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ORIGINAL RESEARCH

Investigating the Relationship Between Cannabis Expectancies and Anxiety, Depression, and Pain Responses After Acute Flower and Edible Cannabis Use

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Abstract

Objective: Cannabis has been touted for a host of pharmacological and therapeutic effects and users commonly report reduced symptoms of physical and mental health conditions, including anxiety, depression, and chronic pain. While there is existing empirical evidence supporting these effects of cannabis use, little is known about the extent to which these effects result from pharmacological versus expectancy factors. We evaluated the associations between participants' cannabis expectancies and their acute self-reported reactions after using legal market forms of cannabis with varying levels of cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC) in three domains: anxiety, depression, and pain.

Methods: Fifty-five flower and 101 edible cannabis users were randomly assigned and asked to purchase at a local dispensary one of three products containing varying levels of CBD and THC. Participants completed a baseline assessment where they reported expectancies about general health effects of cannabis use and an experimental mobile laboratory assessment where they administered their assigned products. Edible users also reported their domain-specific expectancies about cannabis use in improving anxiety, depression, and pain. Following administration, participants completed acute indicators of anxiety, depression, and pain operationalized through subjective acute tension, elation, and a single-item measure of pain.

Results: Among flower users, more positive expectancies for cannabis to improve general health were correlated with greater reductions in tension at acute post-use. This finding was replicated among edible users. Unlike flower users, more positive expectancies for cannabis to improve general health were also correlated with greater increases in elation and greater reductions in pain among edible users. More positive expectancies for cannabis to improve depression and pain were also correlated with greater increases in elation and greater reductions in pain, respectively, among edible users.

Conclusions: Cannabis users' expectancies significantly impacted some of the acute subjective effects of legal market cannabis products. Among both flower and edible users, consistent, significant expectancy effects were found. Results were consistent with prior findings and demonstrate the need to measure and control pre-existing expectancies in future research that involves cannabis administration.

Clinical trial registration number: NCT03522103

Keywords: cannabis; expectancy; placebo; anxiety; depression; pain

Introduction

Cannabis products containing Δ9-tetrahydrocannabinol (THC) remain federally illegal. This presents unique constraints on cannabis research, since institutions that receive federal funding are prohibited from providing legal market cannabis products to study participants. In practice, this prohibits researchers from utilizing gold standard double-blind placebo-controlled

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randomized trials (RCT).[1] To study products *as they are used in the legal market* requires observational designs wherein participants acquire products from dispensaries that must, by law, be accurately labeled.[2] Because it is impossible to conceal the nature of the product from the participant as would happen in a placebo-controlled trial, the extent to which study findings are influenced by participants' expectations of cannabis' effects (i.e., expectancies) remains unclear.

Expectancy effects are the physiological and psychological outcomes of a treatment observed in response to beliefs about the effects of that treatment.[3] They have been observed across myriad domains, including the well-known placebo effect in medical interventions, including pharmaceuticals,[4,5] alternative therapies,[6,7] and even surgery.[8,9] Expectancies can heighten treatment effects across diverse outcomes (e.g., pain,[10] sleep,[11] nausea[12]).

Cannabis has been touted for various medicinal uses, backed by empirical evidence supporting its efficacy for several conditions (e.g., anxiety,[13] depressive symptoms,[14] chronic pain[15]). These reports likely contribute to the formation of expectancies regarding cannabis effects.[16] For example, expectancies regarding cannabidiol (CBD)'s anxiolytic properties predicted self-reported effects of CBD on anxiety.[17]

Although existing data are suggestive, to date, there is no study examining how expectancies shape the effects of the full variety of legal market cannabis (i.e., THC dominant, CBD dominant, THC + CBD). Conducting a placebo-controlled trial of legal market products containing more than trace amounts of THC is currently unfeasible.[1,18] Thus, any difference in certain subjective effects observed across cannabinoid conditions may be exacerbated or driven partly by expectancies.

This study utilizes data from a mobile pharmacology laboratory and naturalistic administrations of legal market edible or flower cannabis.[19] Participants were randomly assigned to a CBD-dominant cannabis flower/edible product, a THC-dominant cannabis flower/edible product, or a cannabis flower/edible product containing approximately equal levels of CBD and THC. Although researchers were blinded to condition assignment, participants were not. Thus, this situation allows the unique ability to test the association of participant expectancies with their acute self-reported reactions to cannabis in domains for which cannabis is commonly used (i.e., anxiety, depression, and pain).

