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Chronic co-use of cannabis and tobacco on short-term recovery from eccentric exercise-induced muscle damage: A pilot study

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ABSTRACT: Cannabis use is increasingly prevalent, particularly among young adults. While the endocannabinoid system (ECS) plays a role in modulating inflammation and pain perception, the influence of chronic cannabis use on recovery from exercise remains unclear. To compare recovery of muscle function, soreness, and circulating biomarkers of muscle damage and inflammation after an exercise-induced muscle damage (EIMD) protocol in chronic cannabis users (CU) compared to non-users (NU), twenty-six physically active participants (12 CU, 14 NU) performed a drop jump protocol to cause EIMD. Isometric and concentric isokinetic peak torque of the quadriceps, serum creatine kinase (CK), myoglobin (Myo), interleukin-6 (IL-6), and perceived muscle soreness were assessed at baseline, immediately post-exercise, and at 24-, 48-, and 72-hour post-exercise. A time and group interaction was observed for isometric peak torque ($p = 0.048$), with CU showing greater isometric strength than NU immediately after exercise (mean difference = 10.53%, 95% CI: 0.12–20.94) and at 72 hours (15.11%, 95% CI: 0.90–29.31), with no differences at other time points. Concentric peak torque, CK and Myo displayed similar kinetics in both groups, with no significant main or interaction group effects. IL-6 showed no clear between-group differences despite a significant time and group interaction, and the overall pattern over time was comparable in CU and NU. Muscle soreness increased after exercise and declined thereafter, with no significant group or time and group interaction effects. Chronic cannabis use does not impair short-term recovery of muscle function or inflammatory response following EIMD.

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INTRODUCTION

Cannabis is the most widely used illicit substance in Western countries [1]. The consumption of cannabis preparation, particularly those containing Δ9-tetrahydrocannabinol (Δ9-THC) may lead to Cannabis Use Disorders (CUD) [1, 2]. Between 1990 and 2019, the number of new cases of CUD more than doubled in 53 out of 204 countries and territories worldwide [3]. Connor et al., [4] estimated that CUD affects approximately 10% of the 193 million cannabis users worldwide, representing a minority of all cannabis users [5]. This trend should be interpreted in the context of a broader increase in cannabis use, partly driven by the progressive liberalization of cannabis policies and greater accessibility in many regions. CUD has been associated with a range of short- and long-term side effects, including respiratory and cardiovascular disorders, cognitive impairment, psychosis, schizophrenia, and mood disorders [2]. Among non-pharmacological therapeutic approaches, structured exercise and physical activity have been proposed as potentially valuable components of CUD management [6].

Exercise is increasingly recognized as a complementary therapeutic strategy for individuals with CUD, with evidence suggesting beneficial effects on both craving and frequency of use. In particular,

aerobic training has been shown to alleviate substance-related symptoms and improve mental well-being in this population [6]. However, the effectiveness of such interventions depends in part on participants' adherence to physical activity programs, which can be influenced by the type of exercise and the sensations it elicits [7]. Certain forms of exercise, especially those involving high eccentric loads, are known to result in exercise-induced muscle damage (EIMD) [8, 9].

EIMD is a well-documented physiological response to unaccustomed or intense eccentric activity. It is characterized by a transient but often prolonged reduction in muscle strength and power [8]. This transitory functional impairment is typically accompanied by delayed-onset muscle soreness (DOMS), reduced joint range of motion, and elevated levels of circulating muscle proteins, such as creatine kinase (CK) and myoglobin (Myo) [9].

Impairment of muscle function, DOMS and other EIMD-related symptoms may negatively impact exercise experience, especially in untrained or physically inactive individuals, who appear to be more susceptible to EIMD [10]. These symptoms may lead to avoidance behaviors, limiting adherence to training programs, particularly in individuals who are already ambivalent toward exercise [11].

Individuals who use Δ9-THC-dominant cannabis may exhibit different responses to EIMD. Acute Δ9-THC consumption has been shown to modulate the activity of the endocannabinoid system (ECS) [12]. The ECS is composed of two primary receptors, cannabinoid receptors 1 and 2 (CB1 and CB2 respectively) whose activity can be influenced by cannabis-derived cannabinoids [13]. These receptors are involved in the regulation of pain perception, inflammatory processes, and muscle regeneration [14–16] and may therefore contribute to the recovery of muscle function following EIMD. Activation of CB1 and CB2 receptors has been associated with alterations in pain sensitivity, cytokine production, and satellite cell functions [14, 15]. Experimental evidence suggests that CB1 stimulation can inhibit myoblast proliferation and differentiation, potentially delaying muscle repair [16], while CB2 activation may exert anti-inflammatory and pro-regenerative effects [14]. Accordingly, acute cannabis use, through the modulation of endocannabinoid receptors by compounds such as Δ9-THC the most abundant cannabinoid in cannabis sativa L, could alter the physiological processes involved in recovery from muscle damage.

Chronic exposure to Δ9-THC, may induce alterations in the ECS function, including receptor downregulation, desensitization, and reduced levels of endogenous ligands [1, 17]. Such adaptations could modify responses to exercise-induced stress, potentially influencing inflammatory responses, and pain perception in cannabis users (CU). Consequently, chronic Δ9-THC-dominant cannabis consumers may exhibit distinct physiological responses to EIMD, particularly in terms of muscle function recovery, inflammatory responses, and pain perception. However, it should be noted that in Europe cannabis is primarily consumed in the form of joints mixed with tobacco [18]. Tobacco cigarette consumption alone could impair the recovery of muscle function following unaccustomed exercise [19, 20], a pattern of use that complicates the determination of the specific effects of cannabis.

