While the current study is not representative of the full adult population in the United States, these findings are similar to Forseth (2019) who, in a nationally representative sample, found that 13% of yoga participants engaged only in yoga, while 86% of yoga participants engaged in additional forms of exercise (Forseth et al., 2019). Due to most yoga participants engaging in additional activities, it is hard to tease out the influence of yoga compared to being generally active. Limited research exists examining characteristics of how the general public engages in yoga (e.g. frequency per week and years of practice). This information is important as researchers

work to better understand what doses of yoga are necessary for improvements in specific health outcomes.

Participants in the yoga group perceived having less stress and their average scores were classified in the low stress category compared to their non-yoga counter parts who had their average scores categorized into the moderate stress category. Due to the significant age difference between the groups, the relationship between age and perceived stress was examined, but no relationship existed within the sample. Thus, these findings support that yoga participants may be better able to handle stress. Previous research supports that many people engage in yoga to help reduce their levels of stress (Quilty et al., 2013; Ross et al., 2012). Improved stress outcomes have also been supported in interventional studies of different populations, including individuals who were emotionally distressed, university students, and the healthy adults (Granath, Ingvarsson, von Thiele, & Lundberg, 2006; Michalsen et al., 2005; Simard & Henry, 2009). This study continues to support the notion that yoga may be a method to improve levels of perceived stress.

Scores from the BDI-II were statistically different between yoga and non-yoga participants of this study, however both groups were classified within the normal ups and down category of the BDI-II. It was expected that non-yoga participants would have a higher BDI-II score than the yoga participants, but also that yoga participants would fall into a lower category. Therefore, the result of both groups being classified within the same BDI-II category was an interesting finding, but is supported by previous research reporting that many people with a mental health diagnosis, such as depression, report doing yoga to improve their diagnosis (Birdee et al., 2008). It should be recognized that data was not collected on mental health diagnoses and therefore the prevalence of depression within the study population cannot be determined. There is limited cross-sectional research examining the relationship between yoga and depression prevalence, but intervention studies commonly report conflicting results regarding the relationship between yoga and depression symptoms (Gatantino et al., 2004; Javnbakht,

Kenari, & Ghasemi, 2009; Kinser, Bourguignon, Whaley, Hauenstein, & Taylor, 2012; Kinser, Goehler, & Taylor, 2012; Ranjita, Badhai, Hankey, & Nagendra, 2016; Rocha et al., 2012; Shapiro et al., 2007; Woolery, Myers, Sternlieb, & Zeltzer, 2004). Interventions that report improvements in depression scores from their participants commonly observe a trend and do not meet statistical or clinical significance. Findings from this study support that yoga may be a means to improve depression symptoms in the general public.

Differences in inflammatory markers between yoga and non-yoga participants were not evident in this study. While significant statistical differences were not observed in ESR values, differences, based on clinical cutoffs were evident between groups, with yoga participants falling within the normal ESR range and non-yoga participants were higher than the normal ESR range. Additionally, seven participants (50%) of the non-yoga group had ESR values above normal compared to only two participants (13%) in the yoga group having ESR values above normal, based on sex and age classifications. This information is encouraging for individuals looking for non-pharmacological methods to improve general inflammation. One reason that this study may not have found a relationship between yoga participation and in inflammatory markers of CRP, TNF-α, and adiponectin is that participants in both groups were primarily healthy and their levels of pro- and anti-inflammatory markers fell within normal/healthy ranges. Forseth et al. (2019) observed similar results from a nationally representative database in which the prevalence rates of elevated and normal CRP levels were similar between individuals who participated in yoga than those who did not. Research interventions examining the impact of yoga on CRP often observe conflicting results, with about half of the studies reporting significant changes (Pullen et al., 2008; Shete, Kulkarni, & Thakur, 2012; Shete, Verma, Kulkarni, & Bhogal, 2017), while the other half of studies find no change in CRP after an intervention (Azami, Reza, Ahmadi, Hossein, & Qavam, 2019; Bower et al., 2014; Cho, Moon, & Kim, 2015; Harkess, Ryan, Delfabbro, & Cohen-Woods, 2016). Similarly, conflicting research exists

regarding the impact of yoga on TNF-α with three studies reporting improvements after yoga use (Chen et al., 2016; Shete et al., 2017; Yadav et al., 2012) while five studies do not observe any changes (Cho et al., 2015; Harkess et al., 2016; Kiecolt-Glaser et al., 2014; Kiecolt-Glaser et al., 2010; Parma et al., 2015). There is not one apparent reason for the differences in reported results from these studies, but the differences may be due to differences in the interventions employed (e.g. yoga style, frequency, or length of study).

Previous research has reported differences in adiponectin corresponding with yoga participation, therefore it was surprising that adiponectin levels were not different between yoga and non-yoga participants in this study. Intervention studies have found significant improvements in adiponectin by ~24% in both overweight men and women (Lee, Kim, & Kim, 2012; Sarvottam, Magan, Yadav, Mehta, & Mahapatra, 2013). A study comparing individuals with over two years of yoga experience compared to novice yoga participants, reported that experienced yoga participants had adiponectin levels that were 28% higher than novice practitioners but did not find a statistically significant difference (Kiecolt-Glaser et al., 2012). Similarly, the present study observed 33% higher adiponectin levels in yoga participants than the non-yoga group. One possible reason for the lack of significance is the age difference in the sample of the present study. Adiponectin levels commonly change with age (Kizer et al., 2010). Thus, the significant age difference between the yoga and non-yoga groups in the present study may have tempered any differences in adiponectin levels had the two groups been more age-matched. Additionally, the adiponectin values of both groups were well within normal ranges, and therefore a significant difference may have been more difficult within the parameters of this study.

No differences were observed in the protein content of Complex V within the mitochondria between the groups. However, the secondary analysis suggests that a relationship exists within the sample between protein content and age, with older participants having lower

values of protein content. Therefore, if the sample was age-matched there may have been a difference between the groups. While the effects of age on oxphos protein content was not within the scope of this study, there is evidence in previous research supporting reductions in oxphos protein content with age (Jonckheere, Smeitink, & Rodenburg, 2012; Kerner, Turkaly, Minkler, & Hoppel, 2001; Xiao et al., 1998; Yaniv, Juhaszova, & Sollott, 2013). One reason to suspect that yoga participation can result in an increase in electron transport chain protein content comes from previous research that has demonstrated that aerobic exercise and markers of habitual physical activity are strongly related with improved mitochondrial functioning (Hedges et al., 2019; Tyrrell et al., 2014). It was also unfortunate that the only quantifiable protein was Complex V. The relationship between yoga participation and protein content of complex IV would be interesting to assess because Complex IV is most impacted by stress and physical activity (Picard, 2018) and yoga participation is supported in this study to reduce percieved stress.

This study examined the relationship between frequency, total minutes per week, and length of yoga practice with each of the health variables, in hopes to find an indication of which, if any, participation characteristics are associated with positive health. Understanding the relationship between practice characteristics and health in a cross-sectional analysis would provide insight into a yoga protocol to implement during interventions to elicit improvements in health outcomes. Unfortunately, none of the correlations in this study were significant, failing to provide insight into this topic. While these findings may be due to the small sample size of yoga participants, they are consistent with previous research that did not report significant findings when examining the between duration of yoga practice (weeks and months) to adiponectin (Kiecolt-Glaser et al., 2012). To the author's knowledge, no other work has been conducted examining associations of yoga characteristics with helath outcomes.

Limitations to this study should be addressed. First, while yoga participants had significantly lower levels of depression symptoms compared to the non-yoga participants, data was not collected from either group on mental health diagnoses. The study included generally healthy participants and therefore cannot speak to the relationship between yoga and markers of health in chronically ill participants. Yoga participation was measured via self-report; this could limit findings based on participant recall bias or over-reporting of their participation. Additionally, the relationship between yoga and mitochondrial protein content could not be thoroughly examined because only complex V was quantifiable and due to differences in age between the groups likely impacting the protein content. Finally, the study sample size was powered for the PSS and BDI-II analyses because there was enough relevant literature to support a power analysis. In this process, the analyses of inflammatory markers were commonly under powered and results should be taken with caution; effect sizes have been reported for future studies to adequately power their analyses. This study also involved many strengths, including the use of objective markers of health, which provide rigorous methodology compared to self-reported perceived health status. Additionally, this study examined seven health variables that are associated with multiple chronic disease pathologies and adds to the literature in understand how yoga may or may not, impact markers that are associated with prevalent, chronic diseases.

Conclusion

This study supports that a relationship exists between yoga participation and psychologic health with yoga participants observing lower perceived stress and symptoms of depression compared to participants who did not engage in yoga. However, significant differences were not observed supporting the relationship between yoga participation on markers of inflammation and mitochondrial protein content. Future work should be performed to build on these results and continue to examine and verify the relationships between yoga and health, within specific populations, and then implement interventions to test these relationships.

