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# Cannabis and Emotion Processing: A Review of Behavioral, Physiological, and Neural Responses

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While previous research has indicated that alcohol use is associated with difficulties in emotion processing and socioemotional functioning, less is known about the effects of cannabis on these functions. The purpose of this review article is to provide the current state of knowledge on the effects of cannabis on emotion processing with regard to behavioral, physiological, and neural responses. This narrative review synthesizes previous research investigating the effects of cannabis on emotion processing across studies that have utilized a number of experimental approaches to determine both the acute and chronic effects of cannabis on emotion processing. Limitations of current research and steps for future directions are discussed. Existing research has shown that cannabis use is associated with difficulties in emotion processing, such as impairments in correctly identifying emotions and problems with emotion differentiation. Electroencephalography (EEG) studies have produced mixed findings, but have considered a number of variables, such as participant sex, and comorbid depression. In addition, while there are mixed findings for the effects of cannabis on amygdalar brain activity across functional magnetic resonance imaging studies, several studies indicate that cannabis use is linked with decreased brain response in the frontal lobe while viewing emotional stimuli. To our knowledge, this is one of the first critical review articles focused on an emerging research area of cannabis and emotion processing. Synthesizing the existing findings in this developing research field is important for future prevention and intervention studies focused on promoting healthy socioemotional functioning in cannabis users.

#### Public Health Significance

Studies synthesized in this review article suggest that cannabis users may have impairments in emotion processing at the behavioral, physiological, and neural level. Understanding these difficulties could aid prevention, intervention, and treatment efforts aimed at promoting healthy socioemotional functioning in cannabis users.

Keywords: cannabis, emotion processing, socioemotional functioning, emotion recognition

Over the past decade, laws and policies decriminalizing and legalizing cannabis have shifted worldwide, notably in the United States. Currently 36 states and 4 territories allow medical cannabis use, and 17 states and 2 districts allow recreational cannabis use (State Medical Marijuana Laws, n.d.). Due to increases in social acceptability, access, and availability, the prevalence of cannabis use has increased. For example, from 2002 to 2017 adult population cannabis use increased from 10.4% to 15% (Compton et al., 2019).

These increases are concerning as a large body of research has reported that cannabis use may have negative impacts on neuro-cognitive functioning, including executive functions, learning and memory, processing speed, and attention (Crean et al., 2011; Kroon et al., 2021). Additionally, there is an emerging research area suggesting cannabis use may affect emotion processing (Gorka et al., 2015; Heitzeg et al., 2015; Hindocha et al., 2014; Metrik et al., 2015; Troup et al., 2016), which could lead to difficulties with

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social relationships, affective processing, and understanding emotions. It is possible that these impairments exacerbate cannabis use, and in return create greater deficits in socioemotional processing, and other cannabis use-related consequences.

Across studies of other substances such as alcohol, impairments in emotion processing have been reported. For example, a systematic literature review found that in comparison to controls, individuals with alcohol use disorder (AUD) tended to have greater deficits in identifying emotions in facial expression recognition tasks, displayed less accuracy recognizing sadness and disgust, and required greater emotional intensity to recognize fear and anger (Donadon & de Lima Osório, 2014). Furthermore, a meta-analysis found that people with AUD and substance use disorder (SUD) had worse facial emotion recognition of anger, disgust, sadness, and fear across a variety of facial emotion recognition tasks, as well as tasks examining emotional intensity and face matching (Castellano et al., 2015). Both preclinical and human studies suggest cannabis may affect emotion processing, including emotion recognition abilities and socioemotional functioning. Specifically, exposure to cannabinoid compounds induces changes in behaviors and neural processes belonging to emotional domains in rats (Trezza et al., 2012). Across human studies, cannabis has been shown to affect emotion recognition behavior (Hindocha et al., 2014; Platt et al., 2010), physiological response to emotions (Papini et al., 2017), neural response as measured by electroencephalography (EEG; Torrence et al., 2019), and functional magnetic resonance imaging (fMRI; Leiker et al., 2019). However, to our knowledge, there are currently no reviews of the literature synthesizing the effects of cannabis on emotion processing in humans. A discussion of this literature is critical to clarify the role of cannabis use's effects on socioemotional processing in humans and begin to examine its effects on clinical outcomes, as well as provide a means for further research to create a basis for clinical interventions.

The purpose of this narrative review is to offer synthesis and interpretation of the current literature on cannabis effects across studies of emotion processing in humans, and to provide recommendations for future work in this emerging research area. Given that previous review articles on cannabis use and emotion processing are lacking, we chose to conduct a narrative review to introduce the literature and provide an overview of the main findings across currently published studies. The review has been organized by method of study to highlight findings across behavioral, physiological, EEG, and fMRI studies of emotion processing. Primary research articles were selected based on the following keyword search criteria: Cannabis AND emotion recognition, cannabis AND emotion processing, cannabis AND socioemotional processing, cannabis AND social processing, cannabis AND amygdala, cannabis AND limbic system, cannabis AND social interactions, cannabis AND emotion functioning, cannabis AND mood; cannabis AND affect; cannabis AND ecological momentary assessment (EMA); cannabis AND daily diary; as well as cannabis AND emotion. The term "cannabis" was also replaced with "marijuana" in all of the above keyword searches, and the searches were conducted again to determine whether additional articles of interest could be found. PubMed (https://pubmed.ncbi.nlm.nih.gov/) was used for all keyword searches. Similar to the reviews of alcohol's effects on emotion processing (Castellano et al., 2015; Donadon & de Lima Osório, 2014), studies selected focused on facial emotion recognition, attention to or reactivity to emotional images, evaluation of emotional images, and socioemotional functioning for both the chronic and acute effects of cannabis. However, studies focused on other affective responses, such as emotion regulation, stress, and/ or coping were excluded, as they were beyond the scope and focus of the current review. Studies of the chronic effects of cannabis use on emotion processing were defined as those that recruited participants with a history of cannabis use who had abstained from cannabis use for a period of time prior to study participation. Where details were provided, this ranged from  $\geq 8$  hr of cannabis abstinence to several months of cannabis abstinence as assessed via participant self-report, urine toxicology screen, observational, and/ or clinical evaluation. Studies of the acute effects of cannabis were defined as those that asked participants to self-administer cannabis orally or via inhalation (tetrahydrocannabinol [THC], cannabidiol [CBD], or both) at the time of study participation in a laboratory setting or investigated the acute effects of intoxication on emotion processing during daily life using EMA or daily diary methods.

# Behavioral and/or Physiological Studies of the Chronic and Acute Effects of Cannabis on Emotion Processing Chronic Effects

With the increasing prevalence of cannabis use, it is important to understand its long-term behavioral and physiological effects. Behavioral effects are often measured through self-report questionnaires or emotion recognition tasks. Physiological effects in response to emotional stimuli have been measured through hormones in blood samples, or skin conductance responses (SCRs) that can supplement behavioral findings. In this section, the effects of chronic cannabis use on human behavioral and/or physiological responses are examined (Table 1).

Impairments in self-reported emotional responses have been reported in chronic cannabis users. A study that used self-report measures, found that in participants with schizophrenia, those who chronically used cannabis (defined as  $\geq 3$  times/week for  $\geq 3$  years) had emotional deficits in expressivity, pleasure, and social functioning compared to those who had no lifetime regular cannabis use. While traits such as anticipatory pleasure can be negatively impacted by schizophrenia, these results suggest that cannabis use may further disrupt emotional responses, which could adversely impact one's interpersonal relationships (Schnakenberg Martin & Lysaker, 2020).