Understanding these potential interactions between Δ9-THC-dominant cannabis use and post-exercise recovery has important public health implications. Accordingly, the present study aimed to compare muscle function recovery, perceived muscle soreness, and circulating biomarkers of muscle damage and inflammation (i.e., CK, Myo, IL-6) following strenuous exercise protocol designed to induce muscle damage in adult CU and non-users (NU). We hypothesized that chronic CU would exhibit altered recovery trajectories compared with NU.

MATERIALS AND METHODS

Subjects

Twenty-six physically active students (engaging more than three 30-minute sessions of physical activity per week) provided written informed consent to participate in the study. Participants were recruited on the university campus and, as far as possible, matched on age (± 5 years), sex, tobacco use (with or without cannabis; ± 5 cigarettes/day), and the type and level of sport participation. They were divided into two groups: regular CU (n = 12) and NU (n = 14). It should be noted that cannabis consumed in the CU was predominantly Δ9-THC-dominant and mixed with tobacco. The sample comprised 20 men (mean age: 22.9 ± 2.8 years; body mass: 76.5 ± 11.7 kg; height: 177.7 ± 7.0 cm) and 6 women (mean age: 20.6 ± 1.9 years; body mass: 56.1 ± 13.4 kg; height: 164.5 ± 9.7 cm) (Table 1).

All participants were instructed to refrain from physical exercise for 48 hours, and from alcohol and caffeine for 24 hours prior to the first laboratory visit and throughout the study protocol. Participants were also asked to maintain their habitual dietary intake, avoid protein supplementation, and refrain from using any additional recovery strategies between sessions. Cannabis users were not instructed to modify their habitual cannabis consumption pattern throughout

TABLE 1. Participant characteristics.

Parameters	CU (n = 12) (Women = 3)	NU (n = 14) (Women = 3)
Age (years)	21.8 ± 3.0 (21.7 ± 1.5)	22.9 ± 2.5 (21.7 ± 1.5)
Height (cm)	174.8 ± 11.2 (162.3 ± 12.7)	174.6 ± 8.6 (166.7 ± 7.8)
Body mass (kg)	66.3 ± 16.3 (47.0 ± 8.2)	76.6 ± 12.6 (65.3 ± 11.7)

CU: Cannabis Users; NU: Non-users. Values in parentheses correspond to women only.
Data are presented as mean ± SD.

