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The Effects of Cannabinoids on the Physical Body.

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ABSTRACT

In this paper we sought to understand what are the effects of cannabinoids on the body and how can we enhance the positive effects of cannabinoids while avoiding any negative side effects. Previous research has suggested that cannabinoids have numerous physiological effects on the body, including effects on the sense of taste, on withdrawal symptoms, and on body mass. In this study we measured cannabinoid consumption (g), synthetic THC consumption (mg), and compared them to measurements of taste palatability, appetite, and withdrawal symptoms rated on subjective scales. Based on pooled standardized data our results supported associations between cannabinoids and palatability of sweet tastes, as well as an association between synthetic THC consumption and withdrawal symptoms, but no support was found for a reduction in appetite with cannabinoid consumption.

1. Introduction

1.1 Research Problem

With the legalization of cannabinoids there has been an overall increase of consumption. We are interested in the physiological effects on the body of consuming cannabinoids and exploring the following questions: After consuming cannabinoids, can senses of taste, touch, and hearing be heightened? What are the effects of long-term marijuana usage on the physical appearance of the body? Does physiological dependence (body withdrawal) occur with cannabinoids and is it greater with synthetic THC?

1.2 Literature Review

A factor that can predict the effects of delta-9-tetrahydrocannabinol (THC) on the body is how consumption of THC affects appetite to sweet tastes (sucrose) and aversive tastes (NaCl). De Luca et al. (2012) was used an implant to infuse rats with NaCl and sucrose to observe behaviour after THC consumption. THC (0.5 or 1.0mg/kg from a volume of 20 ml/kg) induced hedonic reactions with sucrose (5% and 20%) and peaked at 30 minutes as well as having significant observations at 60 and 120 minutes. Palatability of sweet reward was found to have significant results, whereas the aversive tastes had no effect from THC. Taste palatability was measured using hedonic valence on a scale of positive, negative, and neutral behaviours, which were characterised by observing either paw

licks and various tongue movements or gapes, face washing and chin rubs, or rhythmic tongue movements, respectively. Each of the behaviours was given one point if the duration was between one to five seconds, and given two points if duration of behaviour was greater than five seconds. The receptor was discovered to be the cannabinoid CB1 receptor. After systemic THC consumption, sucrose increased dialysate dopamine (DA) in the shell of n.accumbens. After repeated exposure the effects wore off creating a level of high tolerance. De Luca et al. (2012) found this was a natural reward and not the same as a drug reward and that consumption of THC induced palatability of sweets over savery.

Similarly, previous research on the effects of cannabinoids on the body found that chronic use of cannabis was associated with reduced body mass index(BMI) and waistline circumference. In a study by Scheffler et al. (2018) researchers studied the changes in bmi and fasting blood glucose on cannabis users and nonusers who were schizophrenic or had a schizo-affective disorder and were treated according to a standardized treatment regime with depot antipsychotic medication over 12 months. The study included n=109 participants comprising n=40 (37%) Cannabis users and n=69 (63%) non users. The participants were selected from first-admission to psychiatric hospitals and community clinics between April 2007 and March 2011 in Cape Town. The study found that after a period of 12 months, the BMI had significantly reduced in participants who used cannabis which put them at a lower risk for obesity, and in the participants that did not use Cannabis, the researchers found that there was a significant increase in BMI and an elevated waist-line circumference.

Finally, another effect cannabinoids can have on the body is withdrawal after consumption. In an experiment by Trexler et al. (2020) AB-FUBINACA (0−3 mg/kg, i.p.) a member of the indazole carboxamide: family of synthetic cannabinoids, was tested on adult male and female mice. Their response was tested repeatedly measuring catalepsy, antinociception, hypothermia, and locomotor activity. Experiments were carried out by technicians who were blinded to the treatment conditions. For the initial stage the mice were brought to the test room for a minimum of one hour prior to testing, to measure: locomotor activity, catalepsy, tail immersion, and body temperature. Throughout the experiment the mice were weighed daily and injected subcutaneously (s.c.) with AB-FUBINACA (1 or 3 mg/kg) or Placebo- saline, every 12 h for 5 days. On the sixth and final day, all mice received their final injection of AB-FUBINACA or placebo. After 30 min, the mice then received an intraperitoneal injection of rimonabant (3 mg/kg) a drug given to induce withdrawal. The dependent variables measured were: incidences of paw tremors and head twitches. The results were that rimonabant significantly increased both paw tremors and head twitches in mice repeatedly administered AB-FUBINACA, compared to Placebo-treated mice. It is noteworthy that, (using these experimental procedures) mice administered AB-FUBINACA alone did not display spontaneous somatic withdrawal signs. The experiment found that AB-FUBINACA (synthetic cannabinoid) produced classic cannabimimetic effects, including catalepsy, antinociception, hypothermia, and hypolocomotion. The study revealed that AB-FUBINACA, also produces withdrawal effects that diminish much more rapidly than the natural cannabinoids. Therefore we can infer that the withdrawal effects are more significant with use of synthetic

cannabinoids compared to natural, but also decrease much faster.

