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Do trauma cue exposure and/or PTSD symptom severity intensify selective approach bias toward cannabis cues in regular cannabis users with trauma histories?

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ABSTRACT

Trauma cue-elicited activation of automatic cannabis-related cognitive biases are theorized to contribute to comorbid posttraumatic stress disorder and cannabis use disorder. This phenomenon can be studied experimentally by combining the trauma cue reactivity paradigm (CRP) with cannabis-related cognitive processing tasks. In this study, we used a computerized cannabis approach-avoidance task (AAT) to assess automatic cannabis (vs. neutral) approach bias following personalized trauma (vs. neutral) CRP exposure. We hypothesized that selective cannabis (vs. neutral) approach biases on the AAT would be larger among participants with higher PTSD symptom severity, particularly following trauma (vs. neutral) cue exposure. We used a within-subjects experimental design with a continuous between-subjects moderator (PTSD symptom severity). Participants were exposed to both a trauma and neutral CRP in random order, completing a cannabis AAT (cannabis vs. neutral stimuli) following each cue exposure. Current cannabis users with histories of psychological trauma ($n = 50$; 34% male; mean age = 37.8 years) described their most traumatic lifetime event, and a similarly-detailed neutral event, according to an established interview protocol that served as the CRP. As hypothesized, an AAT stimulus type x PTSD symptom severity interaction emerged ($p = .042$) with approach bias greater to cannabis than neutral stimuli for participants with higher ($p = .006$), but not lower ($p = .36$), PTSD symptom severity. Contrasting expectations, the stimulus type x PTSD symptoms effect was not intensified by trauma cue exposure ($p = .19$). Selective cannabis approach bias may be chronically activated in cannabis users with higher PTSD symptom severity and may serve as an automatic cognitive mechanism to help explain PTSD-CUD co-morbidity.

1. Introduction

Posttraumatic stress disorder (PTSD) is characterized by intrusive memories, physiological reactivity to and avoidance of trauma reminders, and negative mood following trauma exposure (American Psychological American Psychiatric Association, 2013). Of

trauma-exposed individuals, 5.9–19.5% will meet diagnostic criteria for PTSD (Atwoli et al., 2015) while others may experience subthreshold PTSD symptoms; though not meeting criteria for a full PTSD diagnosis, subthreshold PTSD symptoms may nonetheless be distressing. Cannabis is commonly prescribed or self-administered to help with PTSD symptom management, with some experts suggesting cannabis as beneficial

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(Walsh et al., 2017). Emerging research provides preliminary support for this (Jetly et al., 2015); however, a recent review suggests the evidence-base supporting using cannabinoids for treating PTSD is currently slim and of low quality (McKee et al., 2021).

Emerging research suggests that cannabis use may be particularly risky for persons with PTSD. For example, cannabis use has been associated with worse PTSD outcomes longitudinally (Wilkinson et al., 2015) and a relationship has also been documented between medicinal cannabis use and cannabis dependence (Yarnell, 2015). High comorbidity rates have been reported between PTSD and cannabis use disorder (CUD; Walsh et al., 2014), leading some to caution against cannabis for PTSD treatment (APA, 2013). Cannabis as a medicant for PTSD remains controversial; nevertheless, experts agree that more research is needed to test potential mechanisms underlying PTSD-CUD co-occurrence.

One set of mechanisms potentially contributing to PTSD-CUD comorbidity involves cannabis-related cognitive processes thought to arise though classical and operant conditioning. Individuals with PTSD who uses cannabis to cope with adverse reactions to trauma reminders form strong memory associations between the trauma cue, cannabis use, and desired relief outcomes (Romero-Sanchiz et al., 2022). On subsequent exposure to trauma cues (e.g., intrusive thoughts or nightmares about the trauma, external trauma reminders), memory associations with substance use and relief are activated, giving rise to trauma cue-elicited cannabis craving, which in turn promotes cannabis use (Romero-Sanchiz et al., 2022). This use of cannabis provides subjective relief from PTSD symptoms, thereby negatively reinforcing future cannabis use (Hawn et al., 2020) and strengthening memory associations. Consistent with this theory, among cannabis users with a history of trauma, exposure to personalized trauma cues led to greater self-reported cannabis craving than did exposure to personalized cannabis cues, particularly among those with higher PTSD symptom severity (Romero-Sanchiz et al., 2022).