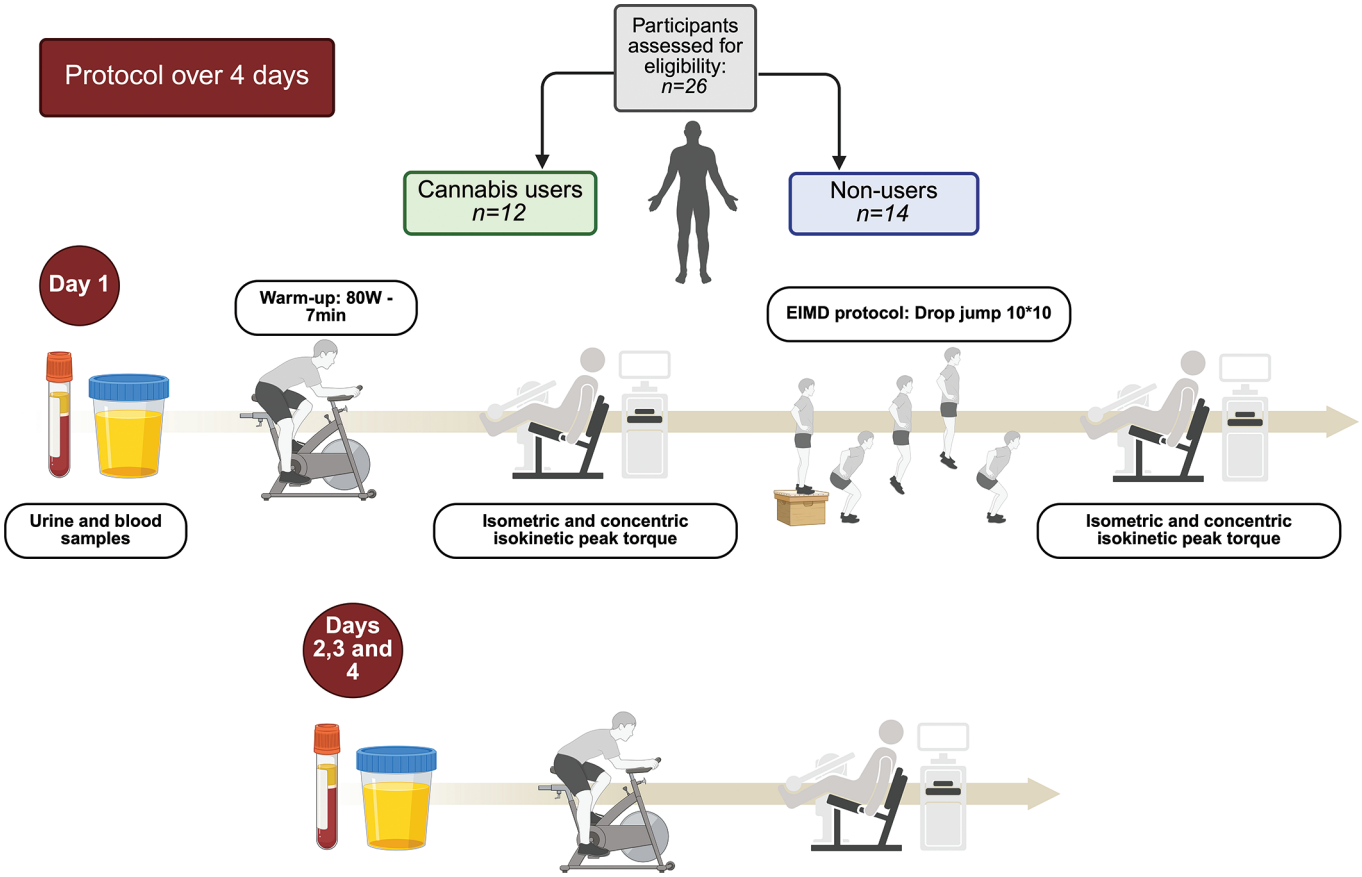


FIG. 1. Timeline of the study design. Illustration of the experimental protocol over the 4-day period. EIMD: exercise-induced muscle damage.

the study period. Participants were familiar with isokinetic testing procedures as part of their physiotherapy training. The study protocol adhered to the Declaration of Helsinki (revised in 2024) and was approved by the Institutional Ethics Committee of the Université Libre de Bruxelles (Belgium), approval number B200-2022-161.

Procedure

The study comprised two groups (CU and NU), each followed over a four-day period (Figure 1). Each participant returned at the same time of day for all subsequent visits, which ensured that conditions remained consistent from one measurement session to the next. At the first laboratory visit, anthropometric measurements were recorded and a venous blood sample was collected to assess serum CK, Myo, and interleukin-6 (IL-6) and, in CU only, Δ9-THC, 11-hydroxy-Δ9-THC (11-OH-THC), and 11-nor-9-carboxy-THC (THC-COOH). Participants then completed a 7-minute warm-up at 80 watts on a cycle ergometer (E894, Monark), followed by assessments of maximal isometric peak torque (IPT) at 60° and maximal concentric isokinetic peak torque at an angular velocity of $60°\cdot s^{-1}$ (CPT) and perceived muscle soreness using a visual analogue scale (VAS). After a 2-minute recovery, participants performed the EIMD protocol, after which torque and soreness were immediately reevaluated. At 24-, 48-, and 72-hours post-exercise (D1, D2, D3), participants returned under identical standardized conditions; one participant did not attend the D3 session.

Maximal isometric and isokinetic peak torque

IPT and CPT of the dominant leg were assessed using an isokinetic dynamometer (Cybex II, Biodex, USA). Following calibration, participants were seated in an upright position, with the thigh secured to the chair using a Velcro strap and the ankle fixed to the lever arm with a padded cuff. The dynamometer's axis of rotation was aligned with the lateral femoral condyle, and the knee joint angle was set at 60° of flexion.

For IPT, participants performed three 5-second maximal voluntary contractions, each separated by 1 minute of rest. After a 3-minute recovery period, CPT of the same leg was assessed during three sets of three maximal knee-extension contractions at an angular velocity of $60°\cdot s^{-1}$, with 1 minute of rest between sets. All participants received standardized verbal encouragement throughout the maximal voluntary contractions. The highest value obtained for both (IPT and CPT) was retained for analysis.

Exercise-induced muscle damage protocol

The EIMD protocol consisted of ten sets of 10 drop jumps from a 60 cm box with 2-minute passive recovery between sets, as previously described [21]. Upon landing, participants flexed their knees to at least 90° before jumping as high and explosively as possible using an arm swing.

Visual Analog Scale pain scores

Muscle soreness was assessed using a 10 cm VAS [22]. Participants were instructed to indicate their perceived level of soreness by marking a cross on the line. This assessment was conducted at five time points: at baseline immediately after the final repetition of the isometric and isokinetic efforts, and at 24-, 48-, and 72- hours post-exercise.

Blood collection and analysis

At each visit, following a 10-minute rest in a seated position, a venous blood sample was collected from an antecubital vein to determine serum concentrations of CK, Myo (markers of muscle damage), IL-6 (marker of inflammation), Δ9-THC (marker of acute cannabis exposure), 11-OH-THC (active intermediate metabolite reflecting recent exposure) and THC-COOH (marker of recent or prior cannabis exposure). Blood samples were drawn into a 9 mL serum tube and immediately centrifuged at 3000 rpm for 5-minute at 4°C, after which samples were aliquoted and stored at -80°C.

Serum CK and Myo concentrations were measured by nephelometry using a BNII analyser (Siemens Healthcare Diagnostics). Serum concentrations of Δ9-THC and its primary metabolites (i.e., 11-OH-THC and THC-COOH) were quantified using a validated quantitative liquid chromatography–tandem mass spectrometry (LC-MS/MS) method. IL-6 was analysed in duplicate using a commercial ELISA kit (RAB0306, Sigma-Aldrich, USA), with a calibration range of 0–1000 pg/mL.