Given existing evidence and lay beliefs about CBD's medical properties,[20] we hypothesized that participants would report more favorable expectancies for CBD-dominant products than for THC-dominant or CBD + THC products. In addition, more positive expectancies for cannabis to improve health were expected to be associated with greater improvement in proxies of anxiety, depression, and pain following acute cannabis use.

Methods

Participants and procedures

The study was approved by the University of Colorado Boulder institutional review board. Participants were recruited as part of a series of RCT examining the acute effects of *ad libitum* cannabis use. Recruitment primarily came from mailed flyers, business cards, and social media announcements.

Researchers screened interested participants for the following inclusion criteria: (1) Age between 21 and 70 years; (2) used cannabis at least four times in the past month; (3) prior experience with using edibles (edible cohort); (4) no other nonprescription drug use in the past 60 days confirmed by urine toxicology screening; (5) tobacco use less than five cigarettes per day; (6) breath alcohol level of 0 at screening and drinking three times or fewer per week and five drinks or fewer per occasion (men) and four drinks or fewer per occasion (women); (7) not pregnant (verified by urine pregnancy test) or trying to become pregnant; (8) and not receiving treatment for psychotic disorder, bipolar disorder, or schizophrenia. Participants provided written informed consent and were compensated for participation during baseline ($50) and mobile laboratory appointments ($100).

Flower cohort: cannabis flower products

Baseline appointment. Participants provided informed consent and completed self-report questionnaires. Participants also received a blood draw to measure plasma cannabinoid concentrations and were randomly assigned to purchase a flower cannabis product with one of three THC/CBD concentration ratios: THC dominant (~24% THC; 1% CBD), THC + CBD (~9% THC; 10% CBD), or CBD dominant (~1% THC; 23% CBD). Participants were instructed to purchase enough of their designated product for 5 days of typical use at a local dispensary. Per State of Colorado law, all study products were labeled with their THC and CBD potencies. Participants were instructed to use their assigned

cannabis product *ad libitum* over the subsequent 5-day period.

Mobile laboratory appointment. Participants were instructed not to use cannabis on the day of their mobile laboratory visit. During this visit, two research team members traveled to the participant's residence in the mobile pharmacology laboratory (a customized Dodge Sprinter van). The visit began with pre-use assessments, including self-report measures and a blood draw. Participants were then instructed to consume their assigned cannabis product inside their home and then return to the mobile laboratory (average total time away from mobile laboratory, 13.3 min), where they completed a battery of post-use assessments, including self-report measures and another blood draw[†]. They remained in the mobile laboratory and completed a final assessment 1 h post-use.

Edible cohort: edible cannabis products

Baseline appointment. The baseline appointment procedures were identical to those for the Flower Cohort, except that participants were randomly assigned to purchase and use an oral cannabis product with one of three THC/CBD concentration ratios: THC-dominant capsule (10 mg THC; 0 mg CBD), THC + CBD capsule (10 mg THC; 10 mg CBD), or CBD-dominant capsule (1.65 mg THC; 25 mg CBD). Consistent with State of Colorado requirements, the THC and CBD potencies of all study products were on the labels following testing in an International Organization of Standards (ISO) 17025-accredited laboratory.

Mobile laboratory appointment. The mobile laboratory visit was the same as for the Flower Cohort, except that because edible cannabis products were being used, participants completed the first post-use assessment *one hour* after consuming the study product (1 h post-use) and the final post-use assessment at 2 h following consumption (2 h post-use).

Measures

Cannabis expectancies. Overall health expectancies were measured at baseline in both cohorts for each of the three cannabinoid profiles with the question, "I believe taking [CBD/THC/THC and CBD together] would improve my health." In the Edible Cohort only, expectancies of the benefits of each cannabinoid profile were also measured specifically for anxiety, depression, and pain. For example, "I believe taking [CBD/THC/THC and CBD together] would improve my depression." All expectancy items were rated on a scale ranging from 0 "Do not at all agree" to 10 "Very much agree."

Alcohol use disorder identification test. Possible scores on the AUDIT range from 0 to 40, and scores greater than 8 are considered harmful or hazardous drinking ($\alpha_{\text{Flower Cohort}} = 0.71$ and $\alpha_{\text{Edible Cohort}} = 0.73$).[22]

Beck Anxiety Inventory. The 21-item Beck Anxiety Inventory (BAI) was used to measure baseline anxiety symptoms.[23] Participants were asked to rate the severity of each symptom (e.g., "unable to relax," "nervous") in the past 2 weeks, on a scale from 0 "Not at all" to 3 "Severely, I could barely stand it" ($\alpha_{\text{Flower Cohort}} = 0.90$ and $\alpha_{\text{Edible Cohort}} = 0.91$).

