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### The Effects of Combined Curcumin Supplementation and High Intensity Interval Training on Time Trial Performance in Moderately Active Individuals

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UNIVERSITY OF NORTHERN COLORADO

Greeley, Colorado

The Graduate School

THE EFFECTS OF COMBINED CURCUMIN SUPPLEMENTATION  
AND HIGH INTENSITY INTERVAL TRAINING ON TIME TRIAL  
PERFORMANCE IN MODERATELY ACTIVE INDIVIDUALS

A Thesis Submitted in Partial Fulfillment  
of the Requirements for the Degree of  
Master of Science

Nora Johnston

College of Natural and Health Sciences  
Sport and Exercise Science

August 2019

This Thesis by: Nora Johnston

Entitled: *The Effects of Combined Curcumin Supplementation and HIIT on Time Trial Performance in Moderately Active Individuals*

Has been approved as meeting the requirement for the Degree of Master of Science in College of Natural and Health Sciences in School of Sport and Exercise Science, Program of Exercise Physiology

Accepted by the Thesis Committee:

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Accepted by the Graduate School

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Research and Sponsored Project

## ABSTRACT

Johnston, Nora. *The Effects of Combined Curcumin Supplementation and HIIT on Time Trial Performance in Moderately Active Individual*. Unpublished Master of Science thesis, University of Northern Colorado, 2019.

Individuals who participate in intensified training programs such as high intensity interval training (HIIT), are at risk for an uncontrolled inflammatory response, which may hinder the body's recovery process. Curcumin is the most recognized compound in turmeric and has a distinctive yellow color. Curcumin has many medicinal actions and is most well-known for its anti-inflammatory activities. More recently, curcumin has emerged as an agent that can potentially optimize performance during intense exercise and may also attenuate pain and muscle soreness. Additionally, curcumin has been linked to improvements in mental health status such as reductions in depression and anxiety.

**PURPOSE:** The specific aim of this study was to explore the performance related and mental health impact of curcumin supplementation during 2-weeks of intensified, HIIT.

**METHODS:** Twenty-three physically active, healthy males and females between the ages of 18-40 years were recruited for this study. Participants were randomly assigned to one of 3 groups: curcumin 1 (LG1 (n=9)), curcumin 2 (LG2 (n=7)), or a rice flour placebo (PL (n=7)). All participants visited the lab 9 times. As part of their assessments, participants completed basic measures of body size and composition as well as a VO<sub>2</sub>max test. Then, they completed a 16.1 km cycling time trial with assessments for pain before and during the test as well as muscle soreness after the test. Mental health was assessed

before the time trials pre and post-intervention. Then, all groups completed HIIT training which included 2 weeks of 3 nonconsecutive days a week of 6, 90 second sprints at 80-90% of their  $VO_2$ max on the cycle ergometer with 3 minutes of active recovery at 50-60% of their  $VO_2$ max. After the training and supplementation period, all groups were reassessed using the time trial with pain and muscle soreness measures and mental health assessment. **RESULTS:** There were no differences among the groups with respect to time trial performance, dolorimetry measures, pain, and mental health at the pre intervention time point. No significant differences in pre to post-intervention time trial performance, dolorimetry, pain, or mental health were observed among groups LV1, LV2 and PL. **CONCLUSION:** Although no main effects related to HIIT or curcumin were observed in this study, results suggest that a larger population may be needed for a more definitive conclusion as to whether or not curcumin may be helpful during intensified training.

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## CHAPTER I

### INTRODUCTION

#### Background

Individuals who participate in intensified training programs such as high intensity interval training (HIIT) are at risk for an uncontrolled inflammatory response, which may hinder the body's recovery process (Zwetsloot, John, Lawrence, Battista, & Shanely, 2014). Various forms of anti-inflammatory supplementation have been used to better control this inflammatory response, and recent literature has shown promise with the spice, turmeric (*Curcuma longa*) (Davis et al., 2007). Curcumin, a compound in turmeric, is associated with reductions in the muscular pain associated with delayed-onset muscle soreness (DOMS), and also as an aid to enhanced muscle recovery, with the potential to improve muscular performance (Nicol, Rowlands, Fazakerly, & Kellett, 2015). In addition to the physical health benefits observed following turmeric/curcumin supplementation, turmeric is also associated with improvements in mental health status (Cox, Pipingas, & Scholey, 2015).

Even though performance research involving turmeric is relatively new, the spice has been used in a plethora of ways over the past few centuries (He et al., 2015). Turmeric, which has been studied for over 3 decades, is a rhizomatous herbaceous perennial plant belonging to the ginger family (Sahin et al., 2016). Grown in southern and southwestern tropical Asian regions, the traditional use of turmeric is as an important



spice to add flavor and color to foods such as curries, pasta, meat, and rice (Kocaadam & Şanlier, 2017). Medicinally, turmeric has also been used to treat various inflammatory conditions and diseases such as inflammatory bowel disease, rheumatoid arthritis, diabetes, obesity, and cancer (He et al., 2015). Both exercise and health-based research have revealed turmeric-induced positive effects related to muscle soreness, pain, recovery, performance enhancement, and mental health (Hewlings & Kalman, 2017).

Many of these health and exercise related benefits are attributed to curcumin (He et al., 2015). Curcumin is the most recognized compound in turmeric and is what gives turmeric its distinctive yellow color (Nicol et al., 2015). The desirable actions of curcumin are similar to nonsteroidal anti-inflammatory drugs (NSAIDS), but without the adverse side effects. Studies addressing transient receptor potential ion channels provide further rationale for the use of curcumin instead of NSAIDS. In fact, curcumin has been shown to decrease tumor necrosis factor-alpha (TNF-alpha), as well as cellular mechanisms mediated by inflammatory nuclear factor (NF-kB) (Di Pierro et al., 2015).

### **Statement of Problem**

The interplay between HIIT and curcumin has not been fully explored in healthy, recreationally active populations. Curcumin has been associated with anti-inflammatory and cognitive benefits related to mental health, yet it has not been examined as a dietary supplement during 2 weeks of cycle based HIIT.

### **Rationale for Study**

This study will be directed towards individuals interested in learning more about how curcumin, when coupled with HIIT, may affect performance, recovery, and mental health in moderately active individuals.

### **Purpose for Study**

The purpose of this thesis research project was to examine the effect of 2 weeks of curcumin vs placebo supplementation during HIIT pre to post-intervention. Outcomes included potential improvements related to time trial performance, dolorimetry measures, pain, and mental health.

### **Hypothesis**

It was hypothesized that 2 weeks of curcumin supplementation during HIIT will improve pre to post-intervention time trial performance, decrease muscle soreness and pain and induce greater mental health benefits when compared to a placebo.

## **CHAPTER II**

### **REVIEW OF LITERATURE**

#### **Introduction**

Individuals who participate in intensified training programs such as HIIT experience an increase in the inflammatory response, which may be beneficial acutely, but on a sustained basis, may hinder the body's recovery process, and decrease an individual's tolerance for exercise (Da Silva Machado et al., 2019). Supplements containing curcumin as the primary ingredient, have emerged as compounds aimed at optimizing the inflammatory response by reducing inflammation and possibly attenuating DOMS. (Verdure Sciences, Inc, 2019). Though previous literature has shown that curcumin can attenuate the inflammatory response (He et al., 2015), minimal research has explored whether a curcumin supplementation improves performance during an acute period of intensified training.

In this chapter, an overview of HIIT, mental health and HIIT performance, turmeric, turmeric and health, curcumin, curcumin and health, curcumin and exercise and curcumin and mental health will be examined and will provide support for the present study.

#### **High-Intensity Interval Training**

HIIT is defined as repeated bouts of high-intensity exercise separated by recovery or rest periods (Buckley, Knapp, & Lackie et al., 2015). Each bout of high intensity

exercise can last between 6 seconds to 4 minutes with recovery periods lasting between 10 seconds to 4 minutes (Romain et al., 2018). The target intensity for HIIT is usually between 80 and 100% of maximal oxygen consumption ( $VO_{2max}$ ) or maximal heart rate ( $HR_{max}$ ; Naves et al., 2018). With time being the main excuse for lack of exercise, HIIT has become increasingly popular in recent decades and allows for a more time efficient way to accomplish exercise training (Foster et al., 2015). This intense training is not only popular with healthy and trained individuals, but the concept is now used effectively with populations with metabolic disorders such as type 2 diabetes and obesity (Bogdanis et al., 2013). In addition to aiding in the treatment of metabolic disorders, previous literature has found that following a 2-week HIIT protocol at 90-100%  $VO_{2max}$  may be a safer option for healthy and clinical populations when compared to super maximal intensities greater than 100%  $VO_{2max}$  (Zwetsloot et al., 2014).

The health and performance benefits of HIIT are of popular interest and well-studied by exercise professionals, rehabilitation, and healthcare providers. These benefits include improved aerobic and anaerobic performance, as well as skeletal muscle oxidative capacity (Buckley et al., 2015). HIIT has the potential to improve cardiorespiratory fitness to a greater extent than the current aerobic fitness recommendation of 150 minutes per week at 60% of  $HR_{max}$ . Additionally, this current recommendation may not be sufficient when the program goal is to elicit improvements in cardiorespiratory fitness in sedentary populations (Gibala, 2018). In an examination of the effects of multimodal HIIT (MM-HIIT), Buckley et al. (2015) compared traditional HIIT with HIIT that incorporated additional resistance and conditioning modalities. Following the exercise interventions, both treatment groups experienced improvements in

VO<sub>2</sub>max (Buckley et al., 2015). In another study, 49 healthy women underwent 8 weeks of HIIT consisting of 4 bouts of 4-min efforts cycling at 90-95% of peak heart rate (HR<sub>peak</sub>) with 3 minutes of active recovery at 50-60% during 3 sessions per week. Following the HIIT intervention, participants experienced a 14.5% improvement in peak rate of oxygen consumption (VO<sub>2</sub>peak) (Naves et al., 2018).

While previous literature clearly shows that HIIT improves aerobic capacity, the duration of HIIT interventions may affect cardiovascular fitness and other outcome variables as well. In one study, 12 weeks of HIIT increased aerobic capacity, lowered physiological stress and glycogen concentrations when compared to 6 weeks of HIIT in rats. In contrast, just seven sessions of HIIT in healthy recreationally active women over the span of 2 weeks, increased both VO<sub>2</sub>peak by 13%, and fat oxidation by 36% (Talanian, Galloway, Heigenhauser, Bonen, & Spriet, 2007). From a mechanistic standpoint, a single cycling session of HIIT (30 second bouts with 2-minute intervals, for a total of 16 minutes) increases antioxidant defense mechanisms as measured by decreases in markers of oxidative stress. This study also compared these single session results to a longer-term training regimen with the same protocol spanning 3 weeks with 3 sessions per week. Both programs resulted in similar reductions in markers of oxidative stress (Bogdanis et al., 2013). Overall, short and long-term HIIT is well studied and the evidence remains somewhat consistent regarding their positive impact on whole body physiological parameters (Talanian et al., 2007).