1.3 Hypotheses

Based on the above literature review, we predicted the following hypotheses:

- Hypothesis #1:If cannabinoids consumption increases, then taste palatability will increase.
- Hypothesis #2: If cannabinoid consumption increases, then appetite will decrease.
- Hypothesis #3: If consumption of synthetic THC is increased, then withdrawal symptoms will increase.

2. Methods

2.1 Participants

The three authors of this paper served as the participants in its studies. The participants ranged in age from 23 to 29 years old, with an average age of 25 years, and included two females and one male, all identifying as cisgender. The participants were all undergraduate students at Camosun College who completed the current studies as an assignment for Psyc 245 ("Drugs and Behaviour") and were grouped together due to their mutual interest in Effects of Cannabinoids on the physical body. Participants have all been consuming Cannabinoids regularly for over twelve months.

2.2 Materials and Procedure

We performed a correlational study to test concurrently all of our hypotheses by examining naturalistic daily changes in their variables longitudinally. Each participant kept a study journal with them at all times over this study's two-week period in order to record self-observations of the following 5 variables: (1) taste palatability, (2) reduced appetite (3) withdrawal symptoms, (4) cannabinoids consumption, and (5) synthetic THC consumption.

Every day a participant recorded a journal for taste palatability and a daily average score was calculated regardless of cannabinoid consumption across all meals. Taste palatability was measured by taste enjoyment for sweet (glucose), or savory (avserive), and a subjective scale from 1 to 5 will be used (1 being not enjoyable, and 5 being very enjoyable) for measuring the specific taste palatability each day. If cannabinoids were consumed participants recorded strain and method of consumption before each meal (see below for cannabinoid type and route of consumption participants may have used).

To measure reduced appetite (the desire to eat food), each participant recorded in their study journals the frequency of food consumption (how many meals per day) and food portions (large, medium, small) each day. a subjective scale from one to five (1= maintained appetite, 3= moderately reduced appetite, 5= extremely reduced) was used to record reduced appetite each day. Participants measured and recorded an average food consumption on days with multiple food consumptions, and on days with no food consumption the participants recorded a score of zero.

To measure withdrawal symptoms, each each participant noted how they felt at the beginning of the day and what symptoms of withdrawal (if any) they experienced. Symptoms were recorded using the Clinical Opiate Withdrawal Scale, which measures the following symptoms: pulse, sweating, restlessness, bone or joint aches, running nose or tearing, GI upset, tremor, yawning, anxiety and irritability. A clinical

withdrawal form (see the Appendix) was filled out explaining symptoms experienced at the beginning of the day before any cannabinoids were consumed for that day. A scoring system was provided in the withdrawal scale: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal.

To measure cannabinoid consumption, each participant recorded in their study journal the type of cannabinoids (sativa, indica, hybrid), amount of cannabinoids consumed in grams (g), and route of consumption (smoke/ joint, pills) each day. On days where multiple cannabinoid consumption occurred, the participants recorded an average of cannabinoid consumption, and on days with no cannabinoid consumption a score of zero was recorded.

To measure synthetic THC consumption, mg of THC in consumed edibles containing synthetic THC were measured. Each participant recorded the number of edibles consumed and the dose of synthetic THC that was contained in the product (mg). On days where multiple edibles were consumed, the participants recorded the number of all edible consumptions, and on days with no cannabinoid consumption a score of zero was recorded.

To assess the strength and statistical significance of associations between variables predicted by our three hypotheses, we performed Pearson product moment correlations of their predictor variables (taste palatability, reduced appetite, and significance of withdrawal symptoms) with their outcome variable (cannabinoids consumption and synthetic THC consumption). For testing Hypothesis #1, we correlated the total amount of cannabinoid consumed by each participant each day with what the participant's taste palatability was. For Hypothesis #2, we correlated the consumption of cannabinoids by each participant each day with how much food the participant consumed. For testing Hypothesis #3, we correlated that the use of synthetic THC edibles, will result in participants experiencing increased withdrawal symptoms. We performed all of the above correlations separately for each participant as well as using data pooled across all of the participants. For the correlations using pooled data, in addition to using the raw data, we also performed correlations after we had first transformed the data from each participant into *z*-scores in order to standardize differences in averages and variability seen between the participants in their data and thus make them more comparable. A correlation coefficient was considered statistically significant if the probability of its random occurrence (p) was $< .05$ (i.e., less than 5% of the time expected by chance alone).

3. Results

As shown in Table 1, withdrawal symptoms, appetite level and palatability to savory and sweet were significantly correlated with cannabinoid consumption. Although not being significant for any single participant (all $r \leq 0.53$, and all $p \geq 0.05$; see Table 1), taste palatability for sweets was significantly correlated with cannabinoids consumed using the pooled standardized data ($r = 0.46$, $p = 0.0021$; see Figure 1B) but not using the pooled raw data ($r = 0.19$, $p = 0.224$; see Figure 1A). Taste palatability for savoury was significantly correlated with cannabinoids consumed for Participant #2 ($r = -0.63$, $p = 0.015$) and Participant #3 ($r = 0.74$, $p = 0.0015$) but not for Participant #1 ($r = 0.08$, $p = 0.802$), where the pooled raw data was significant ($r = 0.31$, $p = 0.046$; see Figure 2A) but the pooled standardized data

was not significant (r = 0.06, p = 0.689; see Figure 2B).