Beck Depression Inventory. Baseline depressive symptoms were measured using a modified 20-item version of the Beck Depression Inventory (BDI), with the suicidality item (#9) omitted.[24] Participants were asked to rate the extent to which they had experienced each symptom (e.g., "loss of interest," "worthlessness") in the past 2 weeks on an item-specific response scale from 0 (least endorsement of symptom) to 3 (greatest endorsement of symptom) ($\alpha_{\text{Flower Cohort}} = 0.92$ and $\alpha_{\text{Edible Cohort}} = 0.90$).

Brief Pain Inventory. The 11-item Brief Pain Inventory (BPI) measures pain intensity, as well as pain interference with daily functioning.[25] Participants rated the extent to which pain had interfered with their daily functioning (e.g., "general activity," "normal work") in the past week by answering 7 items modified from this measure, on a scale from 0 "Never" to 4 "Always" ($\alpha_{\text{Flower Cohort}} = 0.89$ and $\alpha_{\text{Edible Cohort}} = 0.87$).

Marijuana Dependence Scale. Cannabis use disorder symptoms were assessed with the 11-item Marijuana Dependence Scale (MDS), which was developed based on dependence criteria included in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III-R)[26] ($\alpha_{\text{Flower Cohort}} = 0.78$ and $\alpha_{\text{Edible Cohort}} = 0.73$).

[†]Blood samples were obtained to both verify adherence to condition assignment and to examine associations between plasma cannabinoid levels and study outcomes. These data were analyzed and reported in two previously published studies (Bidwell et al., 2020; Gibson et al., 2022).[21] Important to this analysis, these data demonstrated that participants adhered to their assigned study product.

Profile of Mood States questionnaire. A modified 27-item POMS was administered at pre-use and post-use using 5-point Likert-type scales with responses ranging from 1 "not at all" to 5 "extremely."[27] The Tension subscale, calculated as the average of 4 items ("nervous," "anxious," "unable to relax," and "shaky/jittery") assessed acute feelings of anxiety ($\alpha_{\text{Flower Cohort}} = 0.71$ and $\alpha_{\text{Edible Cohort}} = 0.68$). The Elation subscale, calculated as the average of 4 items ("joyful," "euphoric," "elated," and "cheerful"), assessed acute feelings of depression ($\alpha_{\text{Flower Cohort}} = 0.82$ and $\alpha_{\text{Edible Cohort}} = 0.80$). Notably, the 1971 POMS included most of these items (reverse coded) in the original POMS measure of "Depression."

Marijuana Craving Questionnaire. The 10-item Marijuana Craving Questionnaire measures momentary feelings related to cannabis on a scale ranging from 0 "not at all" to 10 "strongest feeling possible."[28] A single item drawn from this scale ("I feel in pain right now") assessed acute pain at each time point.

Analyses

Descriptive statistics were first calculated by cannabinoid ratio to compare across condition. Since we found, in previous analyses, that acute effects on tension and elation could be moderated by baseline anxiety and depression symptoms,[19] we examined correlations between baseline BAI/BDI and acute change in tension/depression. Acute changes were difference scores comparing pre-use and immediate post-use (Flower Cohort)/1 h post-use (Edible Cohort) tension/elation. A within-subjects analysis of variance (ANOVA) tested differences in expectancies associated with the three cannabinoid profiles.

Multilevel models were estimated to examine the relationship between expectancies (i.e., anxiety, depression, pain) and corresponding effects following cannabis consumption. For each participant, a single variable was created which reflected responses to the expectancy item specific to their assigned cannabinoid profile (CBD, THC, or THC + CBD). For example, a participant in the CBD condition would have their CBD expectancies included as the "expectancy" variable. Analyses of the three outcome variables (i.e., tension, elation, or pain) were conducted using mixed-effect models estimating random intercepts for participants.

In each model, we included time, expectancy, and the time by expectancy interaction. For the Flower Cohort, time was contrast coded as pre-use vs. acute post-use. For the Edible Cohort, analyses were conducted across all three time points (pre-use, 1 h post-use, and 2 h post-use). In the case of significant interactions, simple effects tests were conducted for participants with average, higher (1 standard deviation [SD] above average), and lower (1 SD below average) expectancies. To account for any potential variance in outcomes introduced by cannabis condition (i.e., CBD, THC, or THC + CBD), a set of two orthogonal contrast codes for condition were included as fixed effects in all models.

