In the public domain 2024, Vol. 32, No. 3, 285–294 https://doi.org/10.1037/pha0000701

# Reward Learning Capacity in a Community Sample of Individuals Who Use Cannabis

Olivia Turner<sup>1</sup>, Kiran Punia<sup>1, 2</sup>, Diego A. Pizzagalli<sup>3</sup>, James MacKillop<sup>1, 4, 5</sup>, and Iris M. Balodis<sup>1, 4, 5</sup>

Peter Boris Centre for Addictions Research, St. Joseph's Healthcare Hamilton, Hamilton, Ontario, Canada

Department of Psychology, Neuroscience and Behaviour, McMaster University

McLean Hospital, Harvard Medical School

Michael G. DeGroote Centre for Medicinal Cannabis Research, Hamilton, Ontario, Canada

Department of Psychiatry and Behavioural Neurosciences, St. Joseph's Healthcare Hamilton, McMaster University

Cannabis use has been linked to deficient reward processing; however, little is known about its relation to the specific construct of reward learning, in which behavior is modified through associating novel stimuli with a positive outcome. The probabilistic reward task was used to objectively evaluate reward learning in 38 individuals who use recreational cannabis and 34 control comparison participants from the community. Reward learning was evidenced by the development of a response bias, which indicates the propensity to modulate behavior as a function of prior reinforcement. Both cannabis and control groups demonstrated reward learning, with no group differences in response bias development. Among cannabis participants, trending significant relationships between greater chronicity, r(36) = -.30, p = .077, self-reported potency, r(19) = -.33, p = .052, and poorer reward learning were found. Nonsignificant relationships were found between reward learning and frequency, age of initiation, weekly quantity or Cannabis Use Disorder Identification Test–Revised (CUDIT-R) scores (all p > .05). The ability to form noncannabis reward associations is promising for the success of therapeutic interventions for problematic cannabis use; however, indications of severity of use in relation to poorer reward learning suggests a need for a better pharmacological and pharmacokinetic understanding of cannabis.

#### Public Health Significance

This study suggests that individuals who use cannabis maintain the ability to form reward associations outside of the substance, while highlighting the importance of considering severity of use when evaluating this relationship.

Keywords: cannabis, reward processing, reward learning, associative learning, probabilistic reward task

Supplemental materials: https://doi.org/10.1037/pha0000701.supp

Cannabis persists as one of the most widely used drugs worldwide, whereby an estimated 4% of the global population aged 15–64 consumed cannabis in 2020; rates of use have steadily increased in the last decade (United Nations Office on Drugs and Crime, 2022). Despite the popular belief that cannabis use poses little to no risk (Schulenberg et al., 2019; Spackman et al., 2017), several lines of evidence reveal potential negative psychosocial and mental health consequences associated with frequent use, including: lower academic

achievement (Fergusson et al., 2015); higher rates of depression and psychosis (Gobbi et al., 2019); increased risk of developing cannabis use disorder (CUD; Silins et al., 2014); and engaging in other substance use (Lynskey et al., 2003). With more countries moving toward cannabis legalization, understanding the mechanisms through which cannabis use is linked with adverse outcomes is imperative.

Emerging longitudinal studies suggest a dose-dependent relationship between greater cannabis use and poorer psychosocial and

This article was published Online First December 21, 2023.

This research was supported from the Michael G. DeGroote Centre for Medicinal Cannabis Research (CMCR) at McMaster University, the Peter Boris Centre for Addictions Research (awarded to Iris M. Balodis) at McMaster University and from the Ontario Graduate Scholarship Award through McMaster University.

The authors recognize and acknowledge that the land on which this work was completed is the traditional territory of the Mississauga and Haudenosaunee nations, and within the lands protected by the "Dish With One Spoon" wampum agreement.

Iris M. Balodis has received funding from the International Centre for

Responsible Gaming and the Gambling Research Exchange Ontario as well as consulting fees from Bausch. Over the past 3 years, Diego A. Pizzagalli has received consulting fees from Albright Stonebridge Group, Boehringer Ingelheim, Compass Pathways, Engrail Therapeutics, Neumora Therapeutics (formerly BlackThorn Therapeutics), Neurocrine Biosciences, Neuroscience Software, Otsuka, Sunovion, and Takeda; he has received honoraria from the Psychonomic Society and the American Psychological Association (for editorial work) and from Alkermes; he has received research funding from the Brain and Behavior Research Foundation, the Dana Foundation, Millennium Pharmaceuticals, National Institute of Mental Health, and Wellcome Leap; he has received stock options from Compass Pathways,

socioeconomic outcomes (Airagnes et al., 2019; Maggs et al., 2015; Schaefer et al., 2021; Silins et al., 2014; Suerken et al., 2016). This may be due, in part, to impairments in forming positive associations outside of cannabis use; in particular, with increased consumption, cannabis becomes overvalued at the expense of other rewards (Volkow et al., 2016). Therefore, substance use disorders are increasingly conceptualized in the context of altered reward learning (Lewis, 2018). Reward learning is a form of reinforcement learning in which behavior is modified after associating novel stimuli with a positive outcome (National Institute of Mental Health, 2009). Areas of the striatum play a central role in reward learning (O'Doherty et al., 2004), whereby phasic dopamine release facilitates forming an association between behavior and outcome (Schultz et al., 1997). With acute cannabis use, the primary psychoactive component,  $\Delta^9$ -tetrahydrocannabinol (THC), binds to cannabinoid Type 1 receptors (CB1Rs) to indirectly increase dopamine transmission in areas of the mesolimbic dopamine system (Pierce & Kumaresan, 2006). However, chronic use is often associated with hypodopaminergic transmission in these areas (Ginovart et al., 2012; Urban et al., 2012; Volkow et al., 2014), potentially leading to lower gratification from natural reward, and the subsequent pursuit of cannabis as a means to compensate for a diminished reward response (i.e., reward deficiency hypothesis; Blum et al., 2000). Nevertheless, to date, few longitudinal human studies directly examine dopamine release during reward learning and relationships with cannabis use, therefore, a mechanistic understanding of alterations with heavy use remains unclear.

Behavioural reward learning studies in humans evaluate how stimuli acquire rewarding properties and facilitate preference formation, with notable heterogeneity in findings in cannabis populations. While some studies find similar task performance between cannabis and control participants (Bloomfield et al., 2016; Costa Porfirio et al., 2020; Dougherty et al., 2013; Nestor et al., 2010), others show that cannabis use is related to significantly reduced reward learning (Casey & Cservenka, 2020; Moreno et al., 2012; Whitlow et al., 2004). Findings are limited by methodological variability, and inconsistency in cannabis use parameters (e.g., frequency, chronicity, potency, abstinence), which often vary widely or are not reported. Nevertheless, there is some evidence for greater impairment with chronic use (Delibas et al., 2017; Hermann et al., 2009), increased frequency (Bolla et al., 2005; Verdejo-Garcia et al., 2007), higher THC potency (Shannon et al., 2010), and dependence (Gonzalez et al., 2012). With careful consideration of a range of cannabis use characteristics, the present study aims to evaluate reward learning in a recreational cannabis use sample.

