Cannabis Use and Driving-Related Performance in Young Recreational Users: a within-subject randomized clinical study

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ABSTRACT

Introduction: With cannabis legalization, young adults, a group already at high-risk for automobile crashes, may increase cannabis-use which may further increase crash-risk. We examined the effects of inhaled cannabis on driving-related performance in 18-to-24-year-old recreational users. **Methods:** In this within-subject, double-blind, randomized design, participants completed test sessions at no-cannabis state, 1, 3, and 5hrs post-cannabis. Performance was assessed with the Virage simulator and Useful Field of View (UFOV) tests. Self-reported perception of cannabis effects and driving ability/safety were measured. Repeated-measures ANOVA (cannabis effects and time post-use on performance); McNemar's Test (crash-risk [score combining complex simulator tasks] categorization); and, correlations/descriptive statistics (subjective perceptions and performance associations) were employed. **Results:** 180 sessions (n=45 participants) were completed. Significant effects of cannabis vs. no-use were noted on complex UFOV tasks at 3hrs (UFOV-2 ms: 70±24 vs. 37±12; CIs: 28-114 vs. 29-45, t=-2.98 df=41 p=0.004; UFOV-3 ms: 102±66 vs. 64±; CI: 60-144 vs. 53-75, t=-2.42, p= 0.02) and at 5hrs post-use (UFOV-3: 82±29 vs. 61±19, CI: 62-100 vs. 48-75, t=-2.32, p=0.025) when tasks were performed at the 1st test-session. Participants were significantly more likely to be classified as high-crash risk post vs. no-use (24 vs. 8.8%, χ^2= 3.87 df=1, p=0.04, OR=0.42 CI: 0.14-1.30); and reported significantly lower driving ability/safety post vs. no-use. **Interpretation:** We found that among young recreational cannabis-users, while a regular dose of cannabis had no effect on simple and learned tasks, its use led to significant impairments on complex and novel driving-related tasks, and perceived driving ability/safety effects for up to 5hrs post-use.

INTRODUCTION

Cannabis is the most commonly used illicit drug globally (1). Laws legalizing possession and use of cannabis for recreational purposes (2) may further increase its use. In a 2017 general population survey of 1838 current users in Canada, 36% answered "yes" when asked "*Will you consider using marijuana more often once it is legalized?"* (3). The lay public, health professionals and policy makers have raised concern about the impact of changes in cannabis legislation on road safety. This concern is especially pronounced for young drivers who are already known to be at high risk of crashes and who are also the age-group most likely to use cannabis (4).

The literature on the effect of cannabis on driving, primarily in healthy subjects who are either first time or recreational users, suggests there is an impact on different driving-related functions: increased brake and choice reaction time, impaired lane position, headway and dynamic tracking, distortion of time perception, reduced divided/sustained attention (5-9), and increased caution (10). What is less clear given the current research is the time post-cannabis when the deficits in driving-related function subside. Indeed, a recent publication of the research gaps related to cannabis and driving from the United States, suggest insufficient knowledge related to time from consumption to driving safely (5). Given the evidence gaps, the present study aimed to answer two questions: In young recreational cannabis users: 1) to what extent (and for how long) is driving-related performance compromised following a usual dose of inhaled cannabis? and, 2) are there associations between self-reported perceptions (drug effect, driving ability/safety) and performance?

MATERIALS & METHODS

Design/setting

A 'within subject', double-blind (assessors blind to cannabis status of the participants; participants blinded to the randomization sequence), randomized design, where participants acted as their own controls, was used. The study took place at the Center for Innovative Medicine, McGill University Health Center, Montreal, QC, Canada. Ethics approval was obtained from McGill University Ethics Review Board (REB#2018-4138).