Although previously cannabis failed to predict emotion recognition in polysubstance drug users despite it being the most ubiquitously used illicit substance (Fernández-Serrano et al., 2010), more recent research suggests that cannabis users may have impaired ability to recognize emotions, which could lead to difficulty establishing healthy interpersonal relationships. One way to determine cannabis users' emotion processing is through the use of emotion recognition tasks. Using the Dynamic Emotional Expression Recognition Task, Platt et al. (2010) found that frequent cannabis users, who consumed cannabis ≥15 days/month, needed more time to process and identify facial expressions in comparison to controls. Additionally, cannabis users were more liberal in their response criterion for identifying sadness overall during the task, suggesting that they attribute emotions to be more negatively valenced than healthy controls (Platt et al., 2010). However, one confounding factor in these findings could have been elevated schizotypy in

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Behavioral and/or Physiological Studies Examining the Chronic Effects of Cannabis Use on Emotion Processing

Study	и	Age (mean $\pm$ <i>SD</i> )	Cannabis use criteria for cannabis users	Cannabis use criteria for controls	Other substance use criteria for controls	Study task	Main findings
Bayrakçi et al. (2015)	C+: 30	C+: 26.8 ± 4.7 C-: 27.1 ± 4.7	Cannabis dependence; 1-month abstinence	No history of cannabis dependence	<15 lifetime illicit drug uses for any category; <12 alcoholic drinks/ week, negative urine toxicology screen	Facial Emotion Identification Test; Facial Emotion Discrimination Test	Abstinent C+ had deficits in identification towards negative emotions and difficulties in emotion discrimination relative to C-
Fishbein et al. (2016)	C+: 49 C-: 416	I	Any cannabis use initiation at follow-up	No cannabis use initiation at follow-up	At baseline, <1 lifetime drink and The facial recognition task no illicit substance use	The facial recognition task	Youth who were more likely to recognize sad faces were 30% more likely to initiate cannabis use at follow-un
Hindocha et al. (2014)	C+: 25 C-: 34	C+: 22.52 ± 2.57 C: 22.15 ± 2.78	>20 days/month for last 6 months	≤2 times/month during lifetime	No past/present clinically diagnosed self-reported substance use problems; no self-reported illicit substance use >2 times/month in lifetime	Emotional processing task	Ability to recognize and discriminate between emotions impaired in C+ regardless of confounding factors
Papini et al. (2017)	C+: 20 C-: 20	C: 29.0	≥5 days/week for the last 90 days	≤5 lifetime uses, no cannabis use in the last 90 days	No current or past SUD; no illicit or prescription drug use in past 90 days; no past or current alcohol abuse or dependence; negative urine toxicology screen	2-day differential fear conditioning paradigm	C+ associated with \(\perp \) extinction of skin conductance response on Day 1 and Day 2 C+ associated with reduced differentiation between threat and coffer crimitis
Platt et al. (2010)	C+: 29 C-: 27	C+: 19.25 ± 2.14 C-: 21.22 ± 3.07	≥50 lifetime occasions, ≥15 days/month	≤10 lifetime uses	No current or past SUD	Dynamic emotional expression recognition task	sarcy summan C+ had ↑ processing time to identify facial expressions than C- C+ had more liberal in response criterion for sad faces
Schnakenberg Martin and Lysaker (2020)	C+: 36 C-: 35	C+: 49.97 ± 6.70 C-: 49.26 ± 10.06	≥3 times/week, ≥3 years	No lifetime regular cannabis use	No current substance dependence except for nicotine	Emotional Expressivity Scale; The Temporal Experience of Pleasure Scale; Social Functioning Scale	temotional deficits in expressivity,     pleasure and social function in     C+ with schizophrenia
Somaini et al. (2012)	C+: 28 C-: 14	C+: 24.1 ± 2.7 C-: 25.4 ± 3.6	≥2 times/day, ≥3 years	I	Negative urinary drug screen  I week and 2 hr before study; abstinence from smoking 12 hr before study; no polydrug use, ≤3–5 cigarettes/day; no	Emotional response evaluation	Active C+ had ↑ pleasantness ratings for unpleasant images & ↓ arousal compared to abstinent C+ and C− † activity of hypothalamic-pituitaryadrenal axis in C+
Wade et al. (2021)	C+: 38 C-: 45	C+: 21.47 ± 2.2 C-: 20.89 ± 2.72	Smoked cannabis >52 times in past year	Smoked cannabis <10 times in past year	<50 lifetime uses of illicit drugs except for nicotine, alcohol, and cannabis	PennCNP affective processing battery Past year cannabis use related to slower reaction time on emotion recognition	Past year cannabis use related to slower reaction time on emotion recognition
Wilcockson and Sanal (2016)	C-: 15	C+: 23.13 ± 4.16 C-: 24.13 ± 3.94	Daily cannabis users	No lifetime cannabis use		Dot-probe task	C+ had ↑ attentional-avoidance behavior when anxiety-related stimuli present

Note. No information on mean age was reported for the Fishbein et al. (2016) study (participants were 10–12 years old at baseline, and 12–15 years old at follow-up). No information on criteria for the control group was reported in the Wilcockson and Sanal (2016) study. C+ = cannabis users; C- = healthy controls' † = increased; UD = cannabis use et al. (2012) study. No information on other substance use criteria for the control group was reported in the Wilcockson and Sanal (2016) study. C+ = cannabis users; C- = healthy controls' † = increased; UD = cannabis users disorder; SUD = substance use disorder. cannabis users, which was not assessed (Platt et al., 2010). Similarly, however, a recent study by Wade et al. (2021) found that past year cannabis use was associated with slower reaction time on an emotion recognition task, suggesting cannabis use may be related to longer processing times needed for correctly evaluation socioemotional cues in individuals.

A subsequent study conducted by Hindocha et al. (2014), replicated the deficits in emotion recognition observed by Platt et al. (2010). Specifically, Hindocha et al. (2014) found that cannabis users had impairment in identifying all positive and negative emotions and had difficulty discriminating between emotions. Another study, examining cannabis users who were at least 1 month abstinent while they performed both the Facial Emotion Identification Test and Facial Emotion Discrimination Test, found that facial emotion recognition deficits for negative emotions and difficulties in emotion discrimination were still detectable in participants with an average of 3.2 months of cannabis abstinence (Bayrakci et al., 2015). This suggests that cannabis users with several months of abstinence still perform significantly worse when identifying negative emotions relative to healthy controls. This study may indicate that cannabis use causes long-lasting facial emotion recognition deficits, especially in response to negative emotions. However, an alternative explanation suggesting that emotion deficits precede the onset of frequent cannabis use may also be possible. Currently, to our knowledge no longitudinal studies of emotion recognition have been published that include participants prior to the onset of their cannabis use. These studies are critical for determining whether atypical emotion processing may confer risk for engaging in cannabis use.

Physiological responses to emotional stimuli may be another way to understand brain and behavioral markers related to affective processing within cannabis users. In a study conducted by Somaini et al. (2012), 14 chronic cannabis users, 14 abstinent cannabis users, and 14 healthy controls were given an emotional task where neutral and unpleasant images were presented, and participants were asked to complete the Self-Assessment Manikin (SAM) procedure. Results from the SAM indicated that active cannabis users displayed higher pleasantness ratings to unpleasant images and lower levels of arousal compared to abstinent cannabis users and controls. In addition, abstinent cannabis users showed reduced subjective sensitivity to negative emotions and threat, suggesting chronic cannabis use may have long-term effects on emotion processing. Supporting this behavioral effect, hormonal findings from participants' blood samples indicated hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis in cannabis users, which was greatest in active cannabis users. Only partial recovery was seen in abstinent cannabis users, perhaps indicative of the longterm effect of THC on cannabinoid receptor functioning, and hyperactivity of the HPA axis (Somaini et al., 2012).

Cannabis use has been found to modulate emotional response toward fear provoking stimuli. Preclinical findings in rats indicate that chronic cannabinoid administration impairs fear extinction (Lin et al., 2008). In a 2-day differential fear conditioning paradigm experiment conducted by Papini et al. (2017), results suggested that cannabis use may be associated with impaired fear extinction in humans as well. Fear was assessed through SCR, and compared to controls, frequent cannabis users had decreased extinction of their SCR on both days of the experiment in response to sound-bursts that were applied to provoke fear. Furthermore, SCRs demonstrated that

cannabis users had a more difficult time differentiating between threat and safety stimuli in comparison to healthy controls (Papini et al., 2017). Furthermore, cannabis use may affect attentional biases during presentation of fear-provoking stimuli. In a study conducted by Wilcockson and Sanal (2016), attentional biases were examined using a dot-probe task while participants were presented with anxiety-related stimuli, and eye tracking was used to monitor attention. The authors found that daily cannabis users had greater attentional avoidance behavior in the presence of anxiety-related stimuli compared to controls. These findings suggest that cannabis users may use avoidant behavior toward anxiety-provoking stimuli, and such behavior could increase risk for the development of anxiety disorders (Wilcockson & Sanal, 2016).

