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Exploring Health and Fitness in Cannabis and Cannabidiol Users

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ABSTRACT

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Cannabis has been reported to decrease fatigue symptoms and aide in sleep quality, among other use cases. It is unclear whether cannabis is linked to alterations in physical activity and fitness. Cannabidiol, an active compound in cannabis, has also been reported to decrease fatigue symptoms and aide in sleep. Cannabidiol has been reported to aide in recovery from physical activity, but there is no clear connection between cannabidiol use and the likelihood of engaging in physical activity. **PURPOSE:** The aim of this study was to explore fatigue, sleep, physical activity, fitness markers, and fitness outcomes in cannabis and cannabidiol users. **METHODS:** Physically active, healthy male and females (N=12) between the ages of 19 and 28 years were recruited for this study. Participants were cannabis users (CAN [n=4]), cannabidiol users (CBD [n=6]), and control (CON [n=2]). All participants visited the lab 4 times. Participants completed body weight and height assessments, a body composition assessment, and questionnaires/surveys on cannabis use, physical activity history, sleep, and fatigue. Participants were then given the FITBIT Inspire HR to track sleep and physical activity for 1 week. Participants then completed a VO_2peak test, a Wingate test, and a 1-repetition maximum back squat and bench press test. **RESULTS:** There were no significant differences between groups with respect to age, height, weight, or BMI. The CAN group had a significantly lower body fat percent than the CON group ($p = 0.01$). The CBD group spent less time in the fairly active range than the CAN group ($p = 0.009$). The CON group had significantly lower average peak power (p

= 0.01) and average mean power (p = 0.007) when compared to CAN and CBD. This was consistent for relative peak power (p = 0.02) and relative mean power (p = 0.02). The CAN and CBD groups both had higher 1 repetition maximum back squats than CON (p = 0.001, p = 0.007, respectively), and the CAN group had a higher 1 repetition bench press when compared to CON (p = 0.04). There were no differences among groups with respect to fatigue scores, sleep assessment, steps taken per day, minutes spent light and very active, absolute and relative VO_2peak, and fatigue index. **CONCLUSION:** Results from the present study suggest that regular cannabis and cannabidiol users may have the same or better capacity for higher measures of anaerobic power output, and cannabis users may have the same or better capacity for higher measures of muscular strength. These findings provide support for future randomized, controlled clinical trials examining the effects of cannabis and cannabidiol or other health and fitness outcomes.

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CHAPTER I

INTRODUCTION

Background

Cannabis, a psychoactive drug with varying degrees of legality across the United States, has grown in popularity and acceptance over the last decade (Johnston et al., 2012). Cannabis consists of over 140 cannabinoids, of which delta-9-tetrahydrocannabinol (d-9-THC) and cannabidiol are the most recognized (Ribeiro & Ind, 2016). These compounds elicit different responses among users, and various cannabis strains are sold with different concentrations of d-9-THC and cannabidiol. Common side effects of cannabis include tachycardia, impaired memory as well as subjective levels of intoxication (Franz & Frishman, 2016). Cannabis is also proposed as a treatment to offset symptoms and side effects related to depression, anxiety, cancer, and epilepsy (Russo, 2011).

A commonly reported use scenario for cannabis is to improve sleep quality and decrease fatigue symptoms (Consroe et al., 1997). Cannabis increases non-rapid eye movement sleep (NREM), and promotes longer sleep durations (Bradshaw et al., 2019; Goodhines et al., 2019). On the other hand, users have also reported a decrease in fatigue symptoms after using cannabis (Kindred et al., 2017). Findings are inconsistent on whether cannabis use in adults and young adults is associated with a greater or lesser likelihood of achieving physical activity recommendations, though it appears that adolescents engaging in cannabis use are less likely to meet the recommendations (Ames et al., 2020; Korn et al., 2018; Vidot et al., 2017).

Cannabidiol, one of the nonpsychoactive active compounds found in cannabis, is a successful treatment for epilepsy and proposed as a treatment for anxiety, depression, and inflammation (Shannon et al., 2019; Shbiro et al., 2019). Research shows that a commonly reported reason for using cannabidiol is for acute and chronic fatigue. However, the mechanisms associated with these actions of cannabidiol are unclear; one recent study suggests that it may reduce oxidative stress, suppress pro-inflammatory activity, and diminish mitochondrial disfunction (Watt & Karl, 2017).

Cannabidiol is also reported to be a sleep aide by users (Corroon & Phillips, 2018). Cannabidiol improves sleep quality in the short term, though sustained improvements in sleep remain to be fully elucidated (Shannon et al., 2019). In contrast, cannabidiol has potential for the treatment for fatigue and sleepiness in patients with epilepsy and hepatitis (Hussain et al., 2015; Mathur et al., 2020). Lastly, cannabidiol may aide in physical activity recovery and the pain associated with exercise, though it is unclear if there is a connection between cannabidiol use and likelihood of engaging in physical activity (Kasper et al., 2020).

Statement of Problem

Cannabis and cannabidiol are associated with proposed benefits related to fatigue, sleep, physical activity, and fitness. However, further work is needed to understand the impact that these compounds have on these parameters.

Rationale for Study

This study will provide valuable information about cannabidiol and cannabis users with respect to fatigue, sleep, physical activity, body composition, aerobic and anaerobic fitness, and muscular strength. There is relatively little scientific research exploring whether cannabis or cannabidiol are consistently linked to these health-related outcomes.

Purpose for Study

The purpose of this thesis research project was to examine whether regular cannabis or cannabidiol users and non-users differed with respect to fatigue, sleep, physical activity, aerobic and anaerobic fitness, and muscular strength.

Hypothesis

It was hypothesized that regular cannabidiol users would experience better sleep quality and quantity, improved physical activity and aerobic and anaerobic fitness performance, as well as improved muscular strength performance when compared to regular cannabis or non-cannabis/cannabidiol users.

CHAPTER II

REVIEW OF LITERATURE

Introduction

Fatigue is a condition that results in tiredness and a decreased ability to function (Cross, 2019). Individuals dealing with the effects of fatigue may benefit from different treatments such as cognitive behavior therapy and graded exercise therapy (White et al., 2011). Recently, cannabis and cannabidiol have been reported to aid in diminishing fatigue, as both have been shown to have some impact on many of the related effects of fatigue including pain, depression, and sleep (Consroe et al., 1997; Kindred et al., 2017; Russo, 2011).

In this chapter, an overview of fatigue, cannabis, cannabis use, cannabis and fatigue, cannabis and sleep, cannabis and physical activity, cannabidiol, cannabidiol use, cannabidiol and fatigue, cannabidiol and sleep, and cannabidiol and physical activity will be examined to establish support for the present study and hypothesis.

Fatigue

Fatigue is a loosely defined concept that is commonly classified by extreme exhaustion, a lack of energy, and an inability to complete normal daily functions (Aaronson et al., 1999; Shen et al., 2006). Fatigue is a common symptom in various disease states and medical treatments, including chronic fatigue syndrome, inflammation, and cancer treatments such as chemotherapy and radiation (Shen et al., 2006). Fatigue can be loosely separated into 2 categories: acute and chronic (Ross et al., 2021). Acute fatigue can be caused by exercise, illness, and sleep and is often resolved by making life-style changes such as increasing rest or temporarily eliminating

certain activities (Wan et al., 2017). Chronic fatigue persists for more than 6 months and is not alleviated by rest (Rasa et al., 2018). Chronic fatigue is a common symptom of chronic fatigue syndrome (CFS). CFS, also called myalgic encephalomyelitis, is a disease that presents with fatigue, musculoskeletal pain, and flu like symptoms such as headaches, sore throat, lymph node irritation, as well as various cognitive ailments (Chu et al., 2019).

Common treatments for chronic fatigue include cognitive behavior therapy (CBT) and graded exercise therapy (GET) (White et al., 2011). CBT is an interventional approach in which therapists help patients identify and work through thoughts and beliefs that prevent patients from reacting appropriately to everyday situations (Gatchel & Rollings, 2007). GET is a physical activity intervention that employs a gradual introduction of exercise and activity to patients without overtaxing or overreaching (Stiles & Hrozanova, 2016). These treatments may work well in conjunction, as when combined, CBT and GET improve symptoms in patients with post-cancer fatigue (Sandler et al., 2017). Researchers have proposed other treatments for fatigue including nutritional interventions, molecular hydrogen treatment, and acceptance and commitment therapy (ACT) among others (Brugnera et al., 2020; Castro-Marrero et al., 2017; Lucas et al., 2021).

Cannabis

Cannabis (often colloquially known as marijuana, hash, dope, weed) is among the most widely used recreational drugs in the United States, and its use and approval has steadily grown in the past decades (Compton et al., 2004; Johnston et al., 2012). According to the 2016 National Survey on Drug Use and Health (NSDUH), 8.9% of the United States population were current cannabis users, and 2016 was the highest reported use of cannabis in any year since 2002 with

one of the most significant increases observed in people aged 26 years of age and older (U.S. Department of Health and Human Services, 2018).

