



Full length article

Marijuana dependence moderates the effect of posttraumatic stress disorder on trauma cue reactivity in substance dependent patients



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ABSTRACT

Background: Individuals with posttraumatic stress disorder (PTSD) are at heightened risk for marijuana use. Although extant studies speak to the importance of examining the co-occurrence of PTSD and marijuana use as it relates to a variety of clinically-relevant outcomes, no studies have explored the way in which marijuana use may affect in-the-moment emotional responding among individuals with PTSD. Thus, the purpose of this study was to explore the role of marijuana dependence in the relation between PTSD and subjective and biological emotional reactivity in response to a trauma cue.

Methods: Participants were 202 patients with and without current PTSD consecutively admitted to a residential SUD treatment facility. Patients were administered diagnostic interviews, and subjective (negative affect) and biological (cortisol) reactivity to a personalized trauma cue were assessed.

Results: Whereas current PTSD was associated with greater subjective emotional reactivity among participants without marijuana dependence, there were no significant differences in subjective emotional reactivity as a function of PTSD status among participants with marijuana dependence. Moreover, marijuana dependent participants (with and without PTSD) reported less subjective emotional reactivity than participants with PTSD and without marijuana dependence. No significant findings were obtained for cortisol reactivity.

Conclusions: Findings suggest that patients with co-occurring PTSD and marijuana dependence may experience alterations in their emotional processing in response to a trauma cue (i.e., dampening of arousal). Additional research is required to clarify the specific mechanisms through which marijuana use influences emotional reactivity and fear-related emotional processing, as well as how such effects may influence PTSD treatment.

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1. Introduction

Posttraumatic stress disorder (PTSD) is characterized by the presence of re-experiencing, avoidance, and hyperarousal symptoms, as well as negative alterations in cognition and mood, following exposure to a traumatic event (American Psychiatric Association [APA], 2013). The symptoms of PTSD have the potential to result in broad functional impairment (Rodriguez et al., 2012) and contribute to the development of other psychiatric disorders (Kessler et al., 1995), especially substance use disorders (SUD; Chilcoat and Menard, 2003). Within the extant literature, the majority of studies examining the co-occurrence of PTSD and SUD

have focused on alcohol or cocaine use disorders (e.g., Coffey et al., 2007; Jakupcak et al., 2010; Waldrop et al., 2007); however, there is an emerging body of literature exploring the connection between PTSD and marijuana use.

Research has shown that individuals with PTSD are at heightened risk for marijuana use. For example, in the National Comorbidity Survey, current PTSD was found to be uniquely associated with increased rates of past year marijuana use and daily marijuana use (Cougale et al., 2011). Likewise, PTSD symptom severity demonstrates a significant positive association with frequency of marijuana use (Bonn-Miller et al., 2011a; Bremner et al., 1996). Notably, the relation between PTSD and marijuana use is also clinically-relevant. Within a sample of military veterans with PTSD, Bonn-Miller et al. (2013) found that a pretreatment diagnosis of a marijuana use disorder was associated with weaker response to residential PTSD treatment even when other relevant factors (e.g., trauma severity) were considered. Similarly, PTSD symptom sever-

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ity is positively associated with using marijuana to cope, marijuana use problems, and severity of marijuana withdrawal symptoms (Boden et al., 2013; Bonn-Miller et al., 2011b, 2007; Earleywine and Bolles, 2014). Although these studies highlight the importance of examining the co-occurrence of PTSD and marijuana use as it relates to a variety of clinically-relevant outcomes, no studies to date have explored the way in which marijuana use may affect in-the-moment emotional responding among individuals with PTSD.

There is reason to believe that the presence of marijuana use could influence emotional responding to trauma cues among individuals with PTSD; however, the precise way in which emotional responding would be affected is unclear. For example, it is possible that individuals with PTSD may exhibit more intense emotional responses to a trauma cue in the context of marijuana use—consistent with findings that marijuana users report greater emotion dysregulation than non-users (Bonn-Miller et al., 2008). Thus, it is possible that marijuana use may further exacerbate the heightened emotion dysregulation found in PTSD (Tull et al., 2007), contributing to greater trauma cue emotional reactivity within this population. Moreover, findings that individuals with marijuana dependence exhibit greater subjective reactivity to a biological challenge (CO₂ inhalation) than those with marijuana abuse (Bonn-Miller and Zvolensky, 2009) suggest that there may be a dose-response relationship with regard to the level of marijuana use and emotional reactivity.