Withdrawal symptoms were significantly correlated with synthetic cannabinoid consumption for Participants #1 (r = 0.61, p = 0.019) and #3 (r = 0.82, p = 0.0001), but not for Participant #2 (r = 0.50, p = 0.069), although the significance was seen using both the pooled standardized data (r = 0.64, p = 1.938E-06; see Figure 3A) and the pooled raw data (r = 0.53, p = 0.00019; see Figure 3B).

Testing appetite in relation to cannabinoid consumption found significant correlations for Participant #2 (r = -0.61, p = 0.02) and Participant #3 (r = 0.54, p =0.047), but not for Participant #1 (r= 0.17, p= 0.56, see Table 1) and not when using either the pooled raw data (r = 0.20, p = 0.19; see Figure 4A) or the standardized pooled data (r = 0.03, p = 0.83; see Figure 4B).

Based on comparison of the correlation coefficients using both pooled raw data and standardized pooled data, the withdrawal symptoms had the strongest correlation with cannabinoid consumption, as well as taste palatability for sweets had the second strongest correlation with cannabinoid consumption based off the pooled standardized data.

4. Discussion

4.1 Summary of Results

Of the three tested hypotheses, our results found the strongest correlation for cannabinoid consumption was withdrawal symptoms. Similarly, the hypothesis that taste palatability will increase with cannabinoid consumption also found positive correlation results. Whereas, for the hypothesis that if cannabinoid consumption increases then appetite will decrease, we found no significant evidence correlating the two variables.

4.2 Relation of Results to Past Research

For the hypothesis that if cannabinoids consumption increases then taste palatability will increase, support was found in our correlational study. Our findings fall in line with previous research conducted by De Luca et al (2012). Where rats were tested for their taste palatability based off behaviour for sweets (licking of paws and lips; wanting more) and savoury (face washing, chin rubs; and rejection behaviours) after being injected with cannabinoids. De Luca et al. (2012) found that after cannabinoid consumption, rats preferred sweets over savoury. While De Luca et al. (2012) used mice as their research participants, while our study used human participants who regularly consume cannabinoid substances. Our study also compared taste palatability for sweets and savoury variables with cannabinoid consumption to observe separate data for each, and found palatability for sweets was more desirable than savoury after cannabinoid consumption. The findings for both De Luca et al. (2012), and our study had different research design methods, but both had similar findings within the research suggesting that taste palatability for sweets increases as cannabinoid consumption increases.

For the hypothesis that if consumption of synthetic THC is increased then withdrawal symptoms will increase, our study found that the pooled standardized data and pooled raw data both showed significant correlations, where withdrawal symptoms strongly correlated with synthetic cannabinoid consumption. Similarly, the initial experiment by Trexler et al. (2020) found in mice that withdrawal symptoms are more significant with synthetic cannabinoid

use than with natural cannabinoid derivatives. While some details were different such as the mice were injected with the synthetic THC substance subcutaneously, whereas in the human trial the synthetic THC was ingested by mouth and absorbed through the gastrointestinal system.

For the hypothesis that if cannabinoid consumption increases then appetite will decrease, we found no significant correlation between the relationship of cannabinoid consumption and appetite for the pooled data and raw pooled data, even though Participants #2 and #3 both had significant results. Scheffler et al. (2018) had found in their study that participants who tested positive for cannabis had less of an increase in body mass index (BMI), than participants who tested negative for cannabis. The difference between both studies is that Scheffler et al. (2018) had been testing with schizophrenia patients who typically suffer from obesity and cardiometabolic complications and were on antipsychotic medication. They also used a larger sample size (126 participants) over twelve months and recorded BMI, where our study used three participants over a two weeks period and no BMI was recorded, only appetite. Further studies will need to be done in order to directly compare all of these variables.

References

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Table 1

Correlation coefficient (r) values, with number of daily trials (n) per correlation in brackets.