Cannabis contains of over 140 cannabinoids and 2 of the most recognized active compounds are delta-9-tetrahydrocannabinol (d-9-THC) and cannabidiol (Ribeiro & Ind, 2016). Cannabis strains have varying concentrations of both compounds, which are associated with different effects for each user. For instance, *Cannabis sativa* strains contain higher THC content than *Cannabis indica* strains, which contain higher concentrations of cannabidiol (Ribeiro & Ind, 2016). THC is a psychoactive compound with effects that are modulated by cannabidiol, though this is not entirely understood (Chung et al., 2019). Strains with high concentrations of cannabidiol have been reported to reduce the potential for anxiety and psychosis in some subjects and do not appear to have an impact on intoxication or psychomotor impairments due to THC (Freeman et al., 2019).

Some of the risks associated with cannabis use include tachycardia, an increased risk of myocardial infarction, increased supine blood pressure, subjective intoxication, impaired memory, delayed reaction time and decreased attention (Franz & Frishman, 2016). Yet, these findings are not entirely consistent across studies, and there appears to be a dose-response relationship. In 2001, 18 healthy young adults that used cannabis daily took part in a study assessing the effects of cannabis intoxication on cognitive performance (Hart et al., 2001). The participants were given cannabis cigarettes containing 0%, 1.8%, or 3.9% THC concentrations and then took part in a 4-hour smoke session and completed evaluations for reaction time, recall, and reasoning. Recall ability decreased as the concentration of cannabis in the cigarettes increased. Other research has also emphasized the dose-response relationship with respect to these side effects (Heishman et al., 1997; Pope & Yurgelun-Todd, 1996).

Interestingly, in frequent (multiple days per week) smokers, cannabis use seems to be paired with an expectancy effect (Chait & Perry, 1994). In a study by Ramesh et al. (2013), researchers recruited daily smokers to determine what, if any, dose-dependent effects arise from cannabis use. During each session, the participants were given 3 cannabis cigarettes to smoke (2 puffs per cigarette). The cigarettes presented were all active cannabis (6 active puffs), all inactive cannabis (0 active puffs), or a mixture of both. All active conditions, regardless of dose, resulted in an increased rating of perceived strength of the cannabis, "good" effects, and the likeliness that the participants would use the specific dose given to them again. Though, there is evidence of some form of a dose-response relationship as heart rate and expired CO were increased and decreased, respectively in response to the increasing amount of cannabis in each active condition (Ramesh et al., 2013).

While cannabis is used recreationally, and public opinion has shifted to a more positive opinion on the plant, there is evidence that cannabis use can lead to addictive patterns and disorders. According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, the criteria for diagnosing cannabis use disorder include, but is not limited to "use of cannabis for at least a one-year period" accompanied by "repeated failed efforts to discontinue or reduce" usage, "cravings or desires to use" and "use despite awareness of physical or psychological problems attributed to use" (American Psychiatric Association, 2013). Despite concerns over abuse and dependency, between 1991-1992 and 2001-2002 there was a 0.3% increase in cannabis abuse or dependence, as defined by DSM-IV, according to a study that analyzed the prevalence of cannabis use disorders in the United States (Compton et al., 2019).

Cannabis Use and Delivery

Cannabis is used through a variety of methods including smoking, vaporizing, and through food and beverage products. The most common method of use is through smoking (Ramesh et al., 2013). Specifically, cannabis is generally smoked in two forms: a joint, which is cannabis rolled in cigarette paper, and a blunt, which is cannabis rolled in cigar paper that originally held tobacco (Cooper & Haney, 2008). Cannabis can also be smoked through other methods such as water pipes and linear pipes (Mariani et al., 2011). In a 2016 study, Johnson et al. assessed the frequency of cannabis use and delivery system of choice of Colorado high school students, among other variables. Among those that participated in the survey, 85% typically used smoking as their delivery system, with 6% vaporizing, 5% consuming edibles, and 4% using other methods (Johnson et al., 2016). Cannabis smoking may induce symptoms such as chronic cough, wheeze, phlegm; however, these responses vary across studies once any tobacco use was considered (Ribeiro & Ind, 2016). This same report suggested that cannabis use increased forced vital capacity (FVC), which may be due to acute bronchodilator and anti-inflammatory effects of cannabis.

As technology improves and access to cannabis increases, vaping has become for more accessible to the average user. Vaporizing, in contrast to smoking, allows the cannabis to become hot enough to release active cannabinoids without producing smoke and toxins that are often associated with smoking (Earleywine & Smucher Barnwell, 2007). Vaporizing has been proposed as a potentially less-harmful method of using cannabis, and it may be a reasonable alternative to smoking for those with medicinal use cases or those that have developed respiratory issues due to frequent smoking (Van Dam & Earleywine, 2010). One of the reasons that this has been proposed is because vaporizing also allows for a higher potency of cannabis

which, in turn, lowers the amount of inhalation required to yield the psychoactive effects many cannabis users may be seeking. Yet, the risks of vaping are still being studied, and have become a major talking point in the U.S. government. A 2020 CDC report claimed that certain THC-containing vaporizer cartridges contained vitamin E acetate. Vitamin E acetate has been linked to e-cigarette or vaping product use-associated lung injury (EVALI). As of February 2020, the CDC reported 2807 EVALI cases that resulted in hospitalization or death (Centers for Disease Control and Prevention, 2020). A 2020 study examining at EVALI hospitalizations found that 94% of case patients had vitamin E acetate in their bronchoalveolar-lavage (BAL) fluid, with 94% of the patients either reporting the use of THC vaporizing products or having detectable levels of THC in their BAL fluid (Blount et al., 2020).

Due to the lack of combustion and need to inhale the compound, cannabis users may believe that edible or drinkable products may be safer to use. While this thought is based in truth, as the risk for any potential damaging effects to the lungs are potentially mitigated, edible options are often very potent and may take anywhere from minutes to hours for the psychoactive effects to begin. Once these effects begin, they can last for up to around 8 hours (Hammond, 2019). Thus, it is important for users to understand that doses may be higher than they have previously experienced, and that the effects may be delayed and that this delay is not a sign of tolerance or a faulty product.

Cannabis and Fatigue

Cannabis users have reported lower levels of fatigue as a reason for using cannabis products (Consroe et al., 1997). In 2017, an internet-based research study was conducted by Kindred et al. in which participants with Parkinson’s disease (PD) or Multiple Sclerosis (MS) were surveyed on cannabis use patterns. The cannabis users had lower scores on the Fatigue

Severity Scale as well as the fatigue portion of the Guy's Neurological Disability Scale, regardless of disease state (Kindred et al., 2017). Similar findings were reported in a study with cancer patients using cannabis (Bar-Sela et al., 2019). The exact mechanisms for why cannabis may help with fatigue are not determined and it seems that cannabis may impact a spectrum of comorbidities consistent with fatigue states including depression and chronic pain (Hill et al., 2017; Kosiba et al., 2019).

Cannabis and Sleep

Cannabis users have offered improved sleep quality and duration as a reason for consuming cannabis products (Consroe et al., 1997; Kindred et al., 2017). In a study surveying 83 college students, Goodhines et al. (2019) obtained information on quality of sleep, duration of sleep, sleep onset latency, and daytime fatigue post-consumption in students who had used cannabis and/or alcohol in the previous month. The researchers found that cannabis use promoted longer sleep duration with an increase in next-day fatigue (Goodhines et al., 2019). It has also been shown that cannabis use promotes longer sleep durations in middle and older aged adults (Campbell et al., 2020). In another survey-based study, Bachhuber et al. (2019) conducted interviews on customers outside of 2 dispensaries to obtain information on the reasons the customers used cannabis. They found that of the 1000 respondents, 74% reported that cannabis was used to promote sleep. Of those that reported using cannabis to promote sleep, 87% reduced or stopped using over the counter sleep aids and 83% reduced or stopped using prescription sleep aids (Bachhuber et al., 2019).

Cannabis use also seems to be associated with an increase in non-rapid eye movement sleep (NREM), but no change in rapid-eye movement sleep (REM) (Bradshaw et al., 2019). In a study examing the effect of acute vaporized cannabis on sleep in mice, researchers provided the

mice with 1 of 4 treatments (0mg, 40mg, 80mg, or 200mg of cannabis) immediately before recording data. The 200mg group experienced an in increase in NREM sleep time, but only during the first hour of recording (Mondino et al., 2019). It is clear that this work is in its infancy and more exploration into cannabis and sleep is warranted.

Cannabis and Physical Activity

The association between cannabis use and physical activity patterns is a growing area of research interest. In a study surveying Canadian youth, researchers found that chronic users were engaging in less physical activity than nonusers and all other users (Ames et al., 2020). This trend has also been found in adults ranging from 20-59 years old, as a study analyzing the results of the 2007-2014 National Health and Nutrition Examination Surveys found that current and past cannabis users engaged in lower amounts of moderate and vigorous physical activity than nonusers (Vidot et al., 2017).

Interestingly, some cannabis users have reported that cannabis has a positive effect on physical activity performance. In an online survey seeking information on cannabis use in conjunction with physical activity, 92% of respondents reported using cannabis prior to engaging in physical activity (Lisano, Phillips, Smith et al., 2019). Similar findings were revealed in another online survey engaging adult cannabis users about their attitudes and behaviors regarding cannabis use in association with exercise. The researchers found that 81.7% of respondents endorsed using cannabis concurrently with exercise and reported an increase in exercise enjoyment, recovery, and motivation around exercise when using cannabis (YorkWilliams et al., 2019).

