

Towards a Better Understanding of Cannabis and PTSD Recovery: Exploring Outcomes and Possible Mechanisms

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Funding provided by National Institute of Drug Abuse, R34DA040034

39% - 90% of
Americans endorse
lifetime traumatic
stress exposure

Sexual assault
Domestic violence
Combat
Physical assault
Accidents
Childhood abuse
Natural disaster
Life threatening illness
Sudden death

Sequelae of trauma
exposure

Posttraumatic stress
disorder (PTSD)
Depression
Substance abuse
Suicide
Impaired physical
health

PTSD Symptoms

Intrusive memories
Nightmares
Avoidance
Hypervigilance
Concentration
difficulties
Sleep difficulties
Unhelpful beliefs
Lack of interest

Recovery following Trauma Exposure

- Approximately **half** of rape victims have post-traumatic stress (PTSD) symptoms 3 months later
- Reflecting a failure in natural recovery
- Failure in natural fear extinction thought to be key mechanism in the persistence of PTSD (Mahan & Ressler, 2012)

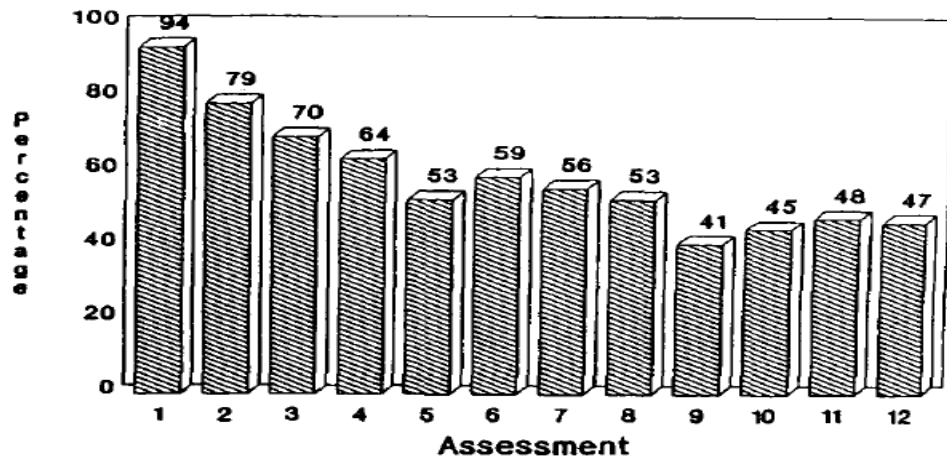
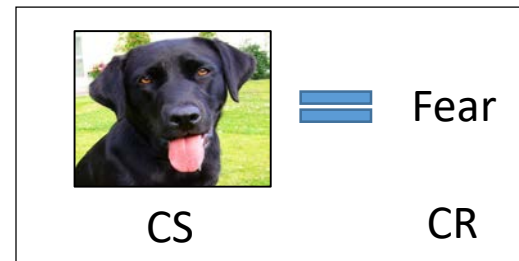
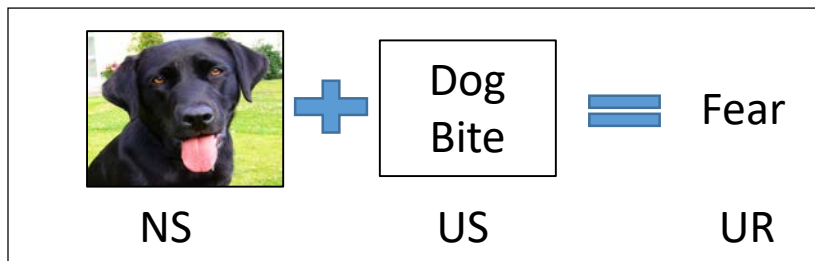


Fig. 1. Percentage of victims with PTSD.

