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Chronic cannabidiol supplementation does not improve ratings of perceived exertion and performance during time-trial cycling

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The research project was supervised by Dr Graeme Close.

Abstract:

Background: Cannabidiol (CBD) supplements are increasingly consumed by athletes to reduce pain during exercise. However, evidence of pain-relieving effects of CBD in healthy participants is limited. Therefore, the present study aimed at investigating the effects of chronic CBD supplementation on perceived pain and performance during cycling exercise. Methods: In a randomized, double-blinded, placebo-controlled study design, 22 healthy participants completed two separated, 10-minute maximal effort time trials on the watt bike, with a 3-week supplementation period in-between. During exercise, ratings of perceived exertion (RPE), heart rate (HR), and blood lactate (BLa) were measured every 2 minutes. Additionally, distance covered, average power, and peak power from the pre- and post-test were recorded. Results: No differences were observed between the CBD and placebo group ($p > 0.05$) or between overall pre- and post-test ($p > 0.05$) in any of the variables. RPE, HR, and BLa increased significantly ($p < 0.001$), and average power decreased significantly ($p < 0.001$) over the duration of the cycling exercise in similar amounts in both groups in the pre- and the post-test. Conclusion: 3-weeks of CBD supplementation does not reduce RPE and does not improve cycling time-trial performance in healthy male and female participants.

Keywords: cannabis; cannabidiol; CBD; pain; performance

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1. Introduction

Cannabis is widely used for both recreational and medicinal purposes and is derived primarily from *cannabis sativa*. This plant contains over 140 cannabinoids with the most notable being tetrahydrocannabinol (THC) and cannabidiol (CBD) [1]. THC is the most well-known and primary psychoactive compound in cannabis. CBD is the second most abundant compound and has no psychoactive effects [2]. In addition, cannabis contains several other molecules which could theoretically have physiological effects, and potentially influence performance [3]. All those cannabinoids can exert a variety of effects via the endocannabinoid system (ECS) [4], which is thought to regulate various behavior processes, including pain [2]. The ECS includes the endocannabinoids, alongside cannabinoid receptor 1 (CB1), cannabinoid receptor 2 (CB2), and enzymes that are required to synthesize and degrade the endocannabinoids [5]. CB1 receptors have a strong presence in the central nervous system (CNS), particularly within regions of the brain and spinal cord that regulate pain perception. The activation of CB1 receptors in those regions inhibits the release of neurotransmitters by decreasing calcium and increasing potassium conductance, which forms the basis for the analgesic action of cannabinoid agonists [6]. CB2 receptors are present in many of the same systems as CB1 receptors but are mainly expressed on immune cells. CB2 receptors play a role in mediating analgesia by reducing inflammation in the periphery and regulating cytokine release [7]. Exogenous cannabinoids can directly trigger CB1 and CB2, activate multiple kinases and channels, and thus exert a diverse range of physiological consequences [8]. Due to their structural differences, THC and CBD have different affinities to CB1 and CB2 receptors [9]. THC acts as a partial agonist to CB1 and CB2 [10]. On the other hand, CBD might function as an agonist to CB2 and as a negative allosteric modulator of CB1 [11]. CBD has also been shown to interact with many other non-endocannabinoid systems, including G-protein coupled, serotonin, vanilloid, dopamine, and opioid receptors [12].

Due to their function in these systems, cannabinoids have been intensively investigated for the treatment of pain [13]. Despite some methodological inconsistencies (e.g., route of delivery, treatment period, pain model), most clinical studies appear to have observed a significant analgesic effect of CBD [1]. A review of clinical trials in pain management showed modest efficacy for cannabinoids across a variety of conditions, including inflammatory pain, neuropathic pain, and cancer pain [2].

Pain has long been linked to success in sports [14], and it is well recognized that repetitive and intensive muscular contraction, which is consistent with endurance performance, leads to exercise-induced pain (EIP) [15]. Therefore, pain tolerance (the maximal level of perceived pain someone can tolerate) may be a significant factor for success in endurance exercise and earlier studies [14–16] showed, that using an intervention to reduce pain can improve exercise performance.

In the elite sports environment, EIP is often modulated via opiates and non-steroidal anti-inflammatory drugs (NSAIDs) [18], but due to their sometimes serious side effects [19], athletes are

beginning to explore alternative pain-relieving therapies with another emerging method being the use of CBD [20]. Although regulations regarding its legality vary between countries, CBD was removed from the World Anti-Doping Agency (WADA) list of prohibited substances in 2018. All natural and synthetic cannabinoids are still prohibited, except for CBD [21]. This recent consideration by WADA opens the door for CBD use by athletes [3].

Studies directly investigating CBD and sports performance are lacking but given CBD´s clinical application use in reducing pain, it could be speculated that CBD might also reduce perceived pain and thus enhance endurance exercise performance. To the authors' knowledge, only one pilot study [22] investigated the effects of CBD on perceived pain and showed that CBD might potentially improve ratings of perceived exertion (RPE) and ratings of pleasure during exercise. Thus, although CBD may improve the ability to sustain pain through several potential mechanisms, further research is still required [3]. Therefore, the aim of the current study was to determine, whether CBD can enhance performance in a 10-minute maximal effort cycling trial by masking pain and reducing the effects of fatigue. The hypothesis of the study is that CBD will reduce RPE and therefore increase cycling performance.

2. Materials and Methods

2.1 Experimental Design

A randomized, double-blind, placebo-controlled study design was conducted to examine the effects of CBD versus placebo (PLA) supplementation on RPE during a 10-minute maximal effort trial on the watt bike. All participants completed two separate 10-minute maximal effort trials on the watt bike, with a 3-week supplementation period in-between. Each experimental trial was completed following 24 hours of diet control. Prior to experimental trials, participants completed preliminary testing including familiarization sessions with the watt bike.