Population

The target population was young adult recreational cannabis users aged 18-to-24 years. Participants were eligible if they: were current recreational users as indicated by cannabis use at least once within the past three months; held a valid drivers' license and had driven in the past three months; had sufficient comprehension of English or French; had sufficient cognitive ability to understand

task requirements as determined by initial phone-interview; provided informed consent; and, had a personal-use cellphone. Participants needed to agree to abstain from cannabis and other illicit drugs for 48hrs prior to each testing day and to provide availability to attend four testing sessions over a 4-to-6 weeks period. Exclusion criteria were: upper and/or lower limb motor and/or sensory deficit(s) precluding simulator/computer use; health conditions (including seizure disorders) that may be triggered by simulator/computer use; conditions/new medications that may lead to health-status fluctuations and decrease test-retest stability; pregnancy; and, participation in another cannabis-related study.

Appendix 1 describes sample size calculations. Participants were recruited through an online social media campaign. Those completing a preliminary eligibility screen and indicating an interest were contacted by the coordinator, who explained study's purpose/procedures, determined eligibility, and scheduled the 1st session following verbal agreement.

Procedures

Each consenting participant was randomised (without stratification, in blocks of 8) to one of 4 sequences on Day 1 (**D1**). The randomization sequence was revealed in front of the participant by opening an opaque, numbered, sealed envelope. Participants were blind to their sequence; they only knew that they were being tested at different times on different days. Each underwent evaluation on 4 separate days over a 4-week period according to their assigned sequence:

Sequence_1: **D1** = no cannabis (NO)→**D2** = 1hr-post→**D3** = 3hrs→ **D** = 5hrs;
Sequence_2: D1 = 3hrs→**D2** = NO→**D3** = 5hrs→ **D4** = 1hr;
Sequence_3: D1 = 1hr→**D2** = 5hrs→**D3** = NO→ **D4** = 3hrs;
Sequence_4: D1 = 5hrs→**D2** = 3hrs→**D3** = 1hr→ **D4** =NO;

The timepoints were chosen given the substantial scientific evidence [11] that delaying driving for at least 6hrs after use of a typical dose allows resolution or near resolution of impairments in those who are recreational users. Driving-related tasks order presentation (UFOV/simulator) was also randomly counterbalanced within sequence, such that half of the participants began with the UFOV. Within participants, this order remained constant.

For all sessions, participants were instructed to continue use of routinely taken medications (if any), and to refrain from smoking cannabis and using other illicit drugs and alcohol for a minimum of 48hrs prior each session. A urine sample was collected to verify adherence. For female participants, a urine pregnancy test was administered. Health-related changes since previous session were inquired on and further information was collected if present. We proceeded with cannabis administration and driving-related testing only if all results were negative and no health-related changes reported.

On Day 1, once the participant had signed the consent form, the following information was collected: basic socio-demographic characteristics (age, gender, education); driving and cannabis-use behaviors. At each testing-session, participant's adherence with the study protocol (questions regarding drug use, urine test, pregnancy test) was verified. After the randomization schedule revealed the procedure for the day, the identified sequence began.

On days when the participant was slated to cannabis-use, the following procedure was followed. In a room with a ventilation system designed specifically for cannabis consumption via inhalation, a standard 100mg dose of dried granulated *Cannabis sativa flowers* was placed into a vaporizer set at 200°C (Mighty Medic, Storz & Bickel GmBH) licensed for medical administration of cannabis in Canada (2016-01-22 Licence No. 96431). The participant was instructed to inhale for 5s, hold their breath for 10s, and wait approximately 45s between inhalations; repeated for 5 inhalations. Research-grade herbal cannabis, with standardized levels of 12.9± 2.8% tetrahydrocannabinol (THC) and <1% cannabidiol (CBD) (Canopy Growth Corporation, reflecting an average street-grade recreational cannabis THC levels (2)) was prepared by the hospital pharmacy and used. A Clinical Trial Application 'no objection letter' was received from the Therapeutic Products Directorate of Health Canada for the study.