Cannabidiol

Cannabidiol is a noneuphoria-producing component of cannabis (Philpott et al., 2017). Cannabidiol is marketed as an anti-depressant, an anti-inflammatory, and as an anxiety medication; however, there are very few human studies which specifically, and thoroughly, address these questions (Linge et al., 2016). Cannabidiol legalization efforts have succeeded in all 50 states in the US. This has led to a growing interest in marketing cannabidiol as a medicine and as a fitness supplement, which may be partially due to the release of restrictions on CBD use by the World Anti-Doping Agency in 2018 (Mareck et al., 2020).

One of the major medicinal uses for CBD, which is widely supported by the scientific community, is as a treatment for epilepsy. In 2018, CBD gained approval by the FDA as a treatment for Dravet syndrome and Lennox-Gastaut syndrome, both of which are highly treatment-resistant forms of epilepsy (Silvestro et al., 2019). In a study exploring the effects of cannabidiol on Lennox-Gastaut Syndrome, a condition involving epileptic encephalopathy, researchers found that 20 mg per kilogram of body weight of cannabidiol reduced the frequency of daily seizures by 41.9% (Devinsky et al., 2018)

Cannabidiol has also been proposed as an anti-inflammatory agent, but the research is less convincing. According to a SingleCare survey, 33% of Americans have used cannabidiol, and of those 64% use it for pain relief or inflammation (SingleCare, 2020). While there is still more research to be done with respect to these outcomes, cannabidiol appears to have little to no side effects for most users. Reported side effects of note include feelings of tiredness, appetite changes, and diarrhea (Iffland & Grotenhermen, 2017).

Public perception of cannabidiol is generally positive, but there is a clear lack of understanding of the potential for cannabidiol to impact health and the details surrounding the

best practices of its use. In fact, a toxic dose of cannabidiol is considered to be 20,000 mg, which is still not widely considered lethal. A 2019 Politico survey found that 5% of respondents believed that cannabidiol is very harmful, and that 46% of respondents are not at all or not very familiar with cannabidiol at all. This survey also showed that one in five adults aged 18-29 used cannabidiol products. In comparison, one in ten adults aged 65 and older reported the same. The results of this study suggested that there are not significant differences in cannabidiol use or perception amongst political and sex demographics (Politico, 2019).

Cannabidiol Use and Delivery

Cannabidiol is available in multiple forms including (but not limited to) smoking, vaporization, topical-transdermal routes, and oral methods such as lozenges. However, the most common forms are vaporization and oral methods (Bruni et al., 2018). Similar to cannabis itself, cannabidiol risks are dependent on the method of use, and even then, those risks are not entirely known nor concrete. The effectiveness of cannabidiol is dependent on the method of use. When smoking or vaping, absorption is dependent on the duration and depth of inhalation. Similarly, consumable and drinkable methods may be dependent on recent food consumption, as a user with an empty stomach will allow the cannabidiol product to be digested and absorbed quicker than a user who had a meal in proximity to taking the product. To date, oral cannabidiol products have no subjective effects in healthy men and women when compared to a placebo (Spindle, et al., 2019).

Cannabidiol and Fatigue

Another common case for cannabidiol use is as a treatment to offset fatigue. Although its mechanisms remain yet to be fully explored, cannabidiol lessens oxidative stress, suppresses pro-inflammatory activity, and diminishes mitochondrial dysfunction (Watt & Karl, 2017). In a study

with children that experience pediatric epilepsy, parents were interviewed on the side effects of their children's disease states before and after using cannabidiol. Prior to using cannabidiol, 70.1% of respondents reported their children experiencing fatigue as a side effect. While using cannabidiol, this response decreased to 9.4% (Hussain et al., 2015). Similarly, in a study with adults with hepatitis, 61% of current cannabidiol users reported a decrease in fatigue symptoms when using cannabidiol (Mathur et al., 2020).

Cannabidiol and Sleep

Similar to cannabis, cannabidiol users have reported sleep duration and quality as reasons for taking cannabidiol (Corroon & Phillips, 2018). In an online survey obtaining information from young adults on their knowledge and attitudes towards cannabidiol, researchers found that of the 135 participants who reported using cannabidiol, 42.22% listed sleep improvement as a primary reason (Wheeler et al., 2020). Similar results were found in another study in which 253 patients taking cannaibidiol were interviewed. Less than half, 31.1%, of the patients listed improved sleep as a side effect of cannabidiol use (Gulbransen et al., 2020). In studies testing for sleep efficiency and improvements, cannabidiol increases sleep duration, efficiency, and generally improve all sleep metrics (Chagas et al., 2014; Nicholson et al., 2004; Winiger & Hewitt, 2020).

Cannabidiol and Physical Activity

There is little research comparing cannabidiol usage and physical activity metrics. In a case series surveying posts on a cannabidiol forum on the social media website Reddit, 376 posts were analyzed to determine the reasons the individuals were using cannabidiol. A very small percentage (1.4%) of the posts listed a physical wellness benefit such as "exercise performance" associated with cannabidiol (Leas et al., 2020). In athletes who currently use cannabidiol during

or within a few minutes of their exercise, it seems that cannabidiol may be used to support well-being and a calm mindset (Zeiger et al., 2019). Another study examined individuals with chronic back disorders who use cannabidiol. Those that were physically inactive were more likely to use cannabidiol overall and more often than those who were physically active. The researchers also found that over time both groups slowly lowered their frequency of use, with the physically active group lowering this frequency at a faster rate (Angarita-Fonseca et al., 2019).

Summary

Fatigue is a common side-effect of many disease states, resulting in pain and exhaustion among other symptoms (Shen et al., 2006). Both cannabis and cannabidiol have been proposed as potential treatments for fatigue and other ailments, and support for these treatments has grown as public opinion and legal guidelines have changed. Cannabis and cannabidiol may be useful as treatments for fatigue, as users have reported decreases in fatigue symptoms (Bar-Sela et al., 2019; Hussain et al., 2015; Kindred et al., 2017; Mathur et al., 2020). Cannabis and cannabidiol have also been proposed as sleep aids, as they both have been shown to improve sleep duration (Bradshaw et al., 2019; Goodhines et al., 2019; Nicholson et al., 2004; Winiger & Hewitt, 2020). Cannabis use has been associated with a lower likelihood of being physically active, though there is a subset of individuals who use cannabis in correlation with exercise (Ames et al., 2020; Lisano, Phillips, Smith et al., 2019; Vidot et al., 2017; YorkWilliams et al., 2019). There is little research on cannabidiol use and physical activity, though some individuals and athletes consider cannabidiol to be a benefit to their ability to perform physical activity and exercise (Angarita-Fonseca et al., 2019; Leas et al., 2020; Zeiger et al., 2019). Cannabis and cannabidiol are of popular interest, and their use as sleep aids, fatigue treatment, and their association with physical activity needs to be studied further.

CHAPTER III

METHODOLOGY

Participants

The purpose of this study was to examine whether regular cannabis or cannabidiol users and non-users differed with respect to fatigue, sleep, physical activity, aerobic and anaerobic fitness, and muscular strength. A total of 12 healthy males (n=8) and females (n=4) between the ages of 19-28 years were recruited from the University of Northern Colorado and the surrounding community to participate in this study. The cannabis group (CAN; n=4) had been using cannabis at least once per week for the past 12 weeks, the cannabidiol group (CBD; n =6) had been using cannabidiol at least once per week for the past 12 weeks and the control group (CON; n=2) had not been using any cannabis or cannabidiol product within the past 12 weeks. All participants were in good health and had been training for 5 days a week for the past 3 months or had performed 150 minutes of moderate to vigorous exercise per week for the past 3 months as per the American College of Sports Medicine guidelines (Liquori et al., 2021). Exclusion criteria included the presence of known chronic disease conditions such as cardiovascular disease, cancer or diabetes, consistent use of anti-inflammatory medications or medications that act through the liver metabolism throughout the duration of this investigation, and a BMI above 29.9 kg/m^2 classifying individuals as obese.

Participants completed 4 total visits over the course of 2 weeks. During these visits, they completed a series of surveys and questionnaires, body size and composition analysis, aerobic and anaerobic fitness analysis, maximal strength testing, physical activity and sleep quantity and

quality analysis. This study was approved by the Institutional Review Board (IRB) at the University of Northern Colorado (Appendix A).

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 to review and sign (Appendix B). Participants were informed that they were free to ask questions prior to signing the form. After signing the form, participants were assigned an identification number that was used in place of their names on all assessments.

Body Weight and Height Assessment

Height and weight were obtained using a stadiometer SECA 220 (Chino, California, USA) and the Detecto standing digital scale (Webb City, Missouri, USA), respectively. Participants were instructed to remove their shoes, socks, and any additional clothing other than the participants base layer prior to height and weight assessment.