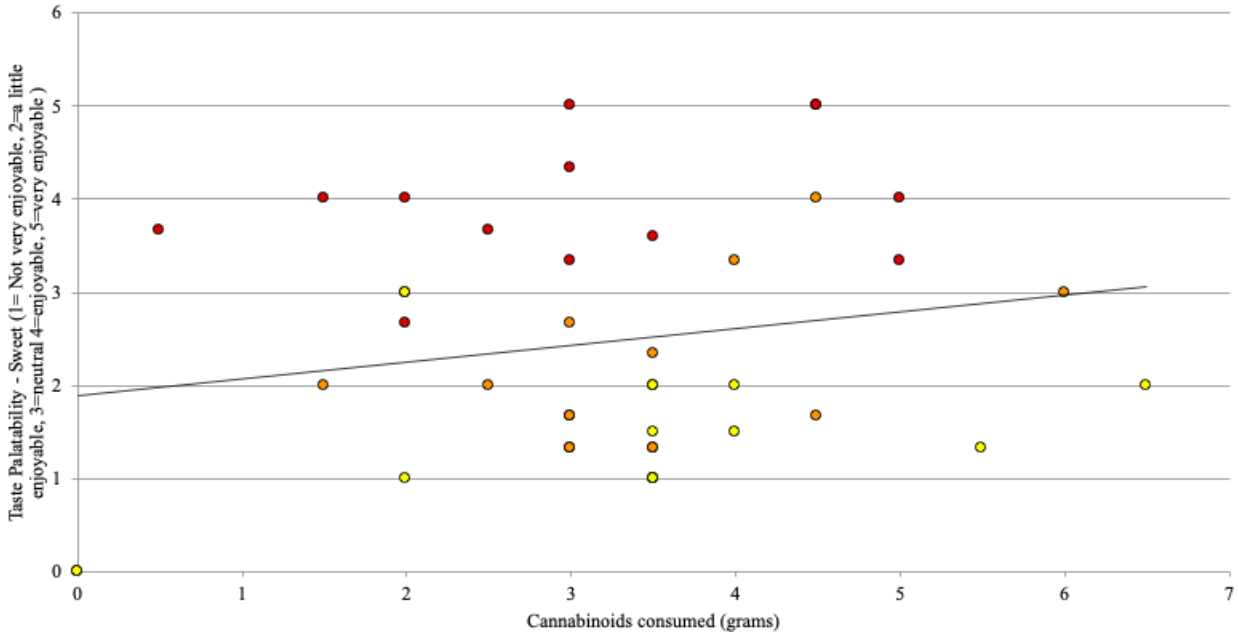
Variables correlated	Participant #1	Participant #2	Participant #3	Pooled raw data	Pooled standardized data
Taste palatability (Sweet) & Cannabinoids consumed	0.36(14)	0.48(14)	0.53(14)	0.19(42)	0.46(42)*
Taste palatability (Savory) & Cannabinoids consumed	0.08(14)	-0.63(14)*	0.74(14)*	0.31(42)*	0.06(42)
Withdrawal symptoms & Synthetic THC consumed	0.61(14)*	0.50(14)	0.82(14)*	0.53(42)*	0.64(42)*
Reduced appetite & Cannabinoids consumed	0.17(14)	-0.61(14)*	0.54(14)*	0.20(42)	0.03(42)

* $p < .05$.

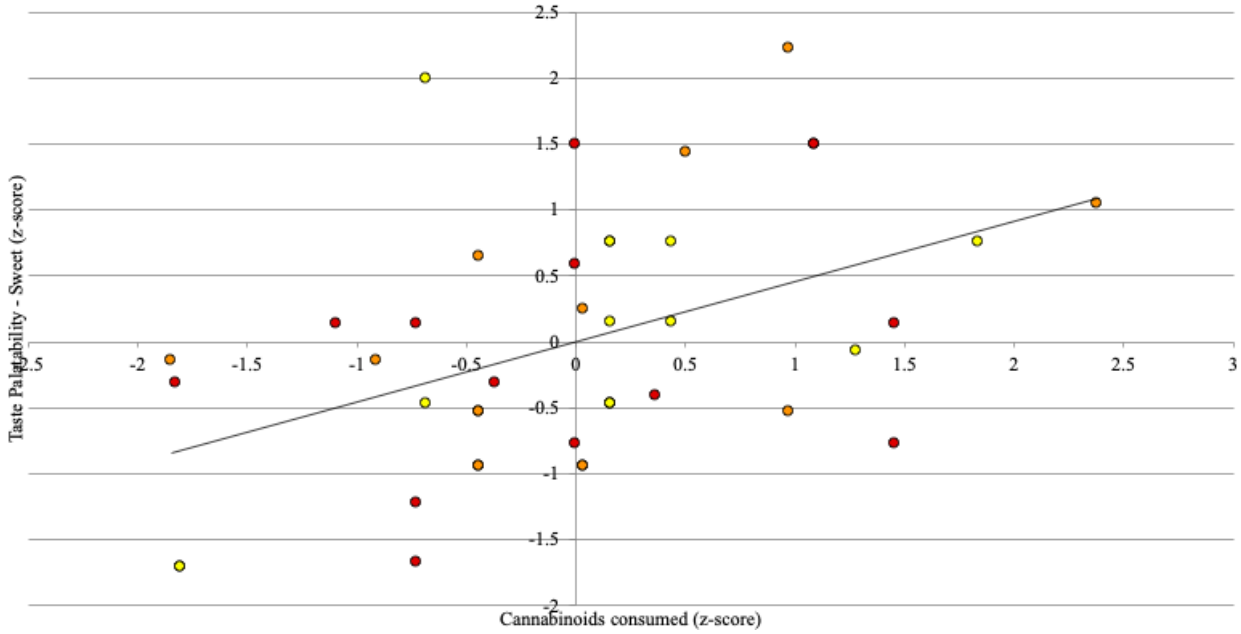
Figure 1

Scatterplot of cannabinoids consumed and taste palatability (sweet) of Pooled raw data (A) and pooled standardized data (B)

A.