On all sessions, 10mins post-use or no-use, participant completed questions regarding: self-perceived driving ability and safety; and, perceived drug effect. Following the randomly-allocated wait times (1, 3, or 5 hours) or immediately (if they were in a no-cannabis session), the participant underwent the driving-related testing. The coordinator accompanied him/her to the testing room housing the UFOV and simulator. The assessor proceeded with the UFOV or simulator, as instructed by the coordinator. For all test-sessions, standardized instructions in French or English and clarifications (as per preference) were provided. Practice trials were performed on each test ensuring participant's understanding of task expectations. During wait times post-use to assessment, participants remained in a private room adjacent to the coordinator's desk and were able to order meals/snacks; listen to music or watch movies (video-games were prohibited).

3 UFOV and 7 simulator tasks were completed (45-to-60-minute period). Breaks were introduced as needed. The order of the 7 simulator and 3 UFOV tasks was kept constant over all test-sessions. In-between UFOV and simulator evaluations, the participant was again asked the questions related to perceived driving ability, driving safety, and perceived "high". All assessors had health-care backgrounds and were trained in driving-related tests administration using standard procedures. Each was blind to the randomization schedule and efforts were made to randomize participants across assessors to reduce the likelihood of any one assessor seeing the same participant repeatedly.

Measures

UFOV Test

The UFOV Test [19] measures Useful Field of View, a function that, when reduced, has strong criterion validity in predicting high-crash risk (12). UFOV, defined as the visual field in which information can be acquired and processed, is measured via 3 tasks. Stimulus presentation varies from a very slow-350ms to an extremely rapid-17ms (i.e. best possible result). In UFOV-1, *a simple processing speed task*, the participant is asked to identify a centrally located object (car or truck). In UFOV-2, *a more complex divided attention task*, the participant is again asked to identify whether the centrally presented target is a car/truck as well as to identify the location of a simultaneously presented peripheral target, again at different time exposures. The final and *most complex task selective attention*, UFOV-3, provides a measure of distractibility by presenting the same task as the UFOV-2, this time with distractors on the screen. The UFOV provides results in ms for each task, indicating the time of the stimulus presentation at which the participant is most successful/providing accurate responses.

The Virage Driving Simulator-VS500M

This simulator includes: 3x55-inch LCD high resolution 1920x1080 pixels screens, providing 180-degree front views; 2 lateral screens positioned in the back, providing blind spots and three mirrors visualization; driving cabin, equipped with automatic transmission and controls (steering wheel, pedals, dashboard) mounted on a motion/vibration system simulating acceleration, braking, pavement-type, and collision effects; and, a surround-sound system, providing realistic engine sounds adjusted to various road scenarios (17). The 7 subtests measure: braking reaction time; steering reaction time; braking vs. steering in combined reaction time and decision accuracy; lane deviation; crossing intersection safety/crash-rate/duration; vigilance accuracy/duration; and obstacle avoidance accuracy/crash-rate (18). For the 3 out of 7 more complex tasks: intersection crossing, vigilance challenge and obstacle avoidance – performances were dichotomized into maximal (100%) vs. submaximal scores (<100%). Crash-risk was operationally defined as combined submaximal score performances on these tasks: intersection crossing accuracy (<100%); obstacle avoidance (crash rate >0% and accuracy <100%); and, vigilance challenge accuracy (<100%). This new variable further dichotomized participants into low vs. high risk. While the predictive validity of the simulator is less well documented than the UFOV, it was chosen given the evidence that simulators are associated with on-road driving, its strong face validity, and the ability to test crash-risk (19, 20).

Statistical Analyses

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc). For

normally-distributed data, a 4*4 *repeated measures ANOVA* (21) with session sequence (1/2/3/4) and cannabis status (no-use/1/3/5hrs post-use) as within-subject factors was used to determine the effects of cannabis and time since use on performance. Effects of cannabis status and sequence as well as their interaction were noted and in cases of significant interaction, pre-determined pairwise comparisons were further conducted with *paired t-tests* (22). Within-subject differences in the proportion of optimal vs. suboptimal complex simulator performances and risk categorization by cannabis status were examined using *McNemar's test for matched pairs* (23). Correlations and descriptive statistics were used to explore the associations between perceived subjective reports with driving-related performance.