A validated behavioral paradigm was used to objectively evaluate reward learning in a community sample of individuals who use

Engrail Therapeutics, Neumora Therapeutics, and Neuroscience Software. Diego A. Pizzagalli has a financial interest in BlackThorn Therapeutics, which has licensed the copyright to the probabilistic reward task through Harvard University. Diego A. Pizzagalli's interests were reviewed and are managed by McLean Hospital and Partners HealthCare in accordance with their conflict of interest policies. No funding from these entities was used to support the current work, and all views expressed are solely those of the authors. All other authors have no conflicts of interest or relevant disclosures.

Olivia Turner played a lead role in data curation, formal analysis, visualization, writing-original draft, and writing-review and editing. Kiran Punia played a lead role in methodology and a supporting role in data curation and writing-review and editing. Diego A. Pizzagalli played a lead

cannabis recreationally (≥2 uses/month). The probabilistic reward task (PRT), based on original signal detection theory, evaluates the propensity to modulate behavior as a function of prior reinforcement (Pizzagalli et al., 2005). Using a modified version of the PRT, a previous study found that cannabis-dependent participants who frequently use high-potency cannabis, showed no reward learning compared to controls (results were lost when controlling for depression and cigarette use; Lawn et al., 2016). However, task performance has not been evaluated in a community sample characterized by a range of recreational cannabis use patterns. Based on the prior findings (Lawn et al., 2016), we hypothesized that compared to nonusing controls, participants in the cannabis group would show reduced capacity to learn nondrug related reward, as evidenced by an impaired ability to form a response bias in the PRT. Moreover, we reasoned that greater cannabis severity (e.g., increased frequency, chronicity, potency, and dependence) would be related to further reward learning impairment. While causality is difficult to establish through a cross-sectional evaluation, these findings would support the notion that deficits in forming novel associations outside of cannabis result in greater use, to supplement for a diminished reward response.

#### Method

#### **Participants**

A total of 106 individuals participated in the study. The population was separated into two groups, including individuals who use cannabis recreationally (n = 55) and control participants (n = 51), recruited from the Hamilton, Ontario community via flyers and online advertisements. Eligibility criteria were: (a) 19 years of age or older; (b) no current organic psychosis; (c) in the control group, no substance dependence, no cannabis use in the past month, and less than 150 days of total lifetime cannabis use; (d) in the cannabis group, participants were included if they used cannabis  $\geq 2$ times/month at the time of assessment. One participant in the control group was removed for meeting alcohol dependence criteria (n = 1). After applying quality control measures on the PRT (see PRT Calculations and Quality Control section below), the final sample reported was N = 72 (cannabis group, n = 38; control group, n = 34). A breathalyzer confirmed no alcohol use prior to the session (n = 64). Individuals in the cannabis group completed a urine toxicology screen on the day of assessment and tested positive for: THC (n = 31), amphetamine (n = 1), benzodiazepines (n = 3), oxycodone (n = 1); n = 4 showed a negative screen for all substances, but met inclusion criteria for self-reported cannabis use; n = 3 had missing

role in validation and a supporting role in data curation, formal analysis, resources, software, and writing–review and editing. James MacKillop played a supporting role in funding acquisition, investigation, methodology, project administration, resources, and writing–review and editing. Iris M. Balodis played a lead role in conceptualization, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing–original draft, and writing–review and editing.

Correspondence concerning this article should be addressed to Iris M. Balodis, Peter Boris Centre for Addictions Research, St. Joseph's Healthcare Hamilton, 100 West 5th Street, D113, Hamilton, ON L8N 3K7, Canada. Email: balodisi@mcmaster.ca

urine screens. Participants were assessed with the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998), to determine psychiatric and substance use diagnoses; n=17 in the cannabis group met criteria for substance dependence (American Psychiatric Association, 1994), with cannabis being the most frequently used substance. Participants met criteria for: generalized anxiety disorder (n=5 cannabis, n=1 control); current major depressive episode (n=4 cannabis, n=1 control). Participants provided informed consent and were reimbursed with gift cards for study completion. The study was approved by the Hamilton Integrated Research Ethics Board (HiREB No. 1600) and was conducted in accordance of the Declaration of Helsinki.

### Physiological Measures

**Breathalyzer.** Blood alcohol concentrations were evaluated through breath alcohol level using a handheld Alco-Sensor Breathalyzer (Intoximeters, Inc, St. Louis, MO, USA).

**Urine Screen.** Participants provided a urine sample on the day of assessment that was tested to qualitatively assess substances in the sample (Rapid Toxicology Cup® II, American Bio Medica Corporation, Kinderhook, NY, USA).

## Self-Report/Clinical Measures

Marijuana History Questionnaire. Evaluates use patterns including weekly quantity and relative THC content of typically-consumed cannabis.

Figure 1

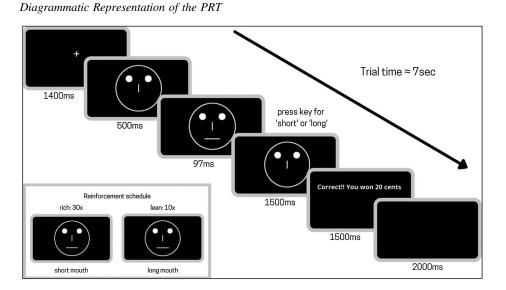
Marijuana Smoking History Questionnaire (Bonn-Miller and Zvolensky, 2009). Assesses frequency of cannabis use; age of initiation; years of use.

Cannabis Use Disorder Identification Test–Revised (CUDIT-R; Adamson et al., 2010). A brief eight-item validated measure used to identify problematic cannabis use.

Beck Depression Inventory–II, (BDI-II; Beck et al., 1961, 1996). A validated 21-item self-report scale that evaluates symptoms of depression.

## Reward Learning Behavioural Task

Probabilistic Reward Task (Pizzagalli et al., 2005). The task followed the protocol established by Pizzagalli et al. (2005). In brief, participants were presented simple cartoon faces with one of two different mouth lengths that were difficult to differentiate and were asked to quickly identify if they saw the short or long mouth (Figure 1). Participants could win money based on correct identification of the stimulus and were not informed that one of the stimuli ("rich" stimulus) was reinforced three times more frequently than the other ("lean" stimulus). An alternate version of the task presented different nose lengths on the cartoon faces; participants were randomized to the mouth/nose version, as well as the version in which the short or long mouth/nose was the more frequently rewarded stimulus. The task contained three blocks of 100 trials, each block lasted approximately 8 min. Participants were informed that only a portion of correct responses would receive reward feedback and were instructed to try their best on the task. Participants were compensated a set amount for study completion, but not specifically for task earnings.



*Note.* Each trial begins with a fixation cross on the screen, followed by a mouthless face. A face with a short or long mouth appears, then a mouthless face for 1,500 ms or until the participant responds with the appropriate "e" or "i" key to indicate which mouth was presented. Feedback is presented on 40 correct trials in each block ("Correct! You won 20 cents"), with 30 reward feedback for the "rich" stimulus and 10 reward feedback for the "lean" stimulus. A blank screen is shown following reward feedback, whereafter the next trial begins. Each trial lasts approximately 7 s; participants complete three blocks of 100 trials each for a total of 300 trials. PRT = probabilistic reward task.