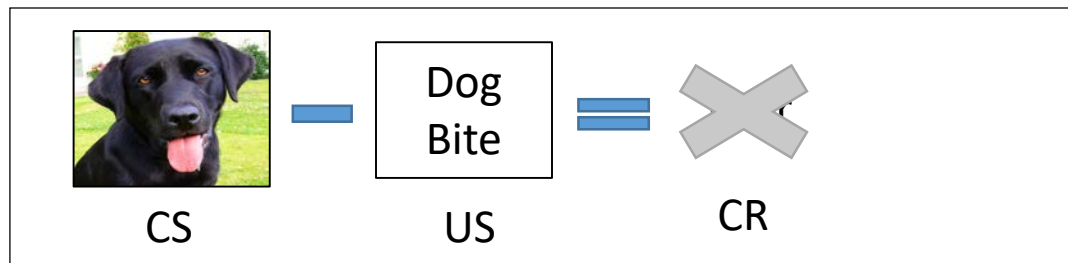
Rothbaum, Foa, Riggs, Murdock, & Walsh (1992)

Fear Conditioning and Extinction Learning

■ Classical fear conditioning

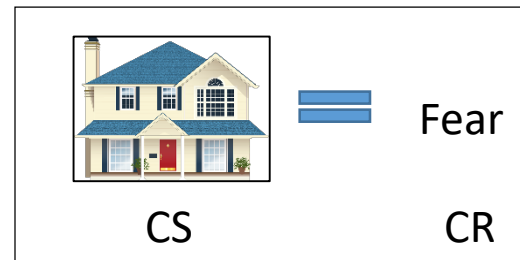
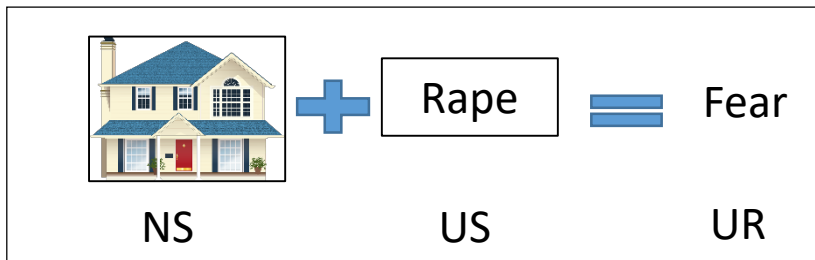


■ Fear extinction

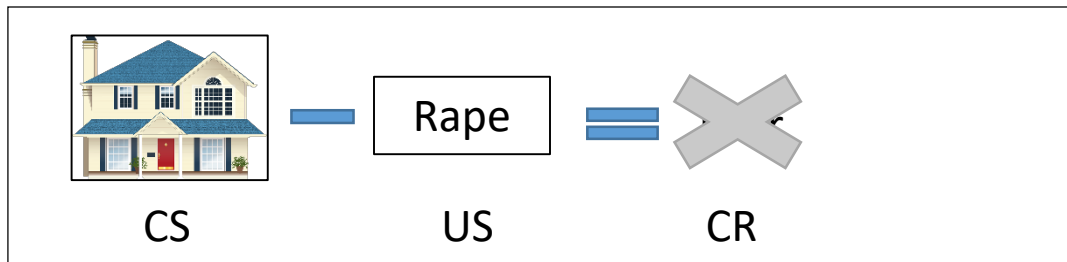


Fear Conditioning and Extinction Learning

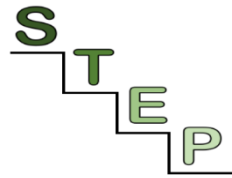
■ Classical fear conditioning



■ Fear extinction



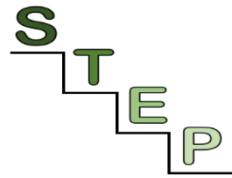
Psychotherapies based on extinction learning have large effects in decreasing PTSD symptoms



Intervention	<i>N</i>	Effect Size (<i>g</i>)
All Psychotherapies	76	1.14
Cognitive Therapies	10	1.63
Exposure Therapies	27	1.08
Mixed Cognitive and Exposure	14	1.38
EMDR	11	1.01
All Medications	56	0.42
SSRIs	20	0.48