Overall, current research indicates that chronic cannabis use may be related to long-term behavioral deficits associated with impaired emotion processing, such as elevated hostility, as well as difficulties in emotion recognition, emotion differentiation, and atypical responsiveness to emotional stimuli. Furthermore, chronic cannabis use has been associated with hyperactivity of the HPA axis in response to emotional images. Longitudinal studies of behavior and physiology are needed to determine the onset of these deficits to better inform prevention and intervention research targeted toward modifying behavioral and physiological responses to emotional stimuli.

#### **Acute Effects**

Other studies have examined the acute effects of cannabis use on socioemotional processing or behavioral response to emotional stimuli (Table 2). In an examination of the effects of acute THC administration on feelings of hostility after social interaction, cannabis users experienced less hostility after smoking a 2.2% THC cigarette following the completion of a group task that involved developing a consensus story for a picture (Salzman et al., 1976). This group task was meant to induce frustration in the participants as they were told their story was inadequate and had to be revised. Feelings of reduced hostility after THC self-administration were opposite to participants who smoked placebo and experienced elevated hostility after the frustration stimulus. However, unlike a more recent study conducted by Ansell et al. (2015), this study did not examine perceptions of hostility in others, and participants were tested in a laboratory setting following acute intoxication. Thus, this study was unable to determine how cannabis users perceived emotions in other individuals following acute THC use. In contrast, in a more recent EMA study conducted by Ansell et al. (2015), 43 recreational cannabis users self-reported feelings of their own hostility and perceptions of hostility in others using a survey on interpersonal hostility. Cannabis users reported greater hostility and perceived others' behavior as more hostile on days that they reported cannabis use (Ansell et al., 2015). Similarly, using EMA to examine reports of hostility following cannabis use over the course of 4 weeks, Trull et al. (2016) found that at the momentary level cannabis use increased feelings of hostility, and more frequent cannabis users also reported overall greater hostility. While these appear to be opposite to those reported by Salzman et al. (1976), they were not collected in a laboratory or group setting, and were also examined in a sample of cannabis users who had co-occurring depressive or borderline personality diagnoses. Thus, it is unclear if similar reports would be observed in a sample of cannabis users

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Behavioral and/or Physiological Studies Examining the Acute Effects of Cannabis Use on Emotion Processing

Study	и	Age (mean ± SD)	Criteria for cannabis users	Study task	Dose of THC/CBD	Main findings
Ansell et al. (2015)	C+: 43	C+: 23.7 ± 4.6	Recreational C+	Daily interpersonal	No specific dose, personal	C+ correlated with ↑ hostility
Amdt and de Wit (2017)	C+: 38	$23.6 \pm 0.66^{a}$	≤100 lifetime cannabis use occasions	Incounty started International affective picture system Dynamic emotion identification task	CBD: 300, 600, or 900 mg	CBD did not change ratings of positive and negative enotional stimuli CBD did not affect emotion identification
Clopton et al. (1979)	C+: 30	23.7 <sup>b</sup>	5–30 days cannabis use/month	Affective Sensitivity Scale	0.33 g cannabis with 6 mg THC or 0.02 mg THC	tenution identification    performance was following THC but not aloosed.
Hindocha et al. (2015)	Heavy C+: 24 Light C+: 24	Heavy C+: 21.42 ± 1.62 (low schizotypy) 21.50 ± 1.38 (high schizotypy) Light C+: 21.00 ± 2.13 (low schizotypy) 22.90 ± 2.02 (high schizotypy)	Heavy C+: ≥25 days/month Light C+: ≤24 days/month	Emotional facial affect recognition	THC: 8 mg CBD: 16 mg THC: 8 mg/CBD: 16 mg	CBD ↑ emotional facial affect recognition at 60% emotional intensity THC ↓ emotional facial affect recognition at 40% emotional intensity THC/CBD not related to impairment
Metrik et al. (2015)	C+: 89	C+: 21.4 ± 4.5	≥2 days/week in the past month, ≥weekly use in the past 6 months	Pleasantness rating; Emotional stroop task	THC cigarette: 2.7%–3%	C+ had ↑ response latency to negative stimuli C+ had no change in response latency to positive stimuli C+ had no attentional bias to affective word etimuli
Salzman et al. (1976)	C+: 60	I	History of cannabis use	Thematic Apperception Test	THC cigarette: 2.2%	THC \ \telings of hostlity after frustration stimulus Placebo \ feelings of hostlity after frustration stimulus
Testa et al. (2019)	183 F and 183 M	24.61 ± 3.13	At least one partner used cannabis ≥2 times/week	Daily diary	No specific dose, personal cannabis use	Cannabis use ↓ morning levels of hostility
Trull et al. (2016)	C+: 35	30.9 ± 11.2 °	I	Ecological momentary assessment	No specific dose, personal cannabis use	Cannabis use ↑ hostility at the momentary level More frequent cannabis use was associated with overall greater hostility

Note. Mean age of participants was not reported in the Salzman et al. (1976) study (participant age ranged from 21 to 30). No cannabis use criteria was reported in the Trull et al. (2016) study. C+= cannabis users; C-= healthy controls;  $\uparrow=$  increased;  $\downarrow=$  decreased; C= cannabidiol; F= females; C= mean C= m

without psychiatric comorbidities. For example, in a community sample of regular cannabis users, a study that used a daily diary method found that cannabis use reduced morning levels of hostility (Testa et al., 2019), which is in contrast to previous reports (Ansell et al., 2015; Trull et al., 2016). However, this study did not examine how moment-to-moment cannabis use affects emotion evaluation in others, indicating more research is needed to understand how cannabis use may alter socioemotional processing when evaluating others' emotions in day-to-day social interactions.

One of the first behavioral studies to examine the effect of acute THC administration on emotion identification in others was conducted by Clopton et al. (1979) using a within-subject design in 30 cannabis users with a history of past month cannabis use. The authors used the Affective Sensitivity Scale, which required participants to identify the emotions being experienced during social encounters by individuals in a series of videos. Emotion identification was examined before and after smoking 6 mg of THC or placebo. The study found that emotion identification performance was significantly worse in cannabis users following THC, but not placebo. The authors suggest that acute THC intoxication could contribute to lack of empathy or difficulties with interpersonal skills in cannabis users.

A study by Metrik et al. (2015) examined the effects of attentional bias toward negative emotions in cannabis users who smoked a cannabis cigarette prior to completing emotion processing tasks. This 2-day study had regular cannabis users (≥2 days/week of cannabis use in the past month and ≥weekly use in the past 6 months) smoke a cannabis cigarette (2.7%–3% THC) or a placebo cigarette on separate occasions. Participants completed two experimental tasks each day: The Pleasantness Rating Task, which measured response latency and perception of pleasantness of affective images, and the Emotional Stroop Task, which identified attentional bias toward affective word stimuli. During the Pleasantness Rating Task, acute cannabis use was found to significantly increase response latency toward negative images compared to neutral ones, suggesting that acute cannabis use created an attentional bias toward negative images. On the contrary, acute cannabis use did not create attentional bias toward positive emotional stimuli. No significant effects were found for attentional bias to affective words in the Emotional Stroop Task (Metrik et al., 2015). Overall, these findings suggest that acute cannabis use may increase allocation of attentional resources toward negative emotional stimuli compared to placebo.

Two of the main cannabinoids found in cannabis, THC, and CBD, may operate to modulate emotional response differently (Hindocha et al., 2015). A four-way, double-blind, placebo-controlled study was conducted with the following groups of participants: Highschizotypy and high frequency of cannabis use, high-schizotypy and low frequency of cannabis use, low-schizotypy and high frequency of cannabis use, and low-schizotypy and low frequency of cannabis use. Prior to completing a Facial Affect Recognition Task where emotions were viewed at different emotional intensities from 20% to 100%, participants were administered 8 mg THC, 16 mg CBD, 8 mg THC, and 16 mg CBD, or a placebo. It was found that at 60% emotional intensity CBD improved emotional facial affect recognition toward all emotions in comparison to placebo, while at 40% emotional intensity THC impaired emotional facial affect recognition in response to all emotions. These findings were present in participants with and without high levels of schizotypy. When THC and CBD were paired together no impairment or improvement was seen while identifying facial emotions (Hindocha et al., 2015). Overall, this study is the first human study to suggest that CBD improves recognition of all facial emotions, while THC impairs them.