Substance Use Monitoring

For substance use monitoring, participants were asked to report their consumption of cannabis, tobacco, and alcohol over the previous month, as well as during the 24 hours preceding the first laboratory session and at 24-hour intervals throughout the study period. Alcohol intake was expressed in international units (IU), and cannabis consumption was estimated using an equivalence of 0.3 grams per joint, in accordance with the guidelines of the French Monitoring Centre for Drugs and Drug Addiction (OFDT).

In addition, frozen urine samples were subsequently analyzed using multi-drug test strips (Multi 5C, nal von minden GmbH, Germany) to verify the presence or absence of Δ9-THC, thereby providing an objective confirmation of self-reported cannabis use.

Statistical analysis

Statistical analyses were performed using GraphPad Prism 10 (GraphPad Software, San Diego, CA, USA). Statistical significance was set at $p < 0.05$. Data are presented as mean ± standard deviation (SD).

For all variables, the normality of data distribution was assessed using the Shapiro-Wilk test. As IL-6values were not normally distributed, they were log-transformed (ln) prior to statistical analysis.

Changes over time between conditions were analyzed using linear mixed-effects models fitted with restricted maximum likelihood (REML) estimation to account for missing values, including "time" and "condition" (CU and NU) as fixed factors, with participants as a random effect. Bonferroni-adjusted post hoc tests were performed to assess specific differences relative to baseline and between-group comparisons at each time point. When assumptions of sphericity were violated for within-subject factors, the Geisser-Greenhouse correction was applied. In addition, Δ9-THC and metabolites concentrations were screened for time effects within the CU group using linear mixed-effects models fitted with REML, with "time" as a fixed factor and participants as a random effect.

Given the relatively small sample size, effect sizes (ES) and associated confidence intervals (CIs) were also reported to aid interpretation of potentially small or non-significant between-group differences. ES for between-group differences at each time point were calculated using Cohen's d with 95% confidence intervals (CI), providing an estimate of the magnitude of differences between CU and NU. Cohen's d was defined as the difference between group means divided by the pooled standard deviation in accordance with Lakens D [23]:

$$d_s = \frac{\overline{X}_1 - \overline{X}_2}{\sqrt{\frac{(n_1 - 1)SD_1^2 + (n_2 - 1)SD_2^2}{n_1 + n_2 - 2}}}$$

Values were interpreted as trivial (< 0.2), small (0.2-0.59), moderate (0.6-1.19), large (1.2-1.9) or very large (2-4) in accordance with thresholds proposed by Hopkins et al. [24] for sports science research.

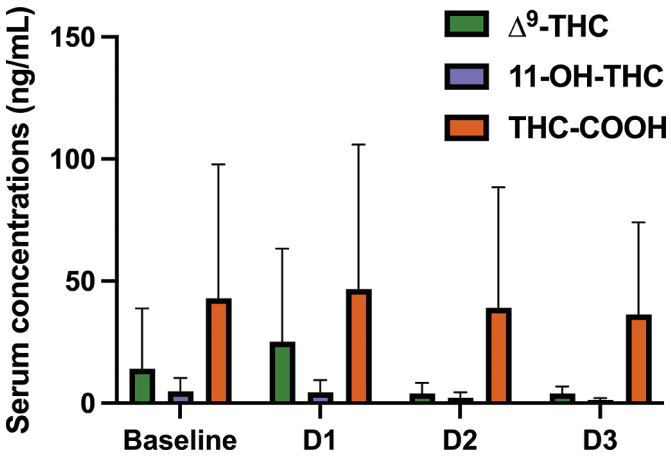


FIG. 2. Serum concentrations of Δ⁹-THC, 11-OH-THC and THC-COOH in cannabis users
Serum concentrations of Δ⁹-THC, 11-OH-THC and THC-COOH, were assessed before drop-jump protocol and reassessed at D1, D2, and D3.

TABLE 2. Patterns of cannabis and alcohol use.

Parameters	CU (n = 12) (Women = 3)	NU (n = 14) (Women = 3)
Joints past 30 days	83.3 ± 44.4 (84.3 ± 42.1)	–
Joints 24 h before V1	2.4 ± 1.6 (3.3 ± 2.5)	–
Joints 24 h before V2	2.1 ± 1.4 (2.7 ± 1.2)	–
Joints 24 h before V3	2.6 ± 2.2 (3.7 ± 1.5)	–
Joints 24 h before V4	1.8 ± 1.4 (2.7 ± 0.6)	–
Tobacco/day past 30 days (cigarettes)	8.5 ± 5.0 (n = 11) (7.3 ± 3.1) (n = 3)	9.4 ± 9.2 (n = 5) (7.5 ± 3.5) (n = 2)
Tobacco past 30 days (cigarettes)	253.6 ± 150.8 (n = 11) (220.0 ± 91.7) (n = 3)	282.0 ± 275.4 (n = 5) (225.0 ± 106.1) (n = 2)
Alcohol (glasses) past 30 days	19.6 ± 17.2 (n = 11) (12.7 ± 6.4) (n = 3)	13.8 ± 10.2 (n = 12) 12.7 ± 8.7 (n = 3)

CU: Cannabis Users; NU: Non-users. Values in parentheses correspond to women only. 1 joint = 0.3 g; 1 glass = 10 g of alcohol. Data are presented as mean ± SD.