## PRT Calculations and Quality Control

Trials where reaction time was <150 ms or >2,500 ms, and remaining trials with reaction time outside the range of  $\pm 3SD$  from the mean, were excluded. Participants with <80% valid trials, and a reward ratio of <2 in any block were removed (Pizzagalli et al., 2005; Diego A. Pizzagalli personal communication, June 2022) reward ratio outlines the proportion of rich to lean stimuli that are rewarded. After application of these criteria, n = 17 in the cannabis group and n = 16 in the control group were excluded. Individuals who did not meet quality control criteria did not differ from participants included in the final sample with respect to age, gender, or cannabis use characteristics, with the exception of a larger range of weekly quantity among participants included in the final sample (p < .05). The main task outcome is response bias, with other important outcomes including discriminability (which captures task difficulty), accuracy and reaction time. Response bias and discriminability (Hautus, 1995) are calculated as:

Response bias: 
$$\log b = \frac{1}{2} \log \frac{\text{rich}_{\text{correct}} \times \text{lean}_{\text{incorrect}}}{\text{rich}_{\text{incorrect}} \times \text{lean}_{\text{correct}}}$$
. (1)

Discriminability: 
$$\log d = \frac{1}{2} \log \frac{\operatorname{rich}_{\text{correct}} \times \operatorname{lean}_{\text{correct}}}{\operatorname{rich}_{\text{incorrect}} \times \operatorname{lean}_{\text{incorrect}}}$$
. (2)

Response bias evaluates the participants' systematic preference of the stimulus paired with reward more frequently; a high response bias score results from a high number of correct responses to the more frequently rewarded stimulus ("rich"), along with a high number of incorrect responses to the less frequently rewarded stimulus ("lean"), resulting in an increased numerator and decreased denominator in the formula above (Pizzagalli et al., 2005). Discriminability is impacted by the differences in the physical properties between the "rich" and "lean" stimuli, offering an index of task difficulty (Pizzagalli et al., 2005).

## Statistical Analyses

All analyses were carried out using International Business Machines Statistical Package for Social Sciences (International Business Machines SPSS Version 28). Data were assessed for normality, homoscedasticity, and outliers. When data violated the aforementioned assumptions, appropriate adjustments were used (e.g., Greenhouse–Geisser correction). T tests and chi-square tests were used to determine differences in demographic characteristics between groups. To evaluate PRT performance, a separate 2 Group (Cannabis, Control)  $\times$  3 Block (1, 2, 3) repeated measures analysis of variance (ANOVA) was conducted, with response bias and discriminability as dependent variables. An additional within-subjects factor of stimulus (rich, lean) was used for accuracy and reaction time. Change in response bias ( $\Delta$ RB; change between Blocks 3 and 1) was correlated with cannabis use characteristics and BDI-II scores, as previously applied in Lawn et al. (2016).

### Results

## **Demographics (Table 1)**

The groups did not differ in age, gender, education, or yearly household income, however, the cannabis group scored significantly higher on depression severity (BDI-II), t(67) = 3.44, p = .05, compared to controls.

 Table 1

 Demographics and Cannabis Use Characteristics

| Measures  | Cannabis $(n = 38)$ | Control $(n = 34)$ |
|---|---------------------|--------------------|
| Age (years)   | 42.2 ± 13.4         | 36.6 ± 14.9        |
| Gender (F/M/O)  | 24/14/0             | 23/10/1            |
| Education   |                     |                    |
| College, university or graduate school/high school/trade school | 24/12/2             | 28/5/1             |
| Yearly household income   |                     |                    |
| <\$15,000   | 18.4%               | 14.7%              |
| \$15–75,000   | 47.3%               | 44.1%              |
| \$75–120,000  | 23.7%               | 14.6%              |
| >\$120,000  | 5.3%                | 5.9%               |
| No response   | 2.6%                | 20.7%              |
| Ethnicity   |                     |                    |
| European/Native North American/Asian/<br>other                  | 24/2/3/9            | 25/2/3/4           |
| Cigarette use (daily)   | n = 13              | n = 2              |
| BDI-II score*   | $12.9 \pm 13.6$     | $4.4 \pm 5.4$      |
| Alcohol use   |                     |                    |
| Never   | 34.2%               | 29.4%              |
| Monthly or less   | 21.1%               | 38.2%              |
| 2–4 times monthly   | 13.2%               | 17.6%              |
| 2–3 times weekly  | 10.5%               | 8.8%               |
| ≥4 times weekly   | 10.5%               | 0%                 |
| Cannabis use frequency  |                     |                    |
| 2–3 times monthly   | 13.5%               |                    |
| 1–6 times weekly  | 24.3%               |                    |
| ≥once daily   | 62.2%               |                    |
| Potency (% THC)   |                     |                    |
| "I do not know"   | 37%                 |                    |
| 0–4   | 2.9%                |                    |
| 5–9   | 2.9%                |                    |
| 10–19   | 17.2%               |                    |
| 20–30   | 40%                 |                    |
| Age of cannabis use initiation                                  | $19.3 \pm 9.7$      |                    |
| Years of cannabis use   | $17.9 \pm 14.7$     |                    |
| Weekly quantity (g)   | $9.0 \pm 9.6$       |                    |
| CUDIT-R score   | $10.2 \pm 6.5$      |                    |

*Note.* F/M/O = female, male, other (self-identified gender); BDI-II = Beck Depression Inventory–II; THC =  $\Delta^9$ -tetrahydrocannabinol; CUDIT-R = Cannabis Use Disorder Identification Test–Revised. \* p < .05.

#### Probabilistic Reward Task (PRT)

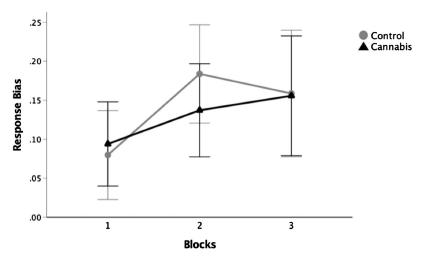
# Response Bias (Figure 2)

A 2 × 3 repeated measures ANOVA revealed a main effect of block, F(2, 140) = 4.63, p < .05,  $\eta^2 = 0.062$ , showing a significant increase in response bias over time; pairwise comparisons showed a significant increase from Block 1  $(0.09 \pm 0.02)$  to Block 2  $(0.16 \pm 0.02, p < .05)$ , from Block 1 to Block 3  $(0.16 \pm 0.03, p < .05)$ , but not between Block 2 and Block 3 (p > .05). There was no significant group difference, F(1,70) = 0.12, p > .05,  $\eta^2 = 0.002$ , or Group × Block interaction, F(2,140) = 0.66, p > .05,  $\eta^2 = 0.009$ , nor was there a significant group difference for  $\Delta$ RB, F(1,70) = 0.02, p > .05,  $\eta^2 = 0.001$ . Response bias findings using alternative PRT quality control criteria are presented in the Supplemental Material (including sensitivity analyses).

## Discriminability (Figure 3)

A 2 × 3 repeated measures ANOVA revealed a main effect of block, F(2, 140) = 3.30, p < .05,  $\eta^2 = 0.045$ , showing higher

Figure 2
Mean Response Bias in Cannabis and Control Groups Across Three Blocks on the PRT



*Note.* Both cannabis and control groups developed a response bias toward the more frequently rewarded (rich) stimulus. A significant increase between Block 1 and Block 2, and from Block 1 to Block 3 emerged. No significant group difference or interaction effects were found. Error bars represent standard errors. PRT = probabilistic reward task.