RESULTS

A total of 191 individuals responded to the social media recruitment and of these, 126 met preliminary eligibility. The first 91 were phone-contacted by the coordinator: 53 were deemed eligible following full eligibility screening. 48 agreed to participate, attended the first session, and signed the informed-consent form. Of these, 45 (94%) completed the study protocol (Figure 1). Table 1 outlines participants' demographics, driving behavior and cannabis use. Unless otherwise indicated, results are presented based on these 45 enrolled subjects: 47% females, mean age of 20.6±1.3 years.

At each cannabis-use session, when asked whether the "high" they were experiencing was the ***same*** or ***different*** from usual at 10mins post-use: 56% at 1hr; 62% at 3hrs; and, 67% at 5hrs reported ***same***. ***Different*** from usual reports across cannabis-use sessions were as follows: ***less*** (22, 17.7, 15.5%), ***more*** (6.6, 8.8, 6.6%), ***other*** – i.e. head high, body high, tired (15.5, 11.1, 11.1%).

Driving-related performances and self-reports of safety/ability

UFOV-1/simplest processing speed: In 91% of all sessions (164/180), regardless of cannabis status, performance was at the maximum best level possible (in ms): *at no cannabis* 17±0; *at 1hr post-use* 17.67±3.16 CI 16.88-18.46; *at 3hrs post-use* 17.31±2.09 CI: 16.79-17.83; and *at 5hrs post-use* 17±0. Effects of sequence, cannabis status and the interaction of sequence*cannabis status were found to be non-significant (χ^2=2.08/2.10/2.10 respectively; df=3/3/5; *p*=0.55/0.55/0.83).

UFOV-2/more complex selective attention: Effects of sequence and cannabis status were both non-significant (*F*=2.34/0.10 df=3, *p*=0.0876 / 0.9584). However, there was a significant interaction of sequence*cannabis status (*F*=3.72 df=9; *p*=0.001) (Figure 1). Subsequent pairwise comparisons revealed significantly worse UFOV-2 scores (in ms) ***3hrs post-use*** vs. no-use when testing was performed at the participant's 1st session - i.e. the task was unfamiliar: 70±24 vs. 37±12; CIs: 28-114 vs. 29-45, *t*=-2.98 df=41 *p*=0.0048.

UFOV-3/highest complexity divided attention: Effects of sequence and cannabis status both were found to be non-significant (F=0.31/0.39 df=3, p=0.8163/0.7600). However, a significant interaction of sequence*cannabis status was found (F=4.58 df=9, p=0.0001). Pairwise comparisons revealed significantly worse UFOV-3 scores (in ms) ***3hrs post-use*** vs. no-use when testing was performed at the participant's 1st session - i.e. the task was unfamiliar: 102±66 vs. 64±18 CI: 60-144 vs. 53-75, t=-2.42 df=41, p= 0.0203. Reduced scores were also found at ***5hrs*** when it was the participant's 1st session: 82±29 vs. 61±19 CI: 62-100 vs. 48-75, t=-2.32 df=41, p=0.0256. The same pattern was noted at ***1hr*** (73+28 vs. 61±25 CI: 54-92 vs. 43-77), but only approached significance (t=-1.46 df=41 p=0.14).

Simulator: Responses on the simplest simulator tasks (braking, steering, lane keeping speed control) did not reveal significant differences in cannabis (combining all post-cannabis states) vs. non-cannabis performance: (F=1.15/1.33/0.61 df=122, braking p=0.36; steering p=0.28; lane keeping speed control p=0.77). The interaction for the more complex task of intersection-crossing (safe-crosses) approached but was not significant (F=1.71 df=9, p=0.14). Interactions for vigilance challenge accuracy (F=0.99 df=9, p=0.47), obstacle avoidance accuracy (F=0.77 df=9, p=0.64), and obstacle avoidance crash-rates (F=1.51 df=9, p=0.21) were non-significant. However, when dichotomizing performances on these more complex simulator tasks into ***maximal*** vs. ***submaximal*** score (100 vs. <100%), participants were significantly more likely to be classified in the ***submaximal*** category at all post-cannabis use time-points combined, on all but one measure (obstacle avoidance accuracy) (Table 2). Furthermore, participants were significantly more likely to be classified as ***high*** crash risk at all post-cannabis use times combined vs. no cannabis (24.13% vs. 8.88%, χ^2= 3.87 df=1, p=0.04, OR=0.42 CI: 0.14-1.30).