B.

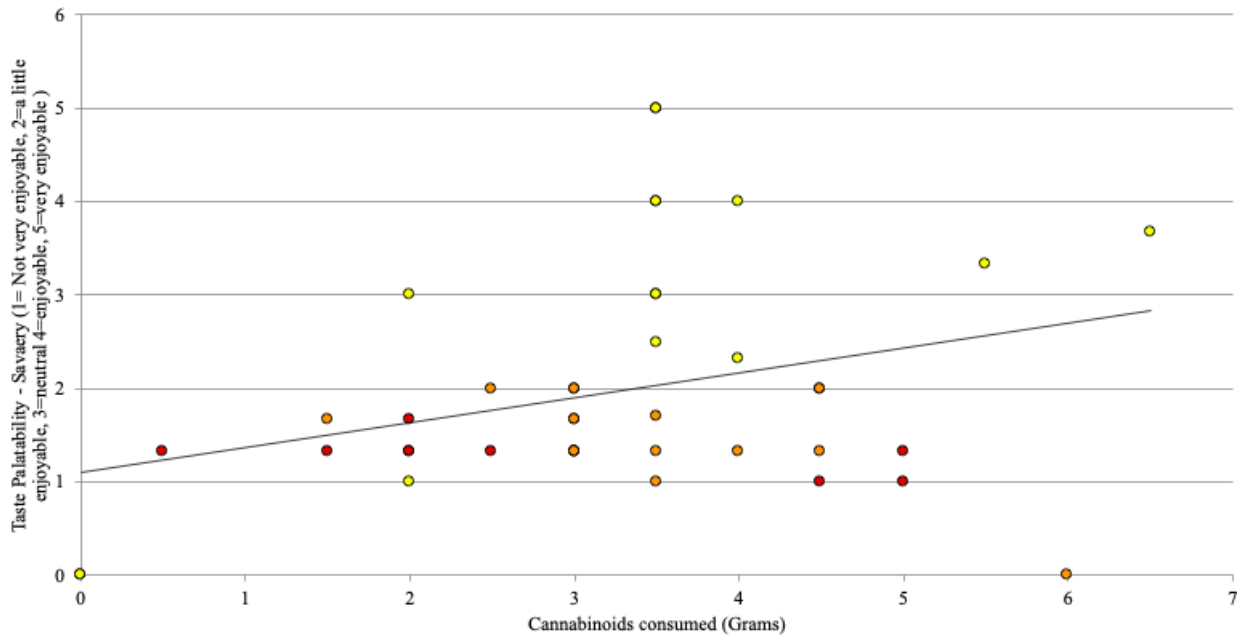


Marker color indicates which participants data is from. Red = participant #1, Orange = participant #2, yellow = participant #3. Some data may not be visible due to overlapping markers.