RESULTS

Patterns of cannabis use and concentrations of THC and metabolites

To corroborate self-reported cannabis use (Table 2), serum concentrations of Δ9-THC and its metabolites were measured across study visits. Detectable concentrations of Δ9-THC and its metabolites were observed in CU, with marked inter-individual variability (Figure 2). No significant differences were observed across time points.

Maximal voluntary contraction

IPT of the quadriceps decreased over time ($F_{(3.315,78.74)}$ = 10.60, $p < 0.0001$). A time and group interaction was detected ($F_{(3.315,78.74)}$ = 2.667, p = 0.048), indicating different recovery trajectories between groups (Fig. 3A). Post hoc comparisons revealed that CU exhibited higher isometric strength than non-users immediately after exercise (mean difference = 10.53%, 95% CI: 0.12 to 20.94, p = 0.048) and at 72-hour post-exercise (mean difference = 15.11%, 95% CI: 0.90 to 29.31, p = 0.038). CPT showed a main effect of time ($F_{(2.704,64.22)}$ = 13.43, $p < 0.0001$), with lower values after exercise and a gradual recovery over the 72-hour follow-up (Fig. 3B). Neither the main effect of group ($F_{(1,24)}$ = 0.08, p = 0.79) nor the time and group interaction ($F_{(2.704,64.22)}$ = 0.44, p = 0.68) was significant, indicating that the kinetics of CPT was similar in CU and NU (all between-group differences at individual time points: $p > 0.44$). ES for maximal voluntary contraction are presented in figure 4 (A).

Muscle soreness and Blood markers of muscle damage and inflammation

Perceived muscle soreness showed a main effect of time ($F_{(2.061,48.42)}$ = 7.39, p = 0.001), with higher ratings after exercise and during the subsequent recovery period (Fig. 3C). Neither the main effect of group ($F_{(1,24)}$ = 1.39, p = 0.25) nor time and group interaction ($F_{(2.061,48.42)}$ = 1.28, p = 0.29) was significant, indicating a similar overall kinetics of soreness in CU and NU. Bonferroni-adjusted post hoc comparisons revealed no statistically significant between-group differences at any time point, although a towards higher soreness in CU was observed immediately after exercise (mean difference = 1.61 a.u., p = 0.055).

Serum CK concentration showed a main effect of time ($F_{(1.854,42.03)}$ = 15.16, $p < 0.0001$), with values increasing from baseline, peaking at 24 hours (D1), and then progressively declining over the 72-hour follow-up period (Fig. 3D). Neither the main effect of group ($F_{(1,23)}$ = 1.51, p = 0.23) nor the time and group interaction ($F_{(1.854,42.03)}$ = 1.21, p = 0.31) was significant, indicating a similar CK kinetics in CU and NU. Bonferroni-adjusted post hoc comparisons revealed no statistically significant between-group differences at any time point.

Serum Myo concentration showed a main effect of time ($F_{(2.494,55.70)}$ = 11.81, $p < 0.0001$), with an increase from baseline, a peak at 24 hours (D1), and a subsequent progressive decline (Fig. 3E). The main effect of group ($F_{(1,23)}$ = 0.05, p = 0.83) and the time and group interaction ($F_{(2.494,55.70)}$ = 0.36, p = 0.75) were not significant, indicating a similar myoglobin kinetics in CU and NU.