Air Displacement Plethysmography

Body composition, lean body mass (LBM) and body fat percentage (BF%) were evaluated using air displacement plethysmography with a BODPOD (COSMED USA Inc., Concord, CA). Prior to testing, participants were instructed to bring a base layer of form-fitting clothing including spandex/lycra shorts for men and a sports bra and spandex shorts or one-piece bathing suit for women. Participants were instructed to remove their shoes, socks, jewelry, and all additional clothing other than the base layer. Participants were then given a swim cap to wear, and body composition analysis was performed via manufacturers guidelines (Davis et al., 2006).

Cannabis Use Assessment

Participants completed the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory *(DFAQ-CU)*. The DFAQ-CU is a 33-item questionnaire that includes items related to smoking rate, quantity, mode, and context of use, among other use patterns. The questionnaire was completed and turned in during the first visit (Cuttler & Spradlin, 2017).

Fatigue Scale

The Piper Fatigue Scale (PFS) is a 27-question screening tool to determine participant fatigue prior to testing. Participants respond to each of the first 23 prompts with a Likert based system of 1-10, with 1 indicating little to no fatigue and 10 indicating extreme fatigue. Example questions from the PFS include “To what degree is the fatigue you are feeling now interfering with your ability to complete your work or school activities?”, and “To what degree would you describe the fatigue which you are experiencing now as being?” The final 4 questions of the PFS are short response questions to allow the participants space to further detail their fatigue. Example questions from the short response section include “Overall, what do you believe is most directly contributing to or causing your fatigue?” and “Are you experiencing any other symptoms right now?” (Strohschein et al., 2003). The assessment was completed and turned in during the first visit.

Wrist Actigraphy Sleep and Activity Assessment

Participants were given the FITBIT Inspire HR to track sleep quantity and quality as well as daily physical activity and steps via wrist actigraphy assessment (Fitbit, San Francisco CA). Participants were instructed to wear the Fitbit Inspire HR band at all times for a full week, except for a brief charging period at the midweek point. Participants were instructed to return the Fitbit at the end of the week.

Visit 2 (Separated from Visit 1 by 7 days)

Hydration Assessment

Upon arrival for performance testing (VO_2peak) participants were instructed to void their bladder into a collection container. The sample provided was analyzed for urine specific gravity using the PAL-10S (4410) urine specific gravity refractometer (ATAGO, Tokyo, Japan). Hydration cutoff was set at USG <1.020. If participants arrived in a dehydrated state (USG >1.020), the participants were rescheduled and instructed to come in at a later date.

Aerobic Fitness Testing

Participants maximal oxygen uptake was assessed through a VO_2peak assessment protocol on a treadmill (Trackmaster, Model: TMX425CP, Full Vision Inc., Newton, KS, USA) using a TrueOne 2400 Metabolic Measurement System (MMS-2400) (Parvomedics, Sandy, UT, USA). The participants completed a modified Bruce protocol (Hall-Lopez et al., 2015). Participants were fitted with a Polar Heart Rate Sensor H1 (Polar Electro Inc., Bethpage, NY, USA) for collection of heart rate (HR) throughout the entirety of the max test. Prior to testing, participant blood pressure was taken. Participants began with a warm-up for 5 minutes at 3.5mph for 5 minutes. Following the warm-up, the treadmill speed increased to a self-selected pace that the participant felt comfortable running at for 5km. This stage, and all following stages until cooldown, lasted 2 minutes. Upon completion of the first stage, speed was increased by 1mph in stage 2 and stage 3 (1: self-selected; 2: self-selected + 1; 3: self-selected + 2). At the completion of stage 3, speed remained consistent (self-selected + 2) until completion of the test, while grade increased by 2% each stage (4: 2%; 5: 4%; 6: 6%). Once participants reached volitional fatigue, the participants engaged in a 5-minute cooldown stage at 0% grade and 3.0mph. Blood pressure was again taken immediately after volitional fatigue was reached, as well as at the end of the

cooldown. Blood lactate was taken at the end of each stage, including warm-up and cooldown (Lactate Plus Meter, Nova Biomedical, Waltham, MA, USA).

Visit 3 (Separated from Visit 2 by at Least 72 Hours)

Anaerobic Testing

Participants were assessed in anaerobic fitness via the Wingate anaerobic power test on a cycle ergometer (Monark Ergomedic 894E, Monark, Varberg, Sweden) (Beneke et al., 2002). Participants began by cycling between 60-75 revolutions per minute (RPM) at a self-selected resistance for 5 minutes. Upon completion of the warm-up, resistance was dropped to 0, and the participant was instructed to begin pedaling at their max cadence. Once participants reached their max pedal cadence, 7.5% of the participant's body weight was added to the cycle ergometer, and the test began. Participants cycled for a total of 30 seconds at a resistance of 7.5% body weight. At the cessation of the 30sec max test, participants cycled for an additional 5 minutes at a self-selected resistance for cool-down. Results included peak anaerobic power, mean anaerobic power, relative peak anaerobic power, total work, and fatigue index.

Visit 4

Strength Testing

Participant strength was assessed via 1 repetition max (1-RM) back squat and bench press (Liquori et al., 2021). Participants completed a warm-up of 5-10 repetitions of the exercise at 40-60% of their estimated 1-RM. Participants then rested for 1-minute. Following 1-minute rest, participants completed 3-5 repetitions of the exercise at 60-80% of their estimated 1-RM. Participants then rested again for 1-minute. Next, weight was added to achieve 100% of their 1-RM. If the participant successfully completed the exercise at this weight, additional weight was added in a conservative fashion and the participant attempted to lift the new weight again

following 3-5 minutes of rest. This procedure continued until the participant failed to lift the set weight, and the previous successful lift was recorded as their 1-RM. All 1-RM testing was spotted by a trained exercise professional to ensure participant safety.

Analysis

All participant data were entered and organized in Microsoft Excel. Further analysis was completed using the statistical package for the social sciences (SPSS) (SPSS, Inc, Chicago, Il). Means and standard deviations were calculated and are reported for all major outcome variables. Data were then averaged for each group and a three-way analysis of variance (ANOVA) was used. Significance was set at alpha = 0.05.

CHAPTER IV

RESULTS

The purpose of this study was to examine if regular cannabis or cannabidiol users and non-users differed with respect to fatigue, sleep, physical activity, aerobic and anaerobic fitness, and muscular strength. A total of 12 participants (n = 8 males, n = 4 females) were assigned to one of three groups; CAN (n=4), CBD (n=6), or CON (n=2). Participant age ranged from 19 to 28 years old with an average of 24 ± 4.6 years old. There were no significant differences with respect to age, height, weight, or BMI among groups. The CON group had a 124% higher average body fat percent than the CAN group (p=0.01) (Table 1).

Table 1

Participant Characteristics

Characteristic	CAN (n=4)	CBD (n=6)	CON (n=2)
Age (years)	23 ± 3.8	24 ± 4.3	27 ± 9.2
Height (cm)	171.33 ± 6.59	169.61 ± 6.25	155.5 ± 6.36
Weight (kg)	69.58 ± 8.68	76.16 ± 10.86	60.83 ± 2.22
Body Mass Index (kg/m^2)	23.65 ± 1.27	24.62 ± 3.81	25.3 ± 2.97
Body Fat (%)	11.68 ± 3.19*	18.98 ± 9.78	26.15 ± 4.74*

Note. CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation.

*Significant difference between the CAN group and CON group in Body Fat (%). (p=0.01).

Cannabis Use Assessment (DFAQ-CU)

The CAN group reported using cannabis between 5 and 6 times a week and 1+ times per day. Three out of 4 participants reported using cannabis within 3 hours of waking up and using a water pipe or bong during these sessions. Half of the participants (n=2) reported using concentrates as the primary form of cannabis use and the other half reported using cannabis plant. The age of first use ranged from 15 to 18 years old, and the onset age for the current usage pattern ranged from 16 to 24 years old (Table 2).

Table 2

Cannabis Use Assessment (DFAQ-CU)

Assessment Information	CAN (n=4)
Sessions Per Week	5-6 Times Per Day: 25% 1+ Times Per Day: 75%
Time of Day For First Session	Within 30 Minutes of Waking: 25% Within 1 Hour of Waking: 25% Within 1-3 Hours of Waking: 25% Within 12-18 Hours of Waking: 25%
Primary Method of Smoking	Vaporizer: 25% Bong/Water Pipe: 75%
Primary Form of Cannabis	Concentrates: 25% Marijuana: 25%
Age of First Use (years)	16.25 ± 1.26
Age For Onset of Current Use Habit (years)	19 ± 3.46

Note. CAN: Cannabis (n=4). Session Per Week, Time of Day For First Session, Primary Method of Smoking, and Primary Form of Cannabis are presented as percentages. Age of First Use and Age Of Onset of Current Use Habit are presented as mean ± standard deviation.

Fatigue Scale (Piper Fatigue Scale)

All groups reported low to moderate levels of fatigue and the total fatigue score among participants ranged from 1.42 to 4.51, with an overall average of 2.58 ± 1.47. There were no significant differences amongst groups in any of the categories of the Piper Fatigue Scale or in total fatigue score (Table 3).