The high neuromuscular and metabolic demands associated with HIIT are linked to feelings of fatigue, which may hinder recovery (Wiewelhove et al., 2016). The muscle damage that hinders recovery and leads to DOMS has symptoms associated with

increased passive stiffness and decreases in strength and power. Symptoms are present post-exercise and usually subside after 3-4 days (Nicol et al., 2015). DOMS is also most associated with eccentric exercise, which causes mechanical stress that triggers a subsequent inflammatory response (Drobnic et al., 2014).

Exercise-induced inflammation is an important mediator of changes in the musculoskeletal and metabolic systems. The myokine, interleukin-6 (IL-6), is an inflammatory cytokine. High circulating serum concentrations are associated with HIIT (Cipryan, 2017). Prolonged aerobic exercise may produce large systemic inflammatory responses, which include elevations in IL-6, which can suppress immune function and increase susceptibility to infections. In contrast, when chronic repeated bouts of the same continuous exercise stimulus occur over a long period of time, the acute inflammatory response associated with one bout of exercise is reduced (Zwetsloot et al., 2014). To summarize, it is generally agreed that HIIT elicits a large inflammatory response, as defined by increases in inflammatory markers such as IL-6 and the muscular inflammation that occurs with DOMS (Wiewelhove et al., 2016; Zwetsloot et al., 2014).

### **Mental Health and High-Intensity Interval Training Performance**

While HIIT is associated with improvements in physiological outcomes such as aerobic and anaerobic performance, there is also evidence of HIIT related improvements in psychological health and quality of life (Romain et al., 2018; Stavrinou, Bogdanis, Giannaki, Terzis, & Hadjicharalambous, 2018). A recent study examined the effects of HIIT on 35 healthy inactive individuals who performed HIIT 2 times a week, 3 times a week, or a non-exercising control group over the course of an 8-week intervention period. The training was performed on a cycle ergometer involving 10 x 60 second cycling

intervals at 83% of peak power output ( $W_{\text{peak}}$ ) with 60 seconds of low intensity cycling between intervals. As expected, the physical health components of  $VO_{2\text{peak}}$ , waist circumference, thigh lean cross-sectional area and physical quality of life were significantly improved in both HIIT groups when compared with the control group. Interestingly, mental health was improved in only the HIIT 3 times a week group. To summarize, this study suggests that a threshold of HIIT 3 times per week may be necessary to induce the mental health benefits (Stavrinou et al., 2018). Similar responses were noted in another study where 90 healthy, inactive individuals participated in a 10-week HIIT or a moderate-intensity continuous training intervention. The HIIT group performed self-selected repeated sprints on a cycle ergometer between 15 and 60 seconds at a  $HR_{\text{max}}$  greater than 90%, with active recovery between 45 and 120 seconds. This group experienced improvements in health perceptions, positive and negative affect, and subjective vitality when compared to the moderate-intensity, continuous exercise training group. Even though HIIT elicits greater levels of immediate fatigue, these findings point to HIIT as a positive experience linked to improvements in both physical and psychological aspects of health (Shepherd et al., 2015).

### **Turmeric**

Nutritional strategies, such as antioxidant rich foods, are used to help regulate inflammation, immune function and oxidative stress, which may be especially important during HIIT (Ortiz-Franco et al., 2017). Ancient and modern cultures have been using medicinal herbs and spices that, to this day, play a pivotal role in the health of people and animals. Plant-based drugs may be more suitable in biochemical terms when compared to

synthetic drugs, although modern medicine does not tend to support natural products for medicinal use (Dias, Urban, & Roessner, 2012).

Turmeric is a spice that has received a great deal of attention over the past few years. Turmeric is obtained from the rhizomatous perennial plant, *Curcuma longa L.*, in the ginger family, Zingiberaceae (Prasad, Gupta, Tyagi, & Aggarwal, 2014). The turmeric plant can grow up to 1 meter high and has tufted, diamond-shaped leaves. The spice is made from the roots, which are boiled, dried, and then ground (Wickenberg, Ingemansson, & Hlebowicz, 2010). Originally turmeric was used as a dye for both skin and clothes (Cooksey, 2017) and was frequently used as a culinary spice in Asian cooking as well as Pakistani, Thai, and Indian cooking (Prasad et al., 2014). Turmeric is also considered a functional food with beneficial properties in supporting health and combating disease. In fact, turmeric has been used medicinally for thousands of years (Kocaadam & Şanlıer, 2017).

Turmeric contains carbohydrate (69.4%), protein (6.3%), fat (5.1), mineral (3.5%), and moisture (13.1%) (Kocaadam & Şanlıer, 2017). It also contains naturally occurring polyphenols that have antioxidant effects. The volatile oil and nonvolatile oleoresin of turmeric comprises diphenylheptanoids, diphenylpentanoids, phenyl propene derivatives, and turmeric oil which are the bioactive components (Nair, Amalraj, Jacob, Kunnumakkara, & Gopi, 2019).

### **Turmeric and Health**

New uses of turmeric shifted from textile dyeing and ancient proposed medicinal properties to exploring potential health effects including anti-carcinogenic, anti-coagulant, anti-inflammatory, antimicrobial, and antioxidant activities (Cooksey, 2017).



The medicinal properties of turmeric over the centuries have many proposed benefits such as aiding in wound healing, allergy, asthma, sinusitis, hepatic disease, and heart disease (Bange et al., 2018). Few studies have examined the whole turmeric root as an agent to help control inflammation or other health concerns. Turmeric by itself is a healthy and safe spice to consume in reasonable amounts (Wickenberg et al., 2010). Side effects that have been observed with individuals include abdominal pain, nausea, constipation, and hot flashes (Amin, Islam, Anila, & Gilani, 2015; Chuengsamarn, Rattanamongkolgul, Phonrat, Tungtrongchitr, & Jirawatnotai, 2014).

### **Curcumin**

Chemists became interested in turmeric during the early 19<sup>th</sup> century. Vogel and Pelletier were the first to discover the yellow colorant component in turmeric, which they named curcumin (Cooksey, 2017). Curcuminoids including curcumin, demethoxycurcumin and bisdemethoxycurcumin are a group of compounds found in turmeric (Moran, Fernandez, Tortosa, & Tortosa, 2016) which have also been approved by the US Food and Drug Administration (FDA) as “Generally Recognized As Safe (GRAS).” The profiles for curcuminoids at doses between 4,000 and 8,000 mg/day are considered safe (Hewlings & Kalman, 2017). Curcumin is found in the rhizome of *Curcuma longa* (turmeric) and is also known as diferuloylmethane. (Moran et al., 2016). Curcumin constitutes 2 to 8% of the turmeric spice (Wickenberg et al., 2010). In one study, 500mg of turmeric contained 22mg of curcumin (Selvi, Sridhar, Swaminathan, & Sripradha, 2015).

## Curcumin and Health

Curcumin has been studied for over 3 decades with numerous identified health benefits related to improvements in the slowing the development and progression of inflammatory diseases, cardiovascular disease, and diabetes (Sahin et al., 2016). For example, when 50 patients with knee osteoarthritis were provided with a commercial compound containing curcumin (Theracurmin) (180mg/day over the course of 8 weeks) or a placebo, knee pain was significantly lower with Theracurmin supplementation when compared to the placebo (Nakagawa et al., 2014). When another product containing curcumin (Algo-cur) was administered in pill form every 12 hours for 5 or 10 days to rugby players suffering from osteo-muscular pain conditions, there were reductions in pain and improved the impaired physical functions compared to the baseline condition (Di Pierro et al., 2017).

Curcumin has also been studied in patients with cardiovascular disease and has been shown to improve serum lipid levels (Qin et al., 2017). Curcumin extract consumption (650mg 3 times daily for 12 weeks) in patients with metabolic syndrome found a lowering effect in low-density lipoprotein cholesterol (LDL) and increased high-density lipoprotein cholesterol (HDL) compared to placebo (Yang et al., 2014). The effects of curcumin are also intriguing with respect to its use for treatment in type 2 diabetes. For example, a curcumin extract (*Curcuma (C.) longa* L. rhizomes, EtOH) at a dose of 0.2/100g or 1.0 g/100g or a control basal diet were fed to Type 2 diabetic KK-A mice for 4 weeks. The supplemented groups were able to resist the increases in blood glucose observed in the control group. These findings may implicate turmeric as a functional food in the amelioration of type 2 diabetes mellitus (Kuroda et al., 2005).

Similar results have been observed in human subjects. For example, the ingestion of 6g of *C longa* increased postprandial serum insulin concentrations at the 30- and 60-minute time points during an oral glucose tolerance test (Wickenberg et al., 2010). Together, these studies, and others, show that curcumin may be effective in controlling circulating blood glucose concentrations and has the potential to slow the progression of type 2 diabetes (Qin et al., 2017; Yang et al., 2014; Kuroda et al., 2005; Wickenberg et al., 2010).

### **Curcumin and Exercise**

As mentioned previously, exercise such as HIIT can increase the inflammatory response and may hinder the body's recovery process (Da Silva Machado et al., 2019). While other supplements have been explored as potential therapeutic targets, curcumin has emerged as an agent with significant potential. One study used curcumin supplementation in a model of exercise-induced muscle damage and found improved recovery time in mice following an eccentric downhill running protocol. Downhill running decreased both treadmill run time to fatigue and voluntary activity, and 10mg of curcumin powder given 3 consecutive days prior to running offset these effects on performance. Lower creatine kinase, IL-6 and TNF-alpha concentrations were also observed in the soleus muscle (Davis et al., 2007). In a similar study, when a turmeric extract (100mg/kg) was administered for 6 weeks to rats, the compound improved endurance time to exhaustion in the exercised group, as well as serum total cholesterol, high-density lipoprotein, triglyceride, and lactate concentrations in both the exercise and non-exercise groups (Sahin et al., 2016).

In human models, other investigators have found that curcumin has the potential to prevent DOMS after downhill running and eccentric leg press exercise (Drobnic et al., 2014; McFarlin et al., 2016). In one study, 20 healthy males took either 200mg curcumin or placebo twice a day for two days prior and 1-day after a 45-minute, constant intensity (lactate 3.5-5 mmol/L) downhill run (grade -10%). The curcumin supplementation group experienced reductions in DOMS-related leg muscle pain at sites located on the anterior right thigh, posterior right thigh, anterior right leg, posterior right leg, anterior left thigh, posterior left thigh, anterior left leg and posterior left leg. Magnetic resonance imaging (MRI) imaging also revealed less muscle injury in the posterior or medial compartment of both thighs. The inflammatory marker, interleukin-8 (IL-8), was also significantly lower 2 hours after the downhill running test when compared to the placebo group (Drobnic et al., 2014). A similar study, involving 28 males/females, who were provided with either a placebo or 400mg/day dose of curcumin, completed eccentric-only dual-leg press exercises and ingested either curcumin or a placebo for 2 days prior to the protocol and 4 days following the protocol. Curcumin reduced creatine kinase at days 1-4 following the eccentric exercise. Additionally, IL-8 was significantly lower in the curcumin group at days 1 and 2 following the exercise, and TNF-alpha was significantly lower in the curcumin group at days 1, 2, and 4, following the exercise when compared to placebo (McFarlin et al., 2016).