Trauma cue-elicited cannabis craving represents only one motivational process arising through learning that might contribute to PTSD-CUD comorbidity. Specifically, automatic cognitive processes are thought to drive a phenomenon reported by many individuals with addictions that they sometimes find themselves engaged in their addictive behaviour without having made a conscious decision to do so and without having experienced a conscious craving to use (Wiers et al., 2016). Exposure to trauma cues in a cannabis user with PTSD could automatically activate strong memory associations between cannabis use and approach behaviour (Wiers et al., 2016). Cannabis approach bias is an automatically activated action tendency to approach cannabis, making cannabis use much more likely following cannabis cue exposure (Cousijn et al., 2011; Walsh et al., 2017). Approach biases can be studied in the lab with the approach-avoidance task (AAT; Cousijn et al., 2011), a computerized reaction time (RT) task that uses substance-related (vs. neutral) visual stimuli to measure individual biases to approach or avoid the substance of interest. Approach bias towards cannabis stimuli appears stronger in heavier cannabis users than current non-users with limited cannabis use history and predicts escalations in cannabis use over time (Cousijn et al., 2011). Heavy cannabis users with deficient control over cannabis action tendencies are also more likely to show increases in cannabis-related problems over time (Cousijn et al., 2012).

The effects of trauma cue exposure on various substance-related cognitive biases can be experimentally examined using the cue-reactivity paradigm (CRP). CRPs involve exposing participants to validated audio and/or visual cues, often personalized to the individual's lived experience, pertaining to both a psychologically traumatic event (e.g., a past car accident) and a similarly detailed neutral control event (e.g., brushing one's teeth; DeGrace et al., 2022). This lab-based cue exposure serves as an experimental analogue for the real-world scenario of being faced with a trauma reminder. CRPs allow for examination of whether exposure to trauma (vs. neutral) cues elicit greater 'reactivity' on addiction-relevant outcomes, including substance-related cognitive biases (e.g., attentional bias towards alcohol cues on a computerized Stroop task; Read et al., 2017).

Recent evidence from a sample of individuals with trauma histories who regularly use cannabis suggests a structured interview protocol (Sinha & Tuit, 2012) focused on an individual's worst lifetime trauma can serve as a valid lab-based CRP (DeGrace et al., 2023). The interview-based CRP elicited greater self-reported cannabis craving and, among those with greater PTSD symptoms, greater negative affect, than the interview-based neutral CRP (DeGrace et al., 2023); however, it remains to be determined whether trauma cue exposure via the interview-based trauma CRP would have similar effects in activating automatic cannabis-related cognitive biases, particularly among participants with greater PTSD symptoms. The present study used the interview-based CRP (DeGrace et al., 2023; Sinha & Tuit, 2012) to examine the impact of personalized trauma versus neutral cue exposure on participants' degree of automatic approach bias towards cannabis stimuli on the cannabis AAT (Cousijn et al., 2011), in the same sample used in our CRP validation study (DeGrace et al., 2023). We also assessed participants' PTSD symptom severity (Blevins et al., 2015) to examine trauma cue-elicited activation of the cannabis approach bias among those with higher vs. lower PTSD symptom severity. We hypothesized: [H1] a greater approach bias towards cannabis than neutral stimuli on the AAT in those with higher versus lower PTSD symptom severity; and [H2] that the stimulus type effect on approach bias (cannabis > neutral) in those with higher PTSD symptom severity would be stronger in the trauma versus neutral cue condition.