Table 3

Piper Fatigue Scale

Subgroups	CAN (n=4)	CBD (n=4)	CON (n=4)
Behavioral/Security	2.75 ± 2.66	1.56 ± 0.59	1.00 ± 0.00
Affective Meaning	2.25 ± 1.30	2.03 ± 1.17	3.20 ± 3.11
Sensory	2.95 ± 0.53	3.2 ± 1.79	2.9 ± 2.69
Cognitive/Mood	3.13 ± 0.71	3.11 ± 1.44	3.09 ± 0.59
Total Fatigue Score	2.77 ± 1.42	2.48 ± 1.43	2.55 ± 1.84

Note. CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation. No significant differences were present.

Wrist Actigraphy Sleep Assessment

Overall, participants slept between 278 and 465 minutes per night with an overall average of 375 ± 58.72 minutes. The number of awakenings per night for each participant ranged widely (9 to 37), though there were no significant differences among groups. There were no statistically significant differences among the groups with respect to time in bed, minutes in REM, light or deep sleep (Table 4).

Table 4

Sleep Characteristics

Sleep Metrics	CAN (n=4)	CBD (n=6)	CON (n=2)
Minutes Asleep (min)	354.55 ± 36.27	385.66 ± 59.73	382.43 ± 116.98
Number of Awakenings	21.42 ± 9.31	30.33 ± 3.76	32.66 ± 7.15
Time in Bed (min)	407.34 ± 47.67	446.08 ± 66.15	434.64 ± 142.74
REM Sleep (min)	71.83 ± 7.85	75.44 ± 12.36	77.22 ± 1.72
Light Sleep (min)	252.56 ± 45.67	251.54 ± 26.00	257.80 ± 44.12
Deep Sleep (min)	61.44 ± 11.92	70.43 ± 15.47	86.66 ± 15.63

Note. CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation. No significant differences were present.

Wrist Actigraphy Activity Assessment

When taken together, all participants in this study took an average of 13967 ± 6537 steps per day and ranged from 6036 steps to 27,986 steps. Distance traveled per day ranged from 2 to 12 miles with an average of 6.0 ± 2.9 miles per day. Overall, the average time spent sedentary was 782 ± 314.1 minutes, ranging from 377 to 1438 minutes per day. The CAN group spent 16.35% more time in the “fairly active” range than the CBD group ($p = 0.009$). There were no significant differences among groups with respect to minutes lightly active and minutes very active (Table 5).

Table 5

Physical Activity Characteristics

Physical Activity Metrics	CAN (n=4)	CBD (n=6)	CON (n=2)
Steps	17127.25 ± 4685.07	10320.83 ± 3611.03	18588 ± 13290.78
Distance (miles)	8.00 ± 1.83	4.17 ± 1.60	8.00 ± 5.66
Sedentary (min)	829.50 ± 207.49	833.33 ± 391.85	733.5 ± 200.11
Lightly Active (min)	348 ± 61.84	263.80 ± 62.95	329 ± 124.45
Fairly Active (min)	86.00 ± 42.49*	73 ± 20.24*	85.00 ± 70.71
Very Active (min)	50.25 ± 9.46	23.6 ± 23.95	48.5 ± 40.31

Note. CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation.

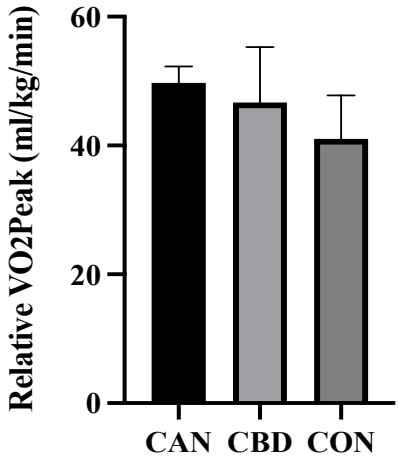
*Significant differences found between the CAN and CBD group in Fairly Active (min) ($p = 0.009$).

Aerobic Fitness Testing (VO_2peak)

The participants reached a relative VO_2peak of 46.75 ± 6.99 ml/kg/min, ranging from 32.8 to 58.5 ml/kg/min (Figure 1a). Absolute VO_2peak ranged from 2.26 to 4.29 L/min, with an average of 3.35 ± 0.61 L/min (Figure 1b). There were no significant differences among the groups.

Figure 1a

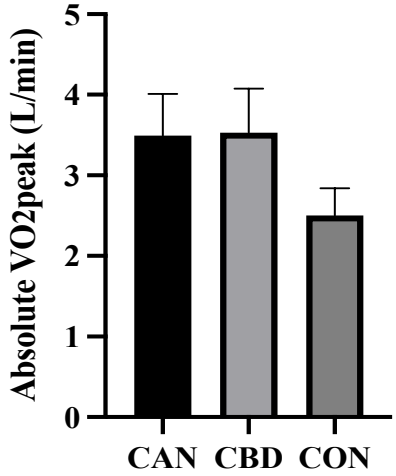
Relative VO_2peak (ml/kg/min)



Note. CAN: Cannabis (n=4) = 49.73 ± 2.56; CBD: Cannabidiol (n=6) = 46.68 ± 8.59; CON: Control (n=2) = 41.00 ± 6.79. Values are presented as mean ± standard deviation. No significant differences were present.

Figure 1b

Absolute VO_2peak (L/min)



Note. CAN: Cannabis (n=4) = 3.50 ± .52; CBD: Cannabidiol (n=6) = 3.53 ± 0.55; CON: Control (n=2) = 2.5 ± 0.34. Values are presented as mean ± standard deviation. No significant differences were present.

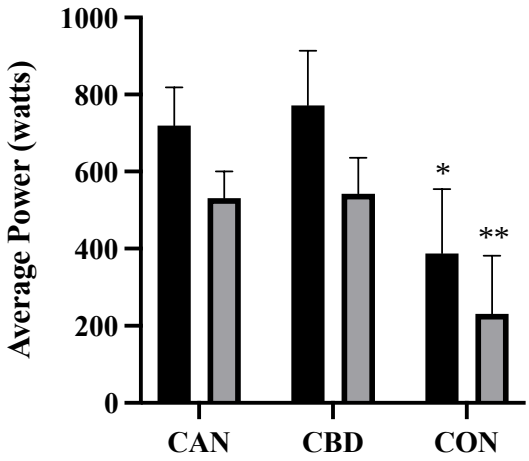
Anaerobic Fitness Testing (Wingate)

The participants had an average peak power of 690.45 ± 187.09 watts when all groups were combined, and the average peak power ranged from 269.44 to 985.75 watts.

The CON group yielded significantly lower average peak power (387.56 ± 167.04 watts, p = 0.01) and average mean power (231.49 ± 150.34 watts, p = 0.007) in comparison to the other groups (Figure 2a). The CON group also yielded significantly lower relative peak power (6.49 ± 2.93 watts/kg, p= 0.02) and average peak power (3.89 ± 2.59 watts/kg, p = 0.02) in comparisons to the other groups (Figure 2b). There were no significant differences in fatigue index, which ranged from 46.07 to 69.79% and had an overall average of 59.31 ± 7.67 percent (Figure 2c).

Figure 2a

Average Peak Power and Average Mean Power (watts)



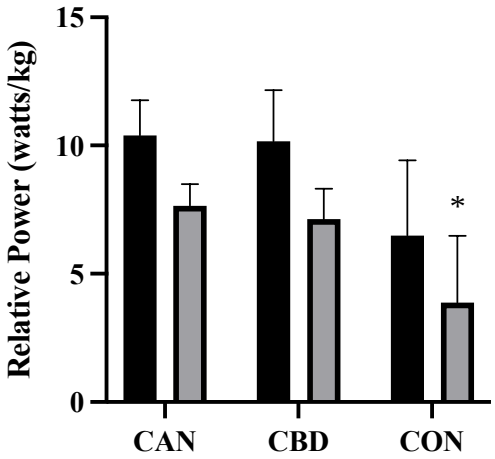
Note. Average Peak Power: black bar; Average Mean Power: gray bar; CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation.

*CON was significantly lower than CAN and CBD (p = 0.01).

**CON was significantly lower than CAN and CBD (p = 0.007).

Figure 2b

Relative Peak Power and Relative Mean Power (watts)

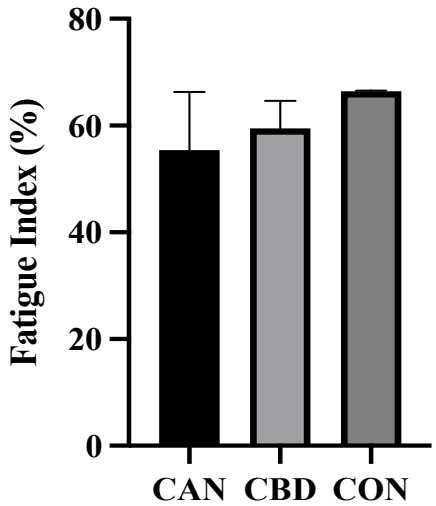


Note. Relative Peak Power (black bar) and Relative Mean Power (gray bar) (watts). CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation.

*CON was significantly lower than CAN and CBD ($p = 0.02$).