Subsequently, a study by Arndt and de Wit (2017) examined the acute effects of CBD on evaluation and recognition of emotional stimuli in past-month cannabis users. Unlike effects that have been reported for THC, CBD did not alter ratings of positive or negative emotional stimuli at any of the doses tested, and in contrast to the study by Metrik et al. (2015), it did not impact participants' ability to identify any of the emotions on an emotion identification task. Thus, findings are mixed with regard to the effects of CBD on responses to emotional stimuli, and long-term effects are still unknown.

Given the paucity of research and some inconsistent findings on the acute effects of cannabis on emotion processing across behavioral and/or physiological studies, more research is needed to understand the effects of intoxication on emotional responses in cannabis users and implications for socioemotional functioning. Diversity of participant characteristics, and dose of CBD and THC administration must be manipulated to fully understand the scope of the behavioral and physiological effects cannabis may have on humans.

# Human EEG Studies of Cannabis and Emotion Processing

The neural correlates of emotion processing in cannabis users have also been studied with the use of EEG and the recording of event-related potentials (ERPs). These methods allow for recording electrical activity from the brain at high temporal resolution while participants perform emotion processing tasks and may be useful for determining whether there are differences in neural activity during affective tasks between cannabis users and controls. In this section, we review the effects of cannabis on emotion processing in human EEG studies (Table 3).

In a study of individuals of Native American ancestry with and without cannabis dependence, the P3 ERP component was examined during a facial discrimination task that included happy, neutral, and sad faces (Ehlers et al., 2008). The authors reported increased latency of the P350 and P450 components of the P3 ERP in those with cannabis dependence, suggesting slower activation of attention to emotional stimuli that could affect socioemotional processing in individuals with cannabis dependence, or be a predisposing risk factor for cannabis use. Understanding these risk factors in high-risk groups who have increased prevalence of cannabis dependence is a critical step toward targeted intervention methods in this population.

Another study that used an emotion processing task in casual to chronic cannabis users was conducted by Troup et al. (2016) and showed that cannabis users had a significant decrease in P3 ERP's compared to controls. P3 complex is particularly interesting in regard to emotion processing and cannabis use as P3 has been associated with attention allocation during tasks and is consistently linked to emotion processing (Sur & Sinha, 2009). Troup et al. (2016) found that chronic cannabis users had reduced P3 amplitude in the centroparietal sites during implicit emotion processing, which was defined as trials that did not require directed attention toward emotional faces; rather, the implicit condition required participants

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 Table 3

 Human EEG Studies Examining the Effects of Cannabis Use on Emotion Processing

Study	n	Age (mean $\pm$ <i>SD</i> )	Cannabis use criteria for cannabis users	Cannabis use criteria for controls	Other substance use criteria for controls	Study task	Main findings
Ehlers et al. (2008)	C+: 47 C+ with other substance dependence: 66 C-: 201	C+: 24.66 ± 7 C+ with other drug dependence: 30.33 ± 8 C-: 30.46 ± 14	C+: cannabis dependence C+ with other substance dependence: Cannabis and other substance dependence diagnosis	No cannabis or other substance dependence	No alcohol use 24 hr before study visit	Facial discrimination task	† latency of P350 and P450 components of P3 ERP when viewing emotional faces
Torrence et al. (2018)	C+: 19 C-: 20	C+: 19.84 ± 2.34 C-: 19.5 ± 2.06	> 1 time/month, > 1 year of cannabis use	No lifetime cannabis use	I	Dot-probe task	↓ attentional bias in C+ measured by P1 amplitude to fearful faces
Torrence et al. (2019)	2 S S C C +: 18 C C -: 18 C C C C C C C C C C C C C C C C C C	C+: 23.94 ± 4.19 C-: 23.56 ± 3.78	>1 time/month, ≥1 year of cannabis use	Never using or not using in last 2 years	No reports of prescription or illicit drug use; no alcohol use 24 hr before study visit	Awareness task	Within C+ ↑ P1 amplitude to happy faces compared to fearful and neutral
Troup et al. (2016)	C+: 27 C-: 43	C+: 21.3 ± 7.18 C-: 19.3 ± 2.07	Casual to chronic cannabis use	Never used cannabis or used >1 year ago	Screened for substance use in 8 and 24 hr before study visit; no specific exclusion criteria	Emotion processing task	↓ P3 amplitude in C+ compared to C− ↓ P3 in C+ to happy faces &↑ to angry faces compared to C−
Troup et al. (2017)	C+: 32 C+ depressed: 43 C- depressed: 27 C-: 20	I	CES-D CES-D	C– Depressed: >16 CES-D	Screened for substance use in 8 and 24 hr before study visit; no specific exclusion criteria	Emotion processing task	C—depressed had ↓ P3 amplitude relative to C— to fearful expressions during implicit processing C+ depressed had ↓ P3 amplitude relative to C— to fearful expressions during
Troup et al. (2019)	Heavy C+, casual C+ and C-: 80F and 64M		Heavy C+: ≥1 time/week Casual C+: <1 time/ week	I	I	Facial-emotion attention task	Male C+ had ↑ P1 compared to female C+ Male C+ had ↑ P3 compared to female C+

Note. No information on age was reported for the Troup et al. (2017) or Troup et al. (2019) studies. Additionally, no information on criteria for the control group was reported in the Troup et al. (2019) study. C+ = cannabis users; C− = healthy controls; ↑ = increased; ↓ = decreased' CES-D = Center for Epidemiological Studies-Depression Scale, F = females' M = males; EEG = electroencephalography; ERP = event-related potentials.

to label the sex of an individual. Cannabis users also had reduced P3 amplitude at frontocentral electrodes during explicit conditions, which were defined as trials that required directed attention; in this study participants were asked to label the emotion expressed in the faces they were presented with (Troup et al., 2016). These findings suggest that cannabis users have reduced neural response to the emotional stimuli presented in comparison to controls, regardless of the level of attention needed for the task's conditions. When examining responses to specific emotions, during the explicit emotion recognition conditions, cannabis users showed increased P3 amplitude in response to angry expressions, and decreased P3 amplitude in response to happy expressions compared to controls. This indicates that cannabis users may be more sensitive to processing angry emotions compared to happy ones. The authors also reported a trend between the frequency of cannabis use and brain activity, such that lower P3 amplitude was related to cannabis use occasions (Troup et al., 2016).

A subsequent study by Troup et al. (2017), recruited cannabis users and controls with and without depression. Participants with depression, regardless of cannabis use status, had a significant reduction in P3 amplitude to the Facial Emotion-Attention Task compared to healthy controls. However, chronic cannabis use further reduced the P3 amplitude, and the group with the largest P3 deficits in response to emotional stimuli were cannabis users who scored highest for subclinical depression. This suggests that cannabis may be interacting with mood state to contribute to a deficit in the amplitude of P3, since P3 is associated with attention to emotion (Troup et al., 2017).

Unlike Troup et al. (2016, 2017), a study conducted by Torrence et al. (2019) suggested cannabis use modulated brain activity in emotion processing that could additionally be measured by P1 amplitude. In this study, instead of an emotion processing task, a backward masking paradigm in an emotion awareness task was used to examine anxiety-related attentional processes. In this experimental design participants had to identify the target facial expression, which would randomly alternate between a fearful, happy, or neutral face, and then a neutral face (the mask). In the restricted awareness (masked) condition, the target face was displayed for 16.66 ms followed by the 150 ms mask, while the aware condition (unmasked) was displayed for 133.33 ms and then the mask was displayed for 33.33 ms. This design was used to mimic restricted awareness in the masked condition. The results of this study indicated that P1 was greater in the masked condition compared to unmasked, and happy faces elicited a greater P1 amplitude than fear and neutral. P1 amplitude, which is thought to reflect an initial increase of attention different from P3, peaks earlier at 80-120 ms in the lateral occipital electrodes. Within cannabis users there was increased P1 amplitude toward happy facial expressions, which suggests cannabis users may have increased early processing of happy facial expressions compared to other emotions (Torrence et al., 2019). A previous study conducted by Torrence et al. (2018) suggested decreased attentional biases toward fearful faces in cannabis users as reflected in a decreased P1 amplitude during a dot-probe task in comparison to controls. This is interesting because anxiety tends to be related to greater attentional bias toward fearful faces. However, in this case cannabis may operate to have anxiolytic effects in the early stages of attention modulation (Torrence et al., 2018).