Perceived driving ability (worse/same/better vs. usual), when combined for the 3 timepoints at 10mins post-cannabis use revealed 50% “worse” and 49% “same”, and 0% “better”. Self-perceived driving safety differed significantly according to cannabis state (F=26.01, df=3, p<0.0001), such that at 1, 3, and 5 hours post-cannabis use – 96%, 89%, and 79%, respectively, scored themselves less safe to drive compared to the no-cannabis state.

No significant associations were found between the UFOV driving-related performance and perceived driving safety and ability on the VAS (Table 3). No significant differences were found for UFOV performances according to the various perceived “high” (i.e. same, less, more, other): UFOV-2 at 1hr/3hrs/5hrs post-use (F=0.13/2.70/1.81, df=3, p=0.94, 0.06, 0.15); UFOV-3 (F=0.12/0.35/2.60, df=3, p=0.94, 0.79, 0.06).

Participants classified as ***high*** crash risk were significantly more likely to indicate “worse” vs. usual ability at all post-cannabis use times combined (68% vs. 32%,

χ^2= 7.40 df=1, *p*=0.0065, OR=0.93 CI: 0.36-3.25).

INTERPRETATION

This study was designed to describe the effects of a standard dose of inhaled cannabis on driving-related performance in young recreational users at 1, 3, and 5 hours after use compared to when they performed these same tasks without cannabis. Three major findings are reported. First, complex driving-related performance is affected at 3hrs and 5hrs post-use such that young drivers are slower to accurately respond when divided attention is required, or distractors are present, and when the stimuli are novel - i.e. they have not experienced the task requirements previously. Second, on the simulator, an individual's crash risk on complex driving tasks was higher post-use versus when they were in a no-cannabis state. Third, self-reported perceptions (driving ability/safety) demonstrated that young recreational users did not find themselves to be as safe to drive in a cannabis state compared to their usual safety and ability, even 5hrs after use.

The measures used in the current study provide important indicators. For instance, the ceiling effect of the UFOV-1, the simplest UFOV task, is important. This suggest that participants gave their best effort at all sessions. This finding is important given the likelihood of a response bias in which participants would potentially have tried to perform more poorly in a cannabis state if they held the belief that cannabis use did not influence driving safety. Participants were particularly challenged when the tasks were novel and complex (i.e. when presented at the 1st session in a cannabis state). In young (20) and older adults (11, 24), UFOV has repeatedly been shown to be a strong predictor of crash rates and overall safety. In the current study, it was useful as a discriminative measure. Future applications for such discrimination ability deserve further research.

The study has limitations. As healthy young recreational users were studied, its results cannot be extrapolated to daily and chronic users, nor to those with health conditions for which medicinal cannabis is prescribed. In addition, driving-related response times and reactions to novel stimuli are different in young versus older individuals (16), suggesting that the differences reported here might be more pronounced in older cannabis users. Subsequent studies should explore these hypotheses. Further, once cannabis use is legalized, investigating its effects on other driving outcomes that were not possible in current study (e.g. on-road performance) is warranted. In conclusion, we found that among young recreational cannabis-users, while a regular dose of cannabis had no effect on simple and learned tasks, its use led to significant impairments on complex and novel driving-related tasks, and perceived driving ability/safety effects for up to 5hrs post-use.

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Appendix 1

Sample size calculations: Sample size calculations were based on the main outcome of interest, performance on driving related measures: UFOV-2 and UFOV-3 (11). A sample of 36 participants was estimated to provide 95% power to detect differences of 40 msec (an outcome that is of clinical importance to safe driving (12-16) in the within-person scores under the different testing conditions (i.e. time since cannabis use/no cannabis). Given an anticipated dropout rate of 15% to 20%, and to permit sub-group analyses, we aimed to enrol 50 participants.