Figure 2c

Average Fatigue Index (%)



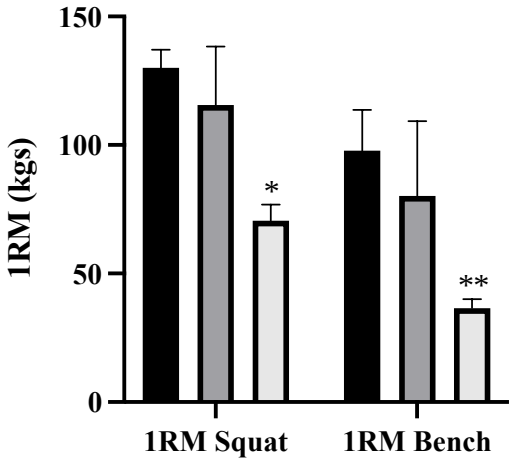
Note. CAN: Cannabis (n=4); CBD: Cannabidiol (n=6); CON: Control (n=2). Values are presented as mean ± standard deviation. No significant differences were present.

Strength Testing (1-RM Back Squat and Bench Press)

The participants average 1RM back squat was 113 ± 26.26 kg. The overall average 1RM bench press was 79 kg ± 30.27. The CAN group average squat 1RM and bench 1RM were 85.7% and 172.2% higher than the CON group ($p = 0.001$, $p = 0.007$). The CBD group average squat 1RM was 64.3% higher than the CON group ($p = 0.039$). There was no difference between the CBD and CON group in the 1RM bench press. (Figure 3).

Figure 3

1-Repetition Squat and Bench Press (kg)



Note. CAN (black bar): Cannabis (n=4); CBD (gray bar): Cannabidiol (n=6); CON (light gray bar): Control (n=2). Values are presented as mean ± standard deviation.

*CON was significantly lower than CAN ($p = 0.001$) and CBD ($p = 0.007$).

**CON was significantly lower than CAN ($p = 0.039$).

CHAPTER V

DISCUSSION AND CONCLUSIONS

The purpose of this study was to examine whether regular cannabis or cannabidiol users experienced differences in fatigue, sleep, physical activity, aerobic and anaerobic fitness, and muscular strength. It was hypothesized that regular cannabidiol users would experience greater sleep quality and quantity, aerobic and anaerobic fitness performance, and muscular strength performance when compared to regular cannabis users and non-users.

All groups were similar with respect to age, height, and weight, as well as body mass index. The average BMI was 24.41 kg/m^2, which places the participant average BMI in normal or healthy weight category (Olfert et al., 2018). In the present study, the CAN group had the lowest BMI (23.65 kg/m^2) amongst groups, though this was not significant. In a previous study, researchers took 15 years of longitudinal data from the Coronary Artery Risk Development in Young Adults (CARDIA) study and assessed cannabis use in conjunction with various health markers. The researchers found that cannabis use was not associated with a higher BMI, even when accounting for a higher calorie intake when compared to nonusers (Rodondi et al., 2006).When all groups were combined, average body fat percentage was 17.74%. This placed the male participants in the “average” category and the female participants in the “good” category when compared to their age ranges (Liquori et al., 2021). There was a significant difference in body fat percent where CON was 124% higher than CAN. Previous research has not shown a relationship between cannabis use and body composition when compared to controls (Lisano, Smith, Mathias et al., 2019; Muniyappa et al., 2013).

Cannabis Use Assessment (DFAQ-CU)

Amongst the cannabis users, 3 out of 4 of the participants had very similar patterns of cannabis use; consuming cannabis 1+ times per day and preferring cannabis plant smoked by way of a water pipe or bong as the primary delivery method. These same 3 participants had the earliest onset age for usage, between 15 and 16 years old. It is possible that there is a correlation between age of onset or length of time using cannabis and frequency of use, though the sample size is a limiting factor in establishing any such relationships. This potential relationship has been proposed in a previous study in which low socioeconomic status males were followed from the ages of 6 to 28 years old. The researchers tracked various trends, including cannabis use. The onset of cannabis usage was observed from ages 13 to 28 years old, and the researchers determined that the risk of addictive behaviors of cannabis were reduced by 31% for each year that the onset of cannabis usage was delayed (Rioux et al., 2018).

Fatigue Scale (Piper Fatigue Scale)

The Piper Fatigue Scale is scored on a 1-10 Likert scale, with higher numbers indicating higher levels of fatigue. All participants reported low to moderate levels of fatigue. Cannabis and cannabidiol have the potential to a beneficially impact fatigue symptoms in users (Consroe et al., 1997; Hussain et al., 2015). The present study found no differences among groups with respect to total fatigue score, nor the subcategories of behavioral/security, affective meaning, sensory, and cognitive/mood. These findings are in contrast to the results of earlier studies. Cannabis increases fatigue symptoms the day after use in college students (Goodhines et al., 2019). In a study comparing patients with multiple sclerosis which used cannabis and non-cannabis using patients, patients were assessed on fatigue symptoms. The participants filled out the Fatigue Severity Scale, a self-report scale consisting of 9 items ranked from 1-7 (7 being the most

severe). The patients who used cannabis were found to have a higher frequency of fatigue symptoms than nonusers (Contentti et al., 2021). Participant health may be a factor in this disparity. It is important to note that all participants in the current study were deemed healthy and physically active individuals.

Wrist Actigraphy Sleep Assessment

The present study utilized the FITBIT Inspire HR to track sleep. A 2019 meta-analysis and systematic review by Haghayegh et al. analyzed 22 research articles to determine the accuracy of sleep tracking by various FITBIT models. The authors found that FITBIT models were effective at differentiating between sleep and waking stages, as well as the time spent in each sleep stage (Haghayegh et al., 2019). In a study specifically comparing sleep tracking on FITBIT to standard actigraphy assessments, the FITBIT was shown to be more effective at tracking sleep stages and duration than the actigraphy assessments (Haghayegh et al., 2020).

It was expected that the CAN and CBD groups would have improved sleep measures when compared to the CON group, with the CBD group performing the best. Unexpectedly, cannabis and CBD use were not related to differences in sleep outcomes. The current literature suggests an increase in total sleep duration in both cannabis and CBD users, as well as an increase in NREM sleep in cannabis users (Bradshaw et al., 2019; Goodhines et al., 2019; Nicholson et al., 2004; Winiger & Hewitt, 2020). In a study in which adults purchasing cannabis products in a dispensary were asked why they took cannabis, 74% of respondents claimed that it promoted sleep (Bachhuber et al., 2019). In another study, rats were given cannabis through vaporization on 2 occasions: a low dose or control session (0 mg, 40 mg or 80 mg), and a high dose or control session (0 mg or 200 mg). The 200 mg trial yielded a small increase in NREM sleep during light sleep in comparison to control, but only during the first hour of recording

(Mondino et al., 2019). In the current study, the small sample size and duration of tracking (7 days) may account for the lack of differences amongst groups.

Wrist Actigraphy Activity Assessment

Physical activity was tracked using FITBIT Inspire HR devices. FITBIT devices have varying levels of accuracy in tracking step count and activity levels. In a study evaluating various pedometers, researchers had participants walk on a treadmill at 3 speeds; 1 km/h, 2 km/h, and 3 km/h. The FITBIT had high to mixed error rates on the two slowest speeds, with a smaller error rate on the 3 km/h speed. The researchers concluded by suggesting that the FITBIT manufacturer focus on the accuracy of step detection at slower walking speeds (Beevi et al., 2016).

All measurements of physical activity were similar among groups except minutes of fairly active, in which the CAN group spent more time in this range when compared to the CBD group ($p = 0.009$). Previous self-report research found that cannabis users are less likely to engage in physical activity, specifically moderate to vigorous activity (Ames et al., 2020; Vidot et al., 2017). This was not the case in the present study, as there were no statistically significant differences in steps tracked or light and vigorous physical activity. In a study utilizing activity tracking through FITBIT devices, researchers found that cannabis users do not have significantly different activity levels than nonusers (Ong et al., 2021). This was found to be consistent in the present study.

Aerobic Fitness Testing (VO_2peak)

The CAN group yielded the highest VO_2peak (49.73 ml/kg/min) when compared to the CBD and CON groups, though there was no statistically significant difference amongst groups. Cannabis has no significant impact on VO_2 testing measures (Renaud & Cormier, 1986). In a study comparing aged (60 and older) cannabis users and nonusers, researchers used data from a

randomized controlled trial entitled Fitness, Older Adults, and Resting State Connectivity Enhancement (FORCE). The participants were assigned to a low or moderate intensity 16-week exercise program. Participants were assessed on VO_2peak before, midway, and after the exercise intervention. There were no significant differences in VO_2peak measurements among nonusers and users at any of the assessment points (YorkWilliams et al., 2020). In another study, aerobic fitness levels of young adults were assessed using VO_2peak. The test followed the Bruce Protocol and consisted of the participants running until reaching volitional fatigue. There were no significant differences among cannabis users or control in VO_2peak measurements (Wade et al., 2021).