(Watts et al., 2013)

Overlap of Trauma Exposure, PTSD and Cannabis Use



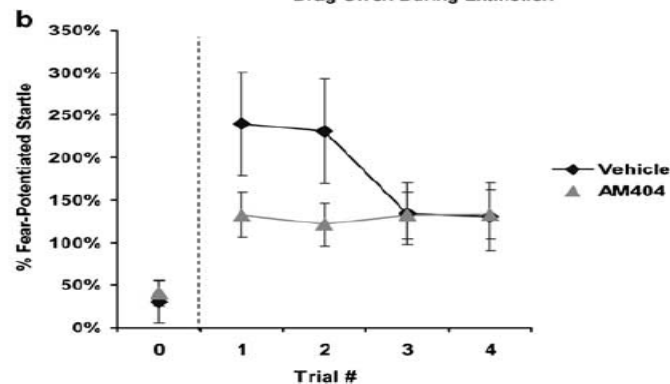
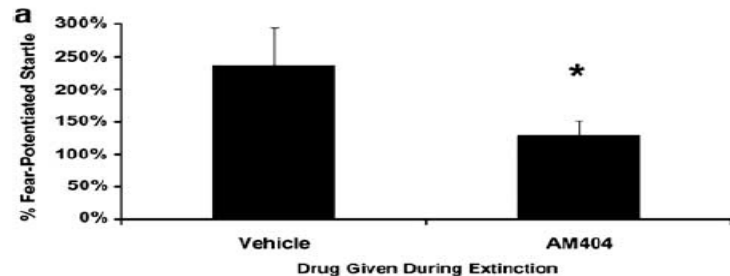
- Rates of cannabis use have increased substantially since 2001 in the US (Hasin et al., 2015)
- Individuals with PTSD are 2.5x more likely to report lifetime cannabis use and almost 2x more likely to report daily cannabis use in the last year (Cougler et al., 2011)
- PTSD is a primary reason that individuals seek out cannabis in states that have legalized medical cannabis (Bowles, 2012)
- Why do patients with PTSD use cannabis? (Bonn-Miller et al., 2010; Bremner et al., 1996)
 - Distress tolerance
 - Symptom management
 - Hyperarousal symptoms (e.g., sleep)

Cannabis as a Treatment for PTSD

- Targeting the endocannabinoid system as treatment for PTSD (Korem et al., 2015)
 - Cannabinoid receptors (CB₁) are implicated in processing of fear, stress, emotion, and reward in the brain
- Potential therapeutic benefits
 - Extinction enhancer- increase the process of new learning associated with recovery
 - Manage the emotional symptoms (e.g., capitalize on anxiolytic effects of cannabis)

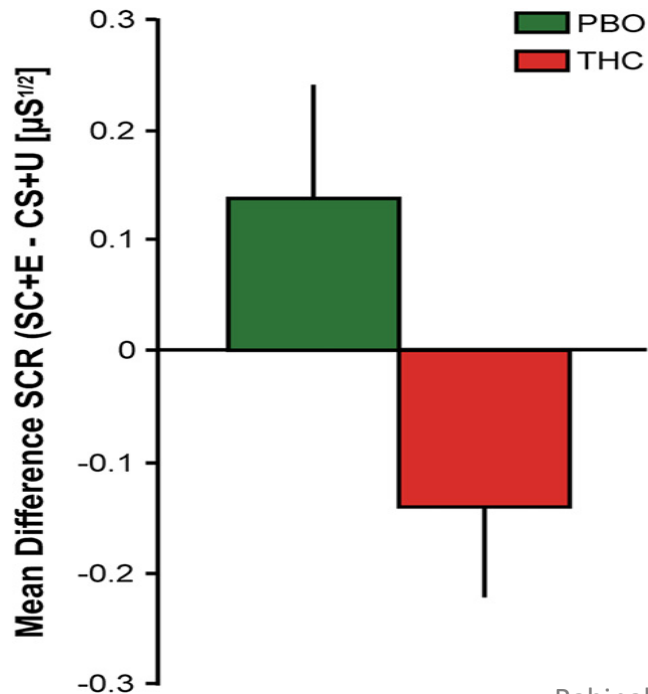
Effects of CB₁ Agonists on Extinction Learning