Alternatively, an emerging body of research on the effects of marijuana use on emotional responding suggests that marijuana use may dampen emotional reactivity in response to a trauma cue among individuals with PTSD. The amygdala (an area of the brain implicated in the development and maintenance of pathological anxiety and PTSD; Liberzon and Sripada, 2007) includes a high density of CB₁ cannabinoid receptors (Perra et al., 2008), activation of which diminishes anxiety responses and amygdala activation in response to aversive stimuli (Patel et al., 2005). Consequently, ingestion of Δ^9 -tetrahydrocannabinol (THC), the primary psychoactive ingredient in marijuana and a selective CB₁ agonist, may correspond with attenuated threat-related emotional reactivity among individuals with PTSD. In support of this notion, studies have demonstrated that marijuana use is associated with reduced amygdala reactivity among individuals with comorbid marijuana dependence and major depression (Cornelius et al., 2010). Likewise, administration of THC in healthy recreational marijuana users (i.e., marijuana users who do not meet criteria for a marijuana use disorder) significantly reduced amygdala reactivity in response to threat signals (Phan et al., 2008). Moreover, Van Leeuwen et al. (2011) found that repeated marijuana users exhibit lower stress reactivity levels (as indexed by cortisol levels) than individuals who

have never used tobacco or marijuana in their lifetime. Finally, individuals with marijuana dependence have been found to exhibit a reduced subjective and biological sensitivity to negative emotion cues (i.e., unpleasant pictures), relative to abstinent marijuana users and healthy controls (Somaini et al., 2012).

The purpose of the current investigation was to explore the role of marijuana dependence in the relation between PTSD and subjective and biological emotional reactivity in response to personalized trauma cues. This investigation was carried out in a sample of substance dependent patients in residential SUD treatment—a clinical population at high-risk for both PTSD and marijuana dependence (Chen et al., 2011). Given the absence of research in this area, as well as conflicting evidence with regard to the particular impact of marijuana dependence on emotional responding in PTSD, no specific hypotheses were made.

2. Method

2.1. Participants

Participants for the current study included 202 patients (100 women) from a SUD inpatient treatment facility who reported exposure to at least one potentially traumatic event. Participants ranged from 18 to 60 years of age (Mean = 34.32, SD = 10.10) and were ethnically diverse (60.4% White; 36.6% African American; 1.5% Latina/o). With regard to educational attainment, 34.1% of participants reported receiving their high school diploma or GED and an additional 38.1% reported completing some form of higher education. The majority of participants were unemployed (67.3%) and had an annual household income of less than \$20,000 (66.3%). Additional clinical and diagnostic data on the participants is presented in Table 1.

2.2. Measures and stimuli

2.2.1. Diagnostic assessment measures. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First et al., 1996) was used to assess for current SUD, including current marijuana dependence. To establish current PTSD diagnoses, all participants were interviewed using the DSM-IV version of the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1990). The CAPS is a structured PTSD diagnostic interview and the most widely used measure of PTSD (Elhai et al., 2005). It assesses the frequency and intensity of the 17 DSM-IV (APA, 2001) PTSD symptoms (plus eight associated symptoms). Frequency items are rated from 0 (never or none/not at all) to 4 (daily or almost every day or more than 80%). Intensity items are rated from 0 (none) to 4 (extreme). The Item Severity ≥ 4 (ISEV4) rule, which requires that at least one re-experiencing, three avoidance/emotional numbing, and two hyperarousal symptoms have a severity rating (frequency + intensity) of ≥ 4 , was used to establish PTSD diagnoses. Frequency and intensity ratings were also summed to create an overall PTSD symptom severity score (Weathers et al., 1999). The CAPS has adequate interrater reliability (0.92–0.99) and convergent validity with the SCID-I (First et al., 1996) and other established measures of PTSD (Weathers et al., 2001). In addition, the robust psychometric properties of the CAPS have been supported in a variety of combat and civilian samples, including patients with substance dependence (e.g., Blake et al., 1990; Brown et al., 1996; Shalev et al., 1997; Weathers et al., 2001).

SUD patients with (vs. without) PTSD exhibit more severe clinical presentations, including elevated rates of co-occurring mood, anxiety, and personality disorders (Najavits et al., 1998; Mills et al., 2006; Tull et al., 2013a). Therefore, to ensure that any observed relations are unique to PTSD rather than elevated levels of psy-

Table 1
Diagnostic and clinical data across all participants.

	% Present
Posttraumatic stress disorder	26.7%
Major depressive disorder	29.2%
Panic disorder with/without agoraphobia	26.7%
Social anxiety disorder	24.8%
Obsessive-compulsive disorder	12.9%
Generalized anxiety disorder	33.7%
Alcohol dependence	66.3%
Cocaine dependence	59.4%
Opioid dependence	25.2%
Marijuana dependence	29.2%
Sedative dependence	21.8%
Stimulant dependence	21.8%
Hallucinogen dependence	3.5%
Borderline Personality disorder	35.6%
Psychotropic Medication use	51.0%

Note: All diagnoses are current.

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