For the Flower Cohort, only general health expectancies of each cannabinoid profile were examined as predictors as this was the only expectancy predictor available. For the Edible Cohort, two models were estimated for each of the three outcome measures: One including general health expectancies and the other including expectancies specific to the outcome domain. The three outcome measures of interest were acute changes in tension (momentary measure of anxiety), elation (momentary measure of depression), and pain after using cannabis. Baseline mental health symptoms and substance use levels such as BDI and MDS scores were controlled for in additional analyses, but results did not differ from models without these predictors. Therefore, results obtained from simpler models were presented.

Results

Demographics and between-cohort differences

Fifty-two participants (females = 19 and males = 33) were recruited for the Flower Cohort, while 101 participants (females = 55, males = 43, and other = 3) were recruited for the Edible Cohort. Participants were primarily recreational cannabis users across both user groups. The two user groups were similar, although participants in the Flower Cohort reported higher MDS, AUDIT, BAI, and BDI scores than those in the Edible Cohort (Table 1). Participants in the Flower Cohort endorsed significantly greater expectancies that health would be improved with the use of CBD alone ($p = 0.040$) and a combination of THC and CBD ($p = 0.048$); however, there were no significant difference in mean expectancies for health benefits of solely consuming THC across cohorts, $p = 0.361$.

Flower cohort: cannabis flower products

Flower Cohort participants expected significantly greater health benefits from consuming CBD (mean [M] = 8.37, SD = 2.51) and THC + CBD ($M = 8.17$, SD = 2.56) than THC alone ($M = 7.0$, SD = 2.79), $p = 0.018$. Baseline anxiety and depression symptoms were unrelated to post-

Table 1. Cohort Comparison on Demographics and Baseline Characteristics

	Flower Cohort (n=52)	Edible Cohort (n=101)	Analysis
Demographics			
			t
Age	40.9 (*16.46*)	37.5 (*14.06*)	−1.34
			χ^2
Gender (% female)	36.5%	54.5%	5.14
Race/ethnicity			4.25
American Indian or Alaska Native	2.7%	8.8%	
Asian	3.4%	2.9%	
Black or African American	1.3%	2.0%	
White	86.6%	81.4%	
Hispanic or Latino	6.0%	4.9%	
Marital status (% married)	23.9%	23.5%	4.91
Employment (% full-time employed)	43.4%	42.2%	3.85
Education (% bachelors or higher)	50.3%	47.1%	2.32
			t
Expectancies on general health			
THC	7.30 (*2.79*)	6.92 (*2.38*)	−0.88
CBD	8.40 (*2.47*)	7.56 (*2.51*)	−2.08*
THC + CBD	8.27 (*2.54*)	7.45 (*2.46*)	−2.00*
Substance use history and current use			
AUDIT	6.57 (*3.64*)	3.46 (*3.11*)	11.25***
Age of onset of regular cannabis use	20.67 (*8.98*)	20.71 (*9.71*)	0.04
MDS	6.94 (*3.63*)	1.98 (*2.27*)	8.80***
Days of cannabis use (past 30 days)	21.43 (*9.63*)	18.92 (*11.92*)	6.29**
%THC in most frequently used flower products	25.50 (*5.31*)	24.13 (*6.04*)	0.87
%CBD in most frequently used flower products	22.32 (*9.26*)	8.64 (*6.63*)	5.73**
THC in most frequently used edible products (mg)	13.13 (*7.89*)	14.86 (*5.27*)	−0.05
CBD in most frequently used edible products (mg)	4.64 (*4.52*)	3.79 (*2.32*)	1.72
Mental and physical health			
Depressive symptoms (BDI)	6.84 (7.48)	10.78 (10.93)	9.96***
Anxiety symptoms (BAI)	27.31 (8.19)	8.76 (8.60)	10.29***
Subjective pain (BPI)	9.32 (10.47)	5.26 (7.14)	2.65**

*$p<0.05$. **$p<0.01$. ***$p<0.001$.
Numbers in Italic are standard deviations.
AUDIT, Alcohol Use Disorder Identification Test; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BPI, Brief Pain Inventory; CBD, cannabidiol; MDS, Marijuana Dependence Scale.

use changes in tension ($r=-0.05$, $p=0.295$) or elation ($r=0.11$, $p=0.177$).