Chapter 3: Study 2
Adherence to and Changes in Physiologic and Psychologic Health during an 8-week Yoga Intervention: A Pilot Study

Abstract

Background: Previous research demonstrates that yoga can improve stress and may improve symptoms of depression, but there is no clear indication of the relationship between yoga and inflammation or mitochondrial functioning. These four markers of health are important as they are markers associated with chronic diseases. Purpose: To investigate the feasibility and impact of an 8-week yoga intervention in an urban university setting on perceived stress, symptoms of depression, inflammation, and oxidative phosphorylation (oxphos) protein content within mitochondria. It was hypothesized that an 8-week yoga intervention would be feasible and would improve markers of health. Methods: The study included nine healthy yoga-naïve adults, (25±4.8 years; 78% female).. Participants had no recent mental health diagnosis, CVD, or limitations to performing yoga. The study was a single-arm 8-week intervention with pre and post intervention data collection for inflammatory and oxphos protein content. Perceived stress and symptoms of depression were measured pre, mid, and post intervention. Mental health variables were assessed via the Perceived Stress Scale (PSS) and Beck Depression Inventory-II (BDI-II). Participants provided a blood sample to measure markers of inflammation (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], tumor necrosis factor alpha [TNF-α] and adiponectin), and the oxphos protein content. Between the visits, participants were asked to attend two 60-minute flow style yoga classes each week. To be deemed feasible, ≥ 85% of participants had to attend 12 of the 16 (≥ 75%) yoga classes. Results: Eight of the nine participants completed the study; one participant dropped out due to a surgery not related to the study. Six participants (67%) attended ≥ 75% of the classes. Scores from the PSS and BDI-II reduced by 13% and 27%, respectively. ESR and CRP values were reduced by 27% and 10%, respectively, but TNF-α values increased by 11% after the intervention. Additionally, over the

course of the intervention adiponectin increased by 21%. Only the protein content from Complex V was visible from western blot procedures; no differences were found in the protein content over the intervention period. Conclusion: While the majority (67%) of participants attended ≥ 12, this failed to meet the criteria of ≥ 85% of participants adhering to the yoga intervention, thus in this small sample feasibility was not supported. Exploratory analyses did provide preliminary support that the intervention reduced perceived stress, symptoms of depression, and systemic inflammation measured by ESR. Further studies are needed to confirm and extend findings and find methods to improve feasibility in yoga interventions.

Introduction

Cardiovascular disease (CVD) is a debilitating, chronic disease that impacts the lives of millions of Americans. In 2016, CVD remained a leading cause of mortality in the United States, accounting for over 750,000 deaths (Nichos, 2017; Xu, Murphy, Kochanek, Bastian, & Arias, 2018). Additionally, it is estimated that ~48% of adults in the United States are living with some form of this disease (Benjamin et al., 2019).

Ongoing research continues to discover and propose new pathologic mechanisms for CVD. Recent studies support that psychologic stress (Brotman, Golden & Wittstein, 2007), inflammation (Libby, 2007; Marsollier, Ferré, & Foufelle, 2011; Pearson et al., 2003; Ridker, 2003; von Hundelshausen & Weber, 2007), and mitochondrial dysfunction (Ballinger, 2005; Marín-García & Goldenthal, 2002; Ren, Pulakat, Whaley-Connell, & Sowers, 2010; Widlansky et al., 2010) may be underlying pathologies of CVD (Ballinger, 2005; Libby, 2007; Marín-García & Goldenthal, 2002; Pearson et al., 2003; Ren et al., 2010). Individually, each condition contributes to thepathology of CVD. Additionally, these conditions appear to act synergistically to worsen CVD outcomes

Yoga may be a modality for prevention and treatment of CVD by eliciting positive changes in the underlying mechanisms. Research supports that yoga may improve some symptoms and risk factors of CVD including: glucose control (Hunter, Tarumi, Dhindsa, Nualnim, & Tanaka, 2013; Monroe, Power, Kumar, & Nagarathna, 1992), hypertension (Damodaran, Malathi, Patil, Shah, & Marathe, 2002), and total cholesterol (Damodaran et al., 2002; Hunter, Dhindsa, et al., 2013). However, the understanding for how yoga improves these health outcomes are still unknown and necessitates further study.

There is strong evidence that yoga is effective in improving stress in groups who have high stress, depression, and/or are in stressful environments (Cowan & Adams, 2005; Granath, Ingvarsson, von Thiele, & Lundberg, 2006; Hartfiel et al., 2012; Michalsen et al., 2005; Michalsen et al., 2012; Simard & Henry, 2009; West, Otte, Geher, Johnson, & Mohr, 2004).

Multi-week yoga interventions observed positive changes in perceived stress in various populations, including medical students (Simard & Henry, 2009; West et al., 2004), chronically stressed or distressed women (Michalsen et al., 2005; Michalsen et al., 2012) and the general population (Hartfiel et al., 2012). Medium to large effect sizes are found within these studies, further encouraging the strong relationship between yoga participation and low levels of stress (Cowan & Adams, 2005; Granath et al., 2006; Michalsen et al., 2005; West et al., 2004). However, the literature does not support linear reductions in stress over the time course of an intervention (Harner, Hanlon, & Garfinkel, 2010).

In contrast to the literature regarding the impact of yoga on stress, the literature assessing the impact of yoga on pro-inflammatory markers is limited. Many interventions report mixed or conflicting findings, resulting in no clear indication of an association or relationship between yoga and inflammation (Azami, Reza, Ahmadi, Hossein, & Qavam, 2019; Bower et al., 2014; Cho, Moon, & Kim, 2015; Harkess, Ryan, Delfabbro, & Cohen-Woods, 2016; J. Kiecolt-Glaser et al., 2014; Parma et al., 2015; Pullen et al., 2008; Shete, Kulkarni, & Thakur, 2012; Shete, Verma, Kulkarni, & Bhogal, 2017; Wolff, Memon, Chalmers, Sundquist, & Midlöv, 2015; Yadav, Magan, Mehta, Sharma, & Mahapatra, 2012). Furthermore, current research in this area is not generalizable due to the selected populations, and intervention variations based on dose of yoga performed. Previous research demonstrated significant improvements in pro-inflammatory markers, such as C-reactive protein (CRP). However, these studies were conducted in chronically ill populations (i.e. in cancer remission or patients with heart failure) and therefore lack external validity (Bower et al., 2014; Kiecolt-Glaser et al., 2014; Pullen et al., 2008). Subsequent studies that reported reductions in inflammatory markers required daily yoga participation, which may not be feasible for the general public(Shete et al., 2012; Shete et al., 2017). In total, less than half of all studies performed that examine the impact of yoga on inflammation reported positive results (Kiecolt-Glaser et al., 2014; Kiecolt-Glaser et al., 2012; Pullen et al., 2008; Rajbjoj, Shete, Verma, & Bhogal, 2015; Shete et al., 2012; Shete et al.,

2017; Yadav et al., 2012). However, yoga appears to have a positive effect on anti-inflammatory markers, such as adiponectin. In the limited research that exists, results demonstrate that yoga commonly increases adiponectin levels by ~24% (Kiecolt-Glaser et al., 2012; Lee, Kim, & Kim, 2012; Sarvottam, Magan, Yadav, Mehta, & Mahapatra, 2013). These results are consistent across three studies, one study comparing novice and expert (2+ years) yoga practitioners and two studies implementing interventions in overweight/ obese adults lasting between 10 days and 16 weeks (Lee et al., 2012; Sarvottam et al., 2013). There is still a gap in knowledge regarding how quickly changes can be observed in adiponectin and the dose of yoga that can elicit changes.

To the author's knowledge, no research has examined the impact of yoga directly on mitochondrial function. Mitochondrial dysfunction contributes to disease progression through the generation of excessive oxidative stress (Jin, 2006; Mancuso et al., 2009). Past research demonstrated that exercise can improve mitochondrial respiration (Busquets-Cortés et al., 2017; MacInnis & Gibala, 2017). Thus, yoga may be a method to improve mitochondrial protein content, and thus function, through its physical activity component.

Accordingly, even though yoga appears to be a viable modality to improve CVD outcomes, research regarding mechanisms on how yoga can impact this disease and its comorbidities is lacking. Throughout the literature, there is limited emphasis on the possibility of using yoga to improve markers of health or disease pathologies prior to disease onset (e.g. CVD or Type 2 Diabetes), thus limiting the understanding of how yoga may impact pathologies of common chronic diseases. Additionally, limitations of the research studies include a lack of reproducibility, consistency in markers studied, and large variations of the yoga performed between studies, including: varying on the style of yoga performed, frequency practiced (daily or two times a week) and length of intervention (10 days to 16 weeks). Despite limitations and lack of methodological rigor of previous studies, the research supports a need for more "evaluation of the feasibility, acceptability, and mechanisms of effects of yoga for [CVD]," (Kinser, 2013).

