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SHORT REPORT

Dose of Product or Product Concentration: A Comparison of Change in Heart Rate by THC Concentration for Participants Using Cannabis Daily and Occasionally

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Abstract

Introduction: Studies show that acute cannabis use significantly increases heart rate (HR) and mildly raises blood pressure in the minutes following smoked or inhaled use of cannabis. However, less is known about how the THC concentration of the product or an individual's frequency of use (i.e., tolerance) may affect the magnitude of the change in HR. It is also relatively unexamined how the physical effects of increased HR after acute cannabis use relate to self-reported drug effects or blood THC levels.

Aims: To describe the relationship between THC concentration of product used, self-reported subjective intoxication, THC blood levels, and frequency of cannabis use with the change in HR after acute cannabis use.

Materials and Methods: Participants ($n = 140$) were given 15 min to smoke self-supplied cannabis *ad libitum*, HR was measured at baseline and an average of 2 min post-cannabis smoking. The ARCI-Marijuana scale and Visual Analog Scales (VAS) were administered, and blood samples were taken at both time points. Participants were asked about their frequency of use. Information about the product used was recorded from the package. Linear regression was used to analyze the relationship between changes in HR (post-pre cannabis use) and post-cannabis use HR, blood THC concentration, THC product concentration, frequency of use, and self-reported drug effect.

Results: There was a significantly higher HR among those who smoked cannabis compared to the controls ($p < 0.001$), which did not significantly differ by frequency of use ($p = 0.18$). Higher concentration THC (extract) products did not produce a significantly different HR than lower concentration (flower) products ($p = 0.096$). VAS score was associated with an increase in HR ($p < 0.05$). Overall, blood THC levels were not significantly related to the change in HR ($p = 0.69$); however, when probed, there was a slight positive association among the occasional use group only.

Discussion: Cardiovascular effects of cannabis consumption may not be as subject to tolerance with daily cannabis use and do not directly increase with THC concentration of the product. This is a departure from other effects (i.e., cognitive, subjective drug effects) where tolerance is well established. These findings also suggest that, at least among those with daily use, higher concentration THC products (>60%) do not necessarily produce cardiovascular physiological effects that are significantly more robust than lower concentration (<20%) products.

Keywords: concentration; THC; heart rate; tolerance

Introduction

After acute cannabis use, heart rate (HR) has consistently been shown to increase.[1] Studies have found that increases in HR after acute cannabis use can surpass the threshold of tachycardia (i.e., >100 beats per min),[2] and this effect has been observed across different modes of

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use (i.e., smoked, edible).[3] The ability to develop toler-
ance to the cognitive impairing effects of cannabis has
been recognized for some time in the literature; how-
ever, there is conflicting data on the tolerance to the
physiological change of increased HR.[4] Benowitz &
Jones[5] found evidence of tolerance to the tachycardic
effect of cannabis. Newmeyer et al.[6] did not find signifi-
cant differences between use groups when comparing
change in HR from pre- to post-cannabis use, but they
did find that tetrahydrocannabinol (THC) concentra-
tion was associated with increased HR and THC blood
levels in occasional users, which was not significant in
daily users. This suggests partial tolerance to cardiovas-
cular effects, irrespective of self-titration.

Few studies of acute cannabis use have included partic-
ipants with a pattern of daily cannabis use or studied the
effects of high THC concentration products. Among the
only studies to consider this, Hendrickson et al.,[2] did not
find a difference in the frequency of tachycardia for those
inhaling flower product compared to concentrate prod-
ucts, based on data taken from a poison control center.

The purpose of this study was to examine the
acute effects of smoking cannabis on HR, exploring
the effects of THC concentration in the product
used, frequency of use, and the relationship with
self-reported effects and blood THC levels. As an
innovation to prior studies, the current study exam-
ined the use of products purchased from a retail
marketplace (including extract products with high
THC concentration) where recreational cannabis
use is legal, allowing us to study these phenomena in
an ecologically valid setting.