2. Method[1]

2.1. Participants

Participants ($n = 50$; 34%M; M age = 37.8 years, $SD = 10.02$) were recruited via social media platforms, Veterans' associations, local mental health clinical services, and community posters (e.g., supermarkets) to take part in an in-person study examining associations between trauma exposure and cannabis use. Eligible respondents had to meet the following inclusion/exclusion criteria: aged 19–65 years; no diagnosis of serious mental illness (i.e., bipolar, schizophrenia, or other psychotic disorder); at least one lifetime exposure to a potentially traumatic event on the Life Events Checklist (LEC-5; Gray et al., 2004); and current regular cannabis use (Gabrys & Porath, 2019; ≥1 g/week in the last month on the Cannabis Timeline Followback (Sobell & Sobell, 1992).

2.2. Measures

Trauma Exposure. The Life Events Checklist (LEC-5; Gray et al., 2004) is a 17-item self-report measure used to assess criterion A of PTSD (APA, 2013). In the present study, the LEC-5 was used to assess participant exposures to qualifying potentially psychologically traumatic events. Participants who indicated exposure to multiple potentially psychologically traumatic events during their lifetimes were instructed to focus on the most distressing event for the PTSD measures and the trauma CRP described below.

Post Traumatic Stress Disorder. The 20-item self-report PTSD Checklist for DSM-5 (PCL-5) was used as a psychometrically-sound continuous measure of DSM-5 (APA, 2013) PTSD symptom severity (Blevins et al., 2015; Bovin et al., 2016). Each item is rated on a 0–4 severity scale and item scores are summed for a total score and four subscales corresponding to each PTSD symptom cluster. PCL-5 scores for our sample showed good internal consistency for the total score ($\alpha = 0.88$) and acceptable-to-good internal consistency for the four subscales ($\alpha \geq 0.6$ for clusters B [re-experiencing], C [avoidance], and E [hyperarousal]; α

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[1] All methods and measures described were approved by the Nova Scotia Health Research Ethics Board (ref #: 1026315).

> 0.8 for cluster D [negative cognitions][2]. The sample was further characterized by quantifying what proportion met DSM-5 (APA, 2013) criteria for past-month PTSD based on the 20-item Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) interview (Weathers et al., 2018).

Cannabis Use and CUD. The sample was also characterized by quantifying what proportion met DSM-5 criteria for past-year CUD based on the 11-item Structured Clinical Interview for DSM-5 Research Version (SCID-5-RV; First, 2015; Osório et al., 2019) SUD module. The Cannabis Timeline Follow Back (C-TLFB; Norberg et al., 2012; Robinson et al., 2014) was used to assess the frequency (number of use days) and dose (in grams) of cannabis used in the past 30 days. Participants were guided by an interviewer to estimate on a calendar how many days in the past month they had used cannabis and how much cannabis (in grams) was used each of those days. The C-TLFB responses were used to verify eligibility ($\geq$1 g/week in the last month).

Anxiety. The Generalized Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006) is a seven-item measure of anxiety disorder symptoms with good reliability and validity (Spitzer et al., 2006). Participants were asked to rate how often they have experienced each anxiety symptom over the past two weeks on a scale from 0 (not at all) to 3 (nearly every day). Scores were summed (possible range: 0–21), with higher scores indicating greater endorsement of anxiety symptoms. The GAD-7 has excellent internal consistency, good test re-test reliability, and procedural validity (Spitzer et al., 2006). This measure was used as a covariate to establish specificity of findings to PTSD symptoms in sensitivity analyses.

Depression. The Beck Depression Inventory (BDI-II; Beck et al., 1996) is a 21-item measure of endorsement of depressive symptoms. Specifically, participants indicated on a 0 (e.g., I do not feel sad) to 3 (e.g., I am so sad that I can't stand it) scale their intensity of each depressive symptom over the past two weeks. Scores were summed (possible range: 0–63), with higher scores indicating greater endorsement of depressive symptoms. The BDI-II has good reliability and discriminant validity (Wang & Gorenstein, 2013). This measure was used as a covariate to establish specificity of findings to PTSD symptoms in sensitivity analyses.