General health expectancies

There was a significant time X expectancy interaction on tension, given greater expectancies for cannabis to improve general health were correlated with greater decreases in tension acutely post-use, $b=-0.07$, $t=3.22$, $p=0.001$ (Fig. 1). Simple effects tests indicated that for participants with higher expectancies, more positive expectancies were associated with significantly greater decreases in tension at acute post-use, $b=-0.19$, $t=-2.91$, $p=0.004$. This effect was not significant for those with average expectancies ($b=-0.02$, $t=-0.62$, $p=0.536$). Those with lower expectancies showed that, as their expectancies for general health increased, they experienced a marginal *increase* in tension after use ($b=0.14$, $t=1.94$, $p=0.056$).

A significant time effect showed that elation significantly increased post-consumption, $b=0.52$, $t=5.58$, $p<0.001$. Similarly, pain significantly decreased after consumption, $b=-0.85$, $t=-4.14$, $p<0.001$. There was no expectancy X time interaction for either elation ($p=0.307$) or pain ($p=0.332$). There was a marginal effect of cannabinoid condition on acute changes in pain after cannabis consumption, where participants who consumed CBD-dominant products reported marginally greater reductions in pain compared to the other two conditions, $b=0.72$, $t=1.73$, $p=0.062$. No other effect of cannabis condition was significant ($ps>0.10$).

Edible cohort: edible cannabis products

There was no significant difference in expectancies by cannabinoid profile on general health, anxiety, or depression (Table 1), $ps>0.14$. Participants reported more positive expectancies for the effects of THC when compared to THC + CBD on pain (Table 2). Baseline anxiety symptoms were marginally negatively correlated with acute changes in tension at 1 h post-use ($r=-0.23$, $p=0.052$). The correlation between baseline depression symptoms and acute changes in elation was not significant ($r=0.13$, $p=0.197$).

General health expectancies

There was a significant time X expectancy interaction given greater expectancies that cannabis would improve general health predicted greater decreases in tension post-use, $b=-0.02$, $t=-2.01$, $p=0.046$. Simple effect tests indicated that more positive expectancies were significantly associated with greater reductions in tension among all participants, but this effect was strongest for those with higher expectancies ($b=-0.15$, $t=-4.62$, $p<0.001$), somewhat weaker for those with average expectancies ($b=-0.10$, $t=-4.57$, $p<0.001$),

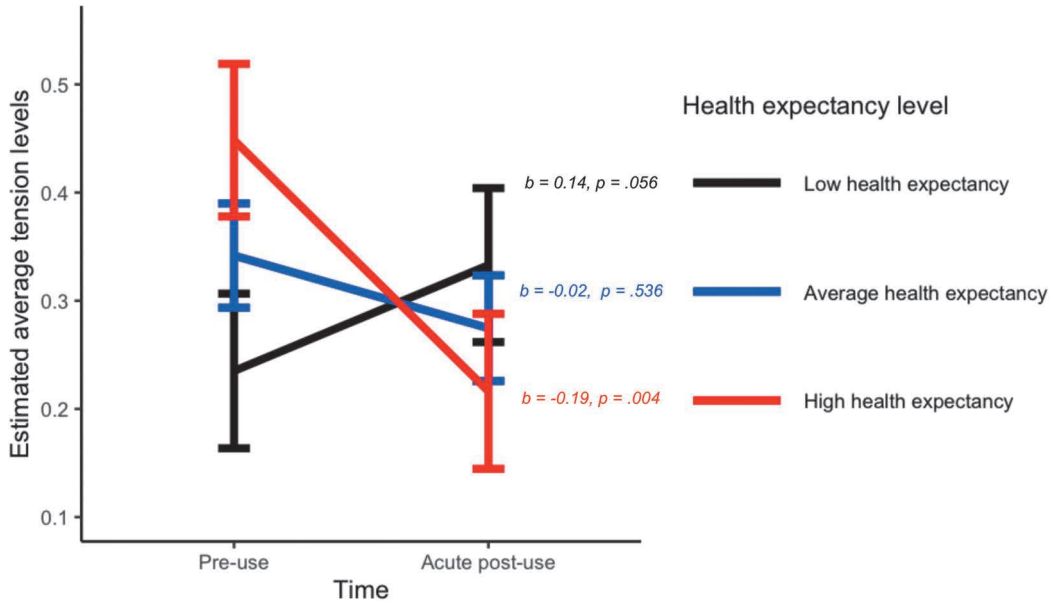

FIG. 1. General health expectancy effect on tension for the flower cohort.

and marginal for those with lower expectancies ($b = -0.06$, $t = -1.79$, $p = 0.076$; Fig. 2).