University students may be an ideal population to engage in and benefit from yoga. Students commonly report moderate to high levels of stress (Brougham, Zail, Mendoza, & Miller, 2009) and have higher prevalence rates of depression (Center for Behavioral Health Statistics and Quality, 2017). Additionally, developing healthy habits during this time period can continued into subsequent adult years because students are independent and can take ownership of their actions (Sparling, 2007). Finally, while most student likely do not have diagnosed chronic diseases, risk factors for chronic disease may be present, making this period of time ideal to engage in behaviors that can reduce the risk for the development of chronic diseases. Thus, college students, through yoga participation, may receive benefits on their perceived stress, symptoms of depression, and can create healthy lifestyle behaviors at an opportune time.

Therefore, the purpose of this pilot study is to evaluate the feasibility of an eight-week yoga intervention on multiple markers of health related to CVD, including: stress, depression, inflammation, and mitochondrial protein content (a surrogate measure for mitochondrial function). The hypotheses are that the intervention will be feasible, with ≥ 85% of participants adhering to the yoga intervention. The study will also explore the impact of yoga on these health markers. It is hypothesized that reductions in stress, symptoms of depression and pro-inflammatory markers and increases in anti-inflammatory markers and mitochondrial protein content will be observed.

Methods

Overview. The study design was a single-arm eight-week intervention. The study was approved by the University of Wisconsin Milwaukee Institutional Review Board. Informed consent was obtained from each participant during the first visit, prior to data collection.

Participants completed three visits to the research laboratory for data collection at baseline, mid- and post intervention. The first and final lab visits were conducted in the morning and participants were asked to come in after an overnight fast. During the first visit height and

weight measurements were performed on each participant following standard procedures (Sawin, Brawner, & American College of Sports Medicine, 2014). Participants also completed a demographic questionnaire and were asked about their current level of activity through the Exercise Vital Sign (Coleman et al., 2012). Participants were asked to complete three additional surveys to assess mental health and sleep quality: Perceived Stress Scale (PSS), Beck Depression Inventory-II (BDI-II), and Pittsburgh Sleep Quality Index (PSQI). The final portion of the visit involved participants providing a small blood sample (~12mL). Participants were provided with the schedule of available yoga classes and encouraged to attend an average of two, 60-minute yoga classes each week. Participants returned to the lab five weeks after their baseline visit, mid-way through the intervention. During this second visit the participants were asked to complete the two mental health surveys (PSS and BDI-II). The final visit was conducted the week following the end of the intervention, nine weeks after their baseline testing. Data collected at this visit was similar to the first visit and involved obtaining a weight, completing the mental health surveys, and providing a small blood sample.

***Participants*.** Participants were recruited from the university and surrounding community through paper flyers, university-wide emails, university social media accounts, and word-of-mouth announcements. Specific groups with potential interest or who many benefit from yoga were targeted (e.g. Greek life, mental health advisory committees, and graduate students). Inclusion criteria for the intervention consisted of men and pre-menopausal women between the ages of 18-44 years, who had not been diagnosed with a mental health condition (e.g. depression, anxiety, or bipolar disorder) or cardiovascular disease, were not currently taking medications that could impact outcome variables, and self-reported being able to participate in yoga. Participants were excluded from the study if they were a current cigarette smoker, had been diagnosed with a mental health and/or cardiovascular disease, regularly participated in yoga prior to the intervention, and women who were currently pregnant. For their involvement, the yoga classes were provided free of charge to participants during the intervention.

Yoga intervention. All participants were asked to attend an average of two, 60-minute flow-style yoga classes each week for eight consecutive weeks (e.g. if they were unable to attend two classes one week due to their schedule, they could attend three classes the following week). All yoga classes were completed at the university recreation center and led by certified yoga instructors. Yoga class attendees were required to obtain a pass for each class and classes were tracked in each student's account, allowing for attendance to be objectively monitored.

Measures

Mental Health Variables. At each visit, participants completed the Perceived Stress Scale (PSS) and the Beck Depression Inventory (BDI-II). The PSS is a 10-question self-report instrument that assesses an individual's perceived stress from the past month; higher scores relate to higher levels of stress (Cohen, 1988; Cohen, Kamarck, & Mermelstein, 1983). The instrument was scored according to standard procedures (Cohen, 1988). This survey is valid and reliable in populations similar to the current study's population (Lee, 2012; Örücü & Demir, 2009; Roberti, Harrington, & Storch, 2006) with a Cronbach's α between 0.84-0.89 (Cohen, Kamarch, & Mermelstein, 1983; Roberti, Harrington, & Storch, 2006) and a test-retest relability > 0.7 in university students (Lee, 2012). The Beck Depression Inventory-II is a 21-question self-reported instrument that assesses symptoms and the intensity of depression from the previous two weeks (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). This tool is one of the most widely used to assess symptoms of depression and is valid and reliable with a Cronbach's α of 0.82 in college females and 0.85 in college males (Dobson & Breiter, 1983) and a test -retest reliability between 0.64-0.93 in a college student sample (Beck, Steer, & Garbin, 1988). Higher scoring on the instrument relates to higher or more intense levels of depression symptoms. This instrument was scored according to standard procedures (Beck, Steer, Ball, & Ranieri, 1996; Beck, Steer, & Brown, 1996; Beck et al., 1961).

***Inflammatory Markers & Mitochondrial Protein Content*.** Blood samples were collected at baseline and post-intervention lab visits for assessment of the following measures: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tumor necrosis factor – alpha (TNF-α), adiponectin and oxidative phosphorylation (oxphos) western blot. A total of ~12mL of blood were collected into two vacutainers with either EDTA anticoagulant or without any anticoagulant or preservation solution. Blood for the ESR analysis was collected in an EDTA tube and was analyzed using Westergren method (Jou et al., 2011). Serum samples were used to assess CRP, TNF-α, and adiponectin. Serum was prepared by isolating it from whole blood, collected in vacutainers without anticoagulants, by centrifugation at 1,000 rpm for 10 minutes and were then frozen at -80°C until analysis. Samples were examined using Quantikine enzyme-linked immunoabsorbent assay (ELISA) using Quantikine Human Kits (R&D System, Minneapolis, MN USA), following kit instructions and a microplate reader (Verza max, Molecular devices, Sunnyvale, CA, USA). Samples were tested in duplicate and were repeated if coefficients of variation were >20%; each analysis include controls of known concentrations and blank wells. Limits of detection for CRP ranged 0.8-50 ng/mL, for TNF- α ranged 4.0-1,000 pg/mL and for adiponectin ranged between 3.9-250 ng/mL.

Protein content of the oxphos complexes (I - V) of peripheral blood mononuclear cell (PBMCs) mitochondria was examined through Western blots. Mitochondrial protein expression is related to enzyme activity and thus is important because impaired or reduced protein assembly can be a marker of mitochondrial dysfunction (No et al., 2018). To accomplish this, PBMCs were separated from whole blood by creating a 1:1:1 ratio of whole blood, Ficoll-Plaque PLUS reagent (GE Healthcare, Chalfont St Giles, UK) and phosphate-buffered saline (PBS) then isolating the PBMCS through a density gradient centrifuge. PBMCs were then washed with PBS and stored at -80°C until analyzed. Protein was isolated from PBMCs with lysing RIPA buffer (EMD Millipore, Temecula, CA) containing complete mini protease inhibitor cocktail tablet (Roche, Basel, Switzerland) and PhosSTOP phosphatase inhibitor (Roche). Western blots on

10ug of PBMC protein were performed by Dr. Michael Lawlor's lab at the Medical College of Wisconsin. Transferred proteins were probed with an antibody against complexes I-V of the oxidative phosphorylation pathway (ab110412; Abcam) and subsequently a horseradish peroxidase conjugated α-mouse secondary (715-035-150; Jackson Labs). Western blots were visualized using enhanced luminol based chemiluminescent substrate (RPN2236; GE Life Sciences) and compared to a molecular weight ladder (Precision Plus Protein Dual Color Standards #1610374, Bio-Rad Laboratories Inc, Des Plaines, IL, USA) to estimate molecular weight. Western blot procedures followed previous protocols from the Lawlor Lab (Lawlor et al., 2014; Siebers et al., 2018). Quantification of protein levels normalized to Vinculin (Cell Signaling #18799) was performed with Image Lab Software (Bio-Rad Laboratories Inc.).

Statistical Analysis

The study sample was described using descriptive statistics (means and standard deviations). To be deemed feasible ≥ 85% of participants had to adhere to the yoga intervention, missing no more than four classes (25%) over the eight-week period. To explore the trends of the markers of health over the course of the intervention, median and ranges were reported. Statistical analyses were performed using SPSS (version 25; IBM, Chicago, IL).

Results

It was estimated that ~4,000 potential individuals were reached via campus-wide emails and, over 200 individuals were reached through emails targeting specific student populations (e.g. graduate students, advisory committees, etc). Social media accounts promoting the intervention had a combined following of 5,800 followers, however it cannot be determined how many followers were duplicated between the sites. Finally, classroom contacts, from either the research team or the academic instructor totaled over 300 students. From these recruiting efforts, Table 3.1 shows a breakdown of how interested individuals heard about the study.