Approach Avoidance Task. The cannabis AAT was adapted from an existing validated alcohol AAT (Wiers et al., 2009) available through Inquisit (Inquisit 5, 2016), a psychological task software. Our within-subjects design used two versions of the AATs with distinct stimuli developed to reduce practice effects across cue conditions. Each AAT included a total of 80 stimuli: 20 cannabis-related (e.g., *bong*) and 20 neutral (e.g., *pencil*), as well as 20 positive (e.g., *diver*) and 20 negative (e.g., *snake*). Positive and negative stimuli were used as fillers (Wiers et al., 2009). Cannabis and neutral stimuli were drawn from an existing, validated stimulus set, with both types of stimuli visually matched for physical attributes (Macatee et al., 2021). Participants were shown 40 cannabis-related stimuli and 40 neutral stimuli across the two AAT versions. Each stimulus appeared in one of two orientations (i.e., portrait or landscape). Participants were instructed to either "pull" the stimulus towards them (by pulling the mouse towards themselves) or to "push" the stimulus away from them (by pushing the mouse away from themselves) as quickly as possible based on the orientation of the stimulus. A pull response resulted in the picture becoming bigger on the screen to give the appearance of movement towards the participant; a push response resulted in the picture becoming smaller on the screen to give the appearance of movement away from the participant. Assignment of push and pull responses to each picture orientation (portrait or landscape) was randomized. Reaction times for each push and pull response were computer recorded (in milliseconds) as were errors in orientation identification. A cannabis approach bias is said to occur when the pull response is completed significantly more quickly than the push response, only for the cannabis stimuli (Cousijn et al., 2011). Stimuli were presented in a pseudo-random order with no more than three of the same orientation or stimulus type in a row (Wiers et al., 2009).

2.3. Procedure

Telephone Screening. In a telephone-administered screening, participants answered questions about their demographics, cannabis use, and history of trauma exposure (LEC-5) to ensure eligibility. If eligible, they then completed the PCL-5 and were booked for an in-person lab session. They were sent a virtual consent form to complete prior to the lab session.

Lab Session. To avoid potential confounding effects on our experimental manipulation, participants were required to remain abstinent from cannabis, nicotine (smoked or vaped), alcohol, and illicit drugs for 12 h, and from caffeine for 2 h, prior to testing. Abstinence from substances (except cannabis) was verified using a urine test and breathalyzer; abstinence from cannabis was verified verbally as short term (<30 days) abstinence cannot be verified biochemically. Participants first completed the C-TLFB and then were assessed for past-month PTSD and CUD using the CAPS and SCID, respectively. Participants were then asked to describe the most psychologically traumatic event in their lifetime and an emotionally neutral event (e.g., a morning routine); participants were asked to share sensory details of the event such as associated sights, smells, and sounds. These semi-structured interviews were administered in randomized order, audio-recorded, personalized to each participant following an established protocol (Sinha & Tuit, 2012), and validated for use as CRPs (DeGrace et al., 2023. Following both the trauma and neutral interview (hereafter referred to as 'cue'), participants completed a different version of the computerized cannabis AAT.

2.4. Data preparation and analysis

Power Analysis. We calculated the number of participants needed for our study design using published guidelines (Judd et al., 2017). We specified a CNC design indicating: participants crossed within condition; targets nested within condition; and two random factors (i.e., target and participants) crossed within condition. With power set at 0.90 and 80 total targets (i.e., cannabis and neutral stimuli), we determined that we would need $n = 50$ participants to detect a medium effect. We reasoned that a medium effect size could be clinically meaningful (i.e., have potential clinical practice implications).

AAT scoring. AAT scores were corrected for outliers by removing all reaction times $\pm$3 standard deviations from the participants' mean reaction time, as well as any scores less than 200ms or more than 2000ms to account for inattention or anticipatory response errors (Cousijn et al., 2011). Error trials (i.e., incorrectly identified orientation) were also removed, and error rates were calculated. If a participant's error rate exceeded 60% on either of the two versions of the AAT, data for that AAT version was treated as missing (Cousijn et al., 2014). One participant had >60% errors on both versions of the AAT and another two had >60% errors on only one version of the AAT (i.e., in only one cue condition[3]). Next, each participant had eight median AAT reaction time scores calculated in the context of each cue type (neutral vs. trauma), stimulus type (neutral vs. cannabis), and response type (pull vs. push). As with prior AAT research (Cousijn et al., 2011), approach bias scores were calculated by subtracting participants' median approach (i.e., pull) from their median avoidance (i.e., push) reaction times, with more positive scores indicating stronger approach bias to the given stimuli (i.