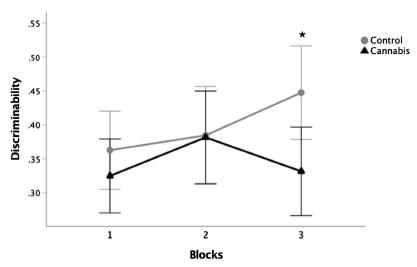
discriminability scores across blocks (Block 1:  $0.34 \pm 0.17$ , Block 2:  $0.38 \pm 0.21$ , Block 3:  $0.39 \pm 0.21$ ). Pairwise comparisons did not reveal any significant differences between blocks (all p > .05). There was no difference between groups overall, F(1, 70) = 1.70, p > .05,  $\eta^2 = 0.024$ . There was a significant Block × Group interaction effect, F(2, 140) = 4.49, p < .05,  $\eta^2 = 0.06$ , where the cannabis group had significantly lower discriminability scores

than the control group on Block 3 (0.33  $\pm$  0.18 vs. 0.45  $\pm$  0.22, p < .05).

# Accuracy (Figure 4A)

A  $2 \times 3$  repeated measures ANOVA with block and stimulus (rich, lean) as factors, revealed a main effect of stimulus,

Figure 3
Mean Discriminability in Cannabis and Control Groups Across Three Blocks on the PRT



*Note.* Discriminability scores increased across blocks, with no significant differences between blocks. Groups did not differ across blocks; however, an interaction effect showed that cannabis participants had significantly lower scores on Block 3 only. Error bars represent standard errors. PRT = probabilistic reward task.

<sup>\*</sup> Indicates a significant group difference in block 3.

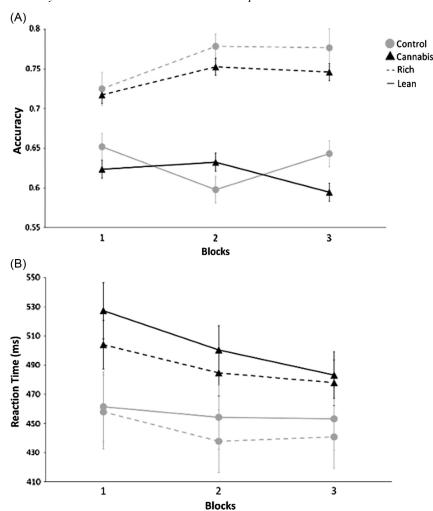


Figure 4
Accuracy and RT in Cannabis and Control Groups Across Three Blocks on the PRT

Note. Panel A: Both groups showed greater accuracy for the rich compared to the lean stimulus in each block. No group differences in accuracy emerged. A Block  $\times$  Stimulus interaction revealed greater accuracy for the rich stimulus in Blocks 2 and 3 compared to Block 1. Panel B: Both groups showed decreased RT across blocks, and faster RT for the rich compared to the lean stimulus in each block. No group differences in RT or interaction effects emerged. Error bars represent standard errors. RT = reaction time; PRT = probabilistic reward task.

F(1, 70) = 66.28, p < .05,  $\eta^2 = 0.486$ , with greater accuracy for the rich stimulus in all three blocks (rich,  $0.75 \pm 0.09$  vs. lean,  $0.62 \pm 0.11$ , p < .001), indicating the PRT elicited the intended effects. There was a significant Block × Group interaction, F(1.81, 126.65) = 3.45, p < .05,  $\eta^2 = 0.047$ ; pairwise comparisons did not reveal any significant results). There was a significant Block × Stimulus interaction, F(2, 140) = 4.43, p < .05,  $\eta^2 = 0.059$ , where rich accuracy in Block 2, and Block 3 were higher than Block 1 (both p < .05). No other effects or interactions were significant.

## Reaction Time (RT; Figure 4B)

A 2 × 3 repeated measures ANOVA revealed a main effect of block, F(1.55, 108.58) = 4.83, p < .05,  $\eta^2 = 0.065$ , showing

a decrease in RT over blocks. There was also a main effect of stimulus, F(1, 70) = 17.60, p < .05,  $\eta^2 = 0.201$ , with shorter RT for the rich stimulus compared to the lean stimulus in all three blocks (rich,  $468 \pm 109$  vs. lean,  $481 \pm 111$ , p < .05), consistent with intended behavioral effects. No other effects or interactions were significant.

#### **Control Analyses**

As in the prior studies (Pizzagalli et al., 2005) and due to the importance of the reinforcement ratio in producing a response bias, we ran control analyses to ensure that groups did not differ in the amount of feedback received during the task. *T* tests revealed that cannabis and control groups did not differ in the number of rewarded

trials received (cannabis rich:  $28.61 \pm 2.22$  vs. control rich:  $28.58 \pm 1.70$ , t(70) = 0.08, p > .05 cannabis lean:  $9.68 \pm .56$  vs. control lean:  $9.67 \pm .36$ , t(70) = 0.08, p > .05; rich/lean ratio: cannabis:  $2.96 \pm .18$  vs. control:  $2.98 \pm .21$ , t(70) = -0.19, p > .50). In addition, groups did not differ in the number of participants allocated (randomized) to the mouth or nose version of the task,  $\lambda^2(1) = 0.076$ , p > .05, nor did they differ in number of participants assigned (randomized) to the version in which the short or long mouth/nose was the more frequently rewarded stimulus,  $\lambda^2(1) = 1.79$ , p > .05.

#### **Correlations With Cannabis Use Characteristics**

A Pearson correlation found no significant relationship between  $\Delta RB$  and cannabis use characteristics: frequency, age of initiation, weekly quantity, or CUDIT-R scores (all p > .05). However, a trend for years of use, r(36) = -.30, p = .077 and potency, r(19) = -.33, p = .052 emerged. To explore differences in "high" THC (20%–30%, n = 14) versus "low" (0%–20%, n = 8), a point biserial correlation was conducted, and revealed a significant negative correlation,  $r_{pb}(19) = -.61$ , p = .003, between  $\Delta RB$  and potency (dichotomized).

The correlation between  $\Delta RB$  and BDI-II score was nonsignificant, r(33) = .28, p > .05. As in Pizzagalli et al. (2005), the cannabis group was dichotomized into "low" BDI (score <16) and "high" BDI-II (score  $\geq 16$ ), as this has been shown to be an accurate cutoff of depression severity (Sprinkle et al., 2002). The point biserial correlation between  $\Delta RB$  and low/high BDI-II was also nonsignificant,  $r_{pb}(33) = .20$ , p > .05.