Similar effects have been observed with lower doses of curcumin, but some speculate that this may decrease the magnitude of the anti-inflammatory response. When participants ingested 150 mg curcumin before and 12 hours after eccentric contractions of the elbow flexors of one arm on an isokinetic dynamometer, maximal voluntary contraction

torque was preserved and recovery occurred 4 days sooner post-exercise in the curcumin group when compared to a placebo controlled group. Interestingly, no significant differences were found with respect to creatine kinase, IL-6, or TNF-alpha suggesting that a larger dose of curcumin and a greater frequency of consumption on recovery days (post-exercise) may be needed to have greater effects (Tanabe et al., 2015). In a similar study, participants ingested 200mg curcumin and 20 mg piperine 3 times a day, and then completed 25 repetitions of 25 meter, one leg jumps on a downhill slope. Concentric and isometric peak torque for knee extension, one leg 6 second sprint performance, countermovement jump performance, muscle soreness, and creatine kinase concentrations were measured, and results revealed a moderately lower sprint mean power output 24 hours post exercise in the curcumin group compared to the placebo. No other effect was found between the two conditions, and, while this dose is greater than the previous studies, the length of supplementation may have been too short to detect significant differences (Delecroix, Abaidia, Leduc, Dawson, & Dupont, 2017).

Few studies have examined the potential for curcumin to improve endurance performance. Eleven recreational athletes took 500 mg/day of curcumin or placebo in a randomized, cross-over design for 3 days prior to the trial day and on the day of the exercise trial. The trial consisted of 2 hours on a cycle ergometer at a power output of 95% of their lactate threshold. Curcumin was associated with a reduced exercise-induced inflammatory response. More specifically, curcumin was associated with lower IL-6 concentrations one hour following exercise compared to placebo. (Sciberras et al., 2015). Together, these studies suggest that curcumin affects performance and the inflammatory

response over the course of short-term interventions; however, more well controlled investigations are needed in the future.

### **Curcumin and Mental Health**

Curcumin is associated with better cognitive function, memory, as well as less stress and anxiety. In fact, curcumin appears to be comparable with current pharmaceuticals as an adjunctive therapy (Cox et al., 2015). There is recent evidence that supports the use of curcumin as an agent to improve psychological health. In human studies, the most common assessments of psychological health involve the use of questionnaires to quantify the signs and symptoms associated with mental health. For example, participants supplemented with curcumin (3 days prior to the trial day and on the trial day) or placebo and then completed a subjective daily analysis of life demands questionnaire to assess stress sources and stress symptoms prior to the exercise sessions. The curcumin group experienced “better than usual” results on the training days when compared to the placebo on the second day of supplementation (Sciberras et al., 2015). Other questionnaires such as the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory scales can be used as a tool for evaluating symptoms of anxiety and depression. To investigate the effects of curcumin on the frequency of anxiety and depression in obese individuals, participants received 1g/day of a C3 Complex formula of curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin) or placebo for 30 days. Curcumin treatment significantly reduced mean BAI scores compared to placebo suggesting curcumin as an anti-anxiety therapy for individuals with obesity (Esmaily et al., 2015). This work was carried a step further with patients with major depressive disorder. Patients at a psychiatric outpatient department were enrolled in this

study for 6 weeks and were assigned to one of the 3 groups: 20mg/day fluoxetine (n=17), 1000mg/day curcumin (n=10), or 1000mg/day and 20mg/day of fluoxetine (n=18). Following the 6 weeks of treatment, curcumin was equivalent to fluoxetine in terms of change in the Hamilton Depression Rating Scale score and the combination group showed a better response than the fluoxetine and curcumin group alone. These results suggest curcumin may be an effective agent in the treatment of major depressive disorder (Sanmukhani et al., 2014).

Cognition and memory are commonly explored in the older adult population. A computerized test of cognition was used with 22 healthy, older males and 38 healthy, older females and evaluated the potential behavioral effects of curcumin. Participants received either curcumin (400 mg Longvida) or placebo once daily for 4 weeks and completed an array of computerized cognitive tasks that preceded and followed the evaluation of state of mood. A single dose of curcumin acutely improved cognitive processes of performance on a measure of sustained attention and working memory. Sustained attention and fatigue measures were also improved after 4 weeks of curcumin supplementation. These results suggest that curcumin may have positive effects related to cognition in healthy elderly populations (Cox et al., 2015).

### **Summary**

In summary, HIIT produces exercise-induced inflammation that can be mitigated by turmeric. There is a growing body of research that has identified curcumin, which is derived from turmeric, as a beneficial agent for improving athletic performance and the severity of DOMS (Davis et al., 2007; Drobic et al., 2014; Sahin et al., 2016; McFarlin et al., 2016; Tanabe et al., 2015, & Sciberras et al., 2015). Additionally, although HIIT is

associated with physical health outcomes, both curcumin and HIIT are also linked to positive effects related to cognition, major depressive disorder, and fatigue (Sciberras et al., 2015; Esmaily, et al., 2015; De la Fuente, Parra, & Sánchez-Queija, 2017; Cox et al., 2015, & Sanmukhani et al., 2014). Supporting evidence related to curcumin and psychological health are of popular interest and further research is needed to study its underlying mechanisms of action.



## **CHAPTER III**

### **METHODOLOGY**

#### **Participants**

A total of 23 healthy, active individuals (ages 18-40 years), were recruited for this study using flyers, word of mouth, and email communications. Physical activity status was defined as meeting the American College of Sports Medicine guidelines for physical activity defined as at least 150 minutes of moderate-intensity exercise per week, along with or including cycling for the past 3 months (Carlier & Delevoeye-Turrell, 2017). To confirm this status, participants were asked to describe their physical activity status by filling out a questionnaire described in visit 1. Participants also were asked to have previous experience cycling as demonstrated by completing at least 1-2 cycling sessions per week for the past 3 months or participating in a structured exercise routine 2-3 times a week. Curcumin 1 (LG1) and Curcumin 2 (LG2) contained 1,000 mg/day of the curcumin compound, and a Placebo (PL) contained 1,000 mg/day of rice flour. Randomization was used to assign participants to the Curcumin 1 (LG1) (n=9), Curcumin 2 (LG2) (n=7), or Placebo (PL) (n=7) groups. Participants were excluded if they met one or more of the following exclusion criteria: regular tobacco or marijuana use and regular use of anti-inflammatory/analgesic/antioxidant supplements or drugs (at least 3 or more days of a typical week), regular ingestion (> 2 times per week) of turmeric or curcumin containing foods or intake of a turmeric or curcumin supplement (within the past 3 months), if the participant thinks she may be pregnant or knows that she is pregnant, or

has known gallbladder, bleeding, endometriosis, uterine fibroids, iron deficiency conditions or a surgery scheduled within 2 weeks of the study completion, as well as allergies to or the potential for the participant's current supplement or medication program to negatively interact with curcumin as well as allergies to soy, sunflower, rice or seed or nut products, previous injuries or orthopedic conditions, and arthritis or other chronic inflammatory injuries in the past 6 months. All participants were encouraged to check in with their physician to evaluate the potential for curcumin to interact with any prescribed medications prior to participating in this study.

### **Data Collection Procedures**

A study overview is presented in Figure C.1.

#### **Visit 1**

##### **Informed Consent**

Upon arrival to the Exercise Physiology Lab (Room 1610) in Gunter Hall, the participants were provided with an informed consent form and given time to review the document. During this visit, participants were educated on which foods contain turmeric and were asked to avoid those foods for the duration of the study while maintaining their normal diet. Then, they completed the questionnaires below.

##### **Medical Health History and Physical Activity Questionnaires**

All study participants completed a medical history form, current medication and allergy form, and a physical activity readiness questionnaire (PAR-Q). The above screening forms and questionnaires were designed specifically with the participant's health in mind by allowing the researchers to become aware of any potential health issues

that might be exacerbated by the training program, allergy to the products used in the study, and the potential for medication interaction with the products used in this study.

## **Visit 2**

### **Height, Weight and Body Composition Assessment**

Participant height (cm) and weight (kg) was obtained using a stadiometer SECA 220 (Chino, California, USA) and the Detecto standing digital scale (Webb City, Missouri, USA), respectively. Body composition including body weight and percent body fat was measured using air displacement plethysmography (BODPOD (COSMED USA Inc., Concord, CA)). Participants were instructed to arrive wearing lycra/spandex shorts (men), or a sports bra and spandex shorts or one-piece bathing suit (women). All participants were asked to remove all jewelry and glasses, and were given a lycra swim cap to wear over their hair. Participants were also instructed to wear the same clothing for all testing procedures, and to avoid consuming food or drink 3 hours prior to testing. All testing was carried out at approximately the same time of day to account for circadian changes in fluid and fecal matter. The BODPOD was calibrated before each test according to the manufacturers' instructions (Cholewa et al., 2018).

### **VO<sub>2</sub>max Exercise Test Protocol**

Participants completed a maximal exercise test protocol on a Monark cycle ergometer (Ergomedic 894E, Monark, Vansbro, Sweden). Oxygen consumption was measured using TrueOne 2400, ParvoMedics, (Sandy UT). The TrueOne 2400 was calibrated prior to each participant's testing session. In order to obtain accurate instantaneous power outputs, the cycle ergometer was fitted with an electronic tachometer to measure crank revolutions per minute (rpm) and a strain gauge to measure

the friction belt tension. The ergometer seat height was individually adjusted to attain an almost fully extended leg (about a 5-degree bend in the knee) at the lowest point in the pedal revolution. Resting lactate measures were obtained by puncturing the participant's finger with a lancet. The first drop of blood was removed with a clean non-alcohol wipe and the strip was placed into the lactate analyzer. Once the screen was on, the second drop of blood was placed at the end of the strip and the measurement was recorded. Participants began the test with a 5-minute warm-up at a workload of 0.5 kiloponds (kp) with a pedaling cadence of 60 revolutions per minute (rpm). Following warm-up, the test began, and participants were required to ride at 75-85 rpm throughout the entirety of the test. The test began at a workload of 0.5kp. Every 3 minutes, resistance was increased by 0.5kp until  $\geq 4$  mMol of blood lactate was obtained. Once blood lactate reached 4mMol, the stage time and increments of workload decreased from 0.5kp every 3 minutes, to 0.2kp every 1 minute (Ziemann et al., 2011). During the test, heart rate was constantly monitored, with blood pressure, rate of perceived exertion (RPE), and blood lactate monitored every 3 minutes. Participants began a prescribed cooldown, which consisted of cycling for 5-minutes at 60 rpm or lower with a 0.5kp workload. Participants HR and blood pressure was continuously monitored throughout cooldown until values return within normal resting ranges. At least 3 days after Visit 2, participants returned to the lab for the following assessments.

### **Visit 3**

#### **Mental Health Assessment**

The Flourishing Scale is a brief eight-item summary measure of self-perceived success in areas such as relationships, self-esteem, purpose, and optimism. Participants

answered a seven-point scale (1 = strongly disagree to 7 = strongly agree) as to how much the participant agreed with each statement relating to indicators of social well-being (e.g., I lead a purposeful and meaningful life). The scale provides a single psychological well-being score. This composite score is created by summing the scores for each item (possible range, 8–56) (De la Fuente et al., 2017). A higher score indicates greater psychological well-being in mental health (Schotanus-Dijkstra et al., 2016).