Another factor contributing to the amplitude of P1 and P3 components in cannabis users is sex. In comparison to female cannabis users, male cannabis users had an increase in P1 and P3 amplitudes. The P1 amplitude in male cannabis users was more robust compared to female cannabis users and controls, suggesting early attentional processes may be affected more in male cannabis users. These findings show that cannabis use and sex could interact and contribute to differing neural responses during emotion processing tasks (Troup et al., 2019).

Only a handful of human EEG studies have been conducted to examine the effects of cannabis on attentional response to emotional faces. Given the differences in populations and tasks used across these studies, it is difficult to make conclusions about the overall effects of cannabis use on the ERP components measured. However, there may be some evidence that compared to controls, cannabis users have decreased P3 amplitudes to emotional stimuli, and within participants who use cannabis, P1 amplitudes may show differences in response to emotional stimuli relative to P3 (Torrence et al., 2019; Troup et al., 2016). Moderating factors like sex and depression diagnosis (Troup et al., 2017, 2019) may affect attentional processing to emotional stimuli, so additional studies focused on individual differences are needed to further understand the effects of cannabis on emotion processing.

## fMRI Studies of the Chronic and Acute Effects of Cannabis on Emotion Processing

### **Acute Effects**

Since it is known that cannabis use can modulate emotions in humans, examining the acute effects of cannabis on brain activity during fMRI tasks of emotion processing is critical for understanding cannabis users' processing of emotional stimuli while intoxicated. Identifying the underlying neural correlates of the acute effects of cannabis on emotion processing could help explain any potential impairments in socioemotional functioning when under the influence of cannabis. This section synthesizes existing findings on the acute effects of cannabis on emotion processing-related brain activity within fMRI studies (Table 4).

Previous studies, like Hindocha et al. (2015) suggest that cannabis has the capacity to increase and reduce anxiety in humans, and these opposing effects are thought to be mediated via THC and CBD, respectively (Hindocha et al., 2015). For example, in studies of individuals who had minimal lifetime occasions of cannabis use, a dose of 10 mg of THC increased anxiety (Bhattacharyya et al., 2010; Fusar-Poli et al., 2009), while a dose of 600 mg CBD tended to decrease anxiety during fearful face processing (Fusar-Poli et al., 2009). During an emotion processing task, CBD reduced the blood oxygen level-dependent (BOLD) signal in the amygdala and the anterior and posterior cingulate cortex (PCC: Fusar-Poli et al., 2009). The suppression of activity in these structures was correlated with a decrease in SCR fluctuations indicating that CBD's effect on the limbic and paralimbic systems could contribute to reductions in anxiety and decreased arousal of the autonomic nervous system (Fusar-Poli et al., 2009). In a similar study conducted by Fusar-Poli et al. (2010), a dose of 600 mg of CBD disrupted ACC-amygdala connectivity, which was believed to decrease anxiety by reducing autonomic arousal via the limbic and paralimbic regions. In contrast, THC decreased activation of the middle frontal gyrus (MFG) and

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 Table 4

 fMRI Studies Examining the Acute Effects of Cannabis Use on Emotion Processing

Study	и	Age (mean $\pm$ <i>SD</i> )	Criteria for cannabis use	Study task	Dose of THC/CBD	Main findings
Bhattacharyya et al. (2017)	C+: 14	C+: $23.79 \pm 4.45$	$\geq 1$ , but <25 lifetime	Fear processing task	THC: 10 mg	THC † anxiety, and † right amygdala activity
Colizzi et al. (2018)	C+: 12 C-: 12 <sup>a</sup>	C+: 27.2 ± 6.9	C+: ≥14 lifetime cannabis joints smoked	Facial expressions of emotion task	THC: 10 mg	uning teat processing. In C+, THC↑ brain activity in fusiform gyrus and ↓ activity in cuneus (similar effects of placebo in C−) ↑ past cannabis use was associated with ↓
Fusar-Poli et al. (2009)	C+: 15	C+: 26.67 ± 5.7	≤15 lifetime occasions	Emotional processing task	THC: 10 mg CBD: 600 mg	cuneus activity during acute intoxication THC ↑ anxiety, and during fearful face processing ↓ activation of MFG and PCC, and ↑ activation in the precuneus and primary
						sensorimotor cortex  CBD ↓ activation in parts of the amygdala, anterior parahippocampal gyrus, anterior and posterior GG, middle occipital gyrus, and nosterior lobe of the cerebellum
Fusar-Poli et al. (2010)	C+: 15	C+: $26.67 \pm 5.7$	≤15 lifetime occasions	Emotional processing	THC: 10 mg	CBD but not THC disrupts ACC-amygdala
Gorka et al. (2015)	C+: 16	C+: 20.8 ± 2.6	≥10 lifetime occasions; No daily use of cannabis	Emotional face matching task	THC: 7.5 mg	THC † connectivity between left basolateral and superficial amygdala with ACC and mPFC
Phan et al. (2008)	C+: 16	C+: 20.8 ± 2.6	≥ 10 lifetime > 10 lifetime occasions; No daily use of cannabis	Emotional face matching task	THC: 7.5 mg	THC ↓ amygdala reactivity to social signals of threat

Note. C+ = cannabis users; C− = healthy controls; ↑ = increased; ↓ = decreased; CBD = cannabidiol; CG = cingulate gyrus; THC = tetrahydrocannabinol; ACC = anterior cingulate cortex; MFG = middle frontal gyrus; mPFC = medial prefrontal cortex; PCC = posterior cingulate cortex; fMRI = functional magnetic resonance imaging.

<sup>a</sup> See Table 5 for cannabis and other substance use criteria for C−.

PCC, and increased activation in the precuneus and primary sensorimotor cortex during fearful face processing (Fusar-Poli et al., 2009).

Other studies have examined the effects of THC on amygdalar activity during emotion processing. In a study conducted by Bhattacharyya et al. (2017), a combination of Positron Emission Tomography (PET) and fMRI were used to see if the availability of Cannabinoid 1 (CB1) receptors was correlated to the degree of modulation of emotion processing in response to THC. Participants had consumed cannabis at least on one occasion but had less than 25 lifetime cannabis use occasions overall. Initially, PET was used to measure CB1 receptor availability at baseline scanning, and during fMRI participants performed a fear processing task. Following a 10 mg dose of THC, cannabis users had greater anxiety and right amygdala activation while processing fear. These effects were positively correlated with CB1 receptor availability in the right amygdala. Overall, the findings suggest that the acute effects of cannabis on anxiety are modulated by THC's effects on the amygdala, the extent of which was determined by the concentration of the local availability of CB1 receptors (Bhattacharyya et al., 2017). On the other hand, some studies have found decreased amygdalar reactivity with acute THC administration (Phan et al., 2008). In a study conducted by Phan et al. (2008), administering 7.5 mg of THC significantly reduced amygdala reactivity to threatening faces during an emotional face matching task, suggesting that THC may have an anxiolytic role in central mechanisms of fear behavior. In a functional connectivity study by Gorka et al. (2015), administering 7.5 mg of THC during an Emotional Face Matching Task, enhanced connectivity between the basolateral amygdala (AMYG-BL) and superficial amygdala (AMYG-SF) subregions, with the rostral anterior cingulate cortex (rACC) and medial prefrontal cortex (mPFC). It has been proposed that the AMYG-BL to rACC/ mPFC functional coupling may be particularly important for perception of social threat, and in prior studies it has been found that greater functional coupling between the amygdala and rACC/mPFC in response to threat is related to reduced stress and anxiety. This enhanced functional connectivity could reflect the regulatory influences of the prefrontal cortex on the subregions of the amygdala in the context of threat, suggesting THC modulates amygdala functional connectivity. Therefore, due to cannabis consumption, increased rACC/mPFC regulatory influences on AMYG-BL and AMYG-SF could be related to diminished perception of threat and anxiety (Gorka et al., 2015).