2.2 Participants

Twenty-four healthy males and females aged between 18 and 45 who had not used cannabis or cannabinoids in the previous three months were recruited for this study and 22 (11 males and 11 females) completed the study. Characteristics from the participants who completed the study were as follows: age, 27 ± 6.3 (SD) years; body mass (BM), 69.4 ± 13.5 kilograms (kg); stature, 170.4 ± 10.1 centimeters (cm); average power, 173.68 ± 46.19 watts (W). Before commencing the first familiarization session, all participants completed a readiness to exercise questionnaire to ensure they were free from illness or injury. All participants were fully informed of all experimental procedures and possible risks before providing their written, informed consent. The study was approved by the Research Ethics

Committee of Liverpool John Moores University (Ethics No. M22_SPS_2273) and all procedures conformed to the ethical standards of the Declaration of Helsinki.

2.3 Sample Size Calculation

Sample size was calculated (G*Power software, version 3.1.9; Düsseldorf, Germany) for an *F* test using repeated-measures analysis of variance with between-subject interaction (Cohen´s effect size [ES] = 1.08, *alpha* = 0.05, ß = 0.8, groups = 2, measurements = 2, allocation ratio N2/N1 = 1). The ES was estimated by between-group differences from previous studies [23] that found a large ES (1.08) for average power on the watt bike. Total sample size was based on average power and 30 participants (15 participants per group) were required for an 81% chance (actual power) of correctly rejecting the null hypothesis.

2.4 Familiarization

Prior to experimental trials participants completed two to five familiarization sessions on the watt bike, consisting of the same protocol that was used for experimental trials. A minimum of 48 hours was set between each session to eliminate muscle damage effects. At the start of the first familiarization session, each participant's body weight was recorded on a SECA scale (model 704, Germany) and height was measured via stadiometer (Leicester height measure MKII, Invicta Plastics, Leicester UK). Participants finished their familiarization after their coefficient of variation of average power and distance covered between their different 10-minute all-out trials on the bike was below 5% [24].

2.5 Randomization and blinding

After the familiarization sessions, participants were block randomized by blinded researchers into two groups (CBD and PLA), using two random number generators. Participants were randomized according to their gender and average power. The randomization was generated in two balanced blocks of ten and one balanced block of four.

2.6 Protocol

All trials were conducted in the laboratory of Tom Reilly Building (TRB) at Liverpool John Moores University. For each participant, the performance trials were conducted at the same time of the day (±1 hour) between 6:30 am and 10:30 am. Resistance of the watt bike was set on 1/1 and 1/5 for females and males, respectively. Each trial started with a 3-minute warm-up on the watt bike at a self-selected pace. After 90 seconds break, the 10-minute maximal effort trial on the bike commenced. Participants were required to maintain a power output as high as possible for the whole 10 minutes and without the use of verbal motivation. RPE, using the scale proposed by Borg [25], heart rate (HR) (Polar

H10, Finland), and average power were collected after 2, 4, 6, 8, and 10 minutes of each trial. Furthermore, blood samples from a fingerpick were obtained at these time points to measure blood lactate (BLa) values (an overview of the research protocol can be viewed in *Figure 1*). During the trials, participants were blinded from on-screen performance data except for time. At the end of each trial, average power, maximal power, and distance covered for the 10-minutes were recorded from the screen of the watt bike. Participants used the same watt bike for pre- and post-trials to minimize systematic bias.