### **Dolorimetry and Pain Questionnaire**

Participants received an explanation of the pain questionnaire and dolorimetry measures that were administered before, during, and after the time trial. Pain intensity was assessed using a 0-10 category scale with ratio properties and verbal anchors associated with the following numbers: 0 no pain at all, 0.5 very faint pain (just noticeable), 1 weak pain, 2 mild pain, 3 moderate pain, 4 somewhat strong pain, 5 strong pain, 7 very strong pain, and 10 extremely intense pain (almost unbearable). No verbal anchors were given in associated with numbers 6, 8, and 9 (Cook, O'Connor, Oliver, & Lee, 1998).

Baseline measures of leg muscle pain and trigger point tenderness were measured with a handheld dolorimeter (Baseline, White Plains, NY) prior to the time trial. The dolorimeter has a maximal range of 11 kg with 100-g divisions. Measurements were made at approximately the mid-point of four muscles: the vastus lateralis, vastus medialis, medial head of the biceps femoris, and lateral head of the biceps femoris. These points were marked and remarked after each measurement over the same point each time. All measurements were taken from the participant's dominant leg. The dolorimetry measures involved providing the following verbal instructions to each participant: "I am

going to measure pressure threshold; that is, how much pressure will induce discomfort. I am going to increase pressure slowly with this device. Say “Yes” when you start to feel pain or discomfort. I will stop the pressure as soon as you say “Yes,” so it will not hurt you. It is important that you understand that this is a test of sensitivity, not a test of endurance. Do you understand or have any questions?’ (Miller, Bailey, Barnes, Derr, & Hall, 2004). After the explanation is given, the dolorimeter was placed exactly over the indelible mark and perpendicular to the muscle under observation. Pressure was increased continuously 1 kg per second until the participant says ‘Yes’. At this time, the pressure was stopped, the meter was removed from the skin, and the measurement recorded. The same measures were obtained following completion of the time trial (Miller et al., 2004).

The following instructions were given for the pain questionnaire prior to the time trial at mile 0 and at mile 9.3:

You are about to undergo a time trial test. The scale before you contains the numbers 0 to 10. You will use this scale to assess the perceptions of pain in your legs now, at rest, and during the test. For this task, pain is defined as the intensity of hurt that you feel in your leg muscles only. Don’t underestimate or overestimate the degree of hurt you feel, just try to estimate it as honestly and objectively as possible. The numbers on the scale represent a range of pain intensity from “very faint pain” (number 1/2) to “extremely intense pain—almost unbearable” (number 10). When you feel no pain in your legs, you should respond with the number zero. When the pain in your legs becomes just noticeable, you should respond with the number 1 or 2. If your legs feel extremely strong pain that is almost unbearable, you should respond with the number 10. You can also

respond with numbers greater than 10. If the pain is greater than 10, respond with the number that represents the pain intensity you feel in relation to 10. In other words, if the pain is twice as great then respond with the number 20. Repeatedly during the test, you will be asked to rate the feelings of pain in your legs. When rating these pain sensations, be sure to attend only to the specific sensations in your quadriceps and not report other pains you may be feeling (e.g., seat discomfort). It is very important that your ratings of pain intensity reflect only the degree of hurt you are feeling in your legs. Do not use your ratings as an expression of fatigue (i.e., inability of the muscle to produce force) or exertion (i.e., how much effort you are putting into performing the exercise (Cook et al., 1998).

### **Time Trial (16.1km) Test**

Participants completed the 16.1km (10 mile) time trial test on the cycle ergometer (SC3 Stages Indoor Cycling, Boulder, CO). A warmup of 10 minutes at 60-75 rpms was required. Participants received no feedback on his or her performance during or after either time trial. A cool-down of 5 minutes similar to the warmup was immediately completed following the completion of the time trial.

### **Visits 4 and 5**

#### **Pre Intervention, Post Time Trial, Dolorimetry Measure, Pain and Mental Health**

After the time trial (24 hours later), participants returned to lab to be evaluated using the mental health and pain questionnaires as well as the dolorimetry protocol described above in Visit 3. After (48 hours following) the time trial, participants returned to the lab and complete the same assessments visit 4.

## **Intervention Period**

### **Supplement and High-Intensity Interval Training Cycle Training**

Following visits 1-5, all participants were required to visit the UNC Campus Recreation Center on 3 nonconsecutive days per week for 2 weeks to perform the HIIT. All HIIT were performed on a cycle stages bike (SC1, Boulder, CO). Participants began each training session with a 5-minute warm-up at an intensity of approximately 50-60% of their VO<sub>2</sub>max measured by HR. Six 90-second cycling bouts at 80-90% VO<sub>2</sub>max using heart rate and were performed. Each 90-second bout was followed by 180 seconds of active recovery at 50-60% for a work-to-rest ratio of 1:2. Participants cooled down for 5 minutes until HR returns to normal resting values. Participants were provided with a training log to record any structured exercise that is completed in addition to the structured training (Ziemann et al., 2011).

### **Curcumin/Placebo Supplementation**

A proprietary curcumin supplement was used for the study. Participants were provided with one of the supplements consisting of 1000 mg of Curcumin 1 (LG1) or Curcumin 2 (LG2) or 1000 mg of rice flour (PLC) in the form of pills to ingest daily for the entire 2 weeks of HIIT. All participants were instructed to take them every morning with food and water and recorded in a food log.

### **Visit 7**

After the Intervention period, participants returned to the lab to complete the same time trial test described in Visit 3



## **Visit 8 and 9**

### **Post Intervention Period, Post Time Trial Measures**

After the TT (24 hours later and 48 hours later), participants returned to the lab and completed the same assessments described in visit 4.

### **Analysis**

All participant data was collected and entered into the Microsoft Teams Excel program. Data was analyzed using statistical package for the social sciences (SPSS) (SPSS, Inc, Chicago, III). Means and standard deviation was calculated for all major outcome variables. Data was then averaged for each group and a two-way multiple analysis of variance (MANOVA) was used to determine whether time trial performance, dolorimetry, pain questionnaires, or mental health were affected by curcumin supplementation. Significance was set at  $\alpha = 0.05$ .

## **CHAPTER IV**

### **RESULTS**

A total of 23 participants (n= 14 females, n=9 males) were randomly assigned to one of three groups; LV1 (n=9), LV2 (n=7) or PL (n=7). Participant age ranged from 18 to 40 years old. There were no differences with respect to age, height, weight, body mass index, percent body fat, or relative VO<sub>2</sub>max at the pre intervention time point (Table 1.).

#### **Time Trial Performance (16.1km)**

Time trial performance averages were  $30.33 \pm 3.85$  minutes for LV1,  $31.53 \pm 5.88$  minutes for LV2 and  $31.55 \pm 5.93$  minutes for PL (Figure 2.). The average times for each group pre- and post-intervention are presented in Figure 2. There were no differences with respect to 16.1 km time trial performance among groups at the pre intervention time point. Additionally, there were no time or supplement main effects or interactions when comparing treatment before and after the intervention.

#### **Dolorimetry**

Dolorimetry measures are presented in Table 2. Values ranged from 2.3 to 10 and there were no significant differences at the pre intervention time point among the groups or with respect to treatment or time in any of the regions of the dominant leg (VL, VM and MHBF and LHBF) as presented in Table 2.

### **Pain Questionnaire**

Overall pain scores ranged from 0.00 to 10.00 across all treatment groups. When all groups were combined, pain scores at mile 9.3 were higher compared to pain scores at mile 0 ( $p=0.01$ ). A trend of significance between LV1 and LV2 at mile 9.3 was found ( $p=0.059$ ) (Table 3).

### **Mental Health Assessment**

There were no differences with respect to Flourishing scale score among the groups at the pre intervention time point or as a result of the intervention with respect to treatment group or time. Average scores were  $49.94 \pm 4.58$  for LV1,  $52.21 \pm 3.46$  for LV2 and  $53.29 \pm 2.73$  for PL (Figure 3.). When all groups and time points were combined, Flourishing scale score totals ranged from 49.22 to 54.