TABLE 1 Study participants: demographics, driving experience and cannabis exposure

	Sample Size (n)	Percentage (%)	Mean
Demographic variables			
Gender			
Male	24	53 %	-
Female	21	47 %	
Age			
18-20	22	48%	20.6 ±1.3
21-24	23	52%	
Education completed			
High School	24	53.3%	-
CEGEP/University	21	46.6%	
Driving experience			
1-3 years	11	24.4 %	-
4-6 years	27	60.0 %	-
>6 years	7	15.5 %	-
Driving frequency			
Daily/weekly	28	62.2 %	-
Monthly	11	24.4%	
Variable	6	13.3 %	
Cannabis use			
Weekly	17	38%	-
Monthly	20	44%	-
Variable	8	18%	-

TABLE 2 Maximal vs. submaximal score performances on the complex Simulator tasks according to cannabis status

	No-cannabis use	Post-cannabis use	McNemar Test & significance	Odds Ratio	95% CI
Vigilance accuracy (higher is better)					
= 100% (**70** test sessions)	16 (35.5%)	54 (37.24%)	43.55, df=1, *p*<0.0001	1.20	0.59-2.43
< 100% (**110** test sessions)	29 (64.4%)	81 (62.75%)			
Obstacle avoidance accuracy (higher is better)					
=100% (**122** test sessions)	34 (75.56%)	88 (60.68%)	2.08 df=1, *p*=0.14	0.60	0.28-1.30
<100% (**58** test sessions)	11 (24.44%)	47 (39.31%)			
Obstacle avoidance – crash rate (less is better)					
= 100% (**13** test sessions)	2 (4.44%)	11 (24.44%)	118.12 df=1, *p*<0.0001	1.90	0.40-8.95
< 100 % (**167** test sessions)	43 (95.55%)	124 (75.55%)			
Intersection crossing – safe crosses (higher is better)					
=100% (**11** test sessions)	1 (2.22%)	10 (6.89%)	122.03 df=1, p<0.0001	3.52	0.43-28.29
<100% (**169** test sessions)	44 (97.77%)	125 (93.10%)			
Intersection crossing – unsafe crosses (less in better)					
=0% (**21** test sessions)	6 (4.13%)	15 (10.34%)	103.14 df=1, *p*<0.0001	0.81	0.29-2.23
>0% (**159** test sessions)	39 (95.86%)	120 (89.65%)			
Crash risk (low vs. high)					
Low (**151** test sessions)	41 (91.11%)	110 (75.86%)	3.87 df=1, *p*=0.0489	0.42	0.14-1.30
High (**29** test sessions)	4 (8.88%)	25 (24.13%)			

TABLE 2 LEGEND: Green vs. pink slots indicate optimal vs. suboptimal performances. Crash risk combines the following outcome variables: Safe crosses <100% & Obstacle avoidance crash rate >%0 & Vigilance accuracy <100% & Obstacle avoidance accuracy <100%. CI: confidence interval; Post-cannabis use combines performances at 1, 3, and 5hrs post-use.

TABLE 3 Correlations between UFOV driving-related performance and perceived driving ability/safety

VAS measure	UFOV2	UFOV3
	No cannabis use	
Perceived driving ability	r=0.13, NS	0.18, NS
Perceived driving safety	r=0.06, NS	0.18, NS
	At 1hr post cannabis use	
Perceived driving ability	r=-0.12, NS	-0.09, NS
Perceived driving safety	-0.11, NS	-0.12, NS
	At 3hrs post cannabis use	
Perceived driving ability	0.08, NS	-0.006, NS
Perceived driving safety	0.11, NS	0.02, NS
	At 5hrs post cannabis use	
Perceived driving ability	**r=-0.40, *p*=0.0056**	-0.005, NS
Perceived driving safety	**r=-0.38, *p*=0.0094**	-0.05, NS