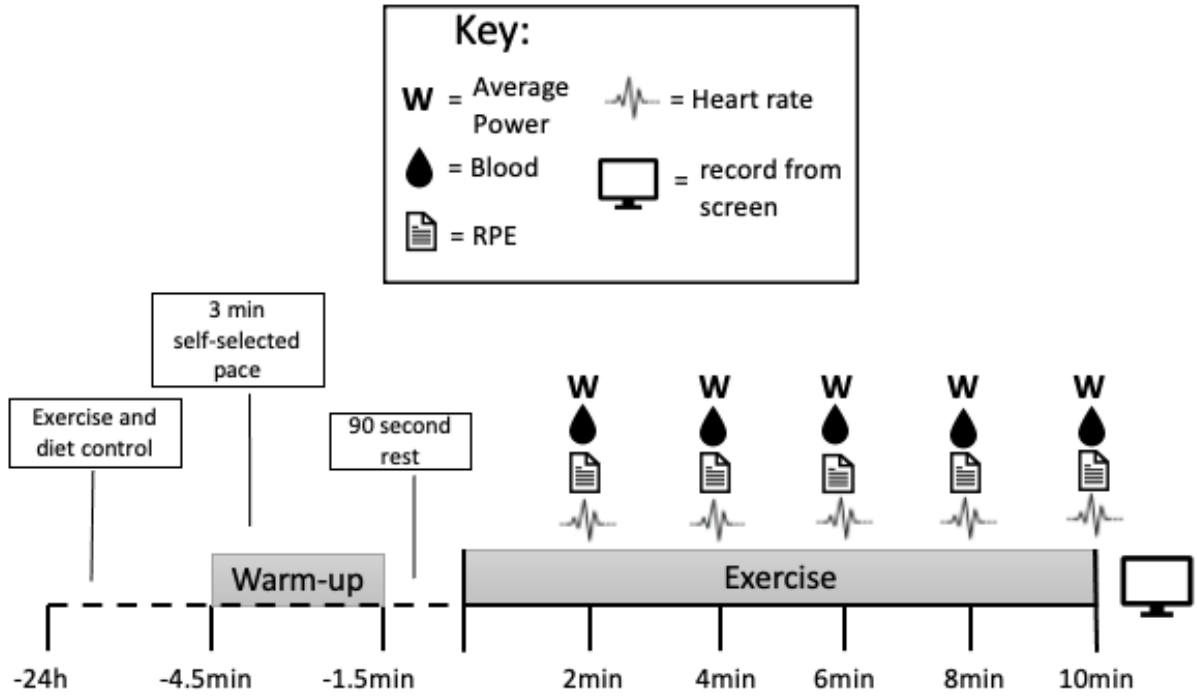

Figure 1. Study Design

2.7 Blood analysis

Blood samples were obtained via finger prick capillary sampling using a 1.8 mm sterile safety-lancet (Sarstedt AG & Co, Nümbrecht, Germany) after sterilization using a pre-injection medical swab (Medlock Medical Ltd., Oldham). A 20µl blood sample was collected in a Biosen capillary tube (EKF Diagnostics, Barleben, Germany) and analyzed using Biosen C-Line for lactate concentrations (EKF Diagnostics, Barleben, Germany).

2.8 Supplementation

Directly after finishing their first experimental trial, participants received their respective supplements. Both the CBD and PLA supplements were provided in identical-looking glass bottles to ensure the blinding of researchers and participants. Participants of the CBD group consumed 150mg of CBD per day in a 40% concentration 100% vegan-certified CBD oral formulation containing plant-

derived CBD (40 mg*mL^{-1} ≥ 98% of the total cannabinoid content) and other minor cannabinoids including CBD, CBG as per the potency analysis in a medium chain triglyceride (MCT) oil (overview of the CBD supplement content can be viewed in *table 1*). The placebo supplement consisted of a taste-matched, visually identical MCT oil (also 100% vegan-certified). Participants started their supplementation directly after the first experimental trial and the last consumption of their supplement was on the morning of the following experimental trial 3 weeks later. Nine drops of the perspective supplement were consumed every morning around 8 am (+/- 1 hour) each day of the three-week period. The drops were held sublingual for 30 seconds and then swallowed afterwards.

Table 1. CBD supplement content

Cannabinoid	Content (in %)
Cannabidiol (CBD)	43.184 %
Cannabichromene (CBC)	0.0135 %
Cannabichromenic Acid (CBCA)	< 0.0025 %
Cannabicyclol (CBL)	< 0.0025 %
Cannabidiolic Acid (CBDA)	< 0.0025 %
Cannabidivarin (CBDA)	< 0.0025 %
Cannabidivarinic Acid (CBDVA)	< 0.0025 %
Cannabigerol (CBG)	0.5955 %
Cannabigerolic Acid (CBGA)	0.0048 %
Cannabinol (CBN)	< 0.0025 %
Cannabinolic Acid (CBNA)	< 0.0025 %
Tetrahydrocannabinolic Acid (THCA)	< 0.0025%
Tetrahydrocannabivarin (THCV)	< 0.0025%
Tetrahydrocannabivarinic Acid (THCVA)	< 0.0025 %
Total CBD (CBD + (CBDA x 0.877))	43.184 %
Total THC (THC + (THCA x 0.877))	< 0.0025 %
Δ8- Tetrahydrocannabinol (Δ8- THC)	< 0.0025 %
Δ9- Tetrahydrocannabinol (Δ9- THC)	< 0.0025 %

2.9 Exercise and diet control

Participants were instructed to abstain from any kind of exercise and alcohol consumption 24 hours before both experimental trials. Dietary standardization was achieved by giving the participants the instructions to consume 6g of carbohydrates per kg of bodyweight the day before each trial, as carbohydrates are the predominant energy source during high-intensity exercise [26]. On the morning of each trial, participants were instructed to have a self-prescribed breakfast, but the same was to be replicated for both trials. Caffeine consumption was optional but should also be repeated across both experimental trials. Participants were also instructed to come to every trial well hydrated. Nutrition was controlled by receiving pictures with a short description of each meal from the participants via WhatsApp, and the composition of dietary macronutrients was calculated with a nutrition assessment software (Nutritics, 2022). If participants needed help with how to reach the 6g of carbohydrates per kg bodyweight, personalized meal plans were sent out to them beforehand.

2.10 Statistical Analysis

Statistical analysis was undertaken using SPSS for Windows (version 25, SPSS Inc, Chicago, IL). Data was assessed for normality by assessing the plot of residuals of the mean values. To compare the performance parameters (distance covered, average power, and peak power) from the CBD and PLA group, which were taken from the screen of the watt bike at the end of each trial, data was analyzed using a two-way mixed design ANOVA, where the within factor was test (pre-test and post-test) and the between factor was group (CBD and PLA). To compare the physiological variables (RPE, lactate, HR) and average power over time, data was analyzed using a two-way mixed-design ANOVA, where the within factors were test (pre-test and post-test) and time (2, 4, 6, 8, 10 minutes) and the between factor was group (CBD and PLA). To ensure sphericity, as an assumption for the ANOVA, the recommendations of Atkinson [27] were used, which state to use the Huynh-Feldt corrected line on the SPSS output if the Greenhouse-Geisser epsilon is greater than 0.75 and to use the Greenhouse-Geisser corrected line if the Greenhouse-Geisser epsilon is 0.75 or lower. Moreover, Bonferroni's tests were used to further identify the investigated main effects. Additionally, t-tests were used to calculate potential differences in the amount of carbohydrates consumed between the groups and between pre- and post-tests. All data in text, tables, and figures are expressed as means and SD with $p < 0.05$ indicating statistical significance.