Methods

Participants ($n = 140$) were consented and enrolled
into one of four cannabis use categories based on
the frequency of their cannabis use (daily vs. occa-
sional) and type of product used during the study
(flower vs. extract products with a high THC concen-
tration, herein referred to as "concentrate"): daily
flower use ($n = 39$), daily concentrate use ($n = 38$),
occasional flower use ($n = 31$), or no-use of cannabis

Table 1. Participant Characteristics and Cannabis Use

	Overall, $n = 140$ n (%)	Daily, flower, $n = 39$ n (%)	Daily, concentrates, $n = 38$ n (%)	Occasional, flower, $n = 31$ n (%)	Non-use, $n = 32$ n (%)
Gender					
Male	78 (56%)	24 (62%)	24 (63%)	18 (58%)	12 (38%)
Female	61 (44%)	14 (36%)	14 (37%)	13 (42%)	20 (63%)
Non-binary	1 (0.7%)	1 (2.6%)	0 (0%)	0 (0%)	0 (0%)
Age					
25–29	57 (41%)	16 (41%)	17 (45%)	13 (42%)	11 (34%)
30–39	64 (46%)	15 (38%)	16 (42%)	16 (52%)	17 (53%)
40–49	14 (10%)	7 (18%)	4 (11%)	0 (0%)	3 (9.4%)
50–55	4 (2.9%)	1 (2.6%)	0 (0%)	2 (6.5%)	1 (3.1%)
Race					
Black or African American	12 (8.6%)	6 (15%)	4 (11%)	1 (3.2%)	1 (3.1%)
Asian	3 (2.1%)	0 (0%)	1 (2.6%)	0 (0%)	2 (6.3%)
White	113 (81%)	29 (74%)	33 (87%)	24 (77%)	27 (84%)
Other	4 (2.9%)	1 (2.6%)	0 (0%)	3 (9.7%)	0 (0%)
Declined/No response	3 (2.1%)	1 (2.6%)	0 (0%)	2 (6.5%)	0 (0%)
Biracial/Multiracial	5 (3.6%)	2 (5.1%)	0 (0%)	1 (3.2%)	2 (6.3%)
Ethnicity					
Hispanic or Latino	23 (16%)	8 (21%)	6 (16%)	4 (13%)	5 (16%)
Not Hispanic or Latino	117 (84%)	31 (79%)	32 (84%)	27 (87%)	27 (84%)
Taking ≥ 1 medication affecting HR	36 (26%)	12 (31%)	9 (24%)	7 (23%)	8 (25%)
Has ≥ 1 condition affecting HR	7 (5.0%)	3 (7.7%)	1 (2.6%)	1 (3.2%)	2 (6.3%)
Mean days of cannabis use in past 30 days (SD)	24.84 (8.58)	29.38 (3.01)	29.71 (1.63)	13.16 (7.07)	—
Mean % Total THC (w/w), (SD)	40.78 (27.05)	22.15 (4.33)	75.57 (11.77)	21.38 (6.04)	—
Mean Number of inhalations (SD)	11.26 (9.50)	15.53 (12.89)	7.47 (4.88)	10.70 (6.62)	—
Mean Consumption time in minutes (SD)	6.89 (4.03)	7.83 (4.10)	6.81 (4.06)	5.87 (3.76)	—
Mean Pre-Consumption Heart Rate	73.36 (12.17)	72.22 (13.82)	72.44 (12.27)	78.00 (10.34)	71.03 (10.96)
Mean Post-Consumption Heart Rate	87.57 (21.19)	95.56 (22.23)	89.50 (16.69)	97.03 (17.54)	66.20 (11.81)
Mean Change in Heart Rate (bmp)	14.33 (18.12)	23.33 (17.09)	17.06 (14.00)	19.43 (16.31)	−4.83 (10.57)
Mean Pre-Consumption Blood THC Levels	1.75 (3.60)	2.37 (3.38)	3.82 (5.22)	0.31 (0.94)	0.00 (0.00)
Mean Post-Consumption Blood THC levels	42.79 (56.22)	43.34 (44.44)	60.92 (75.37)	19.61 (27.20)	—

HR, heart rate; SD, standard deviation.