Table 3.1 Success of Recruiting methods

Method of recruitment	**Percentage of interested individuals**
Campus wide emails	23.3%
Social media posts	18.6%
Paper flyers	14.0%
Contacting specific student groups	11.6%
Classroom contacts	7.0%
Could not be determined	25.5%

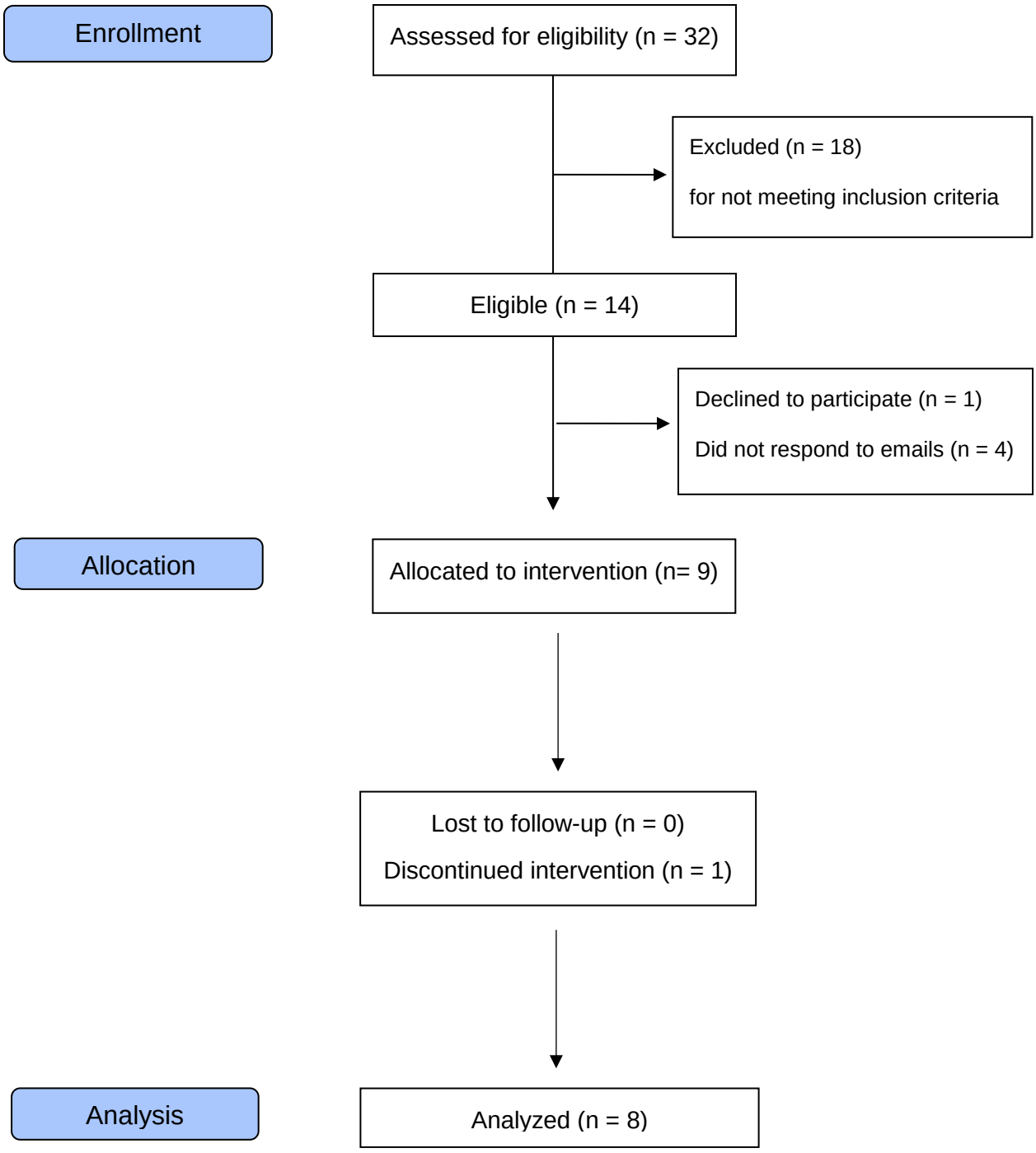
Researchers were contacted by 43 individuals interested in the study, however 11 did not respond to the screening questions. A total of 32 individuals were screened for the study; of those screened, 14 were eligible. The most common exclusion criteria was diagnosis of depression, anxiety, or bipolar disorder. After being deemed eligible, five individuals chose not to participate due to scheduling conflicts, leaving a total of nine enrolled study participants (25 ± 4.8 years; 78% female). Once enrolled in the intervention, one participant dropped out of the study due to a non-study related surgery, leaving eight participants (89%) to be included in the analyses (Figure 3.1). Regarding feasibility, two participants missed more than 25% of the classes. Descriptive statistics of the participants from baseline testing are listed in Table 3.2. At the start of the intervention participants were engaging in an average of 85 ± 99 minutes of exercise per week.

Table 3.2. Participant Descriptive Characteristics

Variable	**Before Intervention**	**After Intervention**
Height (m)	1.6 (0.1)	-
Mass (kg)	69.0 (19.1)	69.1 (20.2)
Body Mass Index (kg/m^{-2})	25.1 (4.9)	25.2 (5.6)

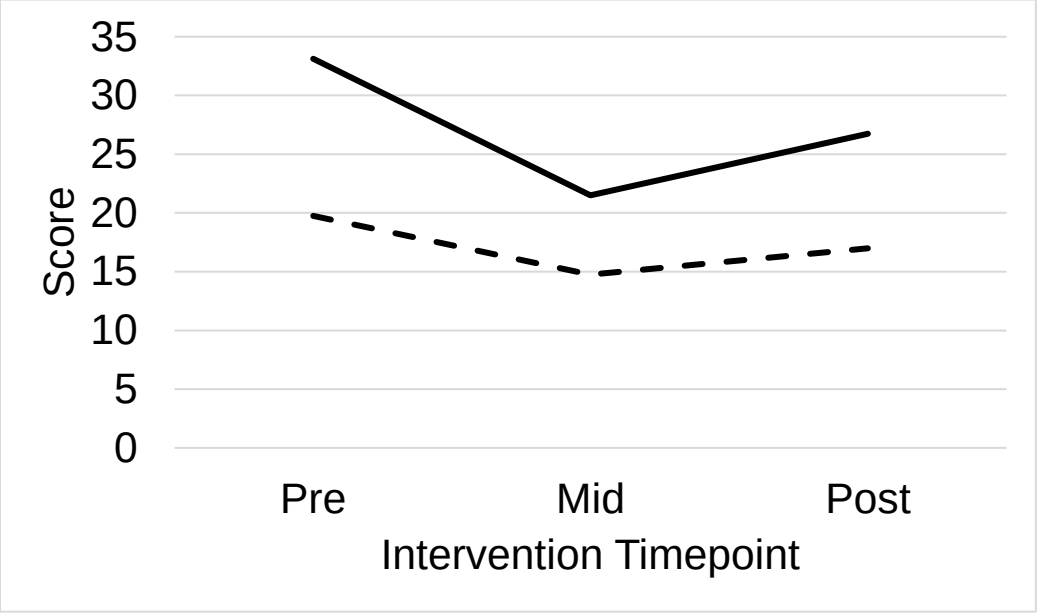
Note. Mean (standard deviation)

Figure 3.1. Enrollment Flow Diagram



Changes to mental health. Differences between the three timepoints were observed in the PSS scores (pre: 18.6 ±7.0 to 14.8 ±7.6 to 17.0 ± 8.9;Figure 3.2) Similarly, BDI-II scores changed between the time points (13.4 ±8.7, to 6.8 ±7.1, to 9.8 ±9.2; Figure 3.2)..