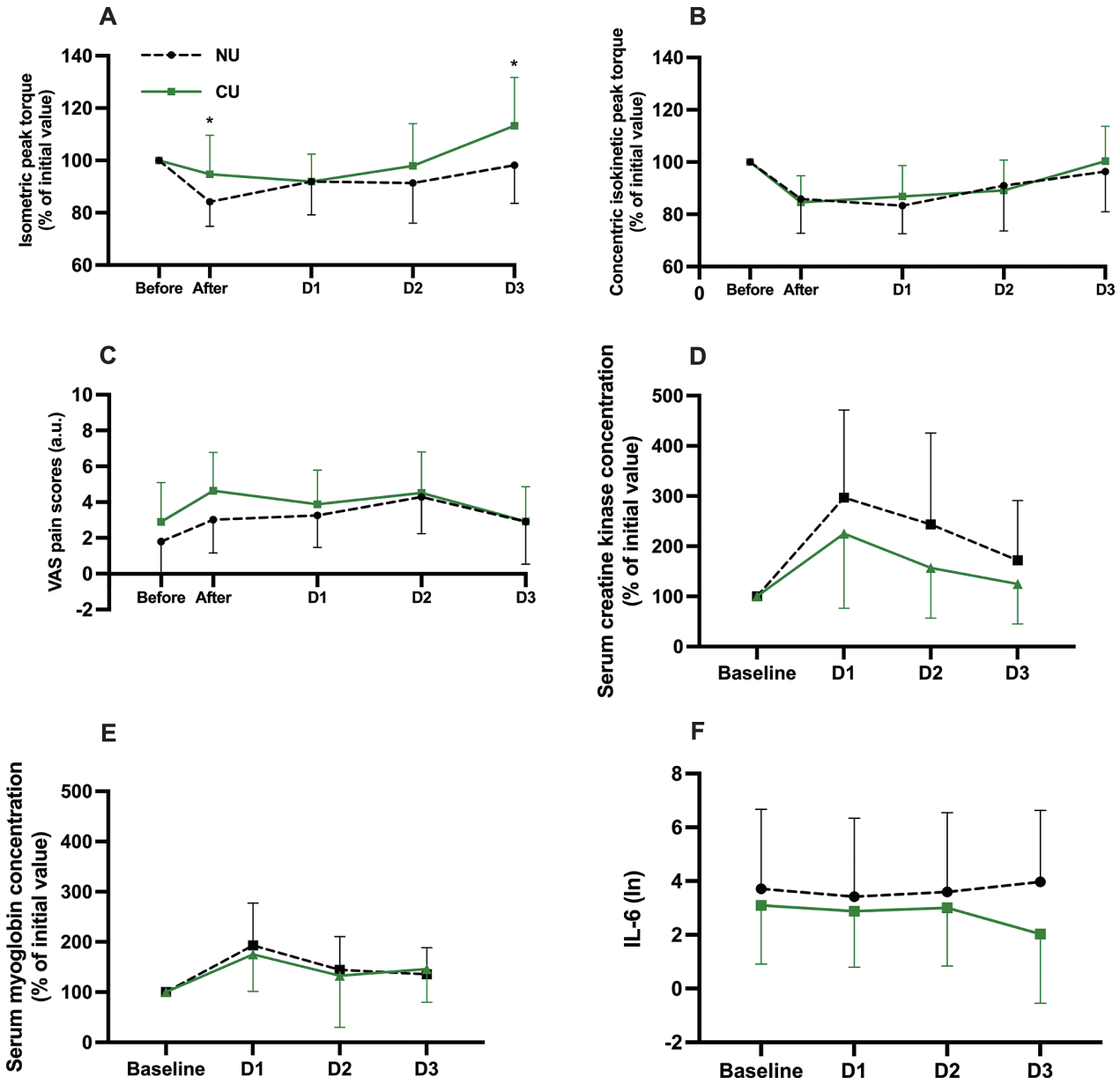


FIG. 3. Maximal voluntary contraction, VAS pain scores and serum markers of muscle damage and inflammation. CU: Cannabis Users; NU: Non-users. (A) Isometric peak torque at 60°; (B) Concentric isokinetic peak torque at 60°·s^{-1} and (C) perceived muscle soreness were assessed before and immediately after the drop-jump protocol (10*10 from a 60cm box) designed to induce muscle damage and reassessed at 24 hours (D1) 48 hours (D2) and 72 hours (D3). (D) Serum creatine kinase; (E) myoglobin; and (F) Interleukine-6 were assessed before drop-jump protocol and reassessed at D1, D2, and D3. *Indicates significant post hoc differences between conditions at that time ($P < 0.05$).

Bonferroni-adjusted post hoc comparisons revealed no significant between-group differences at any time point (all $p \geq 0.58$).

Serum IL-6 concentrations showed no main effect of time ($F_{(2.010,36.18)} = 0.89$, $p = 0.42$) and no main effect of group ($F_{(1,18)} = 0.66$, $p = 0.43$) (Fig. 3F). A time and group interaction was detected ($F_{(2.010,36.18)} = 3.38$, $p = 0.045$), but Bonferroni-adjusted post hoc comparisons revealed no statistically significant differences between CU and NU at any individual time point. Overall, the temporal pattern of IL-6 appeared broadly similar in both groups. ES for VAS pain score are presented in figure 4 (A) and ES for blood markers are presented in Figure 4 (B).

DISCUSSION

The aim of this study was to determine whether chronic Δ9-THC-dominant cannabis use mixed with tobacco influences muscle function recovery following an exercise protocol designed to induce muscle damage in physically active adults. To address this question, we examined the kinetics of maximal isometric and concentric peak torque, circulating concentrations of CK, Myo and IL-6, as well as perceived muscle soreness.

In both groups, the exercise protocol successfully induced muscle damage, as evidenced by marked reductions in IPT and CPT, increased muscle soreness, and elevated serum markers of muscle