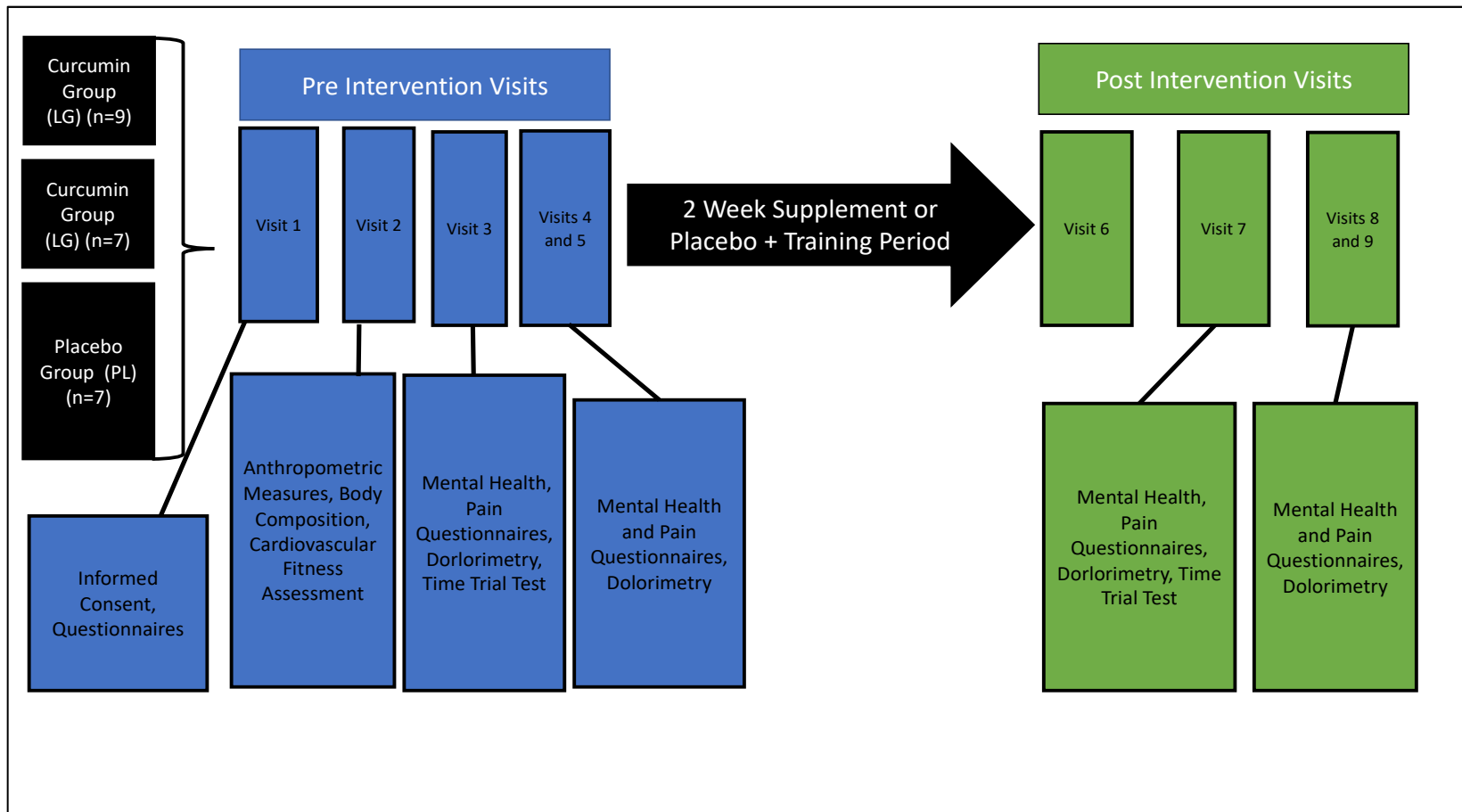


Figure 1. Study Overview

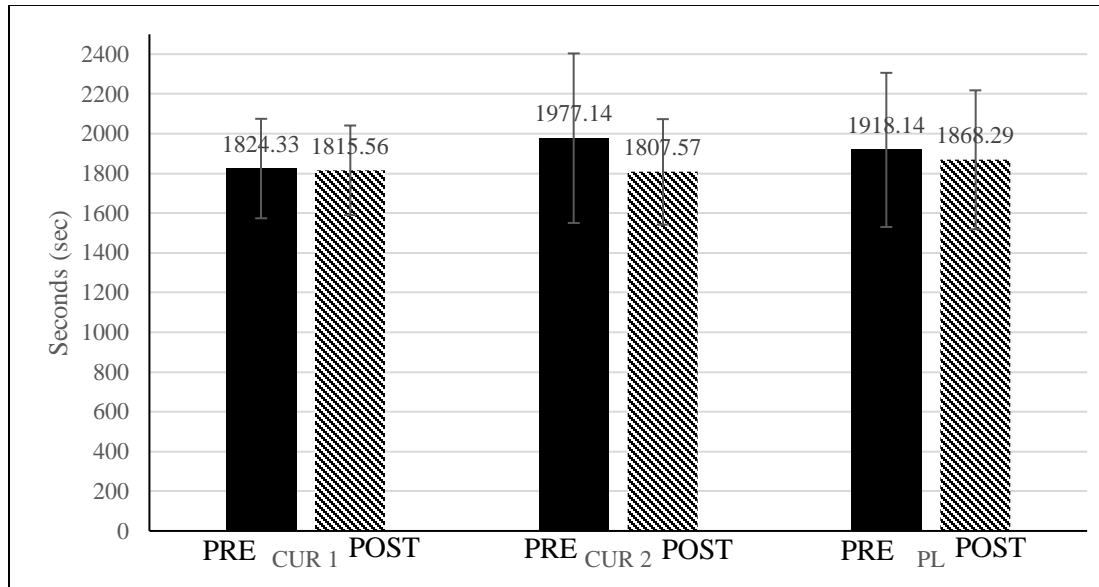
LV1: Curcumin 1 (n=9); LV2: Curcumin 2 (n=7); PL: Placebo (n=7).

Table 1.

*Participant Characteristics*

Participant Characteristic	Overall	LV1	LV2	PL
	(n=23)	(n=9)	(n=7)	(n=7)
Age (years)	25 ± 4.4	25 ± 4.9	25 ± 4.4	24 ± 4.2
Height (cm)	170.43 ± 10.36	170.24 ± 10.49	172.53 ± 11.72	166.85 ± 9.33
Weight (kg)	67.04 ± 10.34	70.20 ± 12.39	67.26 ± 9.61	62.76 ± 7.68
Body Mass Index (kg/m <sup>2</sup> )	23.0 ± 2.04	23.66 ± 1.86	22.61 ± 2.43	22.5 ± 1.90
Body Fat (%)	20.55 ± 7.46	17.47 ± 9.33	22.11 ± 5.50	22.96 ± 5.82
Relative VO <sub>2</sub> max (ml/kg/min)	44.13 ± 8.53	46.73 ± 5.87	41.64 ± 6.45	43.26 ± 12.69

*Note:* LV1: Curcumin 1; LV2: Curcumin 2; PL: Placebo. Values are presented as mean ± standard deviation. There are no main effect or interactions. There are no significant differences present.



*Figure 2.* Time Trial Performance (16.1km) Before and After HIIT Training.

LV1: Curcumin 1 (n=9); LV2: Curcumin 2 (n=7); PL: Placebo (n=7). Values are presented as mean  $\pm$  standard deviation. There are no significant differences present.

Table 2.

*Dolorimetry  
Measures*

	LV1 (n=9)	LV2 (n=7)	PL (n=7)
VL, VM-Pre TT <sub>1</sub>	6.18 ± 2.41	5.88 ± 2.23	7.27 ± 1.89
VL, VM-Post TT <sub>1</sub>	5.97 ± 1.64	5.14 ± 1.56	5.89 ± 2.29
VL, VM-48 TT <sub>1</sub>	7.13 ± 0.72	5.37 ± 0.88	6.99 ± 0.81
VL, VM-Pre TT <sub>2</sub>	5.97 ± 1.64	5.14 ± 1.56	5.89 ± 2.29
VL, VM-Post TT <sub>2</sub>	6.26 ± 1.76	4.78 ± 1.25	5.50 ± 2.53
VL, VM-48 TT <sub>2</sub>	5.70 ± 1.88	4.62 ± 0.92	6.21 ± 2.31
MHBF, LHBF-Pre TT <sub>1</sub>	6.39 ± 2.56	6.01 ± 1.98	7.55 ± 1.12
MHBF, LHBF-Post TT <sub>1</sub>	6.26 ± 1.76	4.78 ± 1.24	5.50 ± 2.53
MHBF, LHBF-48 TT <sub>1</sub>	7.38 ± 0.73	5.79 ± 0.90	7.00 ± 0.83
MHBF, LHBF-Pre TT <sub>2</sub>	6.48 ± 2.42	5.64 ± 1.56	6.41 ± 2.44
MHBF, LHBF-Post TT <sub>2</sub>	6.63 ± 1.98	5.66 ± 1.59	5.93 ± 2.56
MHBF, LHBF-48 TT <sub>2</sub>	6.63 ± 2.11	5.64 ± 0.78	7.34 ± 2.78

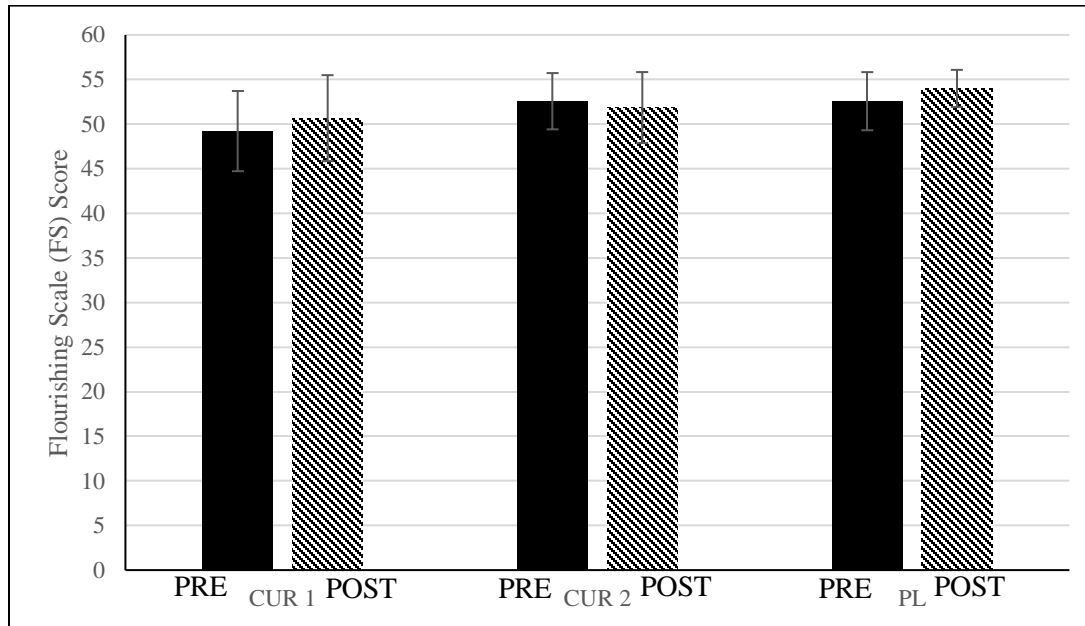
*Note:* LV1: Curcumin 1; LV2:Curcumin 2; PL: Placebo; VL: Vastus Lateralis; VM: Vastus Medialis; MHBF: Medial Head of Biceps Femoris; LHBF: Lateral Head of Biceps Femoris; Pre TT<sub>1</sub>: pre initial time trial; Post TT<sub>1</sub>: post initial time trial; 48 TT<sub>1</sub>:48 hrs post initial time trial; Pre TT<sub>2</sub>: pre time trial 2; Post TT<sub>2</sub>: post time trial 2; 48 TT<sub>2</sub>:48 hrs post time trial 2; All values are measured in kg/cm<sup>2</sup> on a scale 0-10. Values are presented as mean ± standard deviation. There were no significant differences present.

Table 3.

<i>Pain Measures</i>	LV1 (n=9)	LV2 (n=7)	PL (n=7)
PQ0 <sub>1</sub>	0.11 ± 0.33	0.00 ± 0.00	0.29 ± 0.49
PQ9 <sub>1</sub>	4.94 ± 3.11	4.71 ± 2.14	4.86 ± 3.02
PQ0 <sub>2</sub>	0.11 ± 0.22*	0.14 ± 0.38*	0.14 ± 0.24*
PQ9 <sub>2</sub>	6.28 ± 3.01*	3.57 ± 2.44*	4.14 ± 2.54*

*Note:* LV1: Curcumin 1; LV2: Curcumin 2; PL: Placebo; PQ0<sub>1</sub>: Initial Pain Questionnaire at time point 0 mi; PQ9<sub>1</sub>: Initial Pain Questionnaire at time point 9.3 mi; PQ0<sub>2</sub>: Post Pain Questionnaire at time point 0 mi; PQ9<sub>2</sub>: Post Pain Questionnaire at time point 9.3 mi; Values are presented as mean ± standard deviation. \*Significant difference found between the groups of PQ0 and PQ9.





*Figure 3.* Mental Health Assessment

LV1: Curcumin 1 (n=9); LV2: Curcumin 2 (n=7); PL: Placebo (n=7); FS: Flourishing Scale 0-56; Values are presented as mean  $\pm$  standard deviation. There are no significant differences among groups or times are present.

## CHAPTER V

### DISCUSSION AND CONCLUSIONS

The main purpose of this study was to explore the effects of curcumin supplementation over the course of 2-weeks of intensified HIIT. It was hypothesized that when curcumin was taken in conjunction with HIIT, there would be an improvement in pre to post-intervention time trial performance, dolorimetry measures, pain and mental health when compared to placebo. The results of this study did not show statistically significant differences with respect to trial performance, dolorimetry measures, pain questionnaires and mental health. Therefore, we reject our initial hypotheses.