- Endogenous cannabinoid system represents major therapeutic target for anxiety-related disorders such as PTSD
- In rodents, augmented cannabinoid receptor activation typically facilitates extinction (Papini et al., 2015)
- Though chronic higher doses may impair extinction (Lin, Mao, Chen, & Gean, 2008; Pamplona, Prediger, Pandolfo, & Takahashi, 2006)

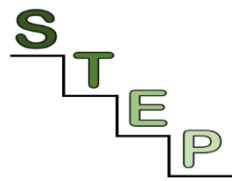


Human Studies of THC and Extinction

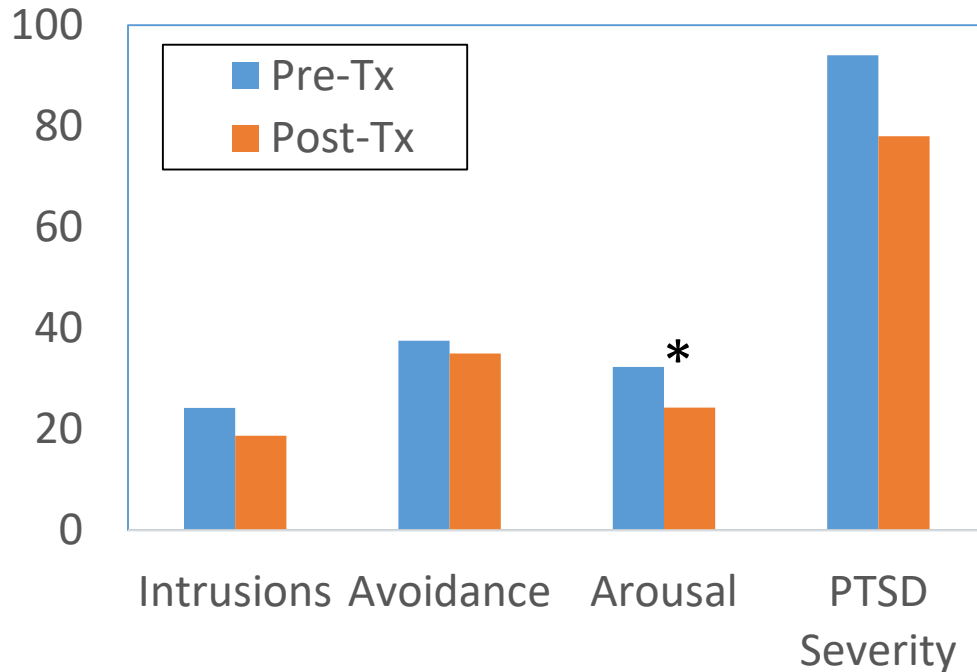
- Administration of THC facilitated short-term extinction as evidenced by decreased skin conductance response when tested 24 hours later (Rabinak et al., 2013)
 - THC prevented the recovery of fear
- Facilitation may be limited to acute effects (Klumpers et al., 2012) and was not found in chronic cannabis users (Papini et al., 2017)
- **All studies were done in healthy volunteers**