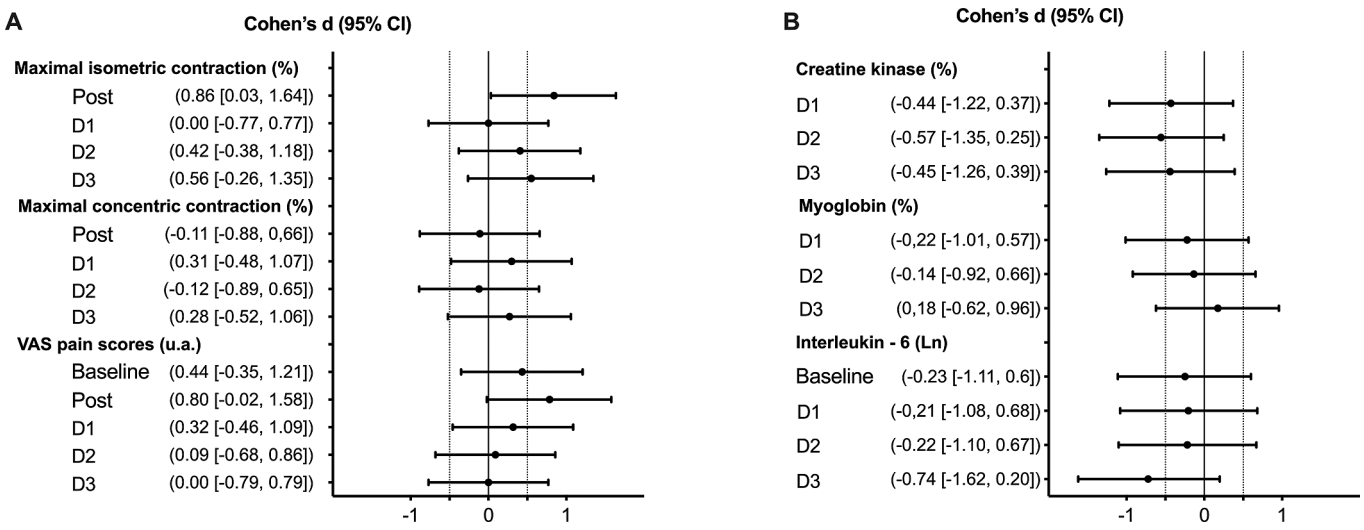


FIG. 4. Effect size (Cohen's d, 95% CI) for Cannabis Users (CU) versus Non-Users (NU).
(A) Effect sizes for maximal isometric and concentric isokinetic peak torque and VAS pain scores measured at baseline, immediately after the EIMD protocol, and during follow-up (D1, D2, D3). (B) Effect sizes for Serum Creatine Kinase, Myoglobin and IL-6 measured at baseline and during follow-up (D1, D2, D3). Dots represent effect sizes (Cohen's d), and error bars indicate 95% confidence intervals. Effect sizes were calculated as CU – NU; positive values indicate higher values in CU, whereas negative values indicate higher values in NU.

damage (CK and Myo) over the 72-hour recovery period. These responses are consistent with established descriptions of EIMD [8, 9, 25].

Contrary to our hypothesis, most recovery markers did not differ between CU and NU. The only exception was IPT, which showed a smaller immediate decrease and better recovery in the CU group. This was evidenced by significant time and group interaction, with higher isometric torque values observed immediately after exercise and at 72 hours in CU compared with NU. In contrast, CPT, CK, Myo, IL-6 and muscle soreness did not differ significantly between groups. The interpretation of the isometric torque findings therefore requires caution, and these results do not allow causal inferences regarding the effects of cannabis on post-exercise recovery.

To our knowledge, no study has examined the effects of Δ9-THC-dominant cannabis on muscle function in the context of recovery from EIMD protocol. The principal finding of the present study is that chronic CU exhibited a different recovery profile of IPT compared with NU, characterized by a smaller initial loss of strength following the muscle-damaging exercise and a more favorable recovery, or adaptation, at 72-hour. It is as though chronic Δ9-THC – dominant cannabis use combined with tobacco exerted a protective effect against muscle damage and accelerated recovery in isometric torque physiology. In both groups, the immediate post-exercise reduction in strength likely reflects a combination of peripheral mechanisms, distal to the neuromuscular junction, and central mechanisms originating within the central nervous system [26]. In principle, cannabis use could influence adversely or favorably one or both of these components, as the ECS is involved in the regulation of motor activity from supraspinal and spinal levels down to the muscle [27]. Our results regarding the decrease in IPT immediately after exercise, together with those of Lisano et al. [28, 29] support this possible cannabis influence. These authors examined fatigue by tracking declines in power output during a 30-second Wingate test in athlete populations regularly inhaling cannabis. In female athletes, CU appeared less susceptible to fatigue than NU [28], whereas in male athletes the same research group reported a tendency towards greater fatigue in CU compared with NU [29]. Taken together, these findings indicate that cannabis use may modulate fatigue-related responses; however, whether such modulation attenuates or exacerbates fatigue remains unclear and may depend on the type of exercise performed, the characteristics of the population studied and the mode of consumption (i.e. Mixed with or without tobacco).

This influence of cannabis use in our study should nevertheless be interpreted with caution. The differences observed in IPT were not replicated under concentric conditions. CPT which showed a similar immediate decline and recovery profile in CU and NU. In general, strength losses following exercise-induced muscle damage are comparable between isometric and concentric contractions [30]. However, it cannot be ruled out that these two indicators may exhibit different time-course responses following an unaccustomed exercise [31]. As these two contraction modes rely on distinct underlying determinants [32], it is possible that cannabis use, whether chronic or acute, may differentially affect IPT and CPT.

To further determine whether chronic CU experienced greater muscle damage and an alteration in recovery, we also evaluated the temporal responses of other markers commonly associated with EIMD, such as circulating concentrations of CK and Myo [9]. In contrast to maximal isometric torque, CK and Myo showed a similar increase

after exercise and a comparable recovery kinetics in both groups. This pattern suggests that, in this setting, chronic Δ9-THC-dominant cannabis use does not substantially affect post-eccentric exercise fatigue, the extent of muscle damage, or the rate of functional recovery.

We initially hypothesized that muscle strength recovery might be impaired in the days following exercise, as chronic Δ9-THC-dominant cannabis exposure has been shown to alter endocannabinoid receptor density and function, as well as endogenous cannabinoid levels [1, 17, 33]. The ECS in skeletal muscle has been implicated in regeneration processes, including satellite cell activation, proliferation and differentiation [14, 16] which are critical for the restoration of muscle function [34]. However, data on the status of the muscular ECS in chronic Δ9-THC-dominant cannabis users are currently lacking. Consequently, although the absence of clear between-group differences in the present study does not exclude a potential effect of cannabis use, it does not support the hypothesis that regular cannabis consumption causes major alterations in this system, at least with respect to short-term functional recovery following exercise-induced muscle damage.