Figure 3.2. Changes in Stress and Depression Scores across an 8-week Intervention

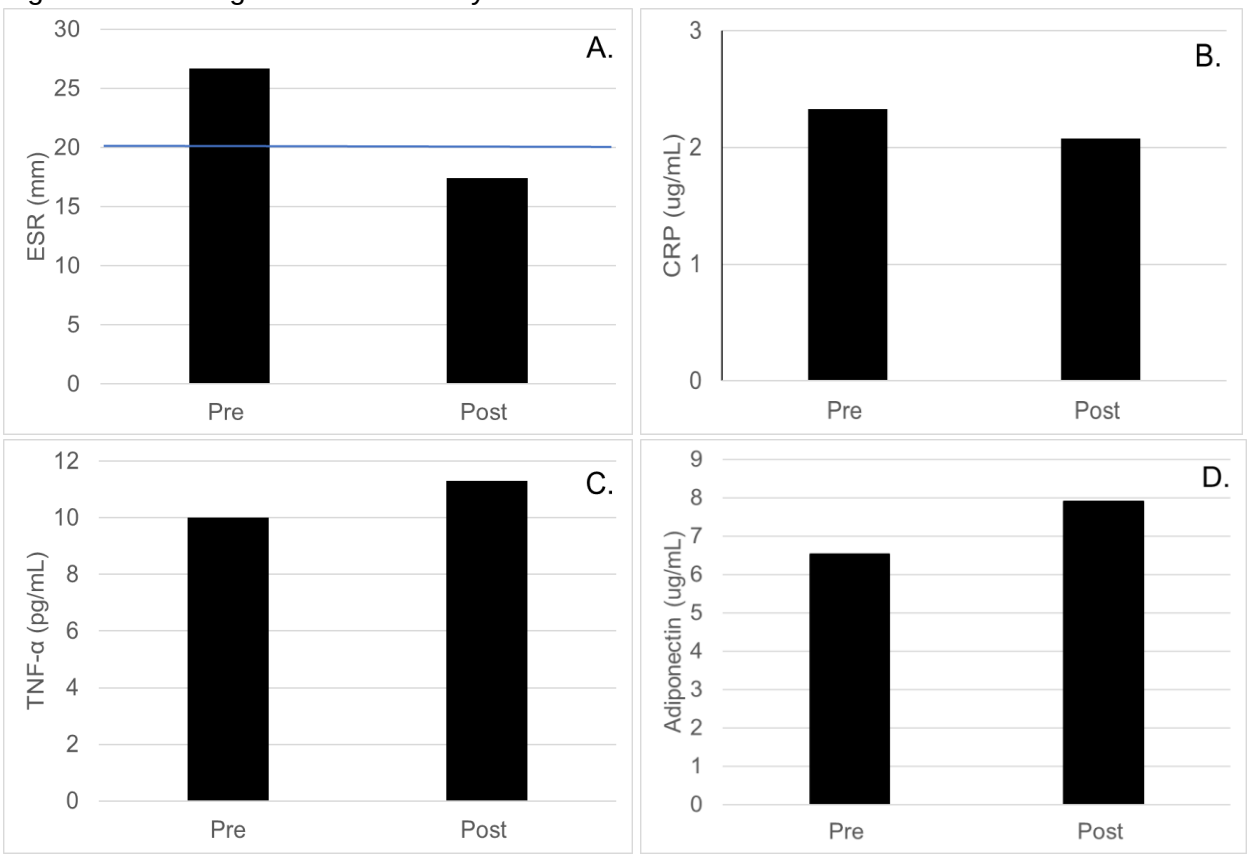


Note. Bold line = Beck Depression Inventory scores; Dotted line = Perceived Stress Scale scores.

Changes to inflammation and mitochondrial protein content. Phlebotomists were not able to collect enough blood from one of the participants to conduct the ESR test, therefore only seven participants were included in this analysis. Within these seven participants a large reduction was observed between the pre and post intervention ESR values (26.71 ± 7.39 to 17.43 ± 6.74; Figure 3.3a). There was a slight reduction in CRP values by 10% (Figure 3.3B) and a slight increase in TNF- α by 11% (Figure 3.3C). The increase observed in TNF- α was contrary to expected changes. Additionally, adiponectin values increased by 21.5% over the eight-week period (Figure 3.3D). Western blot procedures did not produce visible protein content for Complexes I – IV, thus only Complex V was able to be quantified. Protein expression

of Complex V observed a slight reduction between the baseline and post intervention measurements (pre: 0.99 ± 0.94, post: 0.76 ± 0.92).

Figure 3.3. Changes in Inflammatory Markers Pre to Post Intervention.



Note: * $p < 0.05$, Blue line represents the cutoff between healthy vs at-risk limit.

Discussion

University students may be an opportune population to benefit from yoga based on their higher levels of stress, symptoms of depression, and the accumulating presence of risk factors of CVD. The findings of this pilot study suggest that engaging students in an eight-week yoga intervention may present unique challenges in this population. However, throughout the course of the intervention, improvements in some pathologies associated with CVD were observed by participants. While results should be taken with caution, due to the pilot nature of this study,

promising findings were observed regarding perceived stress, depression symptoms, and ESR over the course of the intervention.

During the eight-week intervention, most (n = 6) of participants did adhere to the intervention and attended more than 75% of the yoga classes. However, in the sample of this study, the feasibility criteria for ≥ 85% of the participants completing 12 yoga session was not met. Participants who did not attend the desired 12 yoga classes (≥ 75%) were not asked about their reasons for their low attendance rate, but past studies have found lack of time to be a common barrier for engagement in physical activity or yoga interventions in college students (Kinser, Bourguignon, Whaley, Hauenstein, & Taylor, 2012; Silliman, Rodas-Fortier, & Neyman; 2004). Kinser et al., (2012) reported that a student in their yoga intervention struggled to manage their school work, job, and other life demands. It is interesting to note that during the recruitment and enrollment phase there was a large interest to participate by individuals who were diagnosed with a mental health condition (i.e. depression, anxiety, or bipolar disorder). Unfortunately, these participants did not qualify for the current study. The large interest by this group and belief that yoga may help their mental health condition may be an indicator that, if eligible based on study criteria, yoga interventions would be acceptable to this population and they may be more motivated to adhere to the intervention. Finally, while university students may be a convenient target population for research, their school and work schedules may hinder their engagement in behavioral lifestyle interventions that add additional time commitments to their schedules. Based on the experience of this study, if researchers use a university population, recruiting through campus-wide emails, social media accounts connected to campus activities, and paper flyers posted on campus are encouraged methods for reaching potential participants. Further, it is encouraged to have a location close to or on campus for the yoga classes to be held and a wide range of class times to fit within the busy schedules of students.

Markers of mental health, such as perceived stress and depression symptoms, are important to include in research because these variables are associated with chronic diseases,

including CVD (Dowlati et al., 2010; Fattal, Link, Quinn, Cohen, & Franco, 2007; Gardner & Boles, 2011; Kaplan, Rucklidge, Romijn, & McLeod, 2015; Luft, 1994). Through the course of the intervention, participants reduced their perceived stress by 13.9%, with four of eight participants reduced their stress category (from high to moderate or moderate to low). It should be noted that one participant did increase their perceived stress classification from the moderate to high category during the intervention. Depression symptoms, measured from the BDI-II, were also reduced during the intervention by 27.1%. Observing initial improvements in mental health in response to a yoga intervention is consistent with previous research (Harner et al., 2010; Hewett, Ransdell, Gao, Petlichkoff, & Lucas, 2011; Uebelacker et al., 2010; Woolery, Myers, Sternlieb, & Zeltzer, 2004). In this study, mental health did not have a linear relationship with weeks of the yoga intervention. A possible reason for this is the timing of the intervention and post testing. Some of the participants started the eight-week intervention mid-way through the semester and their post intervention testing was then conducted the week prior to finals, which can be a time of higher stress for students and relate to the increase in both PSS and BDI-II scores. Woolery et al. (2004) also reported significant reductions in depression symptoms in college students over a five-week Iyengar yoga intervention. In contrast to the present findings, Woolery observed depression symptoms decreased in a linear fashion (Woolery et al., 2004). An important difference between the present study and Woolery (2004) is the length of interventions, with the Woolery study only lasting five weeks. Similar to the present study, Harner, et al. (2010) reported non-linear changes in stress and depression symptoms in incarcerated women during a 12-week Iyengar yoga intervention when data was collected at weeks 0 (pre), 4, 8, 12 (post). In their study, stress and depression symptoms declined between week 0 and 4 but increased between week 4 and 8 (Harner et al., 2010). Previous research and the present studysuggest that the largest benefits to mental health may be observed in the first five weeks of a yoga intervention.

Due to the pilot nature of this research statistical analysis (e.g. analysis of variance or t-tests) could not be run with adequate power. Therefore, trends and percentage of changes were reported, but these results should be interpreted with caution due to the small sample size. . The changes observed in ESR values before and after the intervention are promising with a large reduction over the intervention. Further a difference was observed based on the clinical cutoff values for ESR with baseline values categorizing participants within a higher-risk category for CVD and categorized within a lower-risk after the interention Previous studies reported similar results, with significant reductions in ESR after an eight-week yoga intervention in individuals with rheumatoid arthritis and a 10-week intervention in older adults, supporting the results presented here (Gautam, Tolahunase, Kumar, & Dada, 2019; Kim & Ju, 2017). Participants of the present study had non-significant reductions in CRP by 10.5%. Since all participants in this study were well within the normal ranges of CRP, a large decrease in CRP levels may be challenging to observe. Previous research lacks consensus regarding the relationship between yoga and CRP values in populations with healthy elevated levels of CRP (Azami et al., 2019; Cho et al., 2015; Pullen et al., 2008; Shete et al., 2012; Sivasankaran et al., 2006; Wolff et al., 2015). Contrary to the stated hypothesis, TNF- α increased by 11% over the course of the intervention. This change is not supported in the literature as previous research includes conflicting results regarding impact of yoga on TNF- α. Some studies report a significant decrease in TNF- α after a yoga intervention (Bower et al., 2014; Chen et al., 2016; Shete et al., 2017). In contrast, some randomized controlled trials observe no changes in TNF- α after a yoga intervention, but during the intervention time period, control groups observe a a significant increase in TNF- α (Cho et al., 2015; Harkess et al., 2016; Kiecolt-Glaser et al., 2010). Finally, there was an observed increase in adiponectin values by 21%. This is an interesting finding as there was not a substantial change in weight but is comparable to previous interventions examining both overweight males and females, which foundsimilar, but significant, increases in adiponectin by 23-26% (Lee et al., 2012; Sarvottam et al., 2013).