Interestingly, in a study by Colizzi et al. (2018) that examined acute (and chronic) effects of cannabis use, the authors found that under acute THC intoxication, cannabis users showed similar patterns of brain activity to nonusers during the placebo condition, such as activation of the fusiform gyrus and deactivation of the cuneus. Greater past cannabis use was also associated with reduced cuneus activation during acute intoxication, suggesting that chronic effects can modulate the effects of acute intoxication during emotion processing.

fMRI studies of acute cannabis response may demonstrate how cannabis modulates emotion processing brain regions during intoxication. Some studies suggest that THC increases, while CBD may decrease anxiety while processing fearful social stimuli (Bhattacharyya et al., 2017; Fusar-Poli et al., 2009). However, among the limited number of existing studies, several discrepancies have been reported for the effects of THC on amygdalar activity. It is

clear that further fMRI studies of acute cannabis effects are needed to determine the potentially distinct effects of CBD and THC on individuals' neural response to emotional stimuli. These studies could help identify the distinct and overlapping effects of CBD and THC on neural response to emotional stimuli during acute intoxication, which could explain potential positive and negative effects of these cannabinoids on socioemotional functioning in cannabis users.

### **Chronic Effects**

The chronic effects of cannabis use on brain functioning involved in emotion processing can also be examined through the utilization of fMRI. Identifying brain functions altered by chronic cannabis use could help explain differences in socioemotional functioning between cannabis users and healthy controls and offer information about the duration that brain activity may be impacted by cannabis use. This section summarizes the current findings on the chronic effects of cannabis use on brain responses involved in emotion processing using fMRI (Table 5).

Several studies have investigated whether long-term cannabis use alters neural responsiveness to emotionally-provoking stimuli with particular attention toward amygdalar reactivity. For example, some studies have found that the amygdala is hypersensitive to signals of threat. In a study conducted by Spechler et al. (2015), an fMRI affective face processing task (Grosbras & Paus, 2006) was administered to a large group (n = 70) of adolescent cannabis users and substance abstinent adolescent controls (n = 70). During this task short movies displaying angry and neutral faces were presented interchangeably with a control picture (concentric circles) and viewed passively. The findings of this study indicate that in response to angry versus neutral faces, cannabis users had greater reactivity in the bilateral amygdala, which suggests youth cannabis use may be associated with hypersensitivity to signals of threat. This finding may suggest that adolescent cannabis users could be at greater risk for negative affect and the development of mood disorders due to the amygdala's hypersensitivity to threat (Spechler et al., 2015). On the other hand, in a study conducted by Aloi et al. (2018) differences in amygdala reactivity were not found between cannabis users and controls. An Affective Stroop Task was administered during an fMRI scan to adolescents diagnosed with Cannabis Use Disorder (CUD) to examine the effects of CUD symptom severity on neural systems that mediate emotion processing. In the Affective Stroop Task 16 negative, 16 neutral, and 16 positive stimuli were selected from the International Affective Picture System. Participants solely diagnosed with CUD did not differ in amygdala responsiveness to emotional stimuli from controls, however CUD symptom severity was positively related to brain response within the precuneus, PCC, and inferior parietal lobule (Aloi et al., 2018). Another study examined increasing CUD symptom severity in adolescents in response to threat (Blair et al., 2019). In this study, participants were rapidly presented with images, such as human faces, that appeared to loom toward or recede away from them. Increasing CUD symptom severity was associated with decreased response to threatening looming stimuli within the rostral frontal cortex, fusiform gyrus, cerebellum, and amygdala. These data suggest that CUD is associated with a decreased response to threat and indicate that cannabis use may modulate brain systems responsive to emotional stimuli (Blair et al., 2019). Furthermore, in a study conducted by Gruber et al. (2009), similar effects were seen in a group of

(table continues)

 Table 5

 fMRI Studies Examining the Chronic Effects of Cannabis Use on Emotion Processing

				CAN	NABIS AN	D EMOTION				11
	Main findings	† CUD severity associated with † BOLD responses within PCC, precuneus, and iPL during incongruent versus congruent versus	↑ CUB severity associated with ↓ responsiveness to looming threat cues in rostral frontal cortex, fusiform gyrus, cerebellum, and amvedala	C+↑ activity in cingulate gyrus and iPL relative to C–	Higher cannabis use associated with ↓ amygdala reactivity during threat	C+ had \( \psi\$ cingulate gyrus and amygdalar responses to masked affective stimuli relative to C-	C+ had ↓ activation in right insula, prefrontal cortex, amygdala, and occipital cortex in response to negatively valenced stimuli	↑ CUD symptom severity associated with ↓ activity in medial PFC and ACC during face processing	During negative face trials for C+ relative to C-:  † modulation in left amygdala to hypothalamus EC  † modulation in right amygdala to bilateral fusiform gyri EC  † modulation to left centrolateral prefrontal context to bilateral fusiform contex	gyri EC (table continues)
	Study task	Affective stroop task	Looming threat task	Facial expressions of emotion task	Threat-related amygdala reactivity task	Masked facial affect tasks	Emotion-arousal word task	Expression processing task	Emotional face-matching task	
	Other substance use criteria for controls	AUDIT scores = 0	AUDIT scores <4	<ul> <li>≤21 units/week of alcohol, negative urinary drug screen, no smoking for 4 hr, and no alcohol use for 24 hr prior to study. No category of substance use &gt;5 times in lifetime.</li> </ul>	I	No current or past alcohol abuse or dependence; \$\leq\$ lifetime uses of any illicit drug; negative urine toxicology screen	>100 lifetime drinks	Abstinence for 4 weeks prior Expression processing task to testing	No higher than moderate level of nicotine dependence; BAC <0.05 g/210L; negative urine toxicology screen; no alcohol dependence	
	Cannabis use criteria for controls	No alcohol and/or cannabis use	No CUD/AUD symptomatology	<5 lifetime cannabis joints smoked	I	No lifetime cannabis use	1–10 lifetime occasions or no cannabis use	CUDIT scores = 0	No current cannabis use	
•	Cannabis use criteria for cannabis users	CUD severity assessed using CUDIT and participants grouped according to CUDIT scores	CUD severity assessed using CUDIT and participants grouped according to CUDIT scores	≥14 lifetime cannabis joints smoked	CUD diagnosis; MDD diagnosis	≥3,000 joints smoked over lifetime; smoke ≥4 of the last 7 days	>100 lifetime occasions	CUD severity assessed using CUDIT	CUD diagnosis	
3	Age (mean ± <i>SD</i> )	CUDIT ≥ 8: 16.2 ± 1.2 C-: 15.6 ± 1.37	CUDIT ≥ 8: 16.59 ± 0.83 C-: 15.97 ± 1.13	C+: 27.2 ± 6.9 C-: 25.3 ± 4.1	C+: 21.7 ± 2.0	C+: 25 ± 8.8 C-: 26 ± 9.0	C+: 19.84 ± 1.45 C-: 20.51 ± 1.26	C+ and C-: 15.95 ± 1.23	C+: 28.2 ± 3.5 C-: 28.7 ± 3.7	
	и	CUDIT ≥ 8: 29 C-: 33	CUDIT ≥ 8: 28 C-: 34	C+: 12 C-: 12 C-: 13	C+: 6	C+: 15 C-: 15	C+: 20 C-: 20	C+ and C-: 104	C-: 23	
	Study	Aloi et al. (2018)	Blair et al. (2019)	Colizzi et al. (2018)	Cornelius et al. (2010)	Gruber et al. (2009)	Heitzeg et al. (2015)	Leiker et al. (2019)	Ma et al. (2020) C+: 23 C-: 23	

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Table 5 (continued)