We also measured IL-6 concentrations before and after exercise. IL-6 is a cytokine involved in both, systemic inflammation [35], and exercise-induced muscle damage and subsequent regeneration [36]. No clear IL-6 response was observed during the 72-hour follow-up period, and no differences were detected between CU and NU.

This absence of a response could be due to the blood-sampling schedule, as IL-6 concentrations typically peaks during exercise and within the first few hours after exercise, before returning to baseline within 24 hours, suggesting that the main transient IL-6 peak was missed [37].

Regarding cannabis use, previous studies have reported heterogeneous findings, on circulating IL-6 [38, 39] and the present results do not support a clear or consistent effect of chronic cannabis use on circulating IL-6 concentrations.

An additional point of interest in the present study concerns the pattern of DOMS. Trost et al. [11] demonstrated that fear of pain following DOMS can lead to avoidance of physical exertion and reduced performance, thereby limiting engagement in physical activity. Although chronic CU did not differ significantly from NU in overall muscle soreness following the eccentric exercise or in DOMS over the subsequent days, effect-size (Figure 4) estimates suggested a tendency towards slightly higher pain immediately after exercise during peak torque assessments in CU.

Specifically, we observed a small ES for baseline VAS scores and a moderate ES immediately post-exercise in CU compared with NU. Experimental studies indicate that acute cannabis or Δ9-THC administration does not produce robust analgesic effects in healthy volunteers [40, 41] and may even induce hyperalgesia at higher Δ9-THC concentrations [42]. Concerning chronic Δ9-THC-dominant cannabis use, it has been associated with hyperalgesia across several pain models, with higher pain ratings or reduced pain tolerance in users compared with non-users [43]. Beside Zhang-James et al. [44] similarly reported reduced cold pressor pain tolerance in daily CU, particularly when combined with tobacco use, suggesting heightened pain sensitivity in heavy users and a synergistic effect of tobacco and cannabis. A larger sample size would probably have made it possible to demonstrate this effect on pain.

Nevertheless, it is important to consider pain sensitivity in chronic CU when prescribing exercise protocols likely to induce muscle soreness, even when such symptoms are transient.

Limitations

This study has limitations. First, cannabis was predominantly consumed as joints mixed with tobacco. As cigarette smoking has been shown to impair skeletal muscle function and capillarization and to delay tissue healing, we could not separate the respective contributions of cannabis and tobacco use [45]. Although tobacco use was characterized and was matched between groups, residual confounding related to tobacco exposure cannot be excluded. Future studies should quantify tobacco exposure more precisely and, where feasible, compare cannabis-only, tobacco-only, combined-use, and NU groups, ideally using non-combustible cannabis formulations.

Second, the sample size was modest, which may have limited statistical power to detect small between-group differences. Cannabis use was self-reported and heterogeneous in terms of frequency, dose, and product type, precluding any precise quantification of individual dose–response relationships and making it impossible to separate acute from chronic effects within our protocol. Finally, tobacco and alcohol consumption were self-reported, and no formal assessment of problematic cannabis use, cannabis use disorder (CUD), or its severity was conducted, which limits the clinical interpretability of our findings.

CONCLUSIONS

The present study indicates that chronic cannabis use does not impair short-term muscle function recovery following eccentric exercise-induced muscle damage in physically active adults. Despite a divergent isometric torque recovery pattern, concentric strength, circulating markers of muscle damage and inflammation, and perceived soreness showed broadly similar responses in both groups. Effect-size estimates suggested a tendency toward greater acute pain in CU immediately post-exercise, raising the possibility of increased pain sensitivity in this population. These findings have practical implications for exercise prescription, particularly as physical activity is increasingly proposed as a complementary strategy for CUD management, where adherence is critical. The findings of this study suggest that eccentric exercise protocols of this nature do not appear to be contraindicated in individuals with chronic cannabis use from a short-term muscle recovery. This may be relevant when considering exercise as a complementary strategy in the management of CUD. Future studies should employ larger samples, controlled cannabis formulations, and earlier blood sampling to clarify the role of the ECS in post-exercise recovery.

List of abbreviations: CUD: Cannabis use disorders; EIMD: Exercise-induced muscle damage; DOMS: Delayed-onset muscle soreness; CK: Creatine kinase; Myo: Myoglobin; ECS: Endocannabinoid system; Δ9-THC: Δ9-Tetrahydrocannabinol; CU: Cannabis Users; NU: Non-Users; IPT: Isometric peak torque; CPT: Concentric peak torque.

Author's contributions: AM, GC, SB and F-XG, conceived and designed the study. AM, LD, PC and F-XG conducted the experiments and collected the data. AG, J-MG and PM performed the toxicological and biochemical analyses. AM, GC, EH, SB and F-XG analyzed the data. AM and F-XG drafted the manuscript. All authors critically revised the manuscript and approved the final version.

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Data availability statement: The data supporting the findings of this study are not publicly available, as they contain information that could compromise the privacy of the research participants. However, the data are available from the corresponding authors, Antoine Mendes (antoine.mendes@univ-lille.fr) and François-Xavier Gamelin (francois-xavier.gamelin@univ-lille.fr), laboratory URePSSS – ULR7369, upon reasonable request.

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