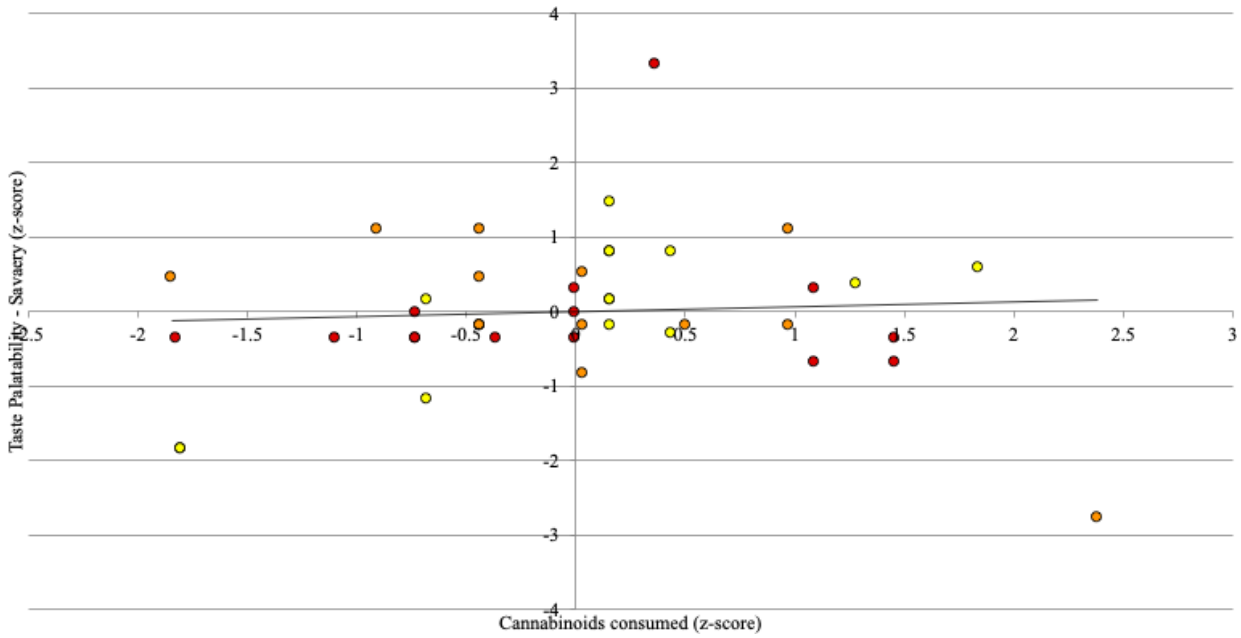
Figure 2

Scatterplot of cannabinoids consumed and taste palatability (savory) of Pooled raw data (A) and pooled standardized data (B)

A.



B

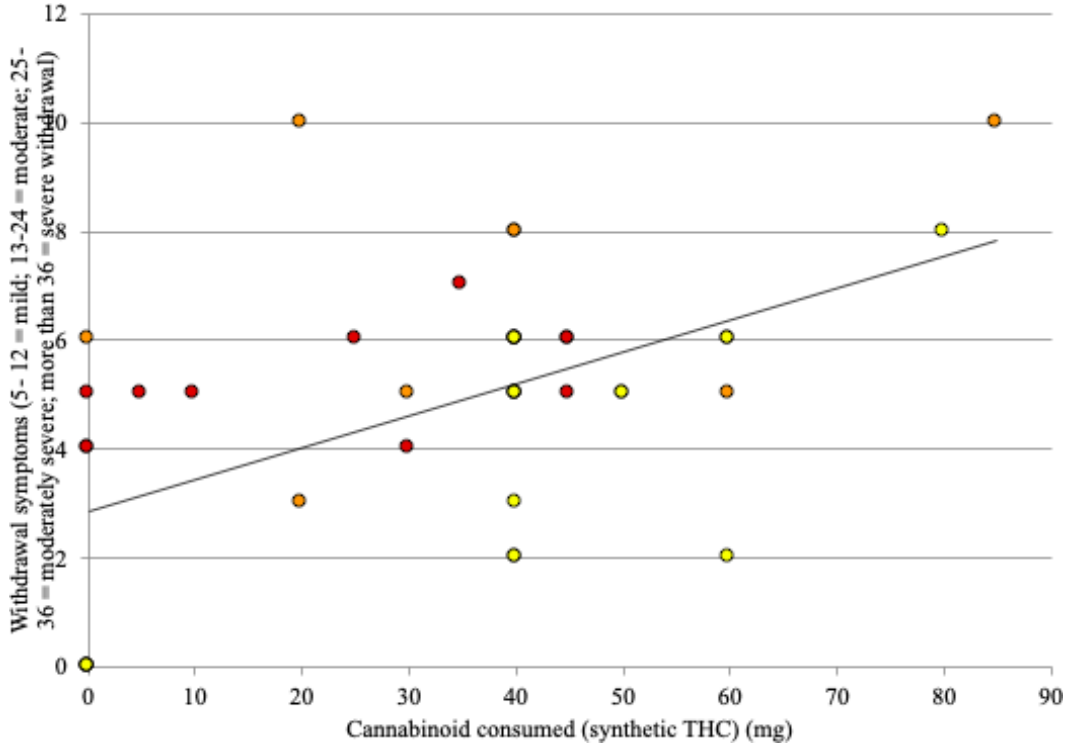


Marker color indicates which participants data is from. Red = participant #1, Orange = participant #2, yellow = participant #3. Some data may not be visible due to overlapping markers.