Study	и	$Age $ (mean $\pm SD$ )	Cannabis use criteria for cannabis users	Cannabis use criteria for controls	Other substance use criteria for controls	Study task	Main findings
Roser et al. (2012)	C+: 15 C-: 14	C+: 26.5 ± 2.9 C-: 27.3 ± 3.5	≥3 times/week, ≥2years	No lifetime cannabis use	No alcohol use prior to testing; negative urine toxicology screen; no substance abuse/ dependence; matched to cannabis users on nicotine use	Theory of mind task	C+ had ↓ activity in parahippocampal gyrus, right precuneus and cuneus and ↑ activity in left cuneus and right anterior cingulate gyrus compared with C-
Spechler et al. (2015)	C+: 70 C-: 70	C+: 14.77 ± 0.40 C-: 14.61 ± 0.66	Cannabis-experimenting adolescents from IMAGEN data set	No lifetime cannabis use	No illicit substance use; no signs of intoxication; matched to cannabis users on lifetime alcohol and cigarette use	Passive viewing of videos with faces	C+ had ↑ reactivity in bilateral amygdala to angry faces
Spechler et al. (2020)	C+: 525 C-: 594	C+: 14.39 ± 0.39 C-: 14.44 ± 0.41	Cannabis-naïve at baseline and then endorsed any level of cannabis use at follow-up	No lifetime cannabis use	Matched to cannabis users on Passive viewing of videos baseline alcohol use with faces	Passive viewing of videos with faces	Right amygdala hyperactivity was predictive of future cannabis use
Wesley et al. (2016)	C+:16 C-: 17	C+: 25.1 ± 3.1 C-: 27.1 ± 6.3	>5 years, >20 days/month, >2 times/day	5 lifetime occasions of cannabis	No current substance dependence other than nicotine; no alcohol abuse or dependence; negative urine toxicology screen; <5 lifetime illicit substance use occasions for any category	Modified international affective picture system task	C+ had ↓ mPFC activity during emotional evaluation compared with C-
Zinmermann et al. (2018)	C+: 19 C-: 18	C+: 23.79 ± 3.24 C-: 24.11 ± 3.14	CUD diagnosis; cannabis abstinence >28 days prior to experiment	<10 g lifetime cannabis consumed	Negative urine toxicology screen	Emotion processing task	Negative emotional stimuli † mOFC activity and † mOFC-dorsal striatal and mOFC-amygdala functional coupling in C+ compared with C-

Note. C+ = cannabis users; C− = healthy controls; ↑ = increased; ↓ = decreased; ACC = anterior cingulate cortex; AUD = alcohol use disorder; AUDT = Alcohol Use Disorder Identification Test; BAC = breath alcohol concentration; BOLD = blood oxygen level-dependent; CUD = cannabis use disorder; CUDIT = Cannabis Use Disorder Identification Test, BC = effective connectivity; iPL = inferior parietal lobule; MDD = major depressive disorder; mOFC = medial orbitofrontal cortex; mPFC = medial prefrontal cortex; PCC = posterior cingulate cortex; PFC = prefrontal cortex; fMRI = functional magnetic resonance imaging.

15 adult chronic cannabis users who had used ≥3,000 joints in their lifetime, and currently smoked ≥four times in the past week. The Masked Facial Affect Tasks were administered by conducting separate scanning runs (angry and happy) with the masked condition (a neutral face) to measure brain activity when consciousness was below the level of awareness. After the task, the participants were given a posttest to identify whether an expression had been seen during the study or not. Results indicated that cannabis users had lower anterior cingulate and amygdalar activity during the presentation of both happy and angry masked affective stimuli compared to controls. Decreased activity in these regions indicates that chronic cannabis users exhibit differences in brain activity to emotional stimuli even at a subconscious level (Gruber et al., 2009). Overall, the studies illustrated prior show conflicting findings toward cannabis's effects for amygdala reactivity when processing threatrelated stimuli. Variables that could account for these discrepancies are type of task conducted, as some studies use tasks that require passive viewing of emotional stimuli (Spechler et al., 2015), others use rapidly presented masked faces (Gruber et al., 2009), while some have images that change in size during the course of the task, described as looming images (Blair et al., 2019). Furthermore, some studies examined group differences in brain activity between cannabis users and controls, while others investigated associations between CUD symptom severity and brain response, indicating that analytical differences may also help explain differences across findings.

Another comorbid factor that may affect emotion processing is the presence of depression. Cornelius et al. (2010), found that amygdala reactivity is inversely related to level of cannabis use in individuals with CUD and major depressive disorder (MDD). This conclusion was drawn from a 3-month double-blind placebocontrolled study in which BOLD fMRI scans were performed prior to participants starting study medication (fluoxetine) and again 12 weeks later after the completion of pharmacological treatment. A threat-related amygdala reactivity paradigm was used during fMRI where subjects viewed emotional faces for a period of 2 s and selected one of two faces at the bottom of a computer screen, which was identical to a target face at the top. During the course of the study, five out of six participants decreased their personal cannabis use, and at study completion were seen to have increased amygdala reactivity, while the one person who increased cannabis use was found to have decreased amygdala reactivity. These results implicate amygdala reactivity is modulated through cannabis consumption due to its role in the endocannabinoid system, and that the differences in amygdala reactivity may have less to do with the presence of depression, and more to do with amount of cannabis consumed (Cornelius et al., 2010). However, a limitation to this study is the possibility that the use of cannabis may be a contributing factor to the development or sustainment of depression.

Theory of Mind (ToM) has been used in prior studies to evaluate ability to empathize with others and has been previously examined to understand biases toward negative emotions (Washburn et al., 2016). In a study by Roser et al. (2012), the effect of cannabis use on ToM was investigated with a task that was made up of six different cartoon stories with four pictures each, showing different scenarios to elicit empathy and emotional reactivity. In response to the ToM Task, cannabis users (who consumed cannabis  $\geq 3$  times/week for  $\geq 2$  years) had decreased activity in the left parahippocampal gyrus, the right precuneus and cuneus, while they had greater activity in the

left cuneus and the right anterior cingulate gyrus (CG) in comparison to controls. Overall, this study suggests that cannabis users may have measurable effects on how their brains process social information as they have deviation from normal activity patterns during the ToM task, and frequent chronic cannabis users may have dysfunctional mechanisms within the endocannabinoid system which resemble those who are at-risk for psychosis (Roser et al., 2012).

There have been some studies focused on cannabis's effects on the prefrontal cortex, and its interaction with the limbic system, such as the amygdala. There is evidence that cannabis use may be related to hypoactivity in response to emotional faces in distinct prefrontal areas. Leiker et al. (2019) examined the effects of CUD symptom severity in adolescent participants during an Expression Processing Task. During this task participants specified whether a face was male or female while viewing a series of photographs that displayed neutral or morphed (50%, 100%, or 150% intensity) happy or fearful expressions. CUD symptom severity was negatively correlated to reactivity within the rostromedial prefrontal cortex (rmPFC) and anterior cingulate cortex (ACC) in response to faces. Similarly, the neural systems of young adults may also be impacted by cannabis use. Wesley et al. (2016) studied young adult chronic cannabis users who consumed cannabis >2 times/day, >20 times/month, and >5 years. For the purposes of this study, a Modified International Affective Picture System task was administered during fMRI. This scanner task consisted of 100 photographic randomized stimuli (80 emotional images, and 20 neutral images), and participants were asked to indicate whether each image was positive, neutral, or negative. While there were limited differences in valence ratings between cannabis users and controls, patterns of brain activity differed between groups. Cannabis users exhibited hypoactive mPFC activity during evaluation of positive and negative images. Since the mPFC is known to deactivate during increased cognitive load, emotional images for cannabis users could represent increased demand for attention and working memory while performing the task (Wesley et al., 2016).

Furthermore, there is evidence that disordered cannabis use may increase neural connectivity of the central autonomic network in response to negative emotional stimuli. In a study conducted by Ma et al. (2020), 23 participants with CUD participated in an Emotional Face Matching Task with images of negative emotional stimuli (pictures of angry and fearful faces) and neutral-shape stimuli presented randomly. In the CUD group there was greater left amygdala to hypothalamus effective connectivity (EC) and greater right amygdala to bilateral fusiform gyri EC, which were both positively associated to participants' stress scores. Additionally, there was decreased brain activation in the left ventrolateral prefrontal cortex to bilateral fusiform gyri ECs, which was negatively associated with participants' stress scores. It is possible that cannabis use may lead to the development or perpetuation of stress-related disorders by increasing connectivity in circuits of the autonomic limbic system that puts one at risk for stress-related disorders and by decreasing connectivity in circuits of the autonomic limbic system that are protective against the development of these disorders (Ma et al., 2020). In another study focused specifically on negative emotional stimuli, Colizzi et al. (2018) recruited cannabis users and nonusers to determine the chronic effects of cannabis use on brain activity during a facial emotion task with varying intensities of fearful faces in which participants were asked to identify the gender of the face. No behavioral differences were found between groups, but cannabis users activated the CG and inferior parietal lobule more than nonusers. Increased activity in these areas could suggest greater responses to emotional states and increased fear response.