Table 2. Analytic Results of Subjective Drug Effects and Cannabis Use/Products, Stratified by Use Group

	Comparison group	Change in Heart Rate, bpm (IQR)		Post cannabis heart rate bpm (IQR)	
		Unadjusted	Adjusted	Unadjusted	Adjusted
Subjective drug effect		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
ARCI[a]: Some parts of my body are tingling	—	**9.746 (3.72, 15.77)**	**9.267 (3.16, 15.37)**	5.492 (−2.09, 13.07)	4.742 (−2.72, 12.2)
ARCI: I notice that my heart is beating faster	—	**11.229 (5.25, 17.21)**	**10.937 (4.92, 16.96)**	**14.659 (7.47, 21.84)**	**14.267 (7.26, 21.27)**
ARCI: Marijuana scale	—	**1.786 (0.71, 2.86)**	**1.625 (0.53, 2.72)**	1.065 (−0.29, 2.42)	0.816 (−0.52, 2.16)
VAS[b]: Are you high right now?	—	**0.242 (0.09, 0.4)**	**0.247 (0.09, 0.41)**	0.187 (−0.01, 0.38)	**0.204 (0.01, 0.4)**
Participant use characteristics					
Use frequency					
Daily use	No Use	**25.028 (18.67, 31.39)**	**24.628 (18.11, 31.15)**	**26.328 (18.77, 33.89)**	**26.602 (19.07, 34.13)**
Occasional use	No Use	**24.267 (16.71, 31.82)**	**24.255 (16.6, 31.91)**	**30.833 (21.85, 39.82)**	**31.644 (22.8, 40.49)**
Daily use	Occasional Use	0.761 (−5.6, 7.12)	0.372 (−6.04, 6.78)	−4.506 (−12.07, 3.06)	−5.042 (−12.44, 2.36)
Use group					
Daily, Concentrates	No Use	**21.889 (14.72, 29.06)**	**21.314 (13.96, 28.67)**	**23.3 (14.73, 31.87)**	**23.781 (15.23, 32.33)**
Daily, Flower	No Use	**28.167 (21, 35.34)**	**27.841 (20.53, 35.15)**	**29.356 (20.79, 37.92)**	**29.338 (20.85, 37.83)**
Occasional, Flower	No Use	**24.267 (16.78, 31.76)**	**24.162 (16.58, 31.75)**	**30.833 (21.89, 39.78)**	**31.565 (22.75, 40.38)**
Daily, Flower	Daily, Concentrates	6.278 (−0.56, 13.12)	6.527 (−0.41, 13.47)	6.056 (−2.11, 14.22)	5.557 (−2.51, 13.62)
Occasional, Flower	Daily, Flower	−3.9 (−11.07, 3.27)	−3.678 (−10.94, 3.58)	1.478 (−7.09, 10.04)	2.227 (−6.21, 10.66)
Occasional, Flower	Daily, Concentrates	2.378 (−4.79, 9.55)	2.849 (−4.37, 10.06)	7.533 (−1.03, 16.1)	7.784 (−0.6, 16.17)
Blood THC level	—	−0.007 (−0.06, 0.05)	−0.012 (−0.07, 0.05)	−0.003 (−0.07, 0.06)	0.003 (−0.06, 0.07)
Cannabis product characteristics					
Concentrates	Flower	−4.505 (−10.93, 1.92)	−4.853 (−11.34, 1.64)	−6.727 (−14.43, 0.98)	−6.825 (−14.41, 0.76)
THC concentration > 50%	THC Concentration < 50%	−4.619 (−11.14, 1.9)	−5.159 (−11.76, 1.44)	−6.375 (−14.2, 1.45)	−6.622 (−14.35, 1.11)

Note: Values are regression coefficients adjusted for age, gender, race/ethnicity, medication use and medical conditions. Bolding indicated values are significant ($p < 0.05$).
[a]The ARCI Marijuana questionnaire states, "I notice that my heart is beating faster" Participants marked "True" or "False".
[b]The drug effect questionnaire (VAS) asked, "Do you feel HIGH right now?" Participants marked on a 100 mm line visual analog scale from "not at all (0 mm)" to "extremely (100 mm)".
CI, confidence interval; IR; interquartile range; VAS, Visual Analog Scales.

as a comparison group ($n = 32$). There was no planned occasional concentrate use group. The Colorado Multiple Institutional Review Board approved the study procedures.