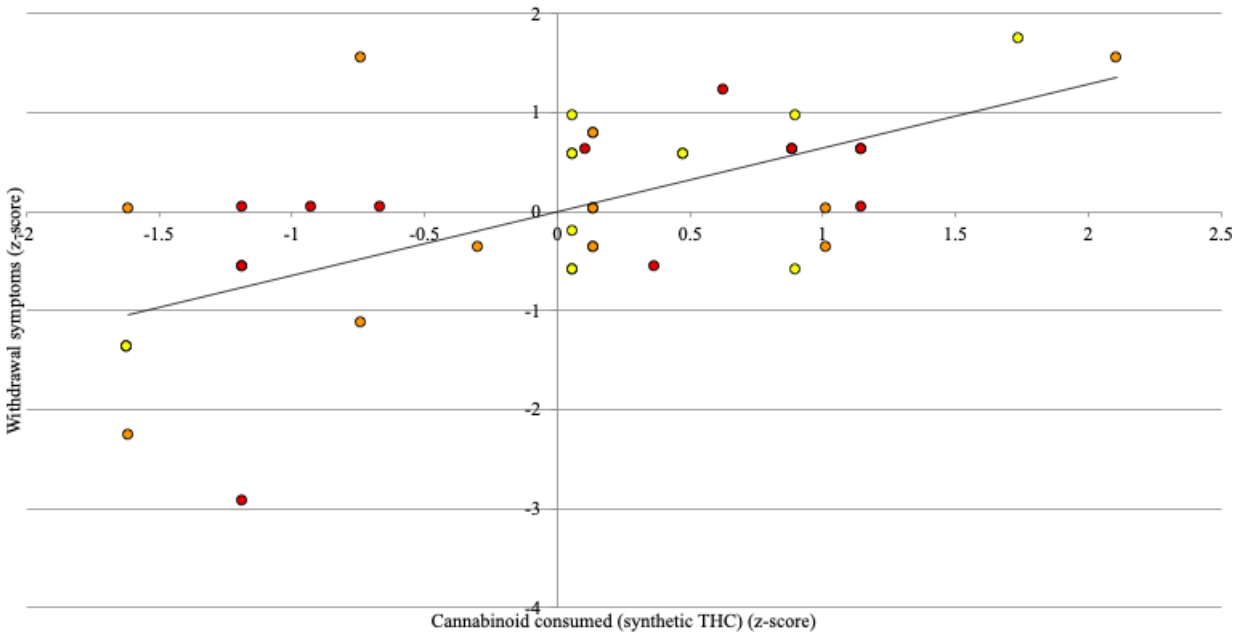
Figure 3.

Scatterplot of synthetic cannabinoids (THC) consumed and withdrawal symptoms of Pooled raw data (A) and pooled standardized data (B)

A.



B.

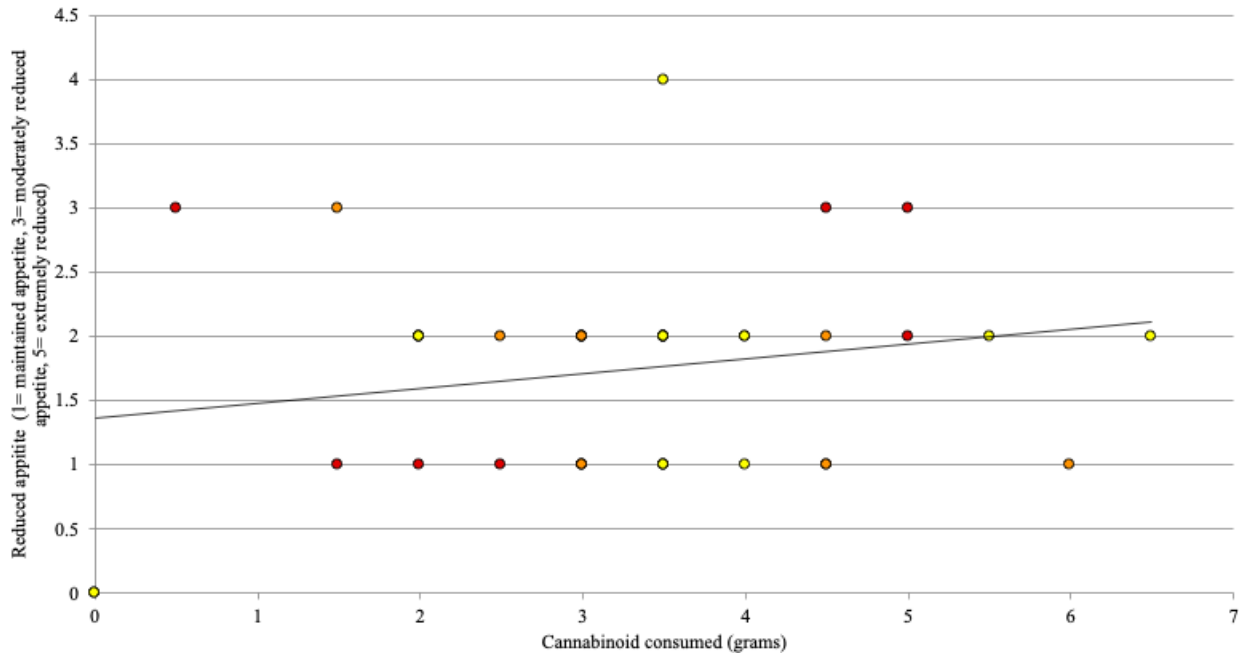


Marker color indicates which participants data is from. Red = participant #1, Orange = participant #2, yellow = participant #3. Some data may not be visible due to overlapping markers.