Anaerobic Fitness Testing (Wingate)

There were significant differences amongst groups with respect to average peak power, relative peak power, average mean power, and relative mean power. The CON group had the lowest recordings amongst all of the previously mentioned variables, as well as the largest fatigue index. In a study measuring exercise responses in chronic cigarette and cannabis users, researchers used a cycle ergometer to assess physical work capacity by way of an increasing work rate protocol. The researchers found no difference among cigarette and marijuana users, marijuana only users, cigarette only users, and neither substance users (Maksud & Baron, 1980). In another study comparing cannabis users and nonusers with a Wingate Anaerobic Power Assessment, there were no significant differences among the groups in power output. Interestingly, there was a trend in the marijuana users to fatigue at a greater rate, represented by power drop, though this trend was not statistically significant (Lisano, Smith, Mathias et al., 2019). This trend was not observed in the present study, as the CON group yielded the highest

anaerobic fatigue percentage among all groups. More work is needed to further determine whether there is a connection between cannabis or CBD use and anaerobic fitness metrics.

Strength Testing (1-RM Back Squat and Bench Press)

The CAN group had the highest 1RM for both the back squat and bench press, and there were significant differences amongst the groups for both tests (back squat: $p = 0.01$; bench press: $p = 0.04$). The CON group had the lowest 1RM in both tests when compared to both groups. There is limited research on cannabis and cannabidiol users and strength testing. Researchers conducted a study comparing a CBD group to a placebo group and skeletal muscle regeneration after resistance training. In this study, researchers had participants complete 1RM back squats as a test of muscular strength. Then, the subjects performed an intensive exercise protocol that consisted of sets of 12 back squats using 70% of their recorded 1RM, followed by drop jumps from a 45 cm box into a deep squat for 3 sets of 15 repetitions. The subjects repeated 1RM testing 24, 48, and 72 hours after the intensive exercise protocol. The researchers found no significant differences in 1RM at any stage of testing (Isenmann et al., 2021). Similar strength comparisons were found in a study in which cannabis users were compared to nonusers on hand grip and lower extremity strength assessments. Participants used a handgrip dynamometer to assess grip strength. Three trials were conducted on each hand and the highest recorded trial for each hand was recorded. Lower extremity strength was assessed on an isokinetic dynamometer and the best of 2 bouts of 100% exertion were recorded. The researchers found no significant differences among cannabis users and nonusers after both of these strength assessments (Lisano, Smith, Mathias et al., 2019).

Limitations

There were several limitations to this study. The small sample size allowed for useful pilot data, but not enough participants to allow us to draw strong conclusions. While not all subjects were college students, this sample consisted entirely of healthy young adults, predominantly male, which may be limiting when attempting to apply the findings to the general population or across sexes.

Another limitation was the inability to control the cannabis products consumed. While the subjects reported their use habits as well as the amount and type they consumed, the variance in dose and timing may lead to inaccuracies in testing. Three out of the 4 CAN participants reported smoking cannabis for all use sessions, though the variance in strains and potency may have also had an effect on testing. Cannabis and CBD timing was another limitation, as the CBD group consumed CBD every night after their last meal, while the CAN group consumed at their leisure.

While physical activity and sleep measures were tracked for all participants, the inaccuracy of the Fitbit product paired with the potential for participants to not follow directions to keep the device on may have produced inaccurate results. Participants were instructed to keep the Fitbit on for an entire week, charging the device for 10 minutes each day when sedentary. The data retrieved do not include any information on time duration of device removal, thus it is possible that some activities and steps were not tracked. Finally, the Fitbit relies on heart rate to produce sleep estimates. This leaves a possibility for inaccurate tracking if the band moves or falls off while the participant slept, as the data may show lower sleep time estimates or split sleep sessions if the band is restored to its correct placement.

Recommendations for Future Research

Research on cannabis and cannabidiol is necessary as these products are legalized and as their use begins to proliferate across the United States. Future studies should attempt to standardize the cannabis consumption, including timing and dosage. A controlled clinical trial in which the cannabis and CBD are administered in a controlled setting would help to alleviate these problems and allow for more accurate testing and data accumulation. Future studies should also seek larger sample sizes and a more even distribution of males and females across groups to account for performance differences among the sexes.

Conclusion

The current study compared the effects of cannabis and cannabidiol on fatigue, sleep, physical activity, sleep aerobic and anaerobic fitness, and muscular strength. In this small pilot study, it was shown that cannabis and cannabidiol use may result in a greater anaerobic power output. Cannabis use may also have a positive impact on muscular strength. Though, cannabis and cannabidiol were not associated with any improvements in fatigue measurements, sleep duration, time spent physically active, or aerobic fitness levels.

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APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL

UNIVERSITY OF
NORTHERN COLORADO

Date: 04/13/2021

Principal Investigator: Laura Stewart

Committee Action: **Expedited Approval - New Protocol**

Action Date: 04/13/2021

Protocol Number: 2101020795

Protocol Title: Cannabis, CBD, and Inflammation

Study Expiration Date:

The University of Northern Colorado Institutional Review Board has granted approval for the above referenced protocol. Your protocol was approved under expedited category (2) (3) (7) as outlined below:

Category 2: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children2, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it
will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

Category 3: Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

Category 7: Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

All research must be conducted in accordance with the procedures outlined in your approved protocol.

If continuing review is required for your research, your project is approved until the expiration date listed above. The investigator will need to submit a request for Continuing Review at least 30 days prior to the expiration date. If the study's approval expires, investigators must stop all research activities immediately (including data analysis) and contact the Office of Research and Sponsored Programs for guidance.

If your study has not been assigned an expiration date, continuing review is not required for your research.

For the duration of the research, the investigator(s) must:

- Submit any change in the research design, investigators, and any new or revised study documents (including consent forms, questionnaires, advertisements, etc.) to the UNC IRB and receive approval before implementing the changes.
- Use only a copy of the UNC IRB approved consent and/or assent forms. The investigator bears the responsibility for obtaining informed consent from all subjects prior to the start of the study procedures.
- Inform the UNC IRB immediately of an Unanticipated Problems involving risks to subjects or others and serious and unexpected adverse events.
- Report all Non-Compliance issues or complaints regarding the project promptly to the UNC IRB.

As principal investigator of this research project, you are responsible to:

- Conduct the research in a manner consistent with the requirements of the IRB and federal regulations 45 CFR 46.
- Obtain informed consent and research privacy authorizations using the currently approved forms and retain all original, signed forms, if applicable.
- Request approval from the IRB prior to implementing any/all modifications.
- Promptly report to the IRB any unanticipated problems involving risks to subjects or others and serious and unexpected adverse events.
- Maintain accurate and complete study records.

- Report all Non-Compliance issues or complaints regarding the project promptly to the IRB.

Please note that all research records must be retained for a minimum of three (3) years after

the conclusion of the project. Once your project is complete, please submit the Closing Report Form.

If you have any questions, please contact Nicole Morse, Research Compliance Manager, at 970-351-1910 or nicole.morse@unco.edu. Please include your Protocol Number in all future correspondence. Best of luck with your research!

Sincerely,

Michael Aldridge
IRB Co-Chair, University of Northern Colorado: FWA00000784

Silvia Correa-Torres
IRB Co-Chair, University of Northern Colorado: FWA00000784

APPENDIX B

INFORMED CONSENT

UNIVERSITY OF
NORTHERN COLORADO

CONSENT FORM FOR HUMAN PARTICIPANTS IN RESEARCH
Title: Cannabis, CBD, and Inflammation Study (CCI)

Researcher: Laura K. Stewart, Ph.D., Professor, School of Exercise and Sport Science
Phone: 970-351-1891

Student Researcher: Blake R. Butler, MS Student, School of Exercise and Sport Science
Email: butl4276@bears.unco.edu

PURPOSE

Chronic inflammation, which is defined as a persistent, low-grade inflammatory response within the body, is associated with many of the negative health conditions which are prevalent in our society today. It is most well-known for its role in the progression of diseases including obesity, metabolic syndrome, cancer, cardiovascular disease, and is linked to many of the underlying factors associated with disease development including perturbations in sleep, and mental health status such as depression, anxiety, fatigue, and quality of life.

Cannabis has been used both recreationally and therapeutically to normalize behaviors of appetite, nausea, and pain. However, there is still much to learn of the therapeutic effects of cannabis. While THC is considered the most recognized component of cannabis, CBD is most associated with its use as a treatment for epilepsy, anxiety, and psychoses, and has been proposed to improve aspects of sleep, mental health, and quality of life.

The goal of this study is to explore differences among regular CBD users, cannabis users and a non-cannabis or CBD using control group with respect to immunological markers, as well as body weight and height assessments, body composition, and surveys and questionnaires addressing marijuana use, physical activity, and mental health. This study will also explore sleep and physical activity as well as cardiorespiratory and muscular fitness.

Data Collection Procedures

Visit 1: Informed Consent, Questionnaires, Blood Draw, Body Composition, Sleep and Activity Assessment, Structured Exercise Assessment

Informed Consent

Upon arrival to visit 1, you will be given the 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 and the researcher will sign two copies of the informed consent (one for the you to take; the other for the researcher's records) if you are willing to participate in the study.