The groups overall were similar in that they did not differ significantly with respect to age, height, and weight. There were also no observed differences in body mass index (BMI) or percent body fat between the groups. The overall average percent body fat was  $20.55 \pm 7.46$  which places them in a moderately lean body fat category for males and a lean body fat category for females. Moderately lean is defined as fat composition that is generally acceptable for good health and lean suggests body fat levels are lower than many people and generally excellent for health and longevity (BOD POD). Previous literature has also suggested that curcumin may be a possible anti-obesity compound. When mice were fed a high fat diet for 23 weeks and then underwent caloric restriction and received curcumin and piperine, they lost more fat than the ad libitum group (Miyazawa et al., 2018). Another study explored the effects of curcumin and patients

with pancreatic cancer. The patients who received curcumin experienced greater losses in fat and muscle mass compared to the control group (Parsons et al., 2016). Although body weight and fat loss may not be entirely desirable in all cancer cases, this study points to the ability of curcumin to alter body weight and composition. Although contradictory to our current study, these studies used mice and unhealthy patients, while our study was comprised of healthy, active individuals. This, coupled with the short intervention time period, could explain why we did not observe any differences with respect to body weight or body composition between the groups as a result of the intervention.

### **Time Trial Performance (16.1 km)**

Relative  $VO_{2max}$  was also not significantly different among the groups and the average  $VO_{2max}$  of the participants placed them in the average category with respect to cardiorespiratory fitness according to ACSM  $VO_{2max}$  normative data (Thompson, Arena, Riebe, & Pescatello, 2013). The current study used a 2-week HIIT protocol and 16.1km time trials were used to assess performance before and after the intervention. The HIIT protocol did not produce significantly faster times pre to post-intervention in either the curcumin or placebo groups. It appeared that the intervention was improving the times of some individuals, but not others. This increased the variability and made it harder for us to detect a training-induced performance effect. Consequently, increasing the number of subjects in each group may help to fully elucidate whether or not the HIIT was effective.

Other research using a 16.1 km cycling time trial performance test was able to detect significantly faster times after ingestion of beetroot juice than in the placebo trial in trained cyclists. (Muggeridge et al., 2013). A similar study that also involved a 16.1

km time cycling time trial test had participants supplement with acetaminophen or placebo. Results revealed significantly faster times with acetaminophen compared to placebo with trained male cyclists (Jones & Williams, 2010). While these studies did not include a HIIT protocol between the time trials, they demonstrate the potential for the time trials used in our study to detect a meaningful performance difference.

The present study did not find significant improvements in time trial performance after the 2-week training period. The protocol included training 3 times a week for 2 weeks, with 6 second sprints of 90 seconds with 3 minutes of passive recovery. Previous literature has shown that a cycling protocol of 4-6, 15-second cycling sprints with 2-minute active recovery at 40%  $\text{VO}_2\text{peak}$  or 4-6, 30-second sprints with 4-minute recovery at 40%  $\text{VO}_2\text{peak}$  twice a week for 9 weeks will improve with a 10 km cycling time trial performance. The training groups also increased their sprint load with time (Yamagishi & Babraj, 2017). Our current study trained individuals for 2-weeks in a total of 6 sessions, compared to previous study which trained for a total of 18 sessions. Our work to rest ratio was also 1:2, while the previous study used a 1:8 ratio. With more intense training, a longer rest period and continual increases in training load, our results may have been different. Another study that used a 2-week cycle training protocol of 3 times a week with 30 second sprints with 4 minutes of rest against a resistance of 0.075 kg/kg body mass with the number of intervals increasing from 4 to 7 over the first 5 sessions and 4 intervals on the final session. Results revealed a significant improvement in cycling time to exhaustion (Burgomaster, Hughes, Heigenhauser, Bradwell, & Gibala, 2005). While our study also included 2-weeks of training, our work to rest ratio included shorter rest periods and the previous study included increasing the intensity of the training sessions

over the course of multiple weeks. Future research should consider increasing load or session number in order to potentially detect more significant improvements.

The curcumin treatment did not appear to significantly effect performance times. Previous literature on endurance performance and curcumin supplementation is limited, and much of the research has only been conducted with animals, making it difficult to translate to human studies. In a study that evaluated exercise performance and physical fatigue, curcumin was administered to 4 groups of mice which received 0, 12.3, 24.6 or 61.5 mL/kg/day by oral gavage for 4 weeks. The mice were tested with a swimming exercise performance test and the curcumin treated groups had significantly longer swimming times to fatigue when compared to control (Huang et al., 2015). Our current study used cycling 16.1km to assess endurance capacity; however, this is not directly related to other endurance performance tests, such as swimming. While there were no significant differences among the groups with regard to cycling performance times, these findings raise questions related to curcumin supplementation dose and the length of intervention time as well. The previous study used the doses of curcumin based on a human weight of 60 kg for 4 weeks (Huang et al., 2015). Our current study was only 2 weeks in duration, which could explain our results.

### **Dolorimetry**

Measures of muscle soreness as evaluated using dolorimetry were not different among the groups at pre, post, and 48 hours post time trial before and after the intervention. Pressure algometers, which include dolorimeters like the one used in this study, are used to measure pressure pain thresholds and maybe influenced by factors including the sex of participant and inter-observer reproducibility (Park, Kim, Park, Kim,

& Jang, 2011). Pressure algometers commonly have a 1-cm<sup>2</sup> pressure application surface and should be perpendicular to the body surface with a 1 kg\*cm<sup>-2</sup> \* s<sup>-1</sup>. Applications of force that are faster or slower may result in a false reading (Kinser, Sands, & Stone, 2009). Pressure algometers have also been used in a study in which trained individuals completed a half marathon. Soreness between the groups was different over time in the medial quadriceps (Levers et al., 2016). Another study did not find any significant differences quadriceps algometer measures after downhill running (Pumpa, Fallon, Bensoussan, & Papalia, 2012).

### **Pain Questionnaire**

As expected, there were statistically significant differences when pre- trial pain (mile 0) was compared to mile 9.3 pain when the groups were combined. This shows that there is more leg pain during the trial. Pain was evaluated using a 0-10 scale and participants were told that pain is defined as “the intensity of hurt that you feel in your leg muscles only and to not underestimate or overestimate the feeling (Cook et al., 1998).” Although pain is a very subjective measure, participants were asked to only focus on sensations in their quadriceps and not report other pains they may be feeling (e.g., seat discomfort). Additionally, they were told not to use their ratings as an expression of fatigue (i.e., inability of the muscle to produce force) or exertion (i.e., how much effort they are putting into performing the exercise) (Cook et al., 1998). Previous research has also used other available measures for pain as it relates to the whole body or to leg specific pain. One study examined psychological measures during submaximal cycling and participants were also given instructions on how to rate feelings of pain in the legs and asked not to focus on sensations from other parts of the body (Duncan & Hankey,

2013). Another study used a 0-10 scale to determine leg pain in a 10 km cycling time trial (Astorino, Cottrell, Lozano, Pratt, & Duhon, 2012). Both studies were able to detect significant differences in leg pain over the course of cycling time trials. Less pain with curcumin supplementation has also been observed 48 hours after a downhill running protocol in the lower limb compared with participants taking a placebo, and a significant difference was found for the right and left anterior thighs (Drobnic et al., 2014). Although not endurance performance specific, curcumin supplementation has been associated with moderate to large reductions in single-leg squat and gluteal stretch pain with a visual analog scale (VAS) at 24- and 48-hours post-eccentric exercise (Nicol et al., 2015).

It is important to note that other non-exercise related assessments such as a VAS have been used to assess pain during curcumin treatment in clinical environment. For example, participants with acute pain related to chronic disease taking either curcumin (Meriva), nimesulide, or acetaminophen experienced a significant reduction in pain perception (estimated on a 5-point VAS) observed after 2 hours of ingestion, with a slightly lower analgesic effect overall in the curcumin group when compared to the other two drugs (Di Pierro et al., 2013). In a longer, more intensive study, 8 weeks of curcumin (180mg/day) revealed lower VAS scores in patients with knee osteoarthritis compared to placebo (Nakagawa et al., 2014). Short-term (10 days) of a curcumin treatment with Algocur, decreased pain that was observed in rugby players with persistent osteo-muscular pain. A VAS (0= none, 10= intolerable) and *functio laesa* (0= complete physical function, 10= maximum impairment of physical function) were used to assess pain and found significant improvements at day 3, 6, 10, and 20 from the initial treatment

in participants with both compounds compared to the condition at baseline. These results potentially support the anti-inflammatory effects of a curcumin (Di Pierro et al., 2017).

In conclusion, it is possible that the pain measure used in this study was not comprehensive enough. Future studies may also want to employ a more pain inducing protocol, such as a Biodex. Furthermore, it is also possible that the curcumin dose and length of supplement intervention in the current study was not sufficient to induce any measurable pain related differences.

### **Mental Health Assessment**

The current study did not find differences with respect to the Flourishing Scale score among the groups. The Flourishing scale is a strong subjective measure of well-being (De la Fuente et al., 2017). High scores on the scale indicate a greater level of flourishing. The Flourishing Scale is widely used in clinical practice and well-being intervention studies, most likely due to its brevity, comprehensiveness, and simplicity (Schotanus-Dijkstra et al., 2016). In our study, the Flourishing scale scores are in the higher ranges (LV1, 49.94; LV2, 52.21 and placebo, 53.29); however, it is important to note that since our sample consisted of mainly college-aged students, this may not be representative of a general population.

### **Limitations**

Although the need for more research in this area was a strong motivator for this study, there were several limitations. The small sample size was a major limitation, which makes drawing conclusions difficult. Since the sample consisted of healthy college-aged students with an average of 25 years, both health status and age can be limiting factors when applying these findings to the general population.



The inability to control for diet is another observed limitation. While participants completed a diet log, there were no other restrictions. Participants were required to record their food intake 24 hours before visits 1 and asked to eat the same meals in the 24 hours prior to visit 6. Participants were asked to avoid making changes to their diet and to maintain their regular food intake during the 2-week intervention period, but this was only measured with three-day food logs which were not included in the scope of this thesis. It is important to note that diets with anti-inflammatory and antioxidant foods can be a confounding factor with respect to muscle recovery, performance, and pain (Serafini & Peluso, 2016).

The daily physical activity of the participants was subjective to each person, and not controlled for in this study. The participants were asked to maintain their current exercise/workouts given that they do not do any unordinary or unfamiliar activity that would cause soreness. While these instructions were given to each participant, the type of workouts/exercise each person completed was not recorded. Lack of control in this area could be a factor in the ability of the participant to perform and respond to the protocol throughout the study.

### **Recommendations for Future Research**

The evaluation of natural products aimed at improving athletic performance has grown rapidly over the past few decades. As physically active individuals are turning more toward natural foods, curcumin is becoming of popular interest. Given the nature of the current study, future studies may want to consider examination of dietary habits and other daily physical activity status of the participants as well as the dose and duration of a curcumin intervention.

## **Conclusion**

To our knowledge, there is a small body of research, which explores the relationship on the beneficial performance related effects of curcumin. The current study examined the effects of curcumin supplementation during 2-weeks of intensified HIIT. In this small pilot study, oral curcumin administration, when coupled with HIIT, was not related to significant improvements in time trial performance, dolorimetry, pain, or mental health.