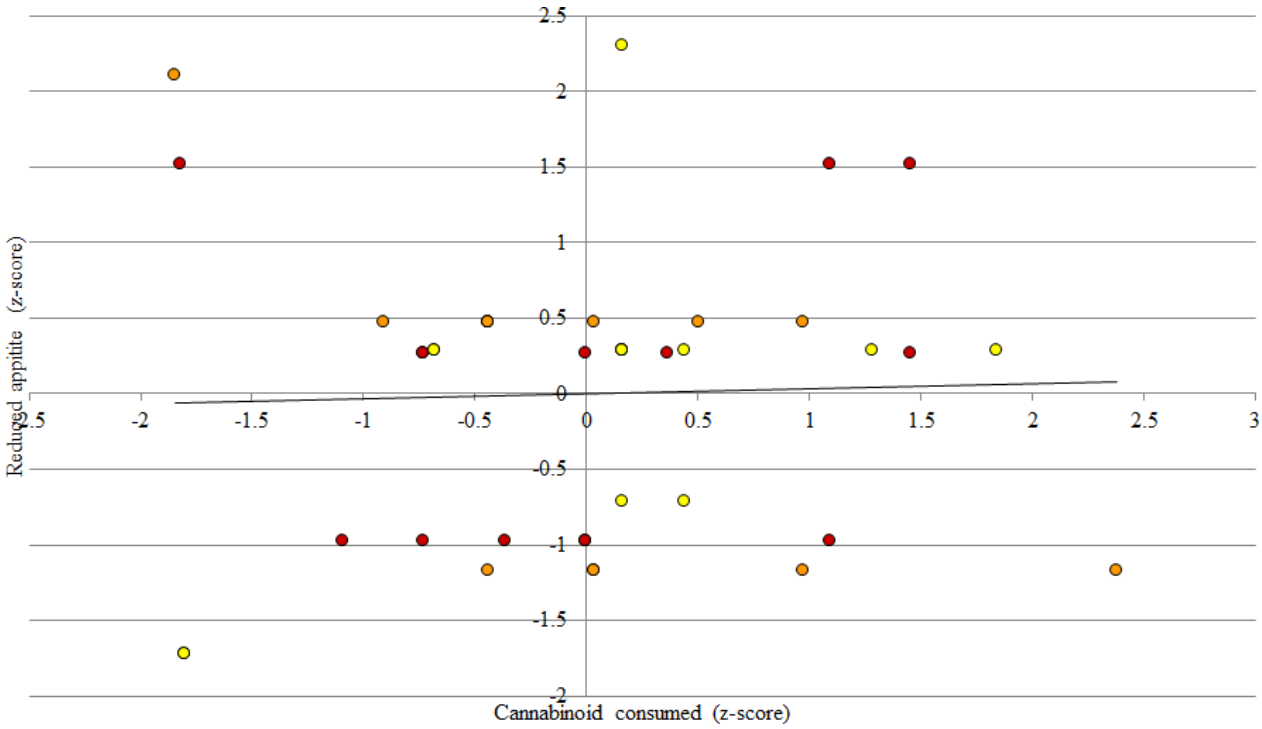
Figure 4

A.Scatterplot of cannabis consumed and reduced appetite using raw data (A) and pooled standardizeddata (B)

A.



B.



Marker color indicates which participants data is from. Red = participant #1, Orange = participant #2, yellow = participant #3. Some data may not be visible due to overlapping markers.

Appendix

Clinical Opiate Withdrawl Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time ___/___/___:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute
Measured after patient is sitting or lying for one minute
0 pulse rate 80 or below
1 pulse rate 81-100
2 pulse rate 101-120
4 pulse rate greater than 120

GI Upset: *over last 1/2 hour*
0 no GI symptoms
1 stomach cramps
2 nausea or loose stool
3 vomiting or diarrhea
5 multiple episodes of diarrhea or vomiting

Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.*
0 no report of chills or flushing
1 subjective report of chills or flushing
2 flushed or observable moistness on face
3 beads of sweat on brow or face
4 sweat streaming off face

Tremor *observation of outstretched hands*
0 no tremor
1 tremor can be felt, but not observed
2 slight tremor observable
4 gross tremor or muscle twitching

Restlessness *Observation during assessment*
0 able to sit still
1 reports difficulty sitting still, but is able to do so
3 frequent shifting or extraneous movements of legs/arms
5 unable to sit still for more than a few seconds

Yawning *Observation during assessment*
0 no yawning
1 yawning once or twice during assessment
2 yawning three or more times during assessment
4 yawning several times/minute

Pupil size
0 pupils pinned or normal size for room light
1 pupils possibly larger than normal for room light
2 pupils moderately dilated
5 pupils so dilated that only the rim of the iris is visible

Anxiety or Irritability
0 none
1 patient reports increasing irritability or anxiousness
2 patient obviously irritable or anxious
4 patient so irritable or anxious that participation in the assessment is difficult

Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored*
0 not present
1 mild diffuse discomfort
2 patient reports severe diffuse aching of joints/muscles
4 patient is rubbing joints or muscles and is unable to sit still because of discomfort

Gooseflesh skin
0 skin is smooth
3 piloerrection of skin can be felt or hairs standing up on arms
5 prominent piloerrection

Runny nose or tearing *Not accounted for by cold symptoms or allergies*
0 not present
1 nasal stuffiness or unusually moist eyes
2 nose running or tearing
4 nose constantly running or tears streaming down cheeks

Total Score _____
The total score is the sum of all 11 items

Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.