### Discussion

The goal of the present study was to investigate reward learning capacity in a community sample of individuals who use cannabis recreationally. In order to capture a range of use patterns, we recruited participants who reported  $\geq 2$  uses/month, however, the majority (62.2%) of our sample reported (at least) daily use. The proportionally higher rates of daily or near daily use are in line with both Canadian (Health Canada, 2021) and U.S. trends (Substance Abuse and Mental Health Services Administration, 2020). Using an objective behavioral measure, we found that both cannabis and control participants demonstrated reward learning over the course of the experiment; specifically, both groups developed a response bias toward the more frequently rewarded stimulus. In contrast to our main hypothesis, the cannabis group did not show significant impairment relative to control participants, in the ability to modulate behavior as a function of prior reinforcement. However, the cannabis group did not exceed the control group in mean response bias on any block. Both groups showed higher accuracy and faster reaction time for the rich compared to the lean stimulus, confirming that the reinforcement schedule was effective in producing a general preference for the more frequently rewarded stimulus; this is consistent with prior PRT studies (Lawn et al., 2016; Liverant et al., 2014; Pechtel et al., 2013; Pizzagalli et al., 2008). Discriminability also did not differ between groups overall, indicating that cannabis and control participants found the task equally difficult. However, on the final block, the cannabis group displayed lower discriminability than controls, perhaps suggesting a state of fatigue by the end of the task, or differences in sustained attention. Finally, contrary to our secondary hypothesis, we did not find that response bias in

the cannabis group was correlated with parameters of cannabis use, with the exception of trending significant relationships with chronicity and potency.

The response bias findings emerging from the present study contrast with the only previous evaluation of a cannabis sample using the PRT (Lawn et al., 2016). In that study, the cannabis group had a significantly lower response bias compared to controls, and in fact, did not develop a response bias across blocks (Lawn et al., 2016). Notably, all participants in their sample met dependence criteria and reported consumption of high-potency cannabis (i.e., "skunk") on >50% of cannabis-using occasions, although the cannabinoid content that constituted "high-potency", was not defined. Moreover, the current sample varied widely in self-reported potency, and when this variable was explored by dichotomizing into "low" versus "high" (relative to the potency range of our sample), a significant relationship emerged with respect to  $\Delta RB$ : Higher reported THC was related to more impaired response bias. However, in Lawn et al. (2016), when BDI score and cigarette use (i.e., cigarettes per day) were included as covariates, the significant group difference in response bias was lost, suggesting a role for confounding psychiatric comorbidities and co-use of other substances in evaluating cannabis use and reward learning.

Other behavioral tasks that tap into elements of reward learning have mixed findings in showing reward learning deficits in cannabis use populations. However, those that demonstrate impaired learning, often find greater deficits in relation to greater chronicity (Delibaş et al., 2017; Hermann et al., 2009) frequency (Bolla et al., 2005; Verdejo-Garcia et al., 2007), higher THC potency (Shannon et al., 2010) and dependence (Gonzalez et al., 2012). Similarly, animal studies show that cannabis administration, particularly high THC doses, results in failure to develop reward associations in a conditioned place preference paradigm, or even led to place aversion (Han et al., 2017; Sañudo-Peña et al., 1997; Vann et al., 2008) and attenuates electrical self-stimulation (Anagnostou & Panagis, 2013; Wiebelhaus et al., 2015). Together, the evidence suggests a potential dose-dependent relationship, where greater reward learning impairment is associated with indications of more severe cannabis use. This is also supported by molecular imaging studies where cannabis-dependent participants show a reduction in amphetamine- and methylphenidate-induced striatal dopamine release, which was inversely related to frequency (Volkow et al., 2014) and dependence severity (van de Giessen et al., 2017). However, functional neuroimaging evidence is inconsistent. A chronic use sample showed reduced striatal activity during reward anticipation on the monetary incentive delay task (Knutson et al., 2000), and importantly, a longitudinal evaluation revealed that increasing cannabis use was associated with subsequent blunted striatal responses (Martz et al., 2016). In contrast, there is evidence for increased striatal activity during reward anticipation on the same task, which positively correlated with chronicity (Nestor et al., 2010), while others report no difference between cannabis and control participants (Enzi et al., 2015; Karoly et al., 2019), including a recent large scale study in 125 adolescents and adults who use cannabis (Skumlien et al., 2022). Future imaging studies are needed to assess the neural substrates, particularly in striatal networks, during reward learning.

Interestingly, we did not find a relationship between response bias and depressive symptoms (BDI-II score) in the cannabis group. This finding contrasts the previous literature showing significantly impaired response bias in populations with depressive (mainly anhedonic) symptoms (Liu et al., 2011; Pizzagalli et al., 2005) and clinical diagnoses of Major Depressive Disorder (Pizzagalli et al., 2008; Vrieze et al., 2013). The average BDI-II score for this group (12.9) suggests mild mood disturbance, not indicative of clinical depression, which may explain the lack of relationship between depression and reward learning in our sample. Moreover, given the heterogeneity in depressive symptomatology, symptoms experienced by those in our cannabis group may not reflect an anhedonic symptom profile.

Overall, the main findings from the present study suggest that individuals who use recreational cannabis are able to form reward associations outside of cannabis use. Therefore, the negative psychosocial and socioeconomic outcomes reported with frequent cannabis use, may be influenced to a greater degree, by impaired motivation to initiate goal-directed behavior (Pacheco-Colón et al., 2018; Skumlien et al., 2021), as opposed to the specific aspect of learning. Future studies should attempt to delineate the role of motivated reward seeking versus associative reward learning in cannabis use populations.

The use of an objective behavioral measure of reward learning is a strength of the present study, as most previous studies in cannabis populations have used tasks that indirectly evaluate facets of reward learning, with alternative primary outcomes (e.g., Iowa gambling task—decision making; monetary incentive delay task—reward anticipation). While the heterogeneity of a community sample allows for greater generalizability, it also results in a large range of cannabis use characteristics, limiting a clear understanding of the role of specific metrics. Moreover, we did not assess quantitative indices of cannabinoid metabolites, which would provide a more refined understanding of residual intoxication or withdrawal, and the effect of THC potency. The latter is particularly relevant considering reports of a steady increase in THC content in cannabis preparations over the past 20 years (ElSohly et al., 2016). A recent recommendation to standardize the quantification of cannabis use metrics across research and clinical settings, outlines a framework that includes the evaluation of cannabinoids in urine or saliva to determine THC potency and recency of use (Lorenzetti et al., 2021). Our high/low THC potency groupings, based on self-report, are considered exploratory, but nonetheless underscore the critical role of potency warranting additional investigation in future studies. Another limitation is that our sample consisted predominately of Caucasian individuals, limiting representation and applicability of the findings to other racial and ethnic groups. The majority of participants also identified with the female gender, although no gender differences emerged in our analyses. Although participants in the cannabis group primarily used cannabis over other substances, noncannabis substance use was not an exclusion criteria, thus leaving the potential for other substances to influence performance. In addition, given the exploratory nature of the correlation analyses, uncorrected p values were used; future studies using a larger sample size should correct for multiple comparisons. A limitation in the PRT literature is the inconsistent quality control criteria applied to the task. However, when applying a variety of criteria to our data set (see Supplemental Material), including criteria used in Lawn et al. (2016), no group differences in response bias emerged. Importantly, regardless of which set of criteria were applied, participant exclusion did not bias one group over the other (cannabis vs. controls).

Given the commonly reported link between cannabis use and an "amotivational syndrome", empirical evidence to characterize reward processing facets in this population is necessary. The present study adds to the limited extant literature on cannabis use and reward learning—a subconstruct of reward processing—and suggests that individuals who use cannabis recreationally, maintain the ability to learn nondrug reward associations. Nevertheless, the evidence indicates a potential role for greater cannabis use severity (i.e., chronicity, potency) and poorer reward learning, which warrants further investigation.