Two Small Trials have tested Cannabis as a Treatment for PTSD

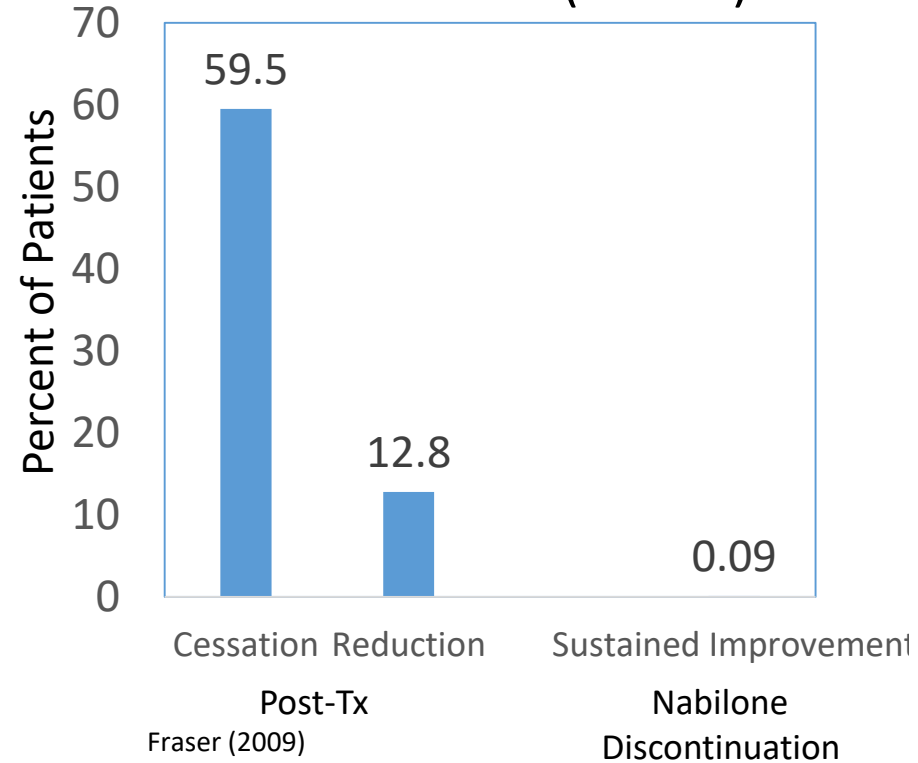


Oral THC for 3 wks ($N = 10$)



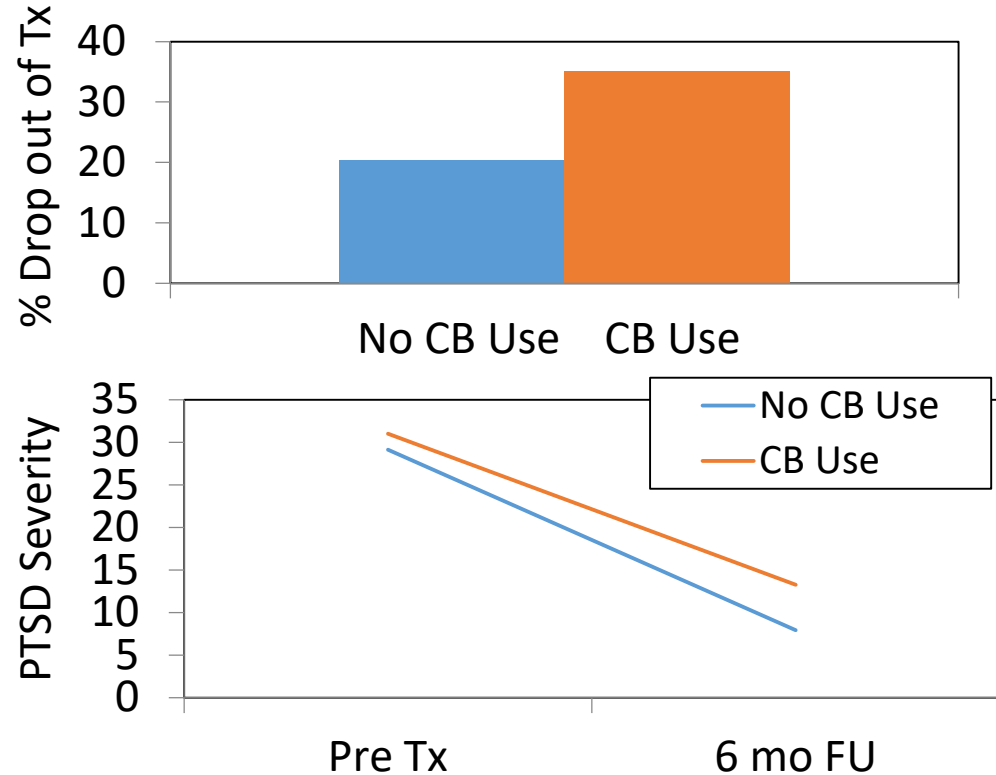
Roitman (2014)