There was a significant time X expectancy interaction for elation given greater expectancies that cannabis would improve general health predicted greater increases in elation post-use, $b = 0.03$, $t = 2.03$, $p = 0.044$. Simple effects tests showed that expectancies were significantly associated with increased elation among all participants, but the effect was strongest for those with higher expectancies ($b = 0.23$, $t = 3.11$, $p < 0.001$), somewhat weaker for those with average expectancies ($b = 0.17$, $t = 4.95$, $p < 0.001$), and weakest for those with lower expectancies ($b = 0.10$, $t = 2.02$, $p = 0.045$).

There was also a time X expectancy interaction for pain, given greater expectancies that cannabis would improve general health predicted greater decreases in perceived pain post-use, $b = -0.09$, $t = -2.91$, $p = 0.004$. Simple effects tests revealed that expectancies were significantly associated with reductions in pain among all participants, but were strongest for those with higher expectancies ($b = -0.66$, $t = -6.05$, $p < 0.001$), somewhat weaker for those with average expectancies ($b = -0.44$, $t = -5.65$, $p < 0.001$), and weakest for those with lower expectancies ($b = -0.21$, $t = -2.67$, $p = 0.009$).

Table 2. Means, Standard Deviations, and Between-Condition Comparisons of Domain-Specific Expectancies for Edible Cohort

	M	SD	*F*	*p*
General health			1.93	0.15
THC	6.92	2.38		
CBD	7.56	2.51		
THC + CBD	7.45	2.46		
Depression				
THC	6.28	2.49	1.97	0.14
CBD	5.96	2.34		
THC + CBD	6.65	2.38		
Anxiety				
THC	6.71	2.38	1.11	0.33
CBD	6.95	2.41		
THC + CBD	7.22	2.32		
Pain				
THC	7.26	2.00	4.11	< 0.05
CBD	7.68	2.17		
THC + CBD	8.10	1.94		

M, mean; SD, standard deviation.

Domain-specific expectancies

The time X expectancy interaction for anxiety was trending in the same direction as the model using general health expectancy as the predictor, $b = -0.01$, $t = -1.77$, $p = 0.078$. There was a significant quadratic time X expectancy interaction for elation, $b = 0.02$, $t = 2.04$, $p = 0.042$ (Fig. 3), given greater expectancies that cannabis would improve depression predicted greater improvement in elation post-consumption. Simple effects tests indicated that expectancies were

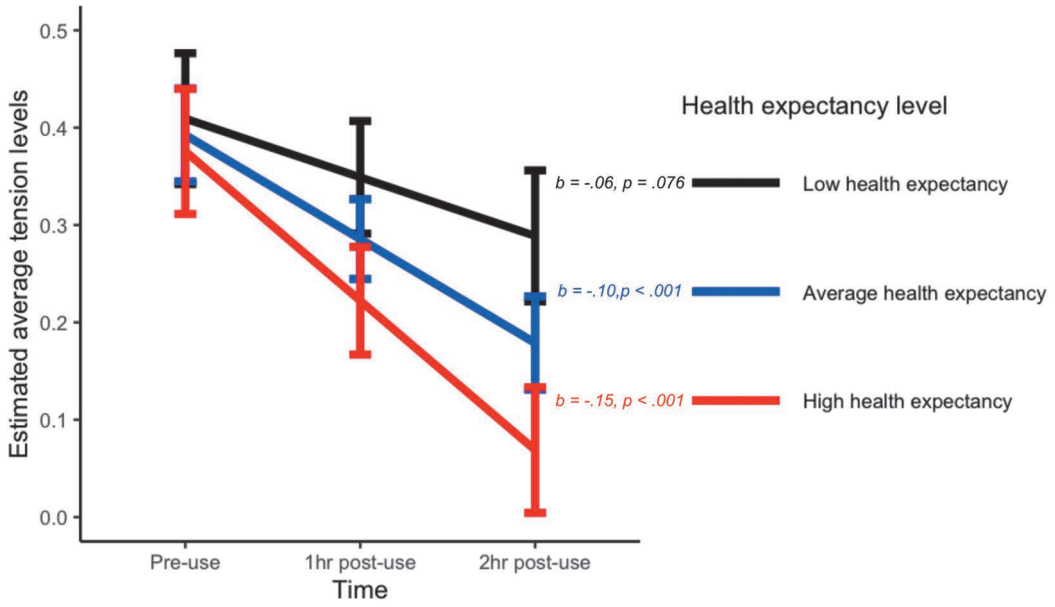

FIG. 2. General health expectancy effect on tension for the edible cohort.

positively associated with increases in elation among participants with higher expectancies ($b = 0.12$, $t = 4.48$, $p < 0.001$), and with average expectancies ($b = 0.08$, $t = 4.28$, $p < 0.001$), but not significant among those with lower expectancies ($b = 0.04$, $t = 1.55$, $p = 0.124$).