Participants were asked to abstain from cannabis use (8 h) before the start of their visit. They self-reported significant medical history and medication use and recalled their cannabis use over the last 30 days or 90 days (for occasional use groups) using a Timeline Followback Calendar to confirm their frequency of use. The ARCI-Marijuana scale and Visual Analog Scales (VAS) were administered to measure self-reported drug effects.[7,8] HR measurements were taken with a digital blood pressure monitor (Omron HEM-907XL). Normal HR was defined as a resting HR between 60 and 100 beats per min.[9] After baseline assessments, participants were given up to 15 min to smoke *ad libitum,* except for the no-use group who did not use cannabis. The end of

cannabis use was noted and typically occurred in fewer than the full 15-min period. Participants were asked to bring their own cannabis labeled with THC concentration, containing less than 2% cannabidiol (CBD), from a licensed Colorado dispensary. Details of the product label were recorded to obtain THC concentration. Venous blood samples were taken at baseline and after inhalation from an intravenous line. An average of 2 min after the participant's end of inhalation, the ARCI and VAS scales were re-administered, and HR was recorded. Blood samples were taken approximately 20 min after the first inhalation of cannabis.

Linear regression was used to analyze the relationship between changes in HR (post-pre cannabis use) and post-cannabis use HR with (1) blood THC concentration, (2) THC product concentration, (3) frequency of use, (4) subjective drug effects, and (5) the interaction between blood THC level and frequency

of use. All models were adjusted for age, gender, and race/ethnicity. Medications and medical conditions that suppress or induce tachycardia were controlled for in the analysis (Supplementary Tables S1 and S2).

Results

Participants used a wide range of cannabis concentrate and flower products procured from licensed dispensaries. These included flower buds, pre-rolled joints, cannabis concentrates (e.g., 'sugar', 'shatter'), and oil. Methods for flower consumption included joints, bongs, 'dry herb' vaporizers; for concentrate consumption, dab rigs, 'nectar collectors', and vaporizers. On average, participants took 5.8 to 7.8 min to inhale their cannabis. The average THC content for flower products were 21.4% for those with occasional cannabis use and 22.2% for those with daily use. The average THC concentrate for concentrate products was 75.6% (Table 1).

Participants in the daily flower and concentrate groups reported use on at least 29 of the last 30 days, while the occasional flower group reported use at least 3 but no more than 36 times in the 90 days prior to data collection, per the eligibility criteria. Participants were mostly White (81%), with 55.7% identifying their gender as male, 43.6% as female, and 0.7% did not identify on the gender binary. Most (46%) participants were

between 30 and 39 years old at the time of data collection (Table 1). Table 1 presents the overall and mean blood THC levels, product THC concentrations, and HR pre- and post-cannabis use, categorized by use group.

Overall, in adjusted models (Table 2), among those who inhaled cannabis, the average increase in post-consumption HR was 26.6 beats per min (bpm) for daily use participants compared to non-users, and 31.6 bpm higher for occasional use participants to non-users ($p < .001$).

The concentration of THC in the product used was not significantly associated with the change in HR ($p = 0.13$). Further, the form of the product used (concentrate vs. flower) was not significantly associated with post-cannabis use HR ($p = 0.08$) or the change in HR ($p = 0.16$; Fig. 1, Table 2). There was no significant difference in HR or change in HR (pre-to-post) between the daily use and occasional use groups (Table 2). Additionally, there were no significant differences in post-consumption HR between daily concentrate vs. daily flower, daily flower vs. occasional flower, or daily concentrate vs. occasional flower ($p \geq 0.07$) (Table 2). Blood THC level was not significantly related to the change in HR ($p = 0.69$) or post-consumption HR ($p = 0.92$) after adjusting for demographics, medications, and conditions (Table 2, Fig. 2).
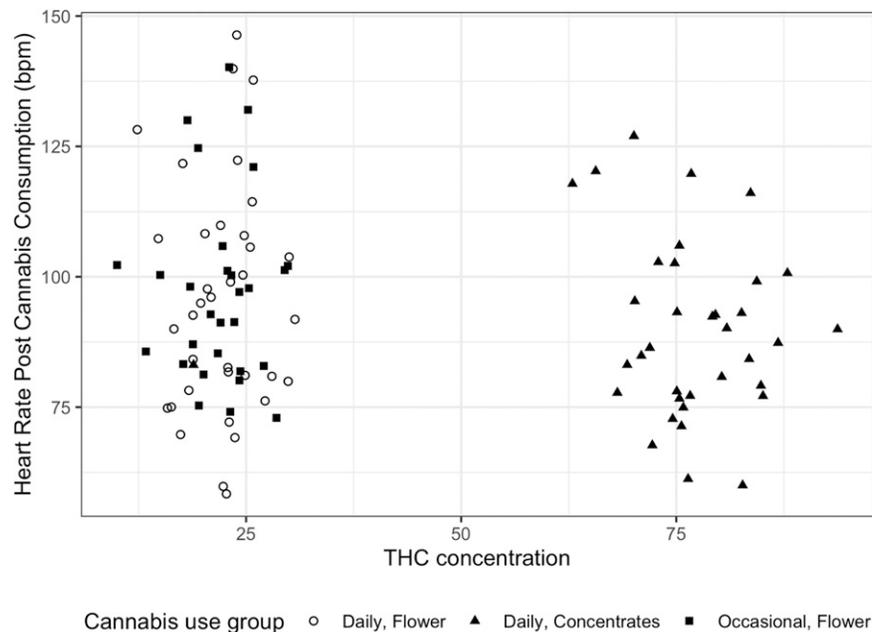