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e., quicker approach [pull] than avoidance [push] responses; Cousijn et al., 2011). A Monte Carlo split-half reliability estimate for the AAT was calculated using an established protocol (Pronk et al., 2022) wherein we calculated an RT difference score (push-pull) for each stimulus and stratified on study design characteristics (AAT stimulus type x cue condition). We obtained evidence of acceptable reliability (Spearman Brown coefficient = 0.83).

3. Results

Sample characteristics. The mean PCL-5 score for the sample was 38.5 (*SD* = 13.4; range = 6–68), which was lower than that of a Canadian psychiatric outpatient sample with diagnosed PTSD (i.e., *M* = 56.6, *SD* = 19.5; Boyd et al., 2022), higher than a trauma-exposed Canadian psychiatric outpatient sample without PTSD (i.e., *M* = 33.56, *SD* = 13.7; Boyd et al., 2022), and above the cut-off for probable PTSD (i.e., ≥33; Bovin et al., 2016). More than half of our sample (62%) scored at or above this PCL-5 clinical cut-off. Approximately half of our sample (58%) met criteria for past-month PTSD based on the CAPS-5 interview (Weathers et al., 2018). The mean scores on the GAD-7 (Spitzer et al., 2006) and BDI-II (Beck et al., 1996) indicated that the average participant was experiencing both anxiety and depressive symptoms of moderate severity. Many (70%) met criteria for past-year CUD on the SCID (First et al., 2015) with mild (2–3 symptoms; 24%), moderate (4–5 symptoms; 12%), or severe CUD (6+ symptoms; 34%; APA, 2013). Demographic and clinical characteristics of the sample are provided in Supplemental Table 1.

Linear mixed models (R v. 4.2.1; package lme4) were used to examine the main and interactive effects of cue type (fixed effect; neutral vs. trauma), AAT stimulus type (fixed effect; neutral vs. cannabis), and continuous PTSD symptom severity on approach bias scores, allowing us to examine both hypotheses in a single analysis. Participants were inputted as a random effect and a restricted maximum likelihood model was used. The omnibus model (see Table 1) evidenced a statistically significant two-way interaction between AAT stimulus type (cannabis vs. neutral) and PTSD symptoms (*t*[137] = 2.05, *p* = .042, *b* = 2.20, 95% CI [0.12–4.28]; see Fig. 1). We probed this two-way interaction by examining the simple main effects of AAT stimulus type at high (+1SD) and low (-1SD) PTSD symptom severity levels, collapsed across cue type (see Fig. 1). Consistent with H1: a statistically significant simple main effect of stimulus type was observed at high PTSD symptom severity (*t*[137] = -2.81, *b* = −45.2, *p* = .006) with greater approach bias towards cannabis than neutral stimuli; and no statistically

Table 1
Linear mixed model omnibus test results predicting approach bias on the Cannabis Approach Avoidance Task (AAT).

Predictors	Estimate (b)	Std. Error	95% CI	t	p
Cue (Trauma = 1; Neutral = 0)	−10.14	84.26	−173.26 – 152.97	1.17	.904
PTSD Symptoms	−0.61	0.86	−2.31 – 1.09	−0.71	.482
Stimuli (Cannabis = 1; Neutral = 0)	−98.85	64.84	−224.36 – 26.66	−1.52	.130
Cue*PTSD Symptoms	0.34	1.39	−2.36 – 3.04	0.245	.806
Cue*Stimuli	128.36	100.59	−66.36 – 323.09	1.28	.204
PTSD Symptoms*Stimuli	2.20	2.20	0.12–4.28	2.05	.042*
Cue*Stimuli*PTSD Symptoms	−2.18	1.67	−5.42 – 1.05	−1.31	.193