3. Results

Characteristics from participants (n=22) completing all trials can be seen in *Table 2.*

Table 2. Participant Characteristics

Characteristics	CBD (n=10)	PLA (n=12)
Age [years]	28 ± 7.3	25.5 ± 5.2
Stature [cm]	169.4 ± 8.4	171.3 ± 11.7
Body mass [kg]	69 ± 14.3	69.7 ± 13.6
Average Power [W]	186.3 ± 46.4	166.5 ± 45

Cm = centimeter, kg = kilogram, W = watts, PLA = placebo

3.1 Performance Variables

All performance variables (distance covered, average power, and peak power) showed no significant difference between the CBD and PLA groups (Figure 2; $p > 0.05$) and no significant difference between the pre- and post-test ($p > 0.05$). There were also no significant interactions between test and group ($p > 0.05$). When comparing average power [W] at each time point during the trials (2, 4, 6, 8, 10 minutes; Figure 3), there was a significant main effect for time ($p < 0.01$), with a significant decrease between all timepoints in both groups ($p < 0.05$), while average power was unchanged between 8 to 10 minutes ($p = 1$). There was also a significant interaction between test and time ($p = 0.034$), with the average power over time being higher in the post-test than in the pre-test, but not when just comparing the overall average wattage of pre-test and post-test from the screen of the watt bike ($p = 0.313$). The average power was also non significantly higher during both tests in the CBD (pre: 185.9 ± 48.76 W; post: 186.6 ± 46.49 W) than in the PLA group (pre: 163.5 ± 43.37 W; post: 169.5 ± 48.35 W; Figure 2A; $p = 0.329$). Peak power in the CBD group increased non significantly from pre- to post-test (405.8 ± 116.23 W, vs. 445.5 ± 123.87 W; $p = 0.225$), whereas peak power in the PLA group decreased non significantly from pre- to post-test (351.9 ± 158.39 W, vs. 345.9 ± 151.46 W; Figure 2B; $p = 0.78$). Distance covered was similar between pre- and post-test in both groups but increased non significantly in the CBD (5.93 ± 0.56 km, vs. 5.95 ± 0.55km; $p = 0.71$) and the PLA group (5.67 ± 0.54km, vs. 5.74 ± 0.59 km; Figure 2C; $p = 0.249$). Even a group division by gender (CBD males compared with PLA males and CBD females with PLA females), showed no significant difference in any performance variable between the CBD and PLA groups ($p > 0.05$).