The amount of protein of each component of the electron transport chain reflects enzyme activity, and thus is a reflection of mitochondrial function(No et al., 2018). Results from this study were only able to assess changes to Complex V, and minimal changes in the protein content could be due to yoga not being a strong enough stimulus to produce changes in PBMC mitochondria over eight weeks. Previous research reports that greater changes to the mitochondria are observed with higher intensities and/or higher volumes of exercise (Busquets-Cortés et al., 2017; Hedges et al., 2019; MacInnis & Gibala, 2017), but yoga is commonly considered a light to moderate intensity activity (Ainsworth et al., 2011). Similar to the present findings, Hedges et al., (2019) did not find changes in Complexes I-V from PBMC mitochondria after two weeks of high intensity training in young men but did observe changes in skeletal muscle mitochondria. The lack of changes observed in oxphos protein content from PBMC mitochondria, observed in both Hedges et al., (2019) and the present study may be a result of mitochondrial PBMCs not responding as quickly to an exercise training stimulus as mitochondria in the skeletal muscle (Hedges et al., 2019).

These results should be interpreted with caution due to limitations within the study. Perhaps the most significant limitations are the study design (i.e. a feasibility study) and the small sample size. Another potential limitation is that the mitochondrial protein content was measured from PBMCs. Mitochondria in the PBMCs were selected because this measurement is less invasive for participants, but this measure may not be as sensitive or change as quickly to exercise as mitochondria in the muscle (Hedges et al., 2019). Thus, mitochondrial changes within the body may be happening but potentially missed based on the tissue examined. A final limitation is that researchers were not able to observe the participants completing the yoga classes. Along with the stated limitations, this study had strengths. This research measured both psychologic and physiologic pathologies, which are all associated with each other and are pathologies to multiple chronic diseases. Through the multiple objective markers of health

examined, this study adds to the literature by examining multiple potential mechanisms through which yoga may impact health. Further, this is one of the first studies to directly examine the mitochondria in relation to yoga participation. Previous research has examined changes in oxidative stress during yoga interventions, as a surrogate measure of mitochondria functioning, but none, to the author's knowledge, have directly examined the mitochondria (Gordon et al., 2008; Hedge et al., 2011; Hegde, Adhikari, Shetty, Manjrekar, & D'Souza, 2013; Patil, Dhanakshirur, Aithala, Naregal, & Das, 2014). While researchers were not able to observe the participation of yoga classes, we were able to objectively monitor their attendance through a check-in process. A final strength of this study is the use of community yoga classes as researchers have urged the yoga research community to move from the lab setting to the community to pursue results that are generalizable to the public (Sherman, 2012).

Due to the possible non-linear relationship between yoga interventions and variables of mental health, future research should consider measuring mental health variables on a weekly or daily basis throughout the intervention. Additionally, researchers should consider assessing and reporting when the last yoga session was performed in relation to the measurement of mental health to better understand the relationship between yoga and mental health. There are many markers of health that yoga has the potential to impact. Research should expand on this pilot study and investigate the impact of yoga on markers of health, both included in this study and additional markers, associated with chronic diseases. This will provide a better understanding of how yoga participation may be associated with improvements in markers of disease progression.

Conclusion

In conclusion, research should continue to find ways to motivate generally healthy college students to regularly engage in yoga. The majority (67%) of participants attended ≥ 75% of the provided yoga classes over an eight-week period. Exploratory findings also observed benefits in perceived stress, symptoms of depression, and systemic inflammation measured by

ESR after the intervention. Future research should work to confirm and expand these findings to better understand the relationship that yoga may have on markers of health associated with cardiovascular disease.

Chapter 4: Summary & Conclusions

The purpose of this research was to examine if individuals who engage in yoga have improved health outcomes of perceived stress, symptoms of depression, inflammation, and oxidative phosphorylation protein content complexes within the mitochondria. It was hypothesized that participation in yoga would be associated with improved markers of psychologic and physiologic health. This hypothesis was tested through a cross-sectional study and a pilot intervention. Specifically, the following hypotheses were tested:

1. Current yoga participants would have improved markers of inflammation (ESR, CRP, TNF-α, and adiponectin), protein content within oxidative phosphorylation complexes, and psychologic health (perceived stress and symptoms of depression) compared to individuals who do not participate in yoga.
2. An eight-week, 16 session yoga intervention would be feasible in a young adult population and that preliminary results would show improvements in psychologic and physiologic variables of health after the intervention.

The studies observed that current yoga participants had lower perceived stress than non-yoga counter parts and that levels of perceived stress were reduced by 13%, both after an eight-week yoga intervention. Similar results were found regarding the relationship between yoga and symptoms of depression; current yoga participants had statistically lower levels of depression symptoms and large reductions (27%) were observed after the pilot intervention. These results provide support for the use of yoga to improve mental health outcomes in the general public.

No differences were observed regarding most inflammatory markers between current yoga participants and their non-yoga counter parts in the cross-sectional study. The primary

difference observed was in ESR values, with current yoga participants being classified more often as having healthy ESR values compared to their non-yoga counter parts (87% vs. 50%, respectively) based on clinical cutoff values. Further, preliminary findings in the pilot intervention reported large reductions of 27% in ESR and participants also observed changes in their categorization from clinical cutoffs (moving from high-risk to low-risk), after an eight-week yoga intervention. However, no other pro-inflammatory markers observed reductions to this magnitude from yoga participation. While it is surprising that the non-specific marker of inflammation was most impacted by yoga no other inflammatory markers observed significant benefits from yoga participation. The lack of significant findings may be due to the generally healthy sample of participants in these studies. Yoga participation in the pilot intervention was associated with an improvement of 10.5% in CRP and 21% in adiponectin. These improvements may become more pronounced in populations at risk for, or diagnosed with, chronic diseases. These findings add to the existing literature that reports conflicting results on the relationship between yoga and inflammation. Future research should continue to include multiple markers of inflammation and expand to markers not considered by this study, to examine the relationship with yoga.

These studies were, to the author's knowledge, the first to directly examine oxidative phosphorylation protein content in relation to yoga participation. While this lack of a difference was an unexpected finding in relation to yoga participation, it may be due to age differences between the groups, with yoga participants being ~10 years older than the non-yoga participants. Thus, if the groups were age-matched, differences may have been observed. Further, limited changes in Complex V protein content were observed over the intervention period; this may have been due to mitochondria within the PBMCs not being sensitive enough to observe changes over a short period (Hedges et al., 2019). Collectively, these findings are unable to provide evidence supporting a relationship between oxidative phosphorylation protein content and yoga participation. However, there are many different assessments / markers of

mitochondrial functioning. Future research should not only examine protein content of election transport chain complexes, but also expand to assess enzyme functioning (e.g. cytochrome C oxidase) within the mitochondria and assess respiration measures (e.g. respiratory control ratio, maximal oxygen consumption rate and leakage within mitochondria).

Change scores for stress, depression, inflammation, and mitochondrial function from the pilot intervention were calculated and correlated to each other. Because research supports that these markers of health are associated with and can impact each other, we were interested to see if changes in variables were correlated, suggesting that yoga could impact each variable to the same extent. Preliminary findings only support that changes in CRP and perceived stress were related to each other and that no other changes in variables were related to each other. These observations add to the literature by supporting that yoga may improve markers associated with disease outcomes through both CRP and perceived stress, however more research should be conducted to determine the mechanisms through which yoga positively impacts chronic diseases.

Finally, the pilot intervention examined the feasibility of implementing a twice-weekly yoga intervention in a college-age population. We observed that while the majority of participants (67%) adhered to the intervention, based on the feasibility cutoff created *a priori* (≥ 85%) this intervention was not feasible in this pilot study. These results are surprising as yoga continues to be a top fitness trend, with over 20 million adults in the United States practicing on a regular basis (Cramer, Ward, et al., 2016; Thompson, 2018). However, attrition rates of ~20% are a common limitation within yoga research, with busy schedules and lack of motivation during at-home yoga practice being common reasons for dropout (Cramer, Haller, Dobos, & Lauche, 2016; Kinser et al., 2012). This study along with past literature, continues to emphasize the need for yoga interventions to be practical and appealing, both for participants of the studies and to encourage yoga participation in the general population. Future research should expand upon the positive results of this study, that the majority of participants attended ≥ 75% of the

classes. Future studies should recruit a larger sample size and continue to find methods to provide yoga classes at a wide variety of times to accommodate the busy schedules of college students. A potential option for administering yoga classes would be through academic courses for credit, this would facilitate students to schedule regular yoga into their schedule and may increase motivation to participant if it is for college credit.