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**APPENDIX A**

INSTITUTIONAL REVIEW  
BOARD APPROVAL



*Institutional Review Board*

DATE:

TO: FROM:

PROJECT TITLE: SUBMISSION TYPE:

ACTION: APPROVAL DATE: EXPIRATION DATE: REVIEW TYPE:

February 12, 2019

Laura Stewart, PhD  
University of Northern Colorado (UNCO) IRB

[1367831-3] The Effects of Combined Curcumin (Longvida) Supplementation and High Intensity Interval Training (HIIT) on Cycling Time Trial Performance

Amendment/Modification

APPROVED February 12, 2019 January 22, 2020 Expedited Review

Thank you for your submission of Amendment/Modification materials for this project. The University of Northern Colorado (UNCO) IRB has APPROVED your submission. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on applicable federal regulations.

Please remember that informed consent is a process beginning with a description of the project and insurance of participant understanding. Informed consent must continue throughout the project via a dialogue between the researcher and research participant. Federal regulations require that each participant receives a copy of the consent document.

Please note that any revision to previously approved materials must be approved by this committee prior to initiation. Please use the appropriate revision forms for this procedure.



All UNANTICIPATED PROBLEMS involving risks to subjects or others and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office.

All NON-COMPLIANCE issues or COMPLAINTS regarding this project must be reported promptly to this office.

Based on the risks, this project requires continuing review by this committee on an annual basis. Please use the appropriate forms for this procedure. Your documentation for continuing review must be received with sufficient time for review and continued approval before the expiration date of January 22, 2020.

Please note that all research records must be retained for a minimum of three years after the completion of the project.

If you have any questions, please contact Nicole Morse at 970-351-1910 or [nicole.morse@unco.edu](mailto:nicole.morse@unco.edu). Please include your project title and reference number in all correspondence with this committee.

Dr. Stewart –

Thank you for the thorough and exceptionally clear amendments/modifications to your study protocols and documentation (informed consent and flyer). Please add a space for participants to initial every page of the informed consent form prior to the signature page (e.g., Page 1 of 8 \_\_\_\_\_ please initial, Page 2 of 8 \_\_\_\_\_ please initial, etc.) before further use in your research. Otherwise, these materials and protocols are approved for use in your research. Best wishes with your research and don't hesitate to contact me with any IRB-related questions or concerns.

Sincerely,  
Dr. Megan Stellino, UNC IRB Co-Chair

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within University of Northern Colorado (UNCO) IRB's records.

**APPENDIX B**

INFORMED CONSENT

# UNIVERSITY OF NORTHERN COLORADO

## Consent Form For Human Participants in Research

### Title: The Effects of Combined Curcumin (Longvida) Supplementation and High Intensity Interval Training (HIIT) on Cycling Time Trial Performance

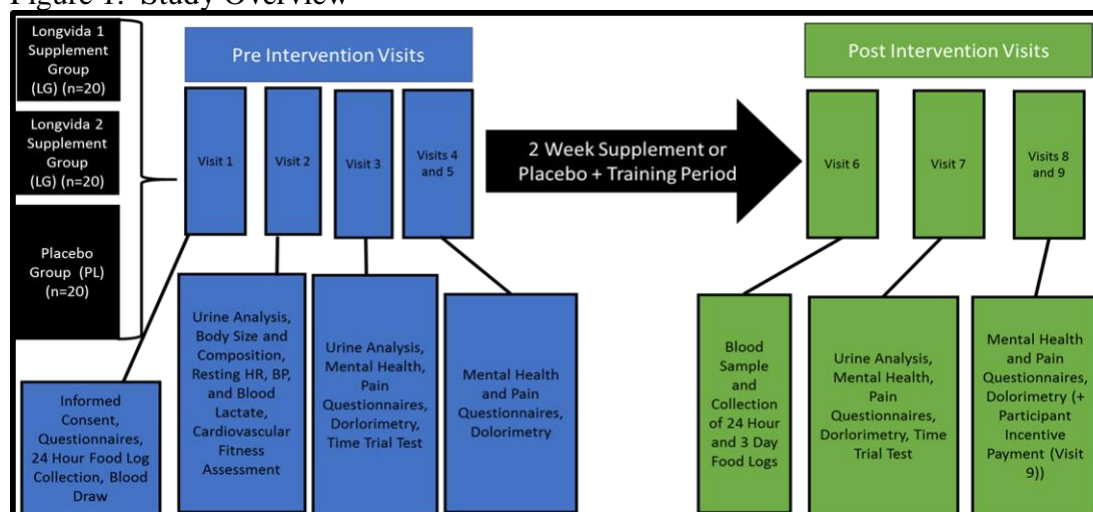
**Researcher:** Laura K. Stewart, PhD, Professor, School of Exercise Sport Science:  
Email: [laura.stewart@unco.edu](mailto:laura.stewart@unco.edu) Phone: 970-351-1891 (office)

**Student Researcher:** Nora J. Johnston, MS student, School of Exercise Sport Science:  
Email: [john9662@bears.unco.edu](mailto:john9662@bears.unco.edu) Phone: 715-651-6543

#### A. PURPOSE

Though previous literature has shown curcumin's ability to control the immune response, minimal research has explored whether curcumin supplementation improves performance during an acute period of intensified training. *Given the current research on the beneficial health effects of curcumin, the specific aim of this study is to explore the relationship between curcumin supplementation (Longvida) over 2-weeks of intensified, HIIT training.* This study will assess your performance and recovery with cycling, dietary information, and mental health. Visits will range in duration of 10 to 60 minutes, with a total anticipated time commitment of about 5 hours. The structure of the visits is outlined below in Figure 1.

Figure 1. Study Overview



## B. DATA COLLECTION PROCEDURES

### Visit 1: (30 minutes)

#### *Informed Consent*

Upon arrival to the Exercise Physiology Lab (Room 1610) in Gunter Hall, you will be provided with an Informed Consent form and given time to review the document. The investigator will explain the experimental protocol and answer any questions you may have. You will be educated on which foods contain turmeric and will be asked to avoid those foods for the duration of the study while maintaining your normal diet. Then you will complete the following questionnaires:

#### *Medical Health History and Physical Activity Questionnaires*

You will be given a Medical History Form, Current Medication and Allergy Form, and Physical Activity Readiness Questionnaire (PAR-Q) to complete. **Please answer these questions honestly. If you have any known allergies to soy, seeds, nuts, turmeric or curcumin products, you may not participate in this study. If have any diagnosed chronic (diabetes, cardiovascular disease, cancer, etc), orthopedic condition, or if you think that you might be or plan to become pregnant, you may not participate in this study. If you are taking any medications prescribed by your doctor, we ask that you consider gaining approval to participate in this study.**

#### *Food Log*

You will be required to record your food intake 24 hours before visits 1 and 6. During the intervention period, you will be asked to record your diet on 2 additional days for a total of 2 week days (Monday-Friday) and 1 weekend day (Saturday or Sunday). We ask that you avoid making changes to your diet and to maintain your regular food intake habits during the 2-week intervention period. Three day food logs will be turned in at visit 6.

#### *Blood Draw*

You will be asked to come into the blood draw having been fasting for 12 hours. Additionally, you will be asked to abstain from alcohol, caffeine, and marijuana for 24 hours and structured exercise for 72 hours. About 3 tablespoons worth of venous blood will be collected from a prominent forearm vein by a registered nurse or trained phlebotomist. You will be asked to be seated quietly for approximately 15 minutes before the blood sample is taken. The blood drawn will be used to conduct analysis related to your overall health and immune system function.

### Visit 2: (1 hour)

#### *Urine Collection*

Prior to arrival for your second visit, you will be asked to come prepared to give a urine collection, which will involve urinating into a small collection cup privately in the bathroom. To ensure dehydration does not affect exercise performance, you will need to

be well hydrated, or you will be asked to return to the lab for the cardiovascular fitness ( $VO_{2max}$ ) testing at a later date.

#### *Body Weight and Height Assessment*

Your height (cm) and weight (kg) will be obtained using a stadiometer SECA 220 (Chino, California, USA) and the Detecto standing digital scale (Webb City, Missouri, USA), respectively.

#### *Body Composition*

Body composition will be measured using air displacement plethysmography, or the BODPOD. You will be instructed to arrive wearing lycra/spandex shorts (men), or a sports bra and spandex shorts or one-piece bathing suit (women). You will be asked to remove all jewelry and glasses, and will be given a lycra swim cap to wear over your hair. You will be instructed to wear the same clothing for all testing procedures, to not consume food or drink 3 hours prior to testing, and to consume a similar quantity of food on both sessions.

#### *Resting Blood Pressure, Resting Heart Rate Measures, and Resting Blood Lactate*

Manual blood pressure and heart rate will be taken 10 minutes prior to the maximal exercise test. Resting blood lactate will also be measured prior to the exercise test as described below. Blood lactate will be measured using a lancet with lactate test strips inserted into the analyzer.

#### *$VO_{2max}$ Exercise Test Protocol with Lactate Testing*

Maximal oxygen consumption, ( $VO_{2max}$ ) is a well-established measure of cardiovascular fitness. In this study,  $VO_{2max}$  will be measured using a structured cycling protocol and a metabolic cart in the Exercise Physiology lab in Gunter Hall (Room 1610). Resting lactate measures will be obtained by puncturing the participant's finger with a lancet. You will begin the test with a 5-minute warm-up at a workload of 0.5 kiloponds (kp) with a pedaling cadence of 60 revolutions per minute (rpm). Following warm-up, the test will begin, and you will be required to ride at 75-85 rpm throughout the entirety of the test. The test begins at a workload of 0.5kp. Every 3 minutes resistance will increase by 0.5kp until  $\geq 4$  mMol of blood lactate is obtained. Once blood lactate reaches 4mMol, the stage time and increments of workload decrease from 0.5kp every 3 minutes, to 0.2kp every 1 minute. During the test, your heart rate will constantly be monitored, with blood pressure, rate of perceived exertion (RPE), and blood lactate monitored every 3 minutes. Following immediate cessation of the max test, your blood lactate, RPE, heart rate and blood pressure values will be recorded. Following the recording of this data, you will begin a prescribed cooldown of; cycling for 5-minutes at 60 rpm or lower with a 0.5kp workload. Following the 5-minute cool down blood lactate will again be measured. Your HR and blood pressure will be continuously monitored throughout cooldown until values return within normal resting ranges.

#### **Visit 3: (1 hour)**

At least 3 days after Visit 2 you will return to the lab for the following assessments.

### *Urine Collection for Hydration Assessment*

Urine collection and analysis will be carried out in the same manner as described in Visit 2.

### *Mental Health Questionnaire*

The Flourishing Scale is a brief eight-item summary measure of self-perceived success in areas such as relationships, self-esteem, purpose, and optimism. You will answer a seven-point scale (1 = strongly disagree to 7 = strongly agree) as to how much you agree with each statement relating to indicators of social well-being (e.g., I lead a purposeful and meaningful life). The scale provides a single psychological well-being score.

### *Pain Assessment- Dolorimetry and Pain Questionnaire*

First you will receive an explanation of the pain questionnaire and dolorimetry measures that will be given before and after the TT. Pain intensity will be assessed using a 0-10 category scale with ratio properties and verbal anchors associated with the following numbers: 0 no pain at all, 0.5 very faint pain (just noticeable), 1 weak pain, 2 mild pain, 3 moderate pain, 4 somewhat strong pain, 5 strong pain, 7 very strong pain, and 10 extremely intense pain (almost unbearable). No verbal anchors are given in associated with numbers 6, 8, and 9.