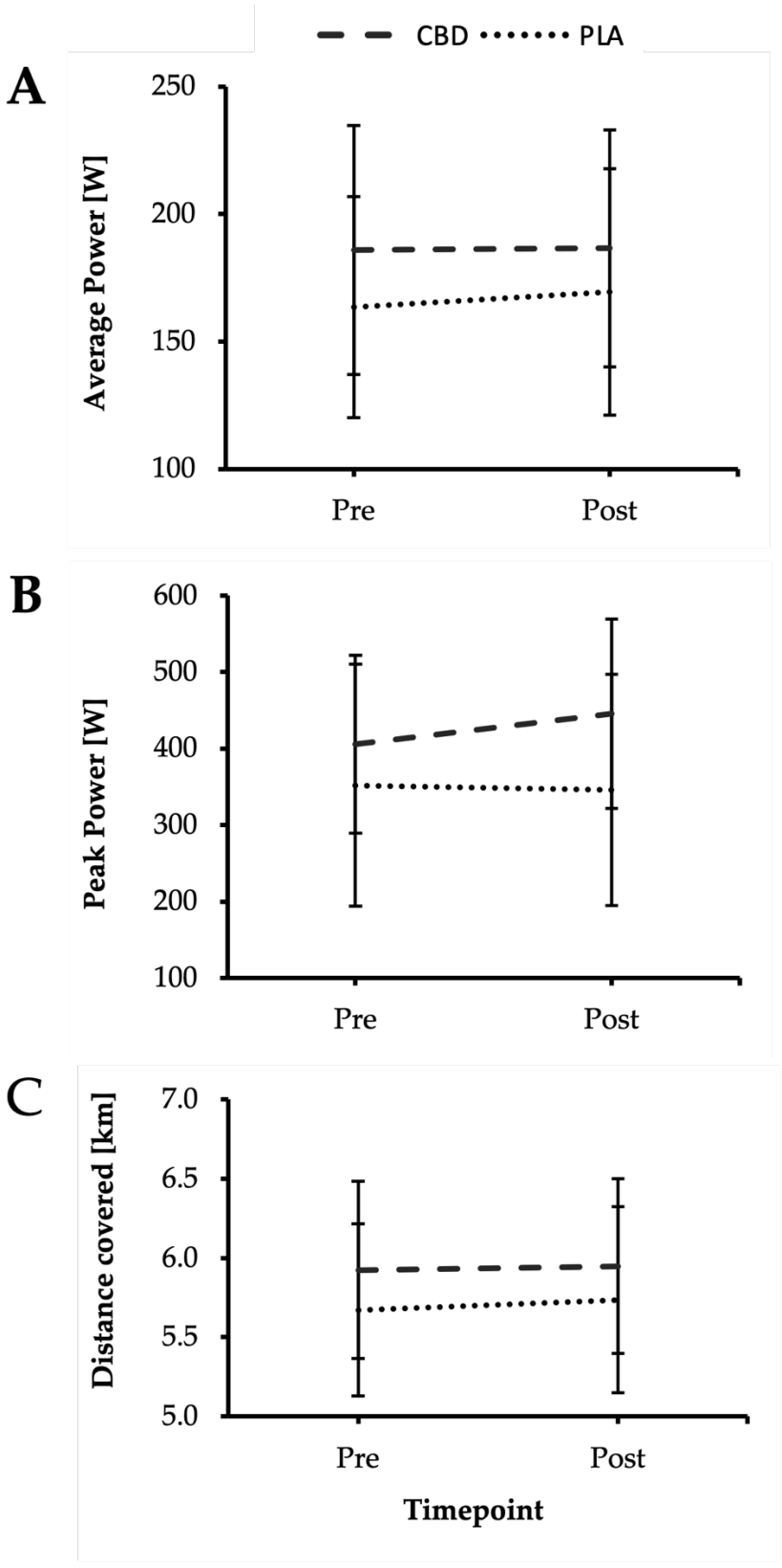

Figure 2. Performance Variables, (A) average power, (B) peak power, (C) distance covered. W = watts, km = kilometer

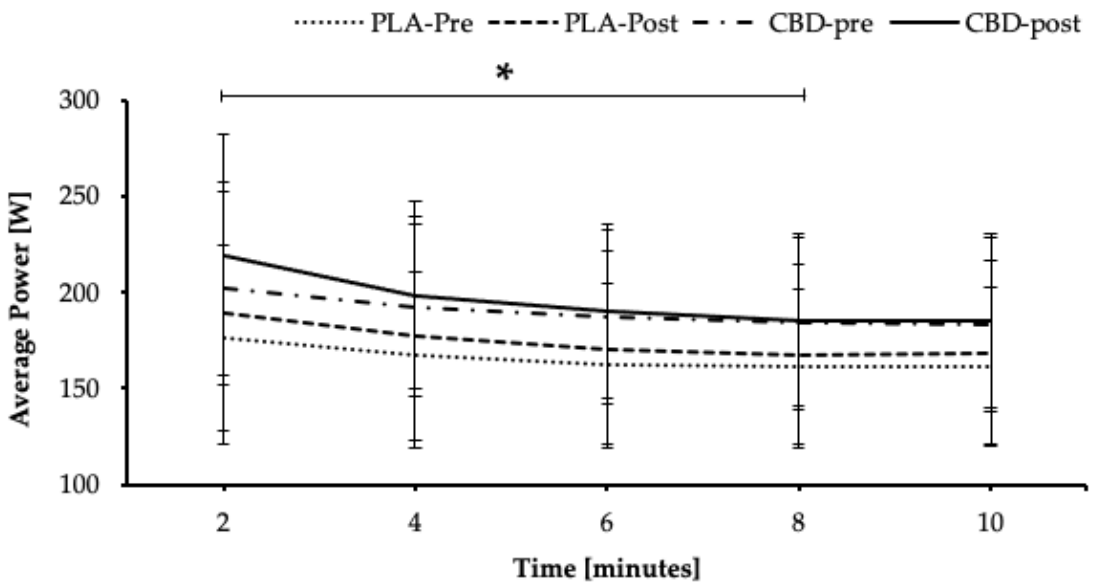

Figure 3. Average power over time. W = watts; (* = p < 0.05)

3.2 Physiological Variables

No physiological variables (RPE, HR, BLa) showed any significant difference between the CBD and PLA group (Figure 4; $p > 0.05$) and no significant difference between pre- and post-test ($p > 0.05$). There were also no significant interactions between test, group, or time ($p > 0.05$). In both groups and during both tests, RPE, HR, and BLa all significantly increased over time ($p < 0.01$), with a significant increase between all timepoints (2, 4, 6, 8, 10 minutes; Figure 4; $p < 0.01$). RPE decreased non significantly in the CBD group from the pre- to the post-test (16 ± 0.45 Arbitrary Units [AU], vs. 15.96 ± 0.45 AU; $p = 0.838$) and increased non significantly in the PLA group (14.88 ± 0.42 AU, vs. 15.27 ± 0.41 AU; $p = 0.103$). Heart rate increased non significantly between pre- and post-test in the CBD (164.28 ± 3.67 beats per minute [bpm], vs. 165.66 ± 4.63 bpm; $p = 0.506$) and decreased non significantly in the PLA group (171 ± 3.35 bpm, vs. 168.73 ± 4.22 bpm; $p = 0.472$). Furthermore, BLa increased non significantly between pre- and post-test in the CBD (6.99 ± 0.68 mmol/L, vs. 7.23 ± 0.65 mmol/L; $p = 0.645$) and the PLA group (6.33 ± 0.62 mmol/L, vs. 7.24 mmol/L; $p = 0.124$). When the groups were divided by gender, there was also no significant difference in any physiological variable between the CBD and PLA groups ($p > 0.05$).