FIG. 1. Post-consumption heart rate by THC concentration.

However, when evaluated by use group, blood THC level was positively associated with both the change in HR ($p = 0.012$) and post-consumption HR ($p = .018$) for the occasional flower group, but was not significant in the daily flower or daily concentrate groups (($p = 0.47$) and ($p = 0.25$), respectively) (Supplementary Table S3).

Self-reported feeling that the heart is beating faster (from ARCI-Marijuana Scale, post-cannabis consumption) were associated with a higher post-cannabis HR ($p < 0.001$). Feeling 'high' right now (from VAS) was associated with a greater increase in HR ($p < 0.01$) and significantly associated with post-consumption HR ($p < 0.05$), after adjusting for demographics, medication use, and medical conditions (Table 2).

Discussion

Definitions of "high" or "higher" THC concentration in products have evolved over time and historically ranged from anything above 2% to 18%.[10–12] Nearly all prior studies no longer reflect what is sold in current retail marketplaces in US states with legal adult cannabis use. Recent studies have used products reflective of today's legal market, such as >60% THC concentration, but much remains unexamined about the differential effects of higher THC concentration products.[13] Our results indicate that high THC concentration cannabis products (e.g., >60%) do not necessarily produce more robust changes in HR than products with lower concentrations (e.g., <20%). These findings corroborate data that previously demonstrated more robust cardiovascular effects were not associated with higher THC concentrate use.[2] It is important to gather more data on the relationship between high concentration products (representative of the modern marketplace) and physiological effects to distinguish the difference between dose (amount consumed) versus concentration of the product used.

We considered participants' frequency of cannabis use as a measure of tolerance to the effects of THC, with daily use equating to potential tolerance. We did not find significant differences in post-use or change
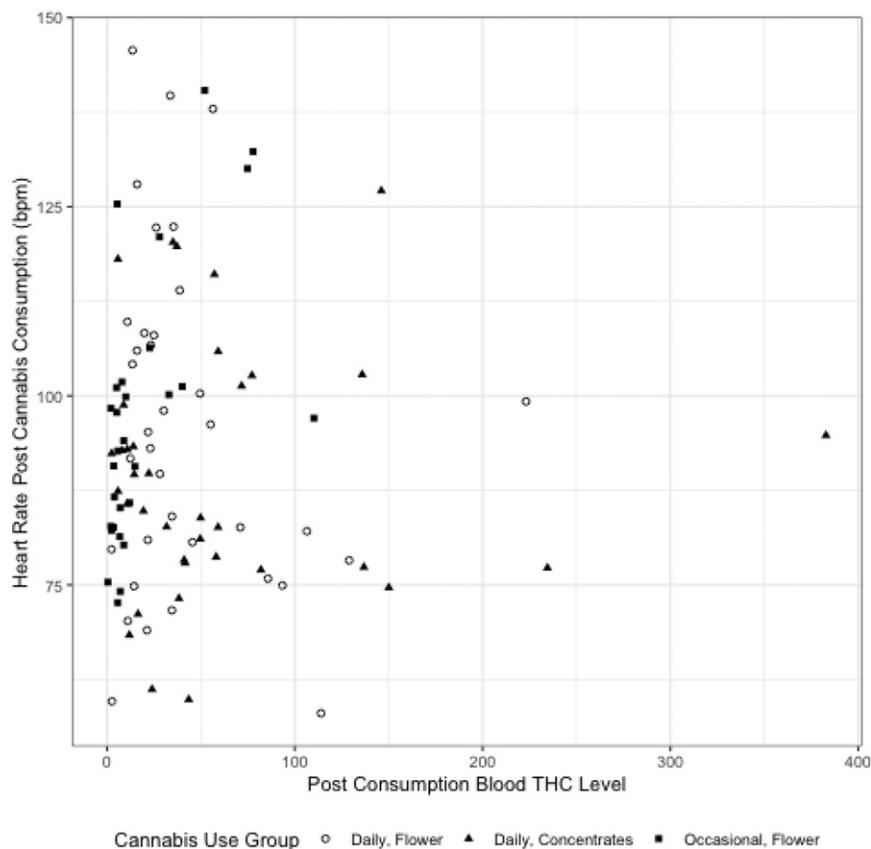