Notes: *p < .05. **p < .01. ***p < .001. Cue and Stimuli were inputted as fixed effects. PTSD Symptoms assessed continuously with the PTSD Checklist (PCL-5; Blevins et al., 2018). Approach bias scores calculated as median push minus median pull reaction time (in msec); higher scores indicate greater approach bias (Cousijn et al., 2014).
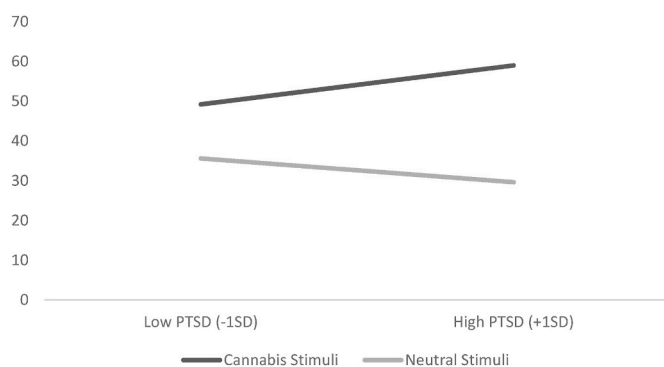

Fig. 1. Two-way interaction between Approach-Avoidance Task (AAT) stimulus type (cannabis vs. neutral) and PTSD symptom severity (continuous PCL-5 scores; Blevins et al., 2015) on AAT approach bias scores (in msec) collapsed across trauma vs. neutral cue condition. Note: Approach bias scores calculated as median push minus median pull reaction time (in msec); higher scores indicate greater approach bias (Cousijn et al., 2014).

significant simple main effect of stimulus type was observed at low PTSD symptom severity (*t*[137] = -0.94, *b* = −15.4, *p* = .36; see Fig. 1). Contrary to H2, the three-way interaction between AAT stimulus type, PTSD symptoms, and cue type was not statistically significant (see Table 1).

Significance of the two-way interaction between AAT stimulus type and PTSD symptoms persisted when order of cue presentation (trauma or neutral first), frequency and quantity of past month cannabis use (on the Sobell & Sobell, 1992Sobell & Sobell, 1992), and past year CUD symptom count on the SCID (First et al., 2018), were controlled for in a single model (*t*[137] = 2.02, p = .045, *b* = 2.20, 95% CI [0.10–4.09]. This interaction also persisted when all three participants with AAT error rates greater than 60% overall were removed entirely (*t*[135] = 2.48, p = .014, *b* = 2.58, 95% CI [0.57–4.60].[4] This interaction further persisted when controlling for depression, measured using the BDI-II (Beck et al., 1996; *t*[137] = 2.04, p = .043, *b* = 2.20, 95% CI [0.12–4.28]) but became marginally significant when controlling for anxiety, measured using the GAD-7 (Spitzer et al., 2006; *t*[137] = 1.85, p = .065, b = 2.29, 95% CI [−0.09 – 4.67]). Nonetheless, probing of the latter marginal two-way interaction revealed that the simple main effect of stimulus type remained significant at high levels of PTSD (*t*[119] = 2.59, p = .011) and non-significant at low levels of PTSD (*t*[119] = 0.97, p = .333) when controlling anxiety scores.

As an additional set of exploratory analyses, we re-ran our original model replacing total PTSD symptoms (PCL-5 total scores) with each PCL-5 subscale score in turn (representing severity of each PTSD symptom cluster). Only one symptom cluster, cluster E (hyperarousal), produced a significant two-way interaction between AAT stimulus type and PTSD symptoms (*t*[137] = 2.49, p = .014, *b* = 8.20, 95% CI [1.84–14.56]) suggesting that the original interaction effect is driven by selective approach toward cannabis stimuli among those with high PTSD hyperarousal symptoms, in particular. See Supplementary Tables 2–9 for a full presentation of these sensitivity and additional exploratory analyses.