There was a significant linear time X expectancy interaction for pain, $b = -0.08$, $t = -2.09$, $p = 0.038$ (Fig. 4). Greater expectancies that cannabis would improve pain predicted greater decreases in pain post-consumption. Simple effects tests indicated that

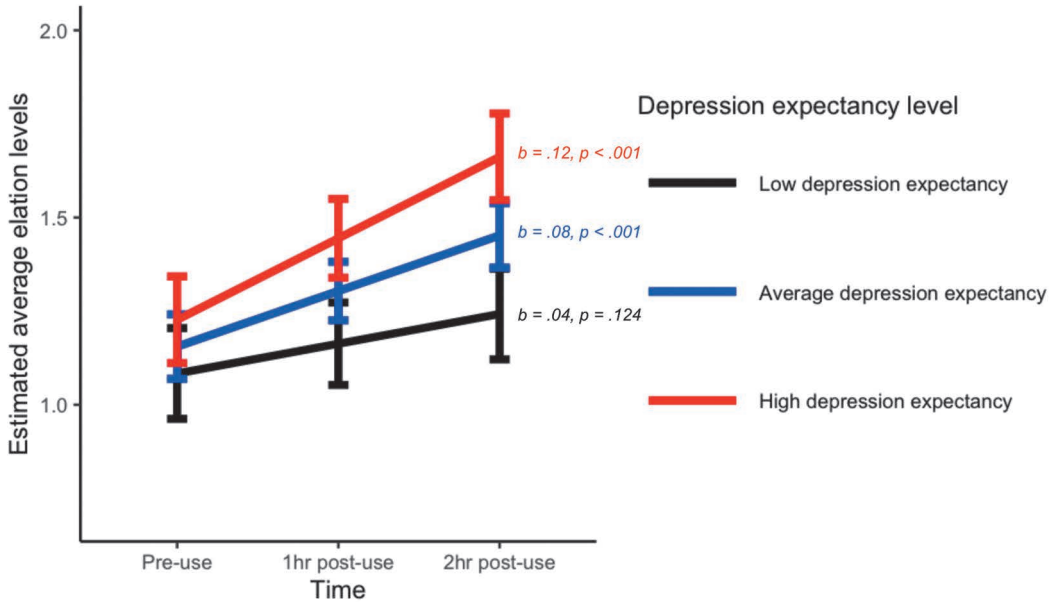

FIG. 3. Depression expectancy effect on elation for the edible cohort.

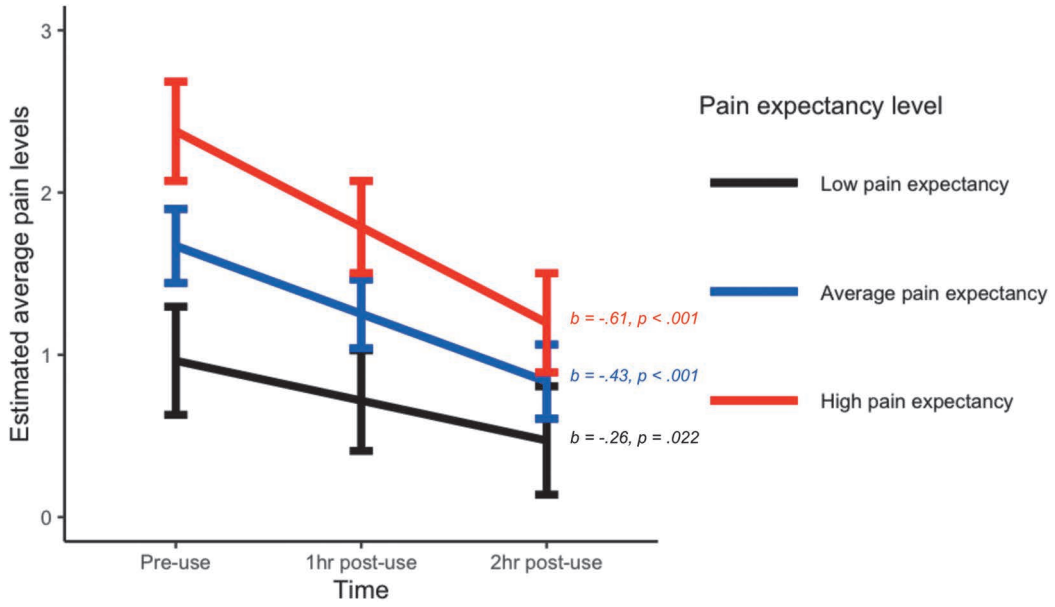

FIG. 4. Pain expectancy effect on pain for the edible cohort.