## References

- Adamson, S. J., Kay-Lambkin, F. J., Baker, A. L., Lewin, T. J., Thornton, L., Kelly, B. J., & Sellman, J. D. (2010). An improved brief measure of cannabis misuse: The Cannabis Use Disorders Identification Test-Revised (CUDIT-R). *Drug and Alcohol Dependence*, 110(1–2), 137–143. https://doi.org/10.1016/j.drugalcdep.2010.02.017
- Airagnes, G., Lemogne, C., Meneton, P., Plessz, M., Goldberg, M., Hoertel, N., Roquelaure, Y., Limosin, F., & Zins, M. (2019). Alcohol, tobacco and cannabis use are associated with job loss at follow-up: Findings from the CONSTANCES cohort. *PLOS ONE*, 14(9), Article e0222361. https://doi.org/10.1371/journal.pone.0222361
- American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders.
- Anagnostou, I., & Panagis, G. (2013). Cannabidiol inhibits the reward-facilitating effect of morphine: Involvement of 5-HT1A receptors in the dorsal raphe nucleus. *Addiction Biology*, 18, 286–296. https://doi.org/10.1111/j.1369-1600.2012.00483.x
- Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II*. Psychological Corporation.
- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961).
  An inventory for measuring depression. *Archives of General Psychiatry*,
  4(6), 561–571. https://doi.org/10.1001/archpsyc.1961.01710120031004
- Bloomfield, M. A. P., Mouchlianitis, E., Morgan, C. J. A., Freeman, T. P., Curran, H. V., Roiser, J. P., & Howes, O. D. (2016). Salience attribution and its relationship to cannabis-induced psychotic symptoms. *Psychological Medicine*, 46(16), 3383–3395. https://doi.org/10.1017/S0033291716002051
- Blum, K., Braverman, E. R., Holder, J. M., Lubar, J. F., Monastra, V. J., Miller, D., Lubar, J. O., Chen, T. J. H., & Comings, D. E. (2000). Reward deficiency syndrome: A biogenetic model for the diagnosis and treatment of impulsive, addictive, and compulsive behaviors. *Journal of Psychoactive Drugs*, 32(sup1), 1–112. https://doi.org/10.1080/02791072.2000.10736099
- Bolla, K. I., Eldreth, D. A., Matochik, J. A., & Cadet, J. L. (2005). Neural substrates of faulty decision-making in abstinent marijuana users. *NeuroImage*, 26(2), 480–492. https://doi.org/10.1016/j.neuroimage.2005 .02.012
- Bonn-Miller, M. O., & Zvolensky, M. J. (2009). An evaluation of the nature of marijuana use and its motives among young adult active users. *The American Journal on Addictions*, 18(5), 409–416. https://doi.org/10.3109/ 10550490903077705
- Casey, J. L., & Cservenka, A. (2020). Effects of frequent marijuana use on risky decision-making in young adult college students. *Addictive Behaviors Reports*, 11, Article 100253. https://doi.org/10.1016/j.abrep.2020.100253
- Costa Porfirio, J. C., Nogueira, R. M. T. B. L., & Corrêa Gomes, B. (2020).
  Executive function, decision-making and impulsivity in undergraduates moderated cannabis users. *Psychology & Neuroscience*, 13(4), 481–492. https://doi.org/10.1037/pne0000216
- Delibaş, D. H., Akseki, H. S., Erdoğan, E., Zorlu, N., & Gülseren, S. (2017). Impulsivity, sensation seeking, and decision-making in long-term abstinent cannabis dependent patients. *Arch Neuropsychiatr*, 55(4), 315–319. https://doi.org/10.5152/npa.2017.19304

- Dougherty, D. M., Mathias, C. W., Dawes, M. A., Furr, R. M., Charles, N. E., Liguori, A., Shannon, E. E., & Acheson, A. (2013). Impulsivity, attention, memory, and decision-making among adolescent marijuana users. *Psychopharmacology*, 226(2), 307–319. https://doi.org/10.1007/s00213-012-2908-5
- ElSohly, M. A., Mehmedic, Z., Foster, S., Gon, C., Chandra, S., & Church, J. C. (2016). Changes in cannabis potency over the last 2 Decades (1995–2014): Analysis of current data in the United States. *Biological Psychiatry*, 79(7), 613–619. https://doi.org/10.1016/j.biopsych.2016.01.004
- Enzi, B., Lissek, S., Edel, M.-A., Tegenthoff, M., Nicolas, V., Scherbaum, N., Juckel, G., & Roser, P. (2015). Alterations of monetary reward and punishment processing in chronic cannabis users: An FMRI study. PLOS ONE, 10(3), Article e0119150. https://doi.org/10.1371/journal.pone.0119150
- Fergusson, D. M., Boden, J. M., & Horwood, L. J. (2015). Psychosocial sequelae of cannabis use and implications for policy: Findings from the Christchurch Health and Development Study. Social Psychiatry and Psychiatric Epidemiology: The International Journal for Research in Social and Genetic Epidemiology and Mental Health Services, 50(9), 1317–1326. https://doi.org/10.1007/s00127-015-1070-x
- Ginovart, N., Tournier, B. B., Moulin-Sallanon, M., Steimer, T., Ibanez, V., & Millet, P. (2012). Chronic  $\Delta^9$ -tetrahydrocannabinol exposure induces a sensitization of dopamine  $D_2/_3$  receptors in the mesoaccumbens and nigrostriatal systems. *Neuropsychopharmacology*, *37*(11), 2355–2367. https://doi.org/10.1038/npp.2012.91
- Gobbi, G., Atkin, T., Zytynski, T., Wang, S., Askari, S., Boruff, J., Ware, M., Marmorstein, N., Cipriani, A., Dendukuri, N., & Mayo, N. (2019). Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: A systematic review and metaanalysis. *JAMA Psychiatry*, 76(4), 426–434. https://doi.org/10.1001/jamapsychiatry.2018.4500
- Gonzalez, R., Schuster, R. M., Mermelstein, R. J., Vassileva, J., Martin, E. M., & Diviak, K. R. (2012). Performance of young adult cannabis users on neurocognitive measures of impulsive behavior and their relationship to symptoms of cannabis use disorders. *Journal of Clinical and Experimental Neuropsychology*, 34(9), 962–976. https://doi.org/10.1080/13803395.2012.703642
- Han, X., He, Y., Bi, G.-H., Zhang, H.-Y., Song, R., Liu, Q.-R., Egan, J. M., Gardner, E. L., Li, J., & Xi, Z.-X. (2017). CB1 receptor activation on VgluT2-expressing glutamatergic neurons underlies  $\Delta^9$ -tetrahydrocannabinol ( $\Delta^9$ -THC)-induced aversive effects in mice. *Scientific Reports*, 7(1), Article 12315. https://doi.org/10.1038/s41598-017-12399-z
- Hautus, M. J. (1995). Corrections for extreme proportions and their biasing effects on estimated values of d'. Behavior Research Methods, Instruments & Computers, 27(1), 46–51. https://doi.org/10.3758/BF03203619
- Health Canada. 2021. Canadian alcohol and drugs survey (CADS): Summary of results for 2019 [WWW Document]. Retrieved July 18, 2022, from https://www.canada.ca/en/health-canada/services/canadian-alcohol-drugs-survey/2019-summary.html
- Hermann, D., Leménager, T., Gelbke, J., Welzel, H., Skopp, G., & Mann, K. (2009). Decision making of heavy cannabis users on the Iowa gambling task: Stronger association with THC of hair analysis than with personality traits of the Tridimensional Personality Questionnaire. European Addiction Research, 15(2), 94–98. https://doi.org/10.1159/000189788
- Karoly, H. C., Schacht, J. P., Meredith, L. R., Jacobus, J., Tapert, S. F., Gray, K. M., & Squeglia, L. M. (2019). Investigating a novel fMRI cannabis cue reactivity task in youth. *Addictive Behaviors*, 89, 20–28. https://doi.org/10.1016/j.addbeh.2018.09.015
- Knutson, B., Westdorp, A., Kaiser, E., & Hommer, D. (2000). FMRI visualization of brain activity during a monetary incentive delay task. NeuroImage, 12(1), 20–27. https://doi.org/10.1006/nimg.2000.0593
- Lawn, W., Freeman, T. P., Pope, R. A., Joye, A., Harvey, L., Hindocha, C., Mokrysz, C., Moss, A., Wall, M. B., Bloomfield, M. A., Das, R. K.,