4. Discussion

The current study was designed to quantify automatic approach bias towards cannabis (vs. neutral) stimuli among trauma-exposed cannabis users with varying PTSD symptom severities following exposure to a

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[4] In this analyses, a main effect of stimulus type also emerged (*t*[135] = -2.00, b = −126.47, p = .047, 95% CI [-248.48 to −4.46] with approach bias to cannabis stimuli (M = 58.0, SE = 11.4) being significantly greater (*t*[135] = −2.46, p = .017) than to neutral stimuli (M = 30.2, SE = 11.0).

personalized trauma (vs. neutral) cue. Consistent with H1, approach bias was stronger towards cannabis than neutral stimuli at higher PTSD symptom severity. Contrary to H2, the selective approach bias towards cannabis in participants with higher PTSD symptoms was not intensified by trauma cue exposure.

The finding that participants with higher PTSD symptoms (particularly PTSD hyperarousal symptoms) showed greater approach bias towards cannabis (vs. neutral) stimuli extends prior work demonstrating that automatic approach towards cannabis stimuli is greater among heavy cannabis users compared to controls (Cousijn et al., 2011). The fact that this AAT stimulus type x PTSD symptoms interaction persisted in sensitivity analyses even after controlling cannabis use levels, CUD, depressive, and anxiety symptoms suggests this approach bias towards cannabis in those with higher PTSD symptoms was not simply due to greater cannabis use/problems or to greater depression or anxiety. The result suggests that selective cannabis approach bias may be a cognitive mechanism contributing to PTSD-CUD comorbidity (Walsh et al., 2014). Moreover, this effect was not intensified by trauma cue exposure, suggesting the tendency to selectively approach cannabis may be chronically activated in those with higher PTSD symptoms. Given research linking cannabis approach bias on the AAT to longitudinal increases in cannabis use (Cousijn et al., 2011), our results suggest that cannabis users with higher PTSD symptoms may be at risk of escalations in their cannabis use over time.

There are several possible explanations for our not observing evidence of the hypothesized three-way interaction between AAT stimulus type (cannabis vs. neutral), PTSD symptom severity, and cue type (trauma vs. neutral) on approach bias scores. The cue manipulation was effective given the trauma verses neutral interview elicited the expected changes in affect and conscious cannabis craving (DeGrace et al., 2023; nevertheless, an interview-based CRP might have been so long as to allow for habituation to the trauma cue and consequent dissipation of the hypothesized trauma cue-elicited enhancement of cannabis approach bias in higher PTSD participants. Alternatively, placement of the AAT immediately following cue exposure may have been too soon to observe our predicted trauma cue effects in intensifying automatic cannabis approach bias at higher PTSD symptom levels. The trauma interview may elicit distractingly high levels of negative affect (DeGrace et al., 2023) and/or rumination among participants with higher PTSD symptoms, interfering with the emergence of a strengthened cannabis approach bias. Alternatively, trauma cue exposure may only intensify selective cannabis approach bias in higher PTSD participants if cannabis is simultaneously available. Trauma cue exposure studies in the PTSD-SUD field often pair trauma cue exposure with in vivo substance cue exposure (DeGrace et al., 2022). Two studies using RT-based cognitive tasks show that trauma cue exposure causes a general slowing of cognitive processing in those with higher PTSD symptoms (Read et al., 2017; Zinchenko et al., 2017). The cannabis AAT is also an RT task, which suggests a reduction in cognitive resources caused by preoccupation with the trauma reminder (DeGrace et al., 2022) could have adversely impacted our cannabis AAT validity following trauma cue exposure in participants with higher PTSD symptoms. Future studies could explore these possibilities using a more standard short audio-visual cue as the CRP (DeGrace et al., 2022a), placing the cannabis AAT further out from the interview-based CRP, simultaneously presenting in vivo cannabis cues when conducting the trauma CRP (DeGrace et al., 2022a), or using non-RT based automatic cannabis-related cognitive bias measures such as word association tasks (Ames et al., 2007).