expectancies were significantly associated with decreased pain among all participants, but that these effects were strongest for participants with higher expectancies ($b = -0.61$, $t = -5.38$, $p < 0.001$), somewhat weaker for those with average expectancies ($b = -0.43$, $t = -5.59$, $p < 0.001$), and weakest for those with lower expectancies ($b = -0.26$, $t = -2.30$, $p = 0.022$).

Discussion

Findings suggest that cannabis flower and edible users' expectancies play a significant role in at least some of the acute effects of legal market cannabis. Consistent with past studies,[16,17] general health expectancies were significantly associated with greater reductions in tension in both cohorts, while effects of anxiety-specific expectancies displayed a similar trend in the Edible Cohort. Expectancy effects in other domains were less consistent. Significant expectancy effects on both depression (i.e., acute changes in elation) and pain were only found within the Edible Cohort. Given established expectancy effects on responses to non-cannabis medications for pain relief,[29] depression,[30] and anxiety,[31] there is no reason to posit that expectancies for cannabis effects on these facets would be immune from this phenomenon.

Among users in the Flower Cohort, we did not find greater expectancies for improving general health for CBD when compared to THC or THC + CBD. Instead, participants reported expecting greater benefits from consuming THC + CBD products. Conversely, among users in the Edible Cohort, no significant difference in general health expectancies were found for different cannabinoid profiles. For pain specifically, greater expectancies were found for THC-dominant products. Thus, contrary to our initial hypothesis, participants did not *expect* greater health benefits from consuming CBD. However, those who consumed CBD-dominant products in the Flower Cohort showed significantly greater reductions in perceived pain post-consumption than participants in the other two conditions. This finding underscores the potential for CBD to reduce pain symptoms and provide medicinal benefits to those with chronic pain conditions.[15,32]

While our findings are novel and significant, there are limitations. First, our sample was a homogeneous group of mostly white regular cannabis users with a college education. Our sample, which was primarily recreational users, also reported low levels of clinical symptoms regarding anxiety, depression, and pain overall, thus limiting generalizability of findings to users who use cannabis to treat these conditions. Although naturalistic administration procedures allowed us to study legal market cannabis effects, we lacked control over dosing and methods of administration. We also lacked a placebo control as such products do not currently exist on the legal market. In addition, this

study did not consider the possibility of users having negative expectations about using cannabis (e.g., harming one's health). More research is needed to determine if an expectancy effect in the opposite direction exists.

This study focused on some of the most common reasons endorsed for using cannabis medicinally (e.g., pain, anxiety, depression). Future studies should assess additional motivations for cannabis use, including improved sleep,[33,34] stress reduction,[35,36] increased sociality,[35,37] increased creativity,[37,38] and even increased exercise enjoyment.[39,40]

In conclusion, this study demonstrates, for the first time, that cannabis expectancies likely contribute to some of the most commonly reported cannabis effects among regular users. Our findings emphasize the need for future placebo-controlled clinical trials involving legal market cannabis use to measure and control pre-existing expectancies that may impact important outcomes.

Authors' Contributions

Concept and design: L.C.B., A.D.B., and K.E.H: Acquisition, analysis, or interpretation of data: All authors. Drafting of the article: M.Y.C., A.D.B., and E.B.K: Critical revision of the article for important intellectual content: M.Y.C., A.D.B., L.C.B., L.P.G., and E.B.K: Statistical analysis: M.Y.C., A.D.B., E.B.K, and L.P.G: Funding acquisition: L.C.B., A.D.B., and K.E.H: Project administration: L.C.B., A.D.B., L.P.G., and K.E.H: Supervision: L.C.B., A.D.B., and K.E.H.

Author Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

ANOVA = analysis of variance
AUDIT = Alcohol Use Disorder Identification Test
BAI = Beck Anxiety Inventory
BDI = Beck Depression Inventory
BPI = Brief Pain Inventory
CBD = cannabidiol
ISO = International Organization of Standards
M = mean
MDS = Marijuana Dependence Scale
POMS = Profile of Mood States
RCT = randomized trials
SD = standard deviation
THC = Δ9-tetrahydrocannabinol