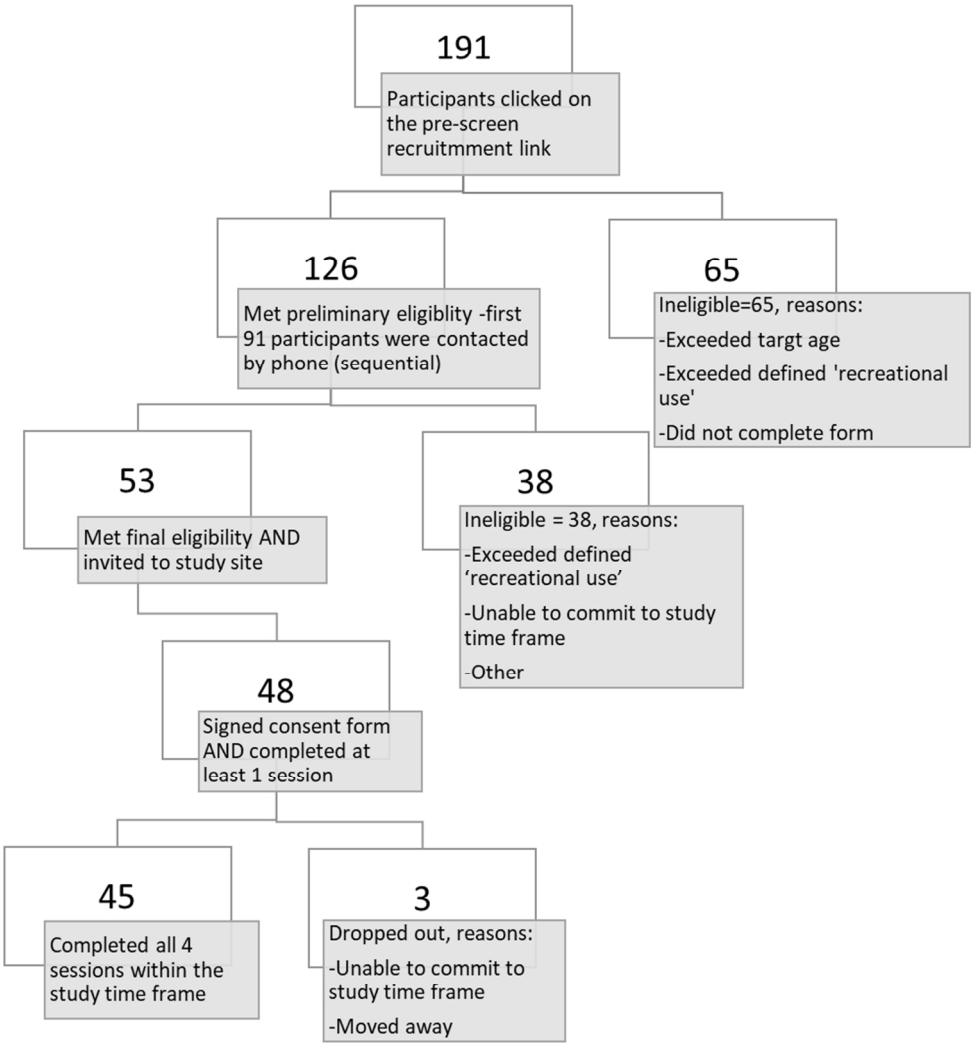

Figure 1. CONSORT diagram

86x97mm (300 x 300 DPI)