- Morgan, C. J., Nutt, D. J., & Curran, H. V. (2016). Acute and chronic effects of cannabinoids on effort-related decision-making and reward learning: An evaluation of the cannabis 'amotivational' hypotheses. *Psychopharmacology*, 233(19–20), 3537–3552. https://doi.org/10.1007/s00213-016-4383-x
- Lewis, M. (2018). Brain change in addiction as learning, not disease. The New England Journal of Medicine, 379(16), 1551–1560. https://doi.org/ 10.1056/NEJMra1602872
- Liu, W. H., Chan, R. C. K., Wang, L. Z., Huang, J., Cheung, E. F. C., Gong, Q. Y., & Gollan, J. K. (2011). Deficits in sustaining reward responses in subsyndromal and syndromal major depression. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 35(4), 1045–1052. https://doi.org/10.1016/j.pnpbp.2011.02.018
- Liverant, G. I., Sloan, D. M., Pizzagalli, D. A., Harte, C. B., Kamholz, B. W., Rosebrock, L. E., Cohen, A. L., Fava, M., & Kaplan, G. B. (2014). Associations among smoking, anhedonia, and reward learning in depression. *Behavior Therapy*, 45(5), 651–663. https://doi.org/10.1016/j.beth.2014.02.004
- Lorenzetti, V., Hindocha, C., Petrilli, K., Griffiths, P., Brown, J., Castillo-Carniglia, Á., Caulkins, J. P., Englund, A., ElSohly, M. A., Gage, S. H., Groshkova, T., Gual, A., Hammond, D., Lawn, W., López-Pelayo, H., Manthey, J., Mokrysz, C., Pacula, R. L., Laar, M., ... Freeman, T. P. (2021). The International Cannabis Toolkit (iCannToolkit): A multidisciplinary expert consensus on minimum standards for measuring cannabis use. Addiction, 117, 1510–1517. https://doi.org/10.1111/add.15702
- Lynskey, M. T., Heath, A. C., Bucholz, K. K., Slutske, W. S., Madden, P. A. F., Nelson, E. C., Statham, D. J., & Martin, N. G. (2003). Escalation of drug use in early-onset cannabis users vs co-twin controls. *JAMA: Journal of the American Medical Association*, 289(4), 427–433. https://doi.org/10.1001/jama.289.4.427
- Maggs, J. L., Staff, J., Kloska, D. D., Patrick, M. E., O'Malley, P. M., & Schulenberg, J. (2015). Predicting young adult degree attainment by late adolescent marijuana use. *Journal of Adolescent Health*, 57(2), 205–211. https://doi.org/10.1016/j.jadohealth.2015.04.028
- Martz, M. E., Trucco, E. M., Cope, L. M., Hardee, J. E., Jester, J. M., Zucker, R. A., & Heitzeg, M. M. (2016). Association of marijuana use with blunted nucleus accumbens response to reward anticipation. *JAMA Psychiatry*, 73(8), 838–844. https://doi.org/10.1001/jamapsychiatry.2016.1161
- Moreno, M., Estevez, A. F., Zaldivar, F., Montes, J. M. G., Gutiérrez-Ferre, V. E., Esteban, L., Sánchez-Santed, F., & Flores, P. (2012). Impulsivity differences in recreational cannabis users and binge drinkers in a university population. *Drug and Alcohol Dependence*, 124(3), 355–362. https://doi.org/10.1016/j.drugalcdep.2012.02.011
- National Institute of Mental Health. 2009. RDoC constructs: Domain: Positive valence systems [WWW Document]. Retrieved July 12, 2022, from https://www.nimh.nih.gov/research/research-funded-by-nimh/rdoc/constructs
- Nestor, L., Hester, R., & Garavan, H. (2010). Increased ventral striatal BOLD activity during non-drug reward anticipation in cannabis users. *NeuroImage*, 49(1), 1133–1143. https://doi.org/10.1016/j.neuroimage .2009.07.022
- O'Doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., & Dolan, R. J. (2004). Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science*, 304(5669), 452–454. https://doi.org/10.1126/science .1094285
- Pacheco-Colón, I., Limia, J. M., & Gonzalez, R. (2018). Nonacute effects of cannabis use on motivation and reward sensitivity in humans: A systematic review. *Psychology of Addictive Behaviors*, 32(5), 497–507. https://doi.org/10.1037/adb0000380
- Pechtel, P., Dutra, S. J., Goetz, E. L., & Pizzagalli, D. A. (2013). Blunted reward responsiveness in remitted depression. *Journal of Psychiatric Research*, 47(12), 1864–1869. https://doi.org/10.1016/j.jpsychires.2013 .08.011
- Pierce, R. C., & Kumaresan, V. (2006). The mesolimbic dopamine system: The final common pathway for the reinforcing effect of drugs of abuse?