Although many individuals who practice yoga believe that it can improve their health, there remains limited and conflicting research to support this notion. Furthermore, the mechanisms for how yoga may influence markers associated with diseases are unknown. This dissertation demonstrates a positive relationship between yoga engagement and psychologic variables of perceived stress and symptoms of depression, both within current yoga participants and in yoga naïve participants after they engaged in 8 weeks of yoga. However, within this dissertation there is limited support between the relationship of yoga and physiologic variables in a healthy population. Future research should continue to pursue understanding the relationship between yoga and physiologic and psychologic health. Additionally, understanding what populations (e.g. at risk for or diagnosed with chronic disease, or general population) can have improved health outcomes through engaging in yoga.

Taken together, this work provides evidence that individuals may observe some health benefits from engaging in yoga. The cross-sectional study examines the relationship between yoga and health outcomes in people who are already engaging in yoga. The pilot intervention then expanded on these results to assess the feasibility of engaging individuals who are not currently participating in yoga to participate in an eight-week yoga intervention and explored changes in health outcomes after eight weeks of yoga participation. The findings from both studies support that participation in yoga can improve perceived levels of stress and symptoms of depression. Further, differences based on clinical cutoffs in the cross-sectional study and exploratory analyses from the pilot study show promising findings regarding the relationship between yoga and systemic inflammation (ESR values). This work was not able to demonstrate

a clear relationship between participation in yoga and markers of inflammation nor mitochondrial protein content. Collectively, these findings support that yoga may be recommended as a lifestyle intervention, complementary to medications, to improve psychologic health outcomes and, with further research, possibly be used for physiologic (inflammation and protein content within oxidative phosphorylation complexes) variables. This information is essential to understanding the impact that yoga may have on markers associated with disease progression to eventually recommend yoga as a lifestyle intervention to improve markers associated with prevalent, chronic diseases, such as cardiovascular disease.

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CURRICULUM VITAE

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EDUCATION

2014-2019 **Doctor of Philosophy** Health Sciences (expected Fall 2019)
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Advisors: Drs. Jeri Lyons, Janis Eells, Michele Polfuss
Dissertation: Examining the Relationship between Yoga Participation and Health. You down, dog?

2015-2019 **Graduate Certificate in Applied Gerontology**
The University of Wisconsin – Milwaukee
Program: Aging and Translational Research

2012-2014 **Master of Science** Kinesiology
The University of Tennessee - Knoxville
Advisor: Dr. David Bassett
Thesis: Accuracy of the SenseWear Armband Across Different BMI Categories

2008-2012 **Bachelor of Science** Exercise and Sport Science - Fitness
University of Wisconsin – La Crosse,

PUBLICATIONS IN REFEREED JOURNALS

1. **Forseth B,** Papanek PE, Schoeller D, Bandini L, Sawin K, Fendrich M, Moosereiner A, Zvara K, & Polfuss M. (2019). Feasibility and Acceptability of a Self-Report Activity Diary in Families of Children with and without Special Needs. *Comprehensive Child and Adolescent Nursing.* [*In Press*] DOI: 10.1080/24694193.2019.1606864

2. **Forseth B,** Boyer WR, Miller A, & Fitzhugh EC. (2019). Demographic, Health Behavior, and Cardiometabolic Risk Factor Profile in Yoga and non-Yoga Participants: NHANES 1999-2006. *Complementary Therapies in Medicine*. 44:123-128.

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4. Polfuss M, Sawin KJ, Papanek PE, Bandini L, **Forseth B**, Moosreiner A, Zvara K, & Schoeller DA. (2018). Total energy expenditure and body composition of children with developmental disabilities. *Disability and Health Journal*. 11(3) 442-446.

5. Lerma N, Keenan K, Strath S, **Forseth B**, Cho C, & Swartz A. (2016). Muscle activation and energy expenditure of sedentary behavior alternatives in young and old adults. *Journal of Physiological Measurement*. 37.10:1686.

MANUSCRIPTS UNDER REVIEW

1. Polfuss M, **Forseth B**, Papanek PE, Schoeller D, Moosereiner A, Sawin K, Zvara K, Young C, Fendrich M, & Bandini L. Variability of Resting Metabolic Rate Equations in Children with Developmental Disabilities. *Under Review at: Research Quarterly for Exercise and Sport.*

2. **Forseth B,** Papanek PE, & Polfuss M. Sedentary Behavior Bout Comparisons between Children with Specials Needs with no Chronic Illness. *Under review at: Disability and Rehabilitation.*

3. **Forseth B.,** Hunter, S. Range of Yoga Intensities from Napping to Sweating: A Systematic Review. Under Review at: *Journal of Physical Activity and Health*. Accepted October 2019.

MANUSCRIPTS IN PROGRESS

1. Polfuss M, Bandini L, Papanek PE, **Forseth B,** Schoeller D. Body Mass Index and Body Fat Percentage Composition in Children with Down Syndrome and Spina Bifida. Intended submission in September 2019.
2. Moosereiner A, **Forseth B**, Polfuss M. Healthy Eating Index in Children with Intellectual and Developmental Disabilities: A descriptive study. Intended submission in September 2019.
3. **Forseth B**, Polfuss M, Hauff C. Differences in Motivational Factors Between Participants of Different Yoga Styles. Intended submission in November 2019.

PUBLISHED ABSTRACTS

1. **Forseth B**, Boyer WR, Fitzhugh EC, & Miller A. (2018). Demographic, Health Behavior, And Cardiometabolic Risk Factor Profiles In Yoga And Non-yoga Participants: Nhanes 1999-2006. Medicine & Science in Sports & Exercise, 50(5S), 77. DOI: 10.1249/01.mss.0000536562.08010.3b

2. Polfuss M, **Forseth B**, Schoeller DA, & Papanek PE. (2018). Accuracy of Parent And Child Self-reported Physical Activity In Children With Special Needs: A Pilot Study. *Medicine & Science in Sports & Exercise*, *50* (5S), 451. DOI: 10.1249/01.mss.0000536562.08010.3b

3. **Forseth B**, Hauff C, Swartz A. (2017). Quantifying Physical Activity Performed During Yoga. *Medicine and Science in Sport & Exercise, 49 (5S), 173-174. DOI:* 10.1249/01.mss.0000517306.85658.59

4. Polfuss M, Schoeller D, **Forseth B**, Sawin K. (2017). The Implication of Total Energy Expenditure on Nutritional Guidance in Children with Special Needs. Journal of Pediatric Rehabilitation Medicine: An Interdisciplinary Approach. 10(2017) S37–S40

5. **Forseth B**, Strath S, Swartz A. (2016). Comparison of Physiological and Accelerometer Responses between Yoga and Slow Walking. *Medicine and Science in Sport & Exercise, 48(5S), 208. DOI:* 10.1249/01.mss.0000485624.51929.78
6. **Forseth B,** Bassett D, Crouter S, Coe D. (2015). Accuracy of the SenseWear Armband Mini-Fly for Estimating Energy Expenditure Across BMI Categories. *Medicine and Science in Sport & Exercise, 47(5S), 14 DOI:* 10.1249/01.mss.0000476430.35948.b5.

SCIENTIFIC PRESENTATIONS (REFEREED)

NATIONAL/INTERNATIONAL

1. **Forseth B**, Polfuss M, Hauff C. (2019). Differences in Motivational Factors Between Participants of Different Yoga Styles. Symposium on Yoga Research. Stockbridge, MA 10/22.

2. **Forseth B** & Polfuss M. (2019). Sedentary Behavior Bout Comparisons between Children with Specials Needs and with No Chronic Illness. Healthy Weight Research Network. Boston, MA 04/05.

3. Polfuss M, Schoeller D, **Forseth B**, & Sawin K. (2017). The Impact of Total Energy Expenditure in Children with Special Needs on Families. International Family Nursing Conference, Pamplona, Spain.

4. Polfuss M, Schoeller D, **Forseth B**, & Sawin K. (2017). The Implication of Total Energy Expenditure on Nutritional Guidance in Children with Special Needs. Spina Bifida Association World Congress Meeting.

5. Polfuss M, Schoeller D, **Forseth B**, Sawin K. (2016) Total Energy Expenditure and Relationship to Fat Free Mass in Children with Special Needs, Council for Advancement of Nursing Science, Washington, DC, 09/2016 (Oral Communication).