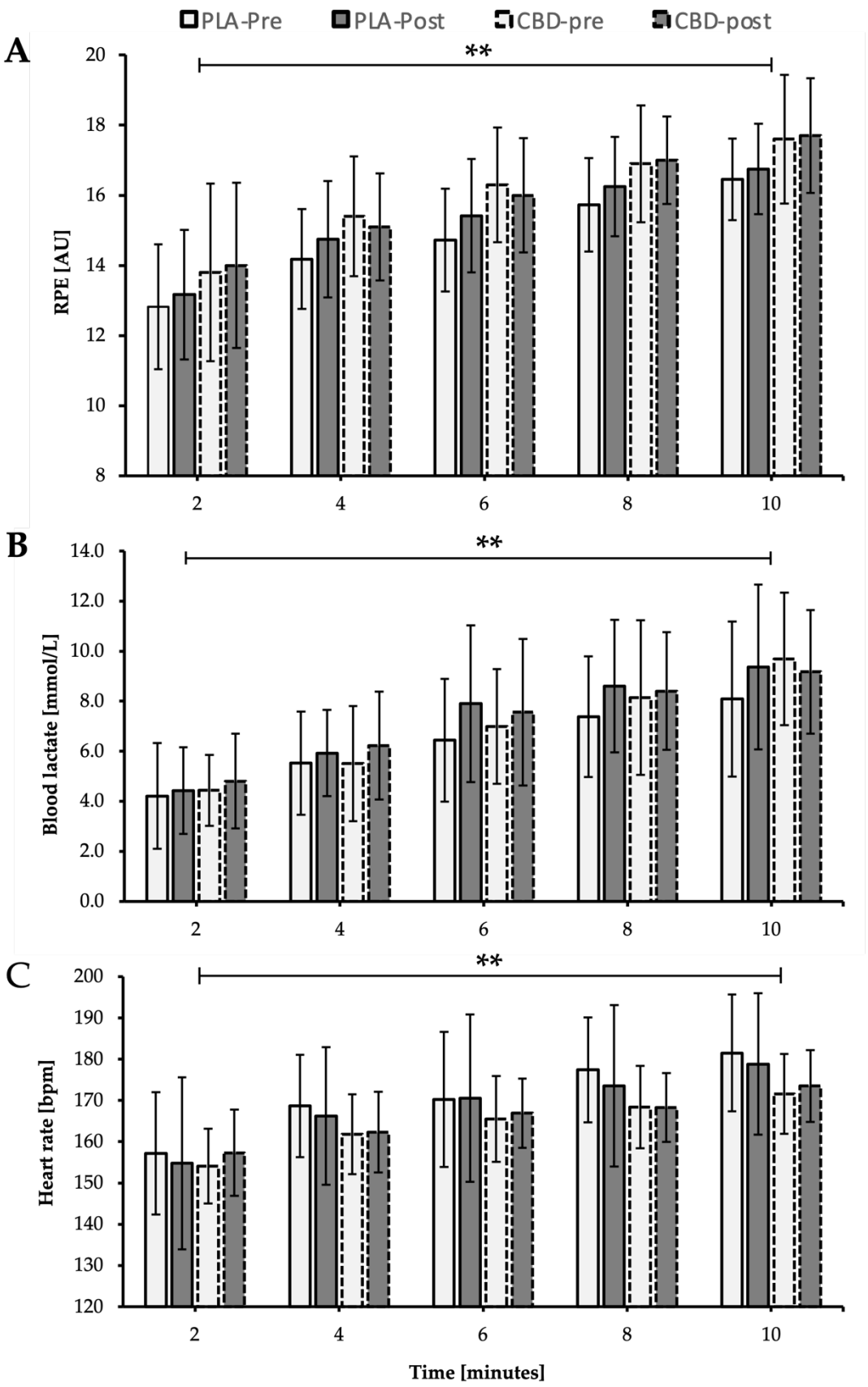

Figure 4. Physiological variables, (A) ratings of perceived exertion (RPE), (B) blood lactate, (C) heart rate. RPE = ratings of perceived exertion; (* = $p < 0.05$; ** = $p < 0.01$)

3.3 Nutrition

There was no significant difference in the amount of carbohydrates consumed per kg body weight between the groups and between pre- and post-test ($p > 0.05$). Even though participants received the recommendations to consume 6g of carbohydrates per kg body weight the day before each trial, both groups consumed an average of 5g of carbohydrates per kg body weight the day before the pre- and before the post-test (Figure 5).

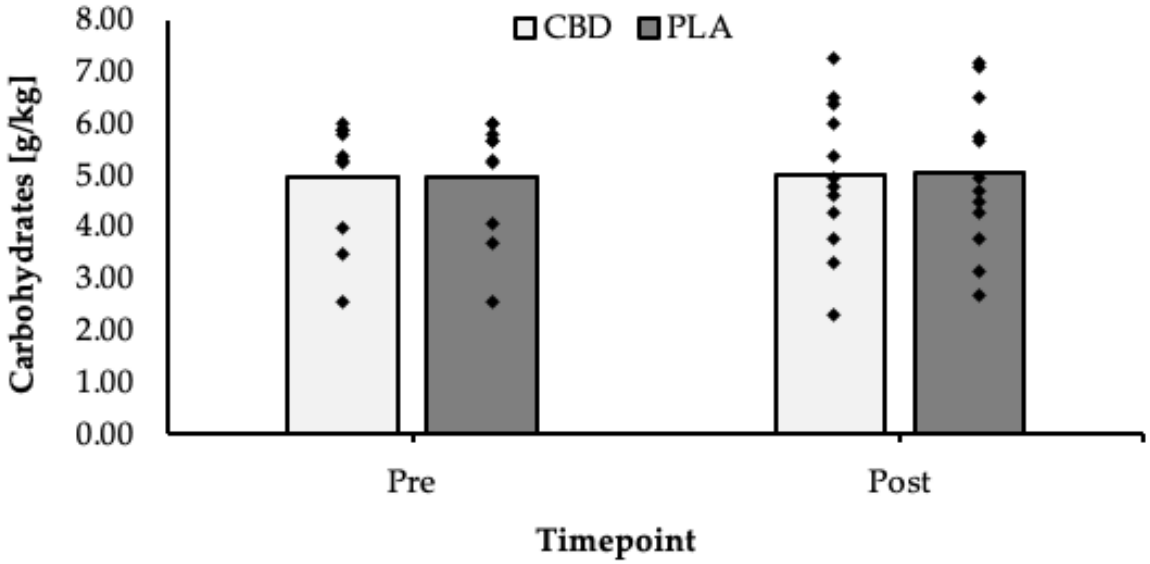

Figure 5. Amount of carbohydrates consumed the day before each trial.