Nabilone (CB agonist) for nightmares for 4-12 mths ($N = 47$)



Effects of Cannabis in Clinical Trials of Therapies for PTSD

- In clinical practice, cannabis use may impair PTSD treatment response to an extinction based treatment
- In our clinical trial ($N = 200$; R01MH066347/R01MH066348) cannabis use predicted
 - Higher likelihood of dropout
 - Slightly worse treatment response



Why this Matters?: Summary of Importance

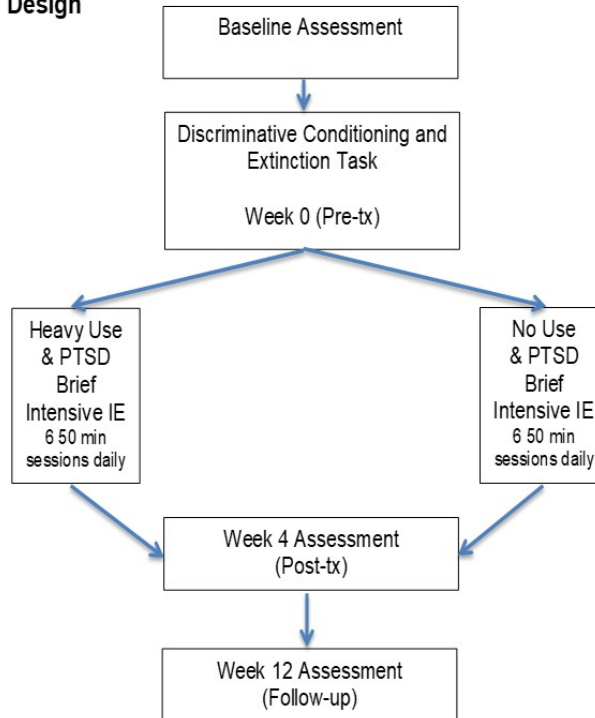
- PTSD is an approved condition for medical cannabis
 - Implies efficacy of approach
 - Data is limited and inconsistent
- Extinction learning contingent on approach behavior
 - Must approach conditioned stimulus
 - Amotivational effects of cannabis
- Anxiolytic effects are temporary
 - Biphasic effects associated with heavy and chronic use
 - Does not lead to behavior change

Moving Forward: Future Directions

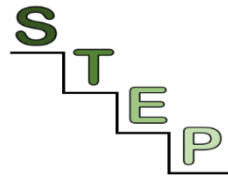
- Cannabis coupled with behavior changes to promote recovery
 - Therapeutic or natural
 - Better understanding of mechanisms of change
- Discrepancy between animal models and human data
 - Real world variability

Project STEP (R34DA040034): Study Design

Figure 1. Design



- Short term Exposure for PTSD (STEP)
- PTSD treatment trial
- Brief imaginal exposure (IE)
 - Facilitation effects
 - Decreasing burden, time
- Naturalistic cannabis use
 - THC/CBD levels at each exposure session



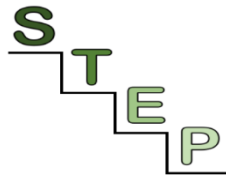
Thank you!

Thanks to collaborators including:

UWCATS: Lori Zoellner, Rick Ries, Heidi Ojahleto, Natalia Garcia, Elizabeth Marks, Rosemary Walker, and Peter Rosencrans

UW Psychiatry and Behavioral Sciences: Cynthia Stappenbeck and Nephi Stella

Funding Agency: NIDA



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