6. Polfuss M, Schoeller D, Strath S, Papanek P, Simpson P, **Forseth B**, Moosreiner A, Zhang L, Zvara K, & Sawin K. (2016). P20 Pilot Project 1 Weight-Related Self-Management in Children with Special Health Care Needs, National Institute of Nursing Research Scientific Symposium.
7. **Forseth B,** Strath S, Cho C, & Swartz A. (2016). Intensity of Yoga, Walking, and Body Weight Calisthenics: A Comparison of Measurement Methods. Pure Action Research Conference, National Meeting. Austin, TX.
8. Lerm N, Keenan K, Strath S, **Forseth B**, Cho C, & Swartz A. (2016). Age Alters Muscle Activation but Not Energy Expenditure During Sedentary Behavior Alternatives. American College of Sports Medicine, National Meeting. Boston, MA.

9. Polfuss M, Schoeller D, Strath S, Papanek P, Simpson P, **Forseth B**, Moosreiner A, Zhang L, Zvara K, & Sawin K. (2016). Weight-Related Self-Management in Children with Special Health Care Needs. NIH Center's Director Meeting, Washington, DC, May.
10. Lerma N, Keenan K, Strath S, **Forseth B**, & Swartz A. (2015) The Effects of Altering Sitting Behavior on Energy Expenditure and Muscle Activation. 4th International Conference on Ambulatory Monitoring of Physical Activity and Movement. Limerick, Ireland.

REGIONAL/LOCAL

1. Xiong K, Polfuss M, & **Forseth B.** (2018). Relationship of Parenting Styles and Obesity with Special Needs Children. College of Health Sciences Research Symposium. Milwaukee, WI.
2. **Forseth B**, Schoeller D, Papenek PE, & Polfuss M. (2017). Accuracy of Parent and Child Self-Reported Physical Activity in Children with Special Needs. Midwest American College of Sports Medicine, Regional Meeting. Grand Rapids, MI.
3. **Forseth B**, Hauff C, & Swartz A. (2016). Development of a Method to Quantify Physical Activity Performed During Yoga. Midwest American College of Sports Medicine, Regional Meeting. Fort Wayne, IN.
4. Polfuss M, Schoeller D, **Forseth B**, & Sawin K. (2016). Measuring Energy Expenditure in Children with Special Needs. Clinical Translational and Science Institute Milwaukee Regional Research Forum, Milwaukee, Wisconsin, October.
5. Polfuss M, Schoeller D, Strath S, Papanek PE, Simpson P, **Forseth B**, Moosreiner A, Zhang L, Zvara K, & Sawin K. (2016). Weight Related Self-Management in Children with Special Health Care Needs. Midwest Nursing Research Society. Milwaukee, WI.
6. **Forseth B**, Strath SJ, & Swartz AM. (2015). Comparison of Physiological and Accelerometer Responses between Yoga and Slow Walking. College of Health Sciences Research Symposium. Milwaukee, WI. Oral communication based on original research.
7. Polfuss M, Schoeller D, Strath S, Papanek PE, Simpson P, **Forseth B**, Moosreiner A, Zhang L, Zvara K, & Sawin K. (2015) Measuring Energy Expenditure in Children with Spina Bifida and Down Syndrome: A Feasibility Study. Clinical Translational and Science Institute Milwaukee Regional Research Forum, Milwaukee, WI, October 15.
8. **Forseth B**, Bassett D, Crouter S, & Coe D. (2015). Accuracy of SenseWear Armband Mini-Fly for Estimating Energy Expenditure in Normal Weight, Overweight, and Obese Individuals. College of Health Sciences Research Symposium. Milwaukee, WI, May 1.

GRANTS

FUNDED GRANTS

1. **Forseth B**, Eells J, & Swartz A. (2017). Comparative Effectiveness Analysis of Yoga and Walking on Glucose Control. College of Health Sciences Student Research Grant Award. $1905.

NON-FUNDED GRANT SUBMISSIONS

1. **Forseth B**, Lyons J, Eells E, & Polfuss M. (2019). Improving Health Through Your Down Dog. College of Health Sciences Student Research Grant Award. $1,885.
2. **Forseth B**, Lyons J, Eells E, & Polfuss M. (2018). Effectiveness of Yoga on Inflammation. College of Health Sciences Student Research Grant Award. $1,932
3. **Forseth B** & Swartz AM, (2016). Quantifying Intensity Performed During Yoga - A Construct Validation. College of Heath Sciences Student Research Grant Award. $2000.

4. **Forseth B** & Swartz AM, (2015). Quantification of Yoga. College of Heath Sciences Student Research Grant Award. $2000.

PROFESSIONAL EXPERIENCE

TEACHING EXPERIENCE

2017 Adhoc Instructor
University of Wisconsin – Milwaukee, Milwaukee, WI
Class: KIN 330 Exercise Physiology

2015-2017 Teaching Assistant
University of Wisconsin – Milwaukee, Milwaukee, WI
Fall 2015: KIN 330 Exercise Physiology
Spring 2016: KIN 230 Health Aspects of Exercise and Nutrition
KIN 430 Exercise Testing for Fitness Assessment and Exercise Prescription
Summer 2016: KIN 330 Exercise Physiology
Fall 2016: KIN 330 Exercise Physiology
Spring 2017: KIN 200 Introduction to Kinesiology
KIN 400 Ethics & Values in the Profession

RESEARCH EXPERIENCE

2015-2018 Graduate Assistant for the College of Nursing,
University of Wisconsin – Milwaukee, Milwaukee, WI
Project 1: Weight-Related Self-Management in Children with Special Health Care Needs
Project Funding: P20 NR 015339-01.
Project 2: Measuring Energy Expenditure in Children with Spina Bifida and Down Syndrome. Project Funding: CTSI of Southeastern Wisconsin. UL1TR000055
Project 3: Measuring Body Composition in Children with Special Needs.

2016-2017 Research Assistant
University of Wisconsin – Milwaukee, Milwaukee, WI
Project: Atwater Standing Desk Project

OTHER PROFESSIONAL EXPERIENCE

2014-2015 Graduate Assistant for The HUB Faculty and Staff Gym,
University of Wisconsin – Milwaukee, Milwaukee, WI

GUEST LECTURES/ INVITED SPEAKER **Forseth B**. (2019). Instruction for Spinning. Department of Exercise Science EXPH 2931. Marquette University, November 14.

Forseth B. (2018). Instruction for Spinning. Department of Exercise Science EXPH 2931. Marquette University, November 15.

Forseth B. (2017) Cardiovascular Health and Exercise. Departments of Biomedical Sciences and Kinesiology NUTR 240.University of Wisconsin-Milwaukee, October 16.

Forseth B. (2017). Body Composition Testing. Departments of Biomedical Sciences and Kinesiology NUTR 430.University of Wisconsin-Milwaukee, March 28.

Forseth B. (2017). Cardiovascular Health and Exercise. Departments of Biomedical Sciences and Kinesiology NUTR 240.University of Wisconsin-Milwaukee, February 27.

Forseth B. (2017) Anthropometric Measurements in Children. Department of Clinical Psychology. BRAIN Lab. University of Wisconsin-Milwaukee, February 21.

Forseth B. (2015). Neuromuscular Adaptations. Department of Kinesiology KIN 330. University of Wisconsin-Milwaukee, November 24.

RESEARCH AND LABORATORY SKILLS

EQUIPMENT

Electrocardiogram

Physical Activity Monitoring (activPAL, ActiGraph, pedometers, Multi-sensor monitors, doubly labeled water administration)

Metabolic Measurement Systems (Cosmed K4b^2, Parvomedics Trueone 2400)

Polar Heartrate monitoring

Colorimetric Analysis (ELISAs)

TESTING PROCEDURES

Body Composition Assessments (DXA, BodPod, anthropometrics, Bioelectrical

Impedance Analysis, skinfolds)

Lactate Assessment (Nova Biomedical Lactate Plus lactate meter)

Maximal and Submaximal Exercise Testing (treadmill and cycle)

Resting Metabolic Rate Testing

Blood Pressure

Phlebotomy

PROFESSIONAL ACTIVITIES

PROFESSIONAL HONORS & AWARDS

2019 2nd Place. 3 Minute Thesis. University of Wisconsin – Milwaukee.
Improving Mental and Physiological Health with Yoga.
2017 Graduate Student Travel Award, Graduate School, University of Wisconsin – Milwaukee.
2016 Helen Bader Age & Community Scholarship, Center for Aging & Translational Research, University of Wisconsin-Milwaukee

2015 Helen Bader Age & Community Scholarship, Center for Aging & Translational Research, University of Wisconsin-Milwaukee
2014 Chancellors Graduate Student Award, University of Wisconsin-Milwaukee

SCHOLARLY ACTIVITIES

PATENT

Forseth, B., Moosereiner, A., Polfuss, M. 2017. 'Arm Span Device Measurement' Patent Application No. 62/447, 964 (Atty. File No. 020870-9132-US01), Filed January 2017. U.S. Provisional Patent.