Baseline measures of leg muscle pain will be measured with a handheld dolorimeter prior to the TT. All measurements will be taken from your dominant leg. The following explanation will be given: ‘I am going to measure pressure threshold; that is, how much pressure will induce discomfort. I am going to increase pressure slowly with this device. Say “Yes” when you start to feel pain or discomfort. I will stop the pressure as soon as you say “Yes”, so it will not hurt you. It is important that you understand that this is a test of sensitivity, not a test of endurance. Do you understand or have any questions?’ After the explanation is given, the dolorimeter will be placed exactly over the indelible mark and perpendicular to the muscle under observation. Pressure will be increased continuously 1 kg per second until you say ‘Yes’. At this time, the pressure is stopped, the meter will be removed from the skin, and the measurement recorded. The same measures will be obtained following completion of the time trial.

You will be given the following instructions prior to the TT and immediately following:

“You are about to undergo a time trial test. The scale before you contains the numbers 0 to 10. You will use this scale to assess the perceptions of pain in your legs now, at rest, and during the test. For this task, pain is defined as the intensity of hurt that you feel in your leg muscles only. Don’t underestimate or overestimate the degree of hurt you feel, just try to estimate it as honestly and objectively as possible. The numbers on the scale represent a range of pain intensity from “very faint pain” (number 1/2) to “extremely intense pain—almost unbearable” (number 10). When you feel no pain in your legs, you should respond with the number zero. When the pain in your legs becomes just noticeable, you should respond with the number 1 or 2. If your legs feel extremely strong pain that is almost unbearable, you should respond with the number 10. You can also

respond with numbers greater than 10. If the pain is greater than 10, respond with the number that represents the pain intensity you feel in relation to 10. In other words, if the pain is twice as great then respond with the number 20. Repeatedly during the test, you will be asked to rate the feelings of pain in your legs. When rating these pain sensations, be sure to attend only to the specific sensations in your quadriceps and not report other pains you may be feeling (e.g., seat discomfort). It is very important that your ratings of pain intensity reflect only the degree of hurt you are feeling in your legs. Do not use your ratings as an expression of fatigue (i.e., inability of the muscle to produce force) or exertion (i.e., how much effort you are putting into performing the exercise.”

You will be asked to answer the pain questionnaire before and during (every 5 minutes) the time trial. Immediately following the time trial the pain questionnaire and dolorimetry will also be administered.

#### *Time Trial (16.1km) Test*

Next, you will complete the 16.1km (10 mile) time trial test. You will be suggested a warmup of 10 minutes at 60-75 rpm. You will be given no indication of completion time and receive no feedback on performance during or after your TT. You will be assessed for pain with the dolorimeter and pain and mental health questionnaire as described above. Blood lactate will be measured at rest, half way through, within the last minute of your test, and after 1 minute and 4 minutes of test completion. You will cool-down for 5 minutes at 60-75rpm immediately following termination of TT.

#### **Visit 4: (less than 10 min) – 24 Hour Measures**

After the TT (24 hours later), you will return to the Gunter 1610 to be evaluated using the mental health and pain questionnaires as well as the dolorimetry protocol described above in Visit 3.

#### **Visit 5: (less than 10 min) – 48 Hour Measures**

After (48 hours following) the TT, you will return to Gunter 1610 and complete the same assessments visit 4.

### **INTERVENTION PERIOD: Supplement and Training Intervention**

#### *Longvida/Placebo Supplementation (2 weeks)*

You will be given the supplement/placebo following the time trial and will be instructed to take one Longvida (LG1 or LG2) capsule daily (1000mg) for the remaining 2 weeks of the study (until visit 6). The placebo will consist of white rice flour (1000 mg) and will have the same physical appearance as the Longvida. Both Longvida (LG1 and LG2) and white rice flour capsules will be ingested in the morning with food and water (breakfast) and recorded on the food log. **If you experience any adverse side effects, please stop taking the pills and contact 911 or Dr. Laura Stewart or Nora Johnston immediately using the contact information on the first page of this document. You will also be**

**provided with a serve allergic reaction information sheet to provide information to you in case of a serious adverse reaction to the supplement.**

*HIIT Cycle Training (2 weeks, 3 nonconsecutive days per week)*

Following visits 1-3, you will be required to visit the UNC Campus Recreation Center on 3 nonconsecutive days per week for 2 weeks to perform the HIIT. You will begin each training session with a 5-minute warm-up at an intensity of approximately 50-60% of your  $VO_{2max}$  measured by HR. Six 90-second cycling bouts at 80-90%  $VO_{2max}$  using HR and will be performed. Each 90-second bout will be followed by 180 seconds of passive rest at 50-60% for a work-to-rest ratio of 1:2. You will cool down for 5 minutes until your HR returns to normal resting values. RPE will be asked at the end of each HIIT training session. You will be provided with a training log to record any structured exercise that is completed in addition to the structured training.

**Visit 6: Blood Sample and Collection of Food Log**

Visit 6 will consist of the collection of a blood sample (described in visit 1) in which you will be asked to consume a 24 hour diet similar to that prior to visit 1, along with the collection of the 3 day food log that was completed during the intervention period. The post intervention time trial test will occur as soon as the next day.

**Visit 7: (1 hour)**

After the Intervention period, you will return to the Gunter 1610 to complete the same time trial test described in Visit 3

**Visit 8: (less than 10 min) – 24 Hour Measures**

After the TT (24 hours later), you will return to the Gunter 1610 and complete the same assessments described in visit 4.

**Visit 9: (less than 10 min) – 48 Hour Measures**

After the TT (48 hours later), you will return to the Gunter 1610 and complete the same assessments described in visit 4. During this visit, you will receive the \$50 Visa gift card for your time.

**C. RISKS, DISCOMFORTS AND BENEFITS**

**Risks**

The Longvida product has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease. While 400 mg of Longvida is not a large amount of the product, users can experience adverse side effects (stomach upset, nausea, dizziness, or diarrhea). The adverse side effects of rice flour are usually mild and may include gastrointestinal upset, abdominal cramping and diarrhea. **It is important to note that if you think you may be pregnant or know that you are pregnant or have known gallbladder, bleeding, endometriosis, uterine fibroids, iron**



**deficiency conditions or a surgery scheduled within 2 weeks of the study completion, as well allergies to or the potential for the participant's current supplement or medication program to negatively interact with curcumin, soy, sunflower, rice or seed or nut products, previous injuries or orthopedic conditions, and arthritis or other chronic inflammatory injuries in the past 6 months, you will not be able to participate in this study. Please contact the study coordinator or 911 if any of these side effects emerge and you may opt to stop taking the supplement or placebo at any time. You will be provided with an information sheet which explains severe allergic reactions and when to call 911.**

Below is list of commonly used medications known to interact with turmeric products. This list only highlights some of the most well-known curcumin – drug interactions and is not comprehensive.

- 1) Taking curcumin in combination with blood thinners can strengthen their effects and increase risk of internal bleeding. Common blood thinning medications include: warfarin (Coumadin), clopidogrel (Plavix), and aspirin.
- 2) When taken in the presence of drugs that reduce stomach acid such as Cimetidine (Tagamet), Famotidine (Pepcid), Ranitidine (Zantac) and Omeprazole, curcumin may cause some negative reactions.
- 3) Curcumin may naturally lower blood sugar concentrations. When taken in combination with drugs for diabetes (that lower blood sugar), the effect may be further lowering blood sugar, causing low blood sugar.
- 4) People who are on anti-histamines experience allergic reactions, including outbreaks such as hives or rashes, or even shortness of breath and anaphylaxis.

**You are strongly encouraged to check in with your physician to evaluate the potential for curcumin to interact with any prescribed medications prior to participating in this study.**

As with any exercise testing and training program, there is a chance that you will experience muscle soreness, fatigue, or even injuries such as sprains or strains. There is also a remote risk of a heart attack or stroke and in very rare cases, death. Precautions to minimize this risk have been taken by the completion of a health history questionnaire and PAR-Q. There is also a risk for self-consciousness during data collection and the training (a psychological risk). HIIT training is also associated with discomforts and including nausea, vomiting, and dizziness. This risk has been reduced by using a trained instructor in a fitness facility with access to an AED onsite. You may withdraw at any time without penalty.

### **Discomforts**

The Longvida and placebo rice flour will be taken in a pill form. There are discomforts with swallowing a pill and there is a remote possibility that the pill could get stuck in the

throat while swallowing, so it is important to take the supplement with plenty of water and food, as it will be taken with breakfast. To help prevent discomforts, you will be instructed to never take the supplement while lying down; instead, you will be instructed to sit or stand when swallowing a pill, and remain upright for at least 30 minutes afterward if possible.

The BODPOD is a small enclosed space. If you are claustrophobic, you will be allowed to opt out of this assessment of body composition. Instead, you will be asked if you would like to try an alternative assessment for body composition, which would include a skinfold assessment as described below. If you are more comfortable with this method, the following protocol will be used. The skinfold measurements will be taken three times from seven sites (chest, midaxillary, triceps, subscapular, abdomen, suprailiac, and thigh) by pinching the skin and then measuring with a spring-loaded Lange skinfold caliper allowing the caliper to pinch the skin. Slight discomfort and possible bruising on rare occasions may be experienced from the pinching and measuring of skinfolds.

As with any exercise test or high intensity training protocol, there is a chance that you will experience some discomfort including muscle soreness, fatigue, nausea or even injuries such as sprains or strains. You will be encouraged to stop any test at any time if there is discomfort beyond your comfort level.

### **Benefits**

You will be given activity assessment, body composition, and aerobic capacity ( $VO_{2max}$ ) information at no cost. You will also receive supervised HIIT personal training and will be provided with individual results after all study participant data has been collected.

## **D. COSTS AND COMPENSATION**

### **Costs**

There are minimal time and resource related costs with this study. Gunter Hall is located on campus and you may be visiting Gunter Hall as a part of your normal classroom activities. The training protocol is located at the UNC Campus Recreation Center which is only about 10 minutes from Gunter Hall. You will have free access to enter the rec center and use of the bikes.

### **Compensation**

You will be compensated for the time that you will spend participating in this study. After all training and study visits are completed, you will receive a \$50.00 Visa gift card. The 5 fastest combined (pre-intervention and post-intervention) 16.1 km time trials will receive an additional \$50 gift card.

### **Participation**

Participation is voluntary. You may decide not to participate in this study and if you begin participation you may still decide to stop and withdraw at any time. Your decision will be respected and will not result in loss of benefits to which you are otherwise entitled, aside from monetary compensation. Having read the above and having had an opportunity to ask any questions, please sign below if you would like to participate in this

research. A copy of this form will be given to you to retain for future reference. If you have any concerns about your selection or treatment as a research participant, please contact Nicole Morse, IRB Administrator, Office of Sponsored Programs, 25 Kepner Hall, University of Northern Colorado Greeley, CO 80639; 970-351-1910.

\_\_\_\_\_  
Signature of Investigator

\_\_\_\_\_  
Signature of Participant

Date: \_\_\_\_\_

Witness: \_\_\_\_\_