FIG. 2. Post-consumption heart rate by blood THC level.

in HR between those with a pattern of daily use versus occasional use. This finding contrasts with other effects observed in prior studies, such as cognitive or subjective drug effects, where tolerance to cannabis is well established.[14,15] Despite not finding an overall effect between blood THC level and HR, we did find a small positive relationship for the occasional use group only. Taken as a whole, our findings may suggest that the physiological effects of cannabis are less impacted by tolerance. This reduced physiological tolerance might be due to self-titration of use, regardless of product concentration. These findings are consistent with those of Leung et al.,[15] who found that self-reported measures did not differ by mode of use or THC concentration and suggested that the lack of discrepancy might be due to tolerance of the neurological effects of THC and self-titration to euphoric symptoms. The observation that even with daily use there are changes in HR supports the use of HR as an objective marker of an isolated cardiovascular effect after recent cannabis use, regardless of pattern or product used, and could be used to validate self-reported use.

A limitation of this study is that HR was taken as a routine part of data collection for the purposes of participant safety and was not intentionally timed to capture near peak cardiovascular effects. We only observed HR at one time point post-consumption. We relied on self-report for medical conditions and prescription medication data. It is possible that medications may have influenced the subject's baseline HR and response to cannabis. Another limitation is that we did not have an occasional concentrate use group and were unable to more extensively examine the relationship between tolerance and THC concentration. Additionally, our blood levels were measured approximately 20 min after the start of smoking, which does not necessarily reflect peak blood THC levels. Future research should examine what contributes to the differences in HR between individuals after acute cannabis use, as we did not find it be related to the product used or use history.

Further study is needed to tease out the nuance of the relationship between THC concentration, tolerance, and the physiological effects of cannabis. Additionally, future research should explore how oral cannabis use (i.e., the use of edibles) relates to cardiovascular effects, which was not examined in the current study. Data exploring and explaining the nature of this relationship may help inform the evolution of regulations regarding high concentration products.

Authors' Contributions

S.L.: Conceptualization, Methodology, Writing, Data Curation, Original Draft Preparation. S.G.: Data curation, Writing—Original draft preparation, Software, Analysis, Validation. J.W.: Reviewing, Editing, Validation, Software, Supervision. G.S.W.: Reviewing, Editing, supervision. A.B.-R.: Writing—Reviewing and Editing, supervision.

Author Disclosure Statement

The authors of this article (Sarah Limbacher, Suneeta Godbole, Julia Wrobel, George Sam Wang & Ashley Brooks-Russell) have no conflicts of interest to disclose related to this work.

Supplementary Material

Supplementary Table S1
Supplementary Table S2
Supplementary Table S3

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Abbreviations Used

ARCI = Addiction Research Center Inventory
bpm = Beats per minute
CBD = Cannabinol
HR = Heart Rate
THC = delta-9 tetrahydrocannabinol
VAS = Visual Analog Scale