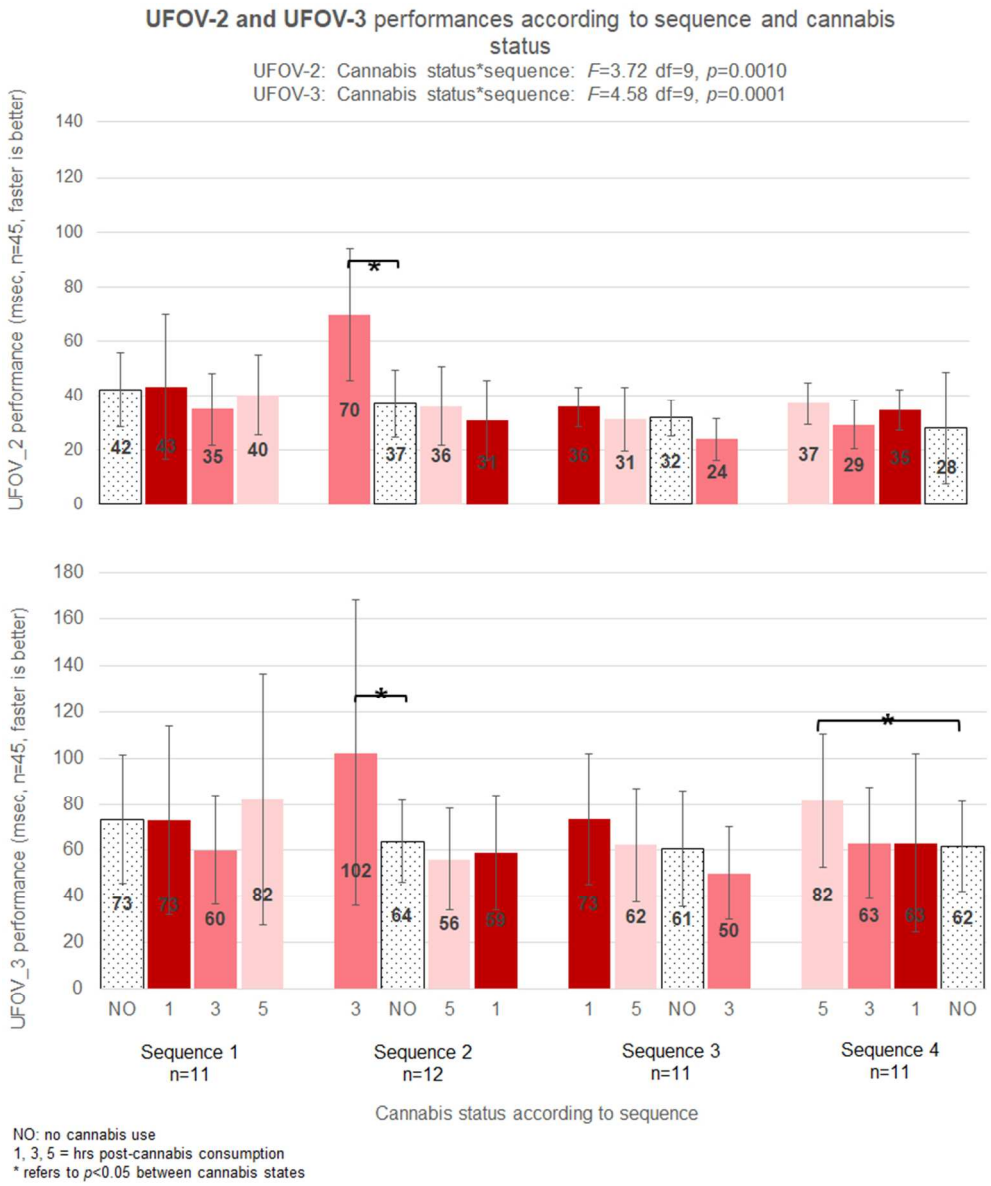

Figure 2. Results of UFOV-2 and UFOV-3 according to sequence and cannabis status. ┼ FIGURE 2 LEGEND: UFOV-2 and UFOV-3 performances (msec, faster is better) at 1, 3 and 5hrs post cannabis use and according the allocated sequence. UFOV-2: Significant sequence x cannabis state interaction (F=3.72, df=9, p=0.001) was found; pairwise comparisons showed a significantly worse performance at 3hrs post cannabis consumption vs. no cannabis use (t= -2.98; df=41; p=0.0048). UFOV-3: Significant sequence x cannabis state interaction (F=4.58, df=9, p=0.0001) was found; pairwise comparisons showed a significantly worse performance at 3hrs post cannabis consumption vs. no cannabis use (t= -2.98; df=41; p=0.0203) and at 5hrs post-use vs. no use (t=-2.32; df=41 p=0)

91x108mm (240 x 240 DPI)