- Neuroscience and Biobehavioral Reviews, 30(2), 215–238. https://doi.org/10.1016/j.neubiorev.2005.04.016
- Pizzagalli, D. A., Iosifescu, D., Hallett, L. A., Ratner, K. G., & Fava, M. (2008). Reduced hedonic capacity in major depressive disorder: Evidence from a probabilistic reward task. *Journal of Psychiatric Research*, 43(1), 76–87. https://doi.org/10.1016/j.jpsychires.2008.03.001
- Pizzagalli, D. A., Jahn, A. L., & O'Shea, J. P. (2005). Toward an objective characterization of an anhedonic phenotype: A signal-detection approach. *Biological Psychiatry*, 57(4), 319–327. https://doi.org/10.1016/j.biopsych .2004.11.026
- Sañudo-Peña, M. C., Tsou, K., Delay, E. R., Hohman, A. G., Force, M., & Walker, J. M. (1997). Endogenous cannabinoids as an aversive or counter-rewarding system in the rat. *Neuroscience Letters*, 223(2), 125–128. https://doi.org/10.1016/S0304-3940(97)13424-3
- Schaefer, J. D., Hamdi, N. R., Malone, S. M., Vrieze, S., Wilson, S., McGue, M., & Iacono, W. G. (2021). Associations between adolescent cannabis use and young-adult functioning in three longitudinal twin studies. *PNAS Proceedings of the National Academy of Sciences of the United States of America*, 118(14), Article e2013180118. https://doi.org/10.1073/pnas.2013180118
- Schulenberg, J. E., Johnstone, L. D., O'Malley, P. M., Bachman, J. G., Miech, R. A., & Patrick, M. E. (2019). Monitoring the future national survey results on drug use, 1975–2018: Vol. II. College students and adults ages 19–60. Institute for Social Research, The University of Michigan.
- Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science*, 275(5306), 1593–1599. https://doi.org/ 10.1126/science.275.5306.1593
- Shannon, E. E., Mathias, C. W., Dougherty, D. M., & Liguori, A. (2010). Cognitive impairments in adolescent cannabis users are related to THC levels. *Addictive Disorders & Their Treatment*, 9(4), 158–163. https://doi.org/10.1097/ADT.0b013e3181c8c667
- Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. The Journal of Clinical Psychiatry, 59(Suppl 20), 22–33.
- Silins, E., Horwood, L. J., Patton, G. C., Fergusson, D. M., Olsson, C. A., Hutchinson, D. M., Spry, E., Toumbourou, J. W., Degenhardt, L., Swift, W., Coffey, C., Tait, R. J., Letcher, P., Copeland, J., Mattick, R. P., & the Cannabis Cohorts Research Consortium. (2014). Young adult sequelae of adolescent cannabis use: An integrative analysis. *The Lancet Psychiatry*, 1(4), 286–293. https://doi.org/10.1016/S2215-0366(14)70307-4
- Skumlien, M., Langley, C., Lawn, W., Voon, V., Curran, H. V., Roiser, J. P., & Sahakian, B. J. (2021). The acute and non-acute effects of cannabis on reward processing: A systematic review. *Neuroscience and Biobehavioral Reviews*, 130, 512–528. https://doi.org/10.1016/j.neubiorev.2021.09.008
- Skumlien, M., Mokrysz, C., Freeman, T. P., Wall, M. B., Bloomfield, M., Lees, R., Borissova, A., Petrilli, K., Carson, J., Coughlan, T., Ofori, S., Langley, C., Sahakian, B. J., Curran, H. V., & Lawn, W. (2022). Neural responses to reward anticipation and feedback in adult and adolescent cannabis users and controls. *Neuropsychopharmacology*, 47(11), 1976–1983. https://doi.org/10.1038/s41386-022-01316-2
- Spackman, E., Haines-Saah, R., Danthurebandara, V. M., Dowsett, L. E., Noseworthy, T., & Clement, F. M. (2017). Marijuana use and perceptions of risk and harm: A survey among Canadians in 2016. *Healthcare Policy*, 13(1), 17–27. https://doi.org/10.12927/hcpol.2017.25194
- Sprinkle, S. D., Lurie, D., Insko, S. L., Atkinson, G., Jones, G. L., Logan, A. R., & Bissada, N. N. (2002). Criterion validity, severity cut scores, and test–retest reliability of the Beck Depression Inventory-II in a university counseling center sample. *Journal of Counseling Psychology*, 49(3), 381–385. https://doi.org/10.1037/0022-0167.49.3.381

- Substance Abuse and Mental Health Services Administration. (2020). Key substance use and mental health indicators in the United States: Results from the 2019 national survey on drug use and health (No. PEP20-07-01-001, NSDUH Series H-55). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.
- Suerken, C. K., Reboussin, B. A., Egan, K. L., Sutfin, E. L., Wagoner, K. G., Spangler, J., & Wolfson, M. (2016). Marijuana use trajectories and academic outcomes among college students. *Drug and Alcohol Dependence*, 162, 137–145. https://doi.org/10.1016/j.drugalcdep.2016.02.041
- United Nations Office on Drugs and Crime. (2022). World drug report 2022 (No. Sales No. 22.XI. 8). UN, Office on Drugs and Crime.
- Urban, N. B. L., Slifstein, M., Thompson, J. L., Xu, X., Girgis, R. R., Raheja, S., Haney, M., & Abi-Dargham, A. (2012). Dopamine release in chronic cannabis users: A [11c]raclopride positron emission tomography study. *Biological Psychiatry*, 71(8), 677–683. https://doi.org/10.1016/j.biopsych.2011.12.018
- van de Giessen, E., Weinstein, J. J., Cassidy, C. M., Haney, M., Dong, Z., Ghazzaoui, R., Ojeil, N., Kegeles, L. S., Xu, X., Vadhan, N. P., Volkow, N. D., Slifstein, M., & Abi-Dargham, A. (2017). Deficits in striatal dopamine release in cannabis dependence. *Molecular Psychiatry*, 22(1), 68–75. https://doi.org/10.1038/mp.2016.21
- Vann, R. E., Gamage, T. F., Warner, J. A., Marshall, E. M., Taylor, N. L., Martin, B. R., & Wiley, J. L. (2008). Divergent effects of cannabidiol on the discriminative stimulus and place conditioning effects of Δ<sup>9</sup>tetrahydrocannabinol. *Drug and Alcohol Dependence*, 94(1–3), 191–198. https://doi.org/10.1016/j.drugalcdep.2007.11.017
- Verdejo-Garcia, A., Benbrook, A., Funderburk, F., David, P., Cadet, J.-L., & Bolla, K. I. (2007). The differential relationship between cocaine use and marijuana use on decision-making performance over repeat testing with the Iowa gambling task. *Drug and Alcohol Dependence*, 90(1), 2–11. https://doi.org/10.1016/j.drugalcdep.2007.02.004
- Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *The New England Journal of Medicine*, 374(4), 363–371. https://doi.org/10.1056/NEJMra 1511480
- Volkow, N. D., Wang, G.-J., Telang, F., Fowler, J. S., Alexoff, D., Logan, J., Jayne, M., Wong, C., & Tomasi, D. (2014). Decreased dopamine brain reactivity in marijuana abusers is associated with negative emotionality and addiction severity. PNAS Proceedings of the National Academy of Sciences of the United States of America, 111(30), E3149–E3156. https://doi.org/10.1073/pnas.1411228111
- Vrieze, E., Pizzagalli, D. A., Demyttenaere, K., Hompes, T., Sienaert, P., de Boer, P., Schmidt, M., & Claes, S. (2013). Reduced reward learning predicts outcome in major depressive disorder. *Biological Psychiatry*, 73(7), 639–645. https://doi.org/10.1016/j.biopsych.2012.10.014
- Whitlow, C. T., Liguori, A., Livengood, L. B., Hart, S. L., Mussat-Whitlow, B. J., Lamborn, C. M., Laurienti, P. J., & Porrino, L. J. (2004). Long-term heavy marijuana users make costly decisions on a gambling task. *Drug* and Alcohol Dependence, 76(1), 107–111. https://doi.org/10.1016/j.druga lcdep.2004.04.009
- Wiebelhaus, J. M., Grim, T. W., Owens, R. A., Lazenka, M. F., Sim-Selley, L. J., Abdullah, R. A., Niphakis, M. J., Vann, R. E., Cravatt, B. F., Wiley, J. L., Negus, S. S., & Lichtman, A. H. (2015). Δ<sup>9</sup>-tetrahydrocannabinol and endocannabinoid degradative enzyme inhibitors attenuate intracranial self-stimulation in mice. *The Journal of Pharmacology and Experimental Therapeutics*, 352(2), 195–207. https://doi.org/10.1124/jpet.114.218677

Received April 10, 2023
Revision received October 29, 2023
Accepted November 5, 2023