4. Discussion

The main finding of the present study is that 3-week supplementation with CBD does not mask pain and does not reduce RPE, and hence does not improve performance during a 10-minute maximal effort trial on the watt bike. Thus, the earlier hypothesis must be rejected. The results show a significant increase in RPE, HR, and BLa, as well as a significant decrease in average power over the duration of the 10-minute maximal-effort protocol in the pre- and the post-test, but with no differences between CBD and PLA groups. This is in line with previous findings from a pilot study [22], which reported no reduction in RPE, nor an improvement in time to exhaustion during running exercise with acute CBD supplementation.

Despite CBD´s growing popularity among athletes [20], evidence in the exercise literature is limited and besides one pilot study [22], the few studies available focused mainly on recovery after training [28–30]. Our initial hypothesis that CBD might reduce pain and thus RPE during exercise was based on previous literature, which shows that in addition to acting on the cannabinoid receptors CB1 and CB2, CBD can also act on multiple other pain targets within the peripheral and central nervous system [31].

CBD can act as an inverse agonist to the orphan G-protein coupled receptors (GPRs) 3, 6, and 12, which are all expressed in neurons in the brain, and GPR3 can also be found in the spinal cord. Therefore, all of them might act as potential targets for CBD when reducing pain perception [32]. Furthermore, CBD has shown agonistic activity at the serotonin (5HT) receptor, which is involved in modulating neuropathic pain [33]. Thus, it could be hypothesized that CBD might regulate EIP by targeting this receptor as well. Additionally, it was shown, that CBD also acts as an agonist at the transient receptor potential vanilloid 1 (TRPV1) [34], which has shown to mediate thermal hyperalgesia by integrating noxious stimuli. Thus, this receptor might also be responsible for some analgesic effects of CBD [34]. Moreover, CBD has shown agonistic activity at dopamine receptor 2 (D2) and has shown to act as a negative allosteric modulator at opioid receptors, which could both potentially be involved in pain modulation [34]. Due to our main finding that CBD does not reduce RPE during exercise, we suggest that its action on these receptors is not involved in regulating EIP.

However, in clinical settings, CBD has been intensively studied for the relief of several pain conditions, although the perceived pain relief effect was shown in products containing CBD and THC, and not with CBD alone [35]. The majority of clinical studies describe the efficacy of CBD and THC co-administered at similar doses [36]. A dose-related effect of cannabis was found, with higher THC contents producing more pronounced pain relief [37]. Furthermore, a real-world evidence study [38] showed that THC-dominant products were more frequently consumed for symptoms related to pain and sleep, while CBD-dominant products were more frequently used to treat anxiety and depression, which might be explained due to their different action on CB1 receptors. Due to their presence in the brain and spinal cord, which are both responsible for pain perception, pain in the ECS is mainly regulated through CB1 receptors. The activation of CB1 receptors inhibits the release of neurotransmitters via decreasing calcium conductance and increasing potassium conductance, which forms the anatomical basis for the analgesic action of cannabinoid agonists like THC [6]. Unlike THC, CBD does not activate CB1, but binds to a separate allosteric site and acts as a negative allosteric modulator, making it more difficult for THC to bind to the CB1 receptor side [11]. Therefore, unlike THC, CBD does not appear to have analgesic effects on CB1 receptors. However, CBD might function as an agonist to CB2 receptors [11], which are expressed mainly on immune cells and mediate analgesia by reducing inflammation in the periphery [7]. EIP from endurance exercise like cycling is likely produced through a combination of increased intramuscular pressure, the release of noxious metabolites, and deformation of tissue associated with muscular contraction, but does not come from inflammation [39]. Therefore, given that CBD does not reduce RPE during cycling exercise, it can be suggested that CBD does also not reduce EIP via targeting CB2 receptors.

Accordingly to our findings, CBD does not appear to influence RPE during exercise and this might be explained due to the inability of CBD to bind to specific receptors. However, there are also other

variables that could potentially influence the efficacy of CBD supplementation, such as differences in tissue accumulation, body fat percentage or gender. Although CBD accumulation in human tissue potentially influences receptor binding, the effects of chronic CBD supplementation on tissue accumulation are poorly understood, as most studies so far focused on THC or a co-consumption of THC and CBD [40]. A recent study by Child et al. [40] measured CBD tissue accumulation and pharmacokinetics in rats and showed, that CBD accumulated similar in adipose tissue, skeletal muscle, and liver, with higher values in adipose tissue than in muscles or liver, which is in line with THC accumulation in humans [10]. While the research from Child et al. [40] offers an insight into the accumulation of CBD, clearly more research is required to understand the molecular pathways as to how CBD is absorbed, stored, and utilized. Due to the potential accumulation of CBD in adipose tissue [40], potential effects of CBD might be influenced by percentage of body fat. Since the present study just measured the overall body weight of the participants, no conclusion can be drawn about the relationship between body fat percentage and different CBD efficacy in the participants here.

Furthermore, earlier studies showed that CBD might show different efficacy between genders. Child et al. [40] observed a different global tissue CBD response between male and female rats. For the same relative CBD dose, females consistently had higher concentrations in adipose tissue, as well as in skeletal muscle and liver. In addition, Redmond et al. [41] showed that the synthetic cannabinoid Nabilone decreased hyperalgesia in healthy human females but not in males. This might be due to the different potency and binding affinity of CB1 receptors between the genders [42]. So far it is not known whether sex differences also exist with CB2 receptors or other targets of CBD [43]. In contrast to Redmond et al. [41], the present study showed no differences in RPE and pain relief with CBD between males and females. This might again be explained due to the high amount of THC (1mg) in the study conducted by Redmond et al. [41], as opposed to < 0.0025 % of THC being present in the broad spectrum used in the present study.