The current study had several potential limitations. First, a variety of cannabis-related stimuli were used in the AAT (e.g., flower, dabs, vapes), but other common stimuli were not (e.g., edibles, oral concentrates like CBD oil). Some participants (e.g., those endorsing edibles but not smoked cannabis; see Supplementary Table 1) may not have identified with the specific cannabis stimuli presented, perhaps reducing their inclination to approach those stimuli. We observed expected effects

of stimulus type on the AAT at higher PTSD symptom severity as hypothesized in H1, but the effect magnitude might have been minimized by lower-than-optimal applicability of the AAT cannabis stimuli for some participants. Second, a power analysis was used to determine that we were adequately powered to detect medium effects, but we were likely underpowered to detect small effects. The insufficient power may have obfuscated evidence supporting the hypothesized three-way interaction in H2, as higher-order interactions do require additional power, particularly for small effect sizes. However, if our study was underpowered to detect the hypothesized three-way interaction due to inadequate sample size, the moderating effect of trauma cue exposure on the selective cannabis approach bias among those with higher PTSD symptom severity may be too small to be practically clinically meaningful. Third, while we saw a significant interaction between AAT stimulus type and continuous PTSD symptom severity, we were underpowered to conduct a sub-analysis among only those participants who met full diagnostic criteria for clinical PTSD on the CAPS (n = 29). In future, researchers may wish to replicate our analyses with a larger sample meeting the diagnostic threshold for PTSD to determine whether the current results stay the same regardless of PTSD diagnostic status or are different in this clinically relevant subgroup. Fourth, PTSD is not only comorbid with CUD but with other SUDs (e.g., Read et al., 2017) which also tend to co-occur with CUD (Budney et al., 2019; however, we did not assess for or exclude other forms of SUD. Thus, while we ruled out CUD symptoms as accounting for our cannabis approach bias findings in those with higher PTSD severity, we cannot rule out the impact of other forms of SUD. Finally, our planned analyses were not pre-registered on a publicly available platform prior to data collection.

Despite limitations, the current study was the first to combine a trauma CRP with a cognitive task used to measure automatic cannabis approach bias. The results were the first to demonstrate that selective cannabis (vs. neutral) approach bias is more pronounced at higher PTSD symptom severity – particularly higher severity of PTSD hyperarousal symptoms. Not finding evidence that trauma cues intensify the selective cannabis approach bias at higher levels of PTSD symptom severity may indicate that selective cannabis approach bias is chronically activated in cannabis users with higher PTSD symptoms. But the absent three-way interaction also raised important considerations for future research methods to determine conditions under which trauma cue exposure might activate or intensify automatic substance-related cognitive biases in those with higher PTSD symptoms. The current study has added to a small literature examining trauma cue exposure effects on automatic substance-related cognitions in substance users with varying PTSD symptom severity levels (DeGrace et al., 2022). Our results show that automatic approach bias towards cannabis stimuli is more pronounced in those cannabis users with higher PTSD symptom severity. This finding points to the role of automatic memory associations in explaining the greater potential of those with PTSD to develop problems with cannabis (Walsh et al., 2014), particularly given research showing that cannabis users with poor control over cannabis-related action tendencies on the AAT are more likely to develop cannabis-related problems over time (Cousijn et al., 2012). Given preliminary results that a cannabis approach bias modification intervention can reduce both conscious cannabis craving to a CRP and cannabis use (Sherman et al., 2018), our results may represent the first step towards opening new avenues for preventing and treating comorbid PTSD-CUD in cannabis users with trauma histories.

CRediT authorship contribution statement

S. DeGrace: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization, Project administration, Funding acquisition. **P. Romero-Sanchiz:** Conceptualization, Methodology, Writing – review & editing, Project administration, Funding acquisition. **P. Tibbo:** Methodology, Writing – review & editing, Funding acquisition. **S. Barrett:** Methodology, Writing

Declaration of competing interest

The authors have no conflicts of interest to declare.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2023.104387.

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