Medical Health History, Physical Activity Questionnaires and Additional Questionnaires
You will complete a Medical History Form and a Physical Activity Readiness Questionnaire (PAR-Q). The above screening form and questionnaire are designed specifically with your health in mind by allowing the researchers to become aware of any potential health issues that might be exacerbated by physical activity.
You will be asked to complete 7 additional questionnaires in varying length, but none will take longer than 7-10 minutes. You will be assessed on your marijuana use, current physical activity levels, as well as your feelings related to depression, anxiety, fatigue, quality of life, and sleep.
Blood Draw
Approximately 30 mL of blood will be taken via venipuncture and will be used to measure various immune markers. All blood samples will be collected with you in a fasted state between the hours of 0600-01000. During the blood draw, you will donate approximately 30ml of an intravenous blood sample.

Body Composition
Height and weight will be obtained using a stadiometer SECA 220 (Chino, California, USA) and the Detecto standing digital scale (Webb City, Missouri, USA), respectively. Body composition, lean body mass (LBM) and body fat percentage (BF%) will be evaluated using air displacement plethysmography with a BODPOD (COSMED USA Inc., Concord, CA). You will be instructed to remove your shoes, socks, jewelry, and all additional clothing other than your base layer. You will then be given a swim cap to wear, and body composition analysis will be performed via manufacturers guidelines.

Sleep and Activity Assessment
You will be given a FITBIT Inspire HR (Fitbit, San Francisco CA) to assess sleep quantity and quality as well as quantity of physical activity via wrist actigraphy assessment. You will be expected to wear the Fitbit Inspire HR band at all hours of the day and night for 1 full week for analysis. Additionally, you will be asked to keep the watch charged. We will be assessing sleep with the watch so charging the watch overnight will not be possible. You will be instructed to return the FITBIT Inspire HR during Visit 4.
Structure Exercise Assessment
You will be instructed to complete a physical activity/structured exercise log. Physical activity logs will include all physical activity completed over the week including but not limited to walking, running, swimming, or any physical activity completed during this week. You will be asked to log intensity, load, weight lifted, and any other details involved in the frequency, intensity, time, and technique of the activity. You will be instructed to return the physical activity logs during Visit 4.

Visit 2: Hydration Assessment and Aerobic Capacity test

Hydration Assessment
Upon arrival for performance testing (VO_{2peak},) you will be instructed to void your bladder into a collection container. The sample provided will be analyzed for urine specific gravity using the PAL-10S (4410) urine specific gravity refractometer (ATAGO, Tokyo, Japan). Hydration cutoff

will be set at USG <1.020. If you arrive in a dehydrated state (USG >1.020) you will be rescheduled and instructed to come in at a later date.

Aerobic Capacity Test

Your maximal oxygen uptake will be assessed though VO_{2peak} assessment on a treadmill (Trackmaster, Model: TMX425CP, Full Vision Inc., Newton, KS, USA) using a TrueOne 2400 Metabolic Measurement System (MMS-2400) (Parvomedics, Sandy, UT, USA). You will be fitted with a Polar Heart Rate Sensor H1 (Polar Electro Inc., Bethpage, NY, USA) for collection of heart rate (HR) throughout the entirety of the max test. You will begin with a warm-up at 0% grade at a speed of 3.5mph for 5 minutes. During warm-up, you will normalize to the Parvomedics system. Following completion of the 5-minute warm up, treadmill speed will increase to a speed of your choosing that you would feel comfortable running at for 5km. Each stage will be 3 minutes in duration, with your blood pressure (BP), blood lactate (BL), HR, and rating of perceived exertion (RPE) measured at the end of each stage. For the first 3 stages, grade will remain at 0% and the speed will increase 1mph every 3 minutes. Following the first 3 stages, speed will remain constant, and grade will be increased by 2% every 3 minutes until volitional fatigue and maximal oxygen uptake will be determined by achieving 2 of the 4 criteria of a true max test; 1) RPE achieving $\geq$8.5 on a modified Borg scale, 2) RER $\geq$ 1.1, 3) HR within 10 beats of your estimated HRmax (220-age), or 4) plateau in VO_2 following an increase in workload.

Visit 3: Anaerobic Fitness Assessment (Separated from Visit 2 by at Least 72 Hours)

You will complete an anaerobic fitness assessment using the Wingate anaerobic power test on a cycle ergometer (Monark Ergomedic 894E, Monark, Varberg, Sweden). You will begin by cycling between 60-75 revolutions per minute (RPM) at a self-selected resistance for 5 minutes. Upon completion of the warm-up, resistance will be reduced to 0, and you will be instructed to begin pedaling at your max cadence. Once you reach your max pedal cadence, 7.5% of your body weight will be added to the cycle ergometer, and the test will begin. You will cycle for a total of 30 seconds at a resistance of 7.5% body weight. At the cessation of the 30 second max test, you will cycle for an additional 5 minutes at a self-selected resistance for cool-down. You will be assessed on peak anaerobic power, mean anaerobic power, relative peak anaerobic power, total work, and fatigue index.

Visit 4: Strength Assessment

Your strength will be assessed via 1 repetition max (1-RM) back squat. You will warm-up by completing 5-10 repetitions of the exercise at 40-60% of your estimated 1-RM. You will then rest for 1-minute. Following 1-minute rest, you will complete 3-5 repetitions of the exercise at 60-80% of your estimated 1-RM. You will then rest again for 1-minute. Next, weight will be added to achieve 100% of your 1-RM. If you successfully complete the exercise at this weight, additional weight will be added in a conservative fashion and you will attempt to lift the new weight again following 3-5 minutes of rest. This procedure will continue until you fail to lift the set weight, and the previous successful lift will be recorded as your 1-RM. All 1-RM testing will be spotted by a trained exercise professional to ensure your safety.

Risk and Discomfort

There may be some minor discomfort associated with blood draws and testing**.** You will be seated comfortably during blood sampling. Any discomfort will be minimized by having a trained nurse or phlebotomist perform the blood draws. There is also a slight chance of skin irritation and discomfort from wearing the heart rate monitor device, but if present, the

discomfort should be minimal. Slight discomfort and possibly bruising on rare occasions may be experienced from the pinching and measuring of skinfolds. As with any exercise test, there is a chance that you will experience some discomfort including muscle soreness, fatigue, or even injuries such as sprains or strains and, or serious illness and death. You will be encouraged to stop any test at any time if there is discomfort beyond your comfort level.

Participation in this study entails minimal risk. There is a risk of bruising and a remote risk of infection with the blood sampling techniques. You may also become lightheaded and faint during these procedures. These risks will be minimized by having trained technicians using sterile, single use supplies for blood sampling. You will also be seated during blood sampling. Fruit juice will also be on hand in the event of a low blood sugar situation. As with any exercise testing, 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.

Participation Benefits

You will be given body composition analysis and aerobic capacity (VO_2peak) evaluations at no cost (valued at $400). Additionally, you will be provided with maximal strength testing and anaerobic fitness analysis. You will be provided with all your individual performance results at the end of the study.

Confidentiality

We will be assessing your marijuana use, which, if you are under 21, is an illegal activity. There is risk associated with reporting this information, but we will keep your information confidential. Because we are not easily linking your name with your substance use behavior and because we are recruiting both marijuana users and non-users, it is extremely unlikely that university authorities or law enforcement could discover that any specific participant used the substances assessed. A waiver has been obtained from the Dean of Students so that Dr. Stewart will not be obligated to report any misconduct as it may relate to marijuana use. Your information will remain confidential unless disclosure is required by law. Examples of two situations are where disclosure is required are: 1) a situation where there is a conversation during the study in which you reveal that you are at serious risk of harming yourself or others and 2) a situation where there is child abuse. No names (only identification (ID) numbers) will be associated with the blood tests and all blood will be analyzed at the same time with other subjects. Samples will be coded so that each collection tube will only be identified with a number so that the technicians or anyone else in the lab will not be able to determine which samples are associated with you.

All information recorded during the study visits will be coded with an ID number, and this ID number will not be readily connected to you. The only person who will have a written record of a person's name and ID number will be the graduate student and this written information will be kept in a locked cabinet in her office (Gunter Hall Room 2790) and shredded after the study data has been collected. Signed consent forms will be stored in a locked cabinet in your office on campus for a period of three years following the completion of the study, and then destroyed. Additionally, all marijuana use survey responses collected in visit 1 will be obtained by a

graduate student who does not know you and is not employed by UNC. In the extremely unlikely situation where the researchers both know you and you disclose marijuana use, the researchers will inform you (if s/he is under 21) that this action is breaking university policy and will provide information and resources to the student about how to quit if you so desire. If you are one of Dr. Stewart's current students, neither your study participation nor drug use information will influence your grade in the course. In this project, will have 3 graduate students working on this project. All data collection will be conducted by a research who does not know you.
All data files will be protected with passwords and paperwork will be locked in filing cabinets. All research assistants will only have access to ID numbers and will be made fully aware of the importance of protecting confidentiality. All staff will be required to sign a certificate of confidentiality, stating that they will not discuss your marijuana use or inappropriately divulge information to you. All procedures will be closely supervised by Dr. Laura Stewart. Research assistant staff will be trained to provide referrals for drug treatment or the counseling center if you request any information.

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. 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.

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Signature of Investigator

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Signature of Participant

Date:_____

Witness:_____