While the majority of research has been cross-sectional, emerging longitudinal studies highlight the potential long-term effects of cannabis use on emotion processing. In a study conducted by Heitzeg et al. (2015) negative emotionality and resiliency were examined in participants from the Michigan Longitudinal Study at three different time points, when participants were on average 13.4, 19.6, and 23.1 years of age. Participants were classified as heavy cannabis users (>100 occasions of cannabis use), or controls with minimal cannabis use (<10 occasions of cannabis use) at the last study visit. Additionally, at the mean age of 20.2 participants completed an emotional-arousal fMRI word task where words with positive or negative valence and arousal were presented in a block design. During this task, heavy cannabis users had less activation in the right insula, prefrontal cortex, and occipital cortex when viewing negatively valenced words. Activation of the dorsolateral prefrontal cortex to negative words in cannabis users was associated with future development of negative emotionality. Additionally, lack of activation of the cuneus/lingual gyrus in cannabis users compared to controls was associated with decreased resiliency, one of the facets used to assess participants' emotional functioning. In controls, resiliency, or one's ability to regulate emotions in challenging circumstances, strengthened across the three time points, however the lack of activation of the cuneus/lingual gyrus in cannabis users suggests that the development of resiliency may have been blunted due to the initiation of cannabis use. These findings suggest chronic cannabis use at the start of adolescence may negatively alter the development of healthy emotional outcomes (Heitzeg et al., 2015). Evidence for persisting emotion processing alterations in chronic cannabis users comes from a study of participants with cannabis dependence who were 28 days abstinent from cannabis use. Participants completed an emotion processing task comprised of four positive, four neutral, and six negative images that were presented for 2 s in a randomized order and viewed passively during an fMRI scan. Following the fMRI scan, participants were asked to rate their emotional perception of the images (in regard to valence and arousal) on the SAM scale. In participants with cannabis dependence, increased medial orbitofrontal cortex (mOFC) activity and stronger mOFC-dorsal striatal and mOFC-amygdala functional coupling was seen during the presentation of negative emotional stimuli. Thus, the findings suggest persistent alterations in emotion processing in cannabis dependent individuals, present even following abstinence (Zimmermann et al., 2018). A recent longitudinal study suggested that increased right amygdala reactivity to angry faces could significantly predict cannabis use 5 years later; thus, examining amygdalar response to socioemotional information may have important predictive utility for identifying those at risk for cannabis use (Spechler et al., 2020). Furthermore, a longitudinal study of substance-naïve adolescents who were followed from ages 10-12 to ages 12-15 found that among all of the neurocognitive tasks examined, performance on a facial emotion identification task was the strongest predictor of cannabis initiation during the study period. Specifically, individuals who were more likely to recognize a sad face were 30% more likely to initiate cannabis use, which could reflect a bias toward negative emotions in those who go on to

use cannabis (Fishbein et al., 2016). However, more longitudinal studies are needed to test this relationship.

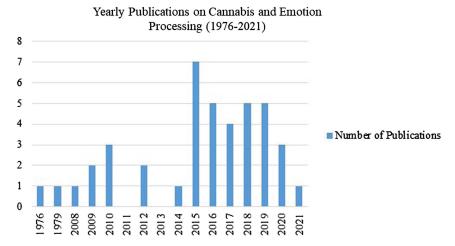
Emerging literature on the effects of cannabis use on emotion processing utilizing fMRI indicates a hypoactive effect of cannabis on emotion processing in the frontal lobe, including the prefrontal cortex. The prefrontal cortex is implicated in processes related to identification and differentiation (Siddiqui et al., 2008), which could be why cannabis users have a harder time identifying the intensity of an emotion, as well as differentiating between what emotion is being displayed to them. Additionally, there are discrepancies in the literature regarding the effects of cannabis use on amygdalar function. In some studies, amygdala activity is greater in response to fearful or threatening faces or predictive of future cannabis use, while other studies suggest that amygdala activity is lower in cannabis users relative to controls. Further studies, including longitudinal designs are needed to determine preexisting neural activity in emotion processing brain regions, including the amygdala, that could predispose individuals to use cannabis and distinguish those from the effects of cannabis use on brain activity after substance use initiation. Furthermore, greater standardization in task design when examining amygdala reactivity in response to cannabis use may be helpful to determine whether variations in task requirements may have accounted for differences in previous study findings.

## **Conclusions**

Findings from this narrative review suggests that cannabis and emotion processing represents an emerging research area as the majority of studies on this topic have been published within the last 10 years (Figure 1), more than half of which have been published even more recently in the past 5 years. Studies across humans indicate that both acute and chronic cannabis use may be associated with effects on emotion processing. Findings include elevated hostility, lack of responsiveness to emotional stimuli, and difficulties with accuracy and response time when identifying and differentiating between emotions (Ansell et al., 2015; Papini et al., 2017; Platt et al., 2010; Somaini et al., 2012; Wade et al., 2021). Additionally, the components of cannabis, specifically CBD and THC, modulate emotion processing differently. For example, THC increases anxiety, while CBD tends to decrease anxiety while processing fearful social stimuli (Bhattacharyya et al., 2017; Fusar-Poli et al., 2009).

Across EEG studies, there is evidence that cannabis users have decreased P3 amplitudes to emotional stimuli. In addition, there are opposing P1 and P3 amplitudes to positive versus negative emotional stimuli (Torrence et al., 2019; Troup et al., 2016). In general, fMRI studies indicate that cannabis has a hypoactive effect on emotion processing in the frontal lobe, including the prefrontal cortex and medial prefrontal cortex (Blair et al., 2019; Heitzeg et al., 2015; Leiker et al., 2019; Wesley et al., 2016). Cannabis use may also affect amygdalar reactivity during emotion processing (Bhattacharyya et al., 2017; Cornelius et al., 2010; Fusar-Poli et al., 2009; Gruber et al., 2009; Leiker et al., 2019; Phan et al., 2008; Spechler et al., 2015, 2020). However, conflicting results suggest more studies are needed to determine the directionality of these effects. Furthermore, cannabis use has been shown to affect functional connectivity in the brain between the basolateral and

Figure 1
Yearly Publications on Cannabis and Emotion Processing (1976–2021)



*Note.* This histogram illustrates the number of yearly publications related to cannabis and emotion processing that fall within the scope of the current review article, published between 1976 and 2021. Forty-one publications were identified; 33 of 41 were published in the last 10 years, and 23 of 41 were published in the last 5 years, suggesting behavioral, physiological, and neural studies on cannabis and emotion processing represent an emerging area of cannabis research. See the online article for the color version of this figure.

superficial subregions of the amygdala and the rACC and the mPFC (Gorka et al., 2015).

Limitations across the current literature include lack of detail on method of consumption and amount of cannabis used across participants, as cannabis can be smoked, vaporized, ingested, and used topically. Future studies are needed that categorize cannabis users by duration of use, age of cannabis use initiation, and frequency of daily use. Overall, more research on individual differences is needed to determine the effects of sex, polysubstance use, and comorbid psychiatric disorders on socioemotional functioning, and studies should also expand to middle-aged and older adult cannabis users, as the majority of currently published research is limited to adolescents and young adults. Additionally, there are a lack of longitudinal studies of emotion processing in cannabis users. Specifically, there appear to be no longitudinal EEG studies examining the effects of cannabis use on emotion processing, and no studies of the acute effects of cannabis use on emotion processing using EEG.

Further studies are critical to clarify the role of cannabis on regions of the brain involved in emotion processing. Existing research suggests cannabis has atypical effects on emotion processing, such that cannabis users have deficits recognizing and evaluating emotions. Additionally, there are differences in how cannabis users respond to affective information compared to healthy controls, indicated by altered brain responses, sometimes in the absence of behavioral differences. All of these factors may put cannabis users at risk for negative impacts in their interpersonal relationships and may lead to the increase of cannabis use to cope with these arising problems, which perpetuates the cycle of use and emotional distress. Furthermore, cannabis use could be a factor in the development or perpetuation of comorbid psychiatric illnesses. Clarification on the role cannabis plays in emotion processing can lead to understanding

its effects on socioemotional functioning and provides a means to create a basis for clinical interventions to aid those who have altered emotion processing related to their cannabis use.

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