In addition, the tool of measurement used to measure the potential pain-reliving effect of CBD might influence current findings. In clinical studies pain is often measured via rating scales of pain perception [44–46], whereas in sport and exercise science pain is often measured as part of perception of effort and fatigue [47], which can be described with Borg´s RPE scale [25]. Earlier exercise studies already used RPE in context with other potential pain-relieving supplements. Chtourou et al. [48] for example showed that caffeine consumed in form of an energy drink can reduce RPE and pain perception during trainings sessions, which can be explained through the increased secretion of ß-endorphins with caffeine [49].

Additionally, RPE in the present study significantly increased from the start to the end of each trial in both groups in pre- and post-test. This is in line with earlier studies [50], which showed a linear rise in RPE over the duration of exercise, with maximum levels at exercise completion. According to the

original concept of Borg [25], the linear increase in RPE indicates that the brain perceives that the exercise is becoming more demanding, even when the work rate remains the same. Additionally, Scherr et al. [51] indicated that RPE is strongly correlated with HR and BLa, which can also be seen in the present results. The significant increase in RPE, HR, and BLa between all timepoints from start to end of each trial in the present study highlights the high intensity of the exercise [51]. As EIP increases proportional with exercise intensity, it can be shown that the performed time-trial was hard enough to induce EIP in the participants [52].

Even though the present study showed no reductions in RPE, Kasper et al. [20] investigated CBD use in rugby players and found that 26% of the players had previously used CBD supplements and 80% of those players used CBD to reduce pain or improve recovery. Therefore, even though in the present study CBD does not seem to reduce RPE or pain during exercise, it might instead improve pain and recovery from exercise-induced muscle damage after exercise [28] or have some sort of placebo effect [53], as it is well-known that CBD can reduce pain in many clinical conditions [48–50]. Moreover, rugby players could potentially face a different kind of pain during exercise than seen during cycling [56]. Therefore, CBD might potentially be able to reduce pain in rugby players and future studies would be valuable, as reducing pain and improving performance is a desirable goal for athletes [14].

Despite many athletes currently using CBD supplements [20], so far CBD is the only cannabinoid that is legal to use for athletes, with THC and all other cannabinoids prohibited in and out of competition [21]. THC is considered a threshold substance, with a decision limit of 150 ng/ml, but all other cannabinoids are completely prohibited [57]. According to WADA [21], substances or methods are prohibited in and out of competition if they meet at least two of the following criteria: 1.) enhance performance, 2.) adversely affect health, and 3.) be against the spirit of sport. The product used in the present study was a broad spectrum, consisting of many different cannabinoids, as well as terpenes and flavonoids. Working synergistically, they are supposed to produce a wide variety of benefits including a reduction of pain or inflammation [58]. Following the prohibited list, the broad spectrum used in the present study is prohibited for athletes in and out of competition, due to the presence of several other cannabinoids, like CBG and CBC. This raises the question about the prohibition of those cannabinoids other than CBD when the present study shows that the use of CBD broad spectrum does not improve performance. Further studies with larger sample sizes are needed to further investigate the effects of cannabinoids on performance and their effect on health. Furthermore, it is questionable whether the consumption of other cannabinoids is against the spirit of sport [13].

Although this study provides important findings concerning the effects of chronic CBD supplementation on RPE and performance during time-trial cycling, there are also some limitations. Even though the amount of carbohydrates consumed the day before each trial was similar between both groups and between pre- and post-test, individual participants consumed partially different amounts

of carbohydrates the day before the pre- and the post-test. As muscle glycogen stores have been shown to influence high-intensity exercise [26], potential differences in performance might be due to the amount of carbohydrates consumed and not due to the supplement. As this study included male and female participants, it must be taken into consideration that this study did not measure the menstrual cycle of the females. As the supplementation period lasted three weeks, females were in different phases of their menstrual cycle in the pre- and the post-test. Although both groups included a similar number of female participants, being in different phases of their menstrual cycle might have influenced their performance levels [59]. Furthermore, sleep was not tracked or measured the days before the trials, although it has shown to potentially influence performance [60]. Moreover, CBD is metabolized in the liver by CYP450 enzymes [61], but earlier studies already showed high inter-subject variability in those enzymes and therefore in CBD metabolism and pharmacokinetics [62], which might present a limitation of transferability. Therefore, future studies should include larger sample sizes to be able to make conclusions for a wider population. In addition, all participants in the study received the same amount of CBD oil, although metabolism and efficacy might be influenced by body weight, percentage of body fat, or gender. Furthermore, it is not known whether different dietary habits might also influence the CBD metabolism of the participants. Future studies should focus on answering any questions concerning potential influences of CBD metabolism and recommendations concerning exact dose requirements. Moreover, an omics approach may provide a potential insight into the molecular and cellular function of CBD as well as clarification on its exact mechanisms.

5. Conclusion

The current study indicates that 3 weeks of CBD supplementation did not reduce RPE during time-trial cycling exercise and thus did not improve performance. RPE, HR, and BLa increased significantly over the duration of the cycling exercise and average power decreased significantly over time, but with no difference between CBD and PLA or overall pre- and post-test. Athletes should therefore carefully consider the advantages and disadvantages of taking CBD supplements.

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6. References

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