

CBD for Treating SUDs

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***CLINICAL EVIDENCE FOR CANNABIDIOL FOR
TREATING SUBSTANCE USE DISORDERS***

- **There is a perception in the lay literature that cannabis or cannabidiol has a potential to treat:**
 - Opiate Use Disorder (**OUD**)
 - Cannabis Use Disorder (**CUD**)
 - Tobacco Use Disorder (**TUD**)
 - Other SUDs

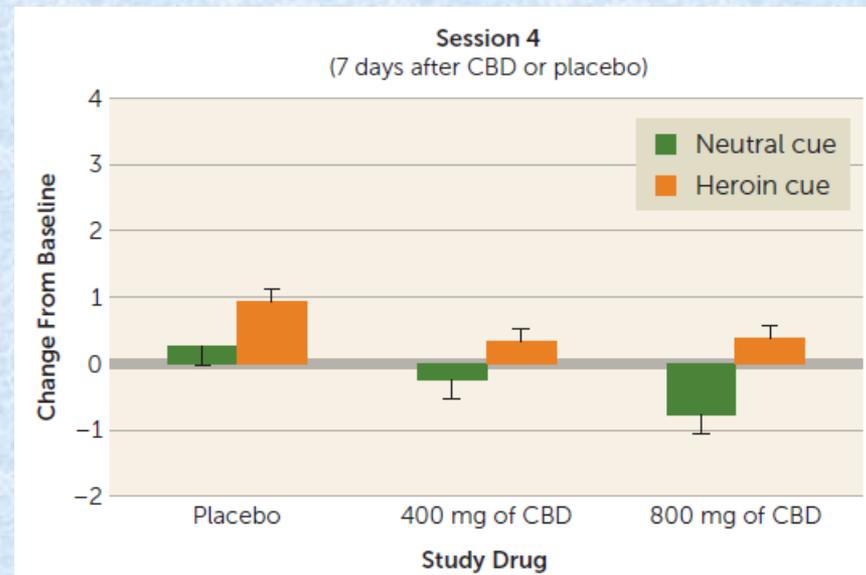
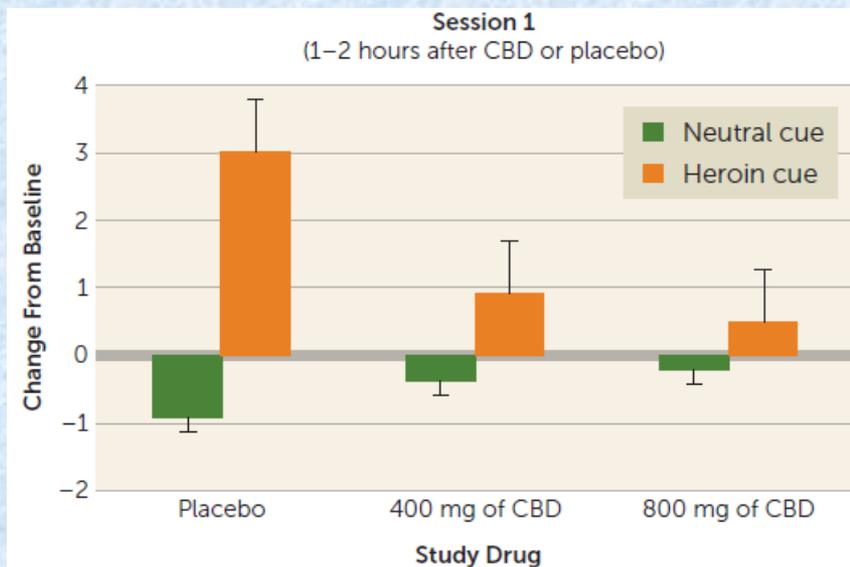
- **Bachhuber et al. (2014):** The states of California, Oregon and Washington, that had medical marijuana laws prior to 1999, had a 24.8% lower mean annual opioid overdose mortality in each year compared with states without medical cannabis laws (Alaska, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Mexico, Rhode Island, and Vermont).
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- **Finney, Humphreys and Harris (2015):** The legalization of medical marijuana reduced the number of overdose deaths from opioid pain relievers, an effect that strengthened in each year following the implementation of legislation.
- **However, population-based nature of the study does not establish a causal relation or evidence for changes in behavior of patients with pain.**
- **Reduction in opiate overdoses in those states could be related to factors including distribution of naloxone kits and overdose prevention efforts, utilization of prescription monitoring programs, greater access to medication assisted treatment and increased regulation of opiate prescriptions.**

- **Bradford and Bradford (2016):**
- **Medical marijuana laws significantly reduced the prescribing of opioids for pain.**
- **However, the current evidence is insufficient to support the claim that legalizing marijuana will reduce opioid use and opiate overdose deaths.**
- **Need large epi and clinical studies/trials are needed to show that cannabis or CBD can be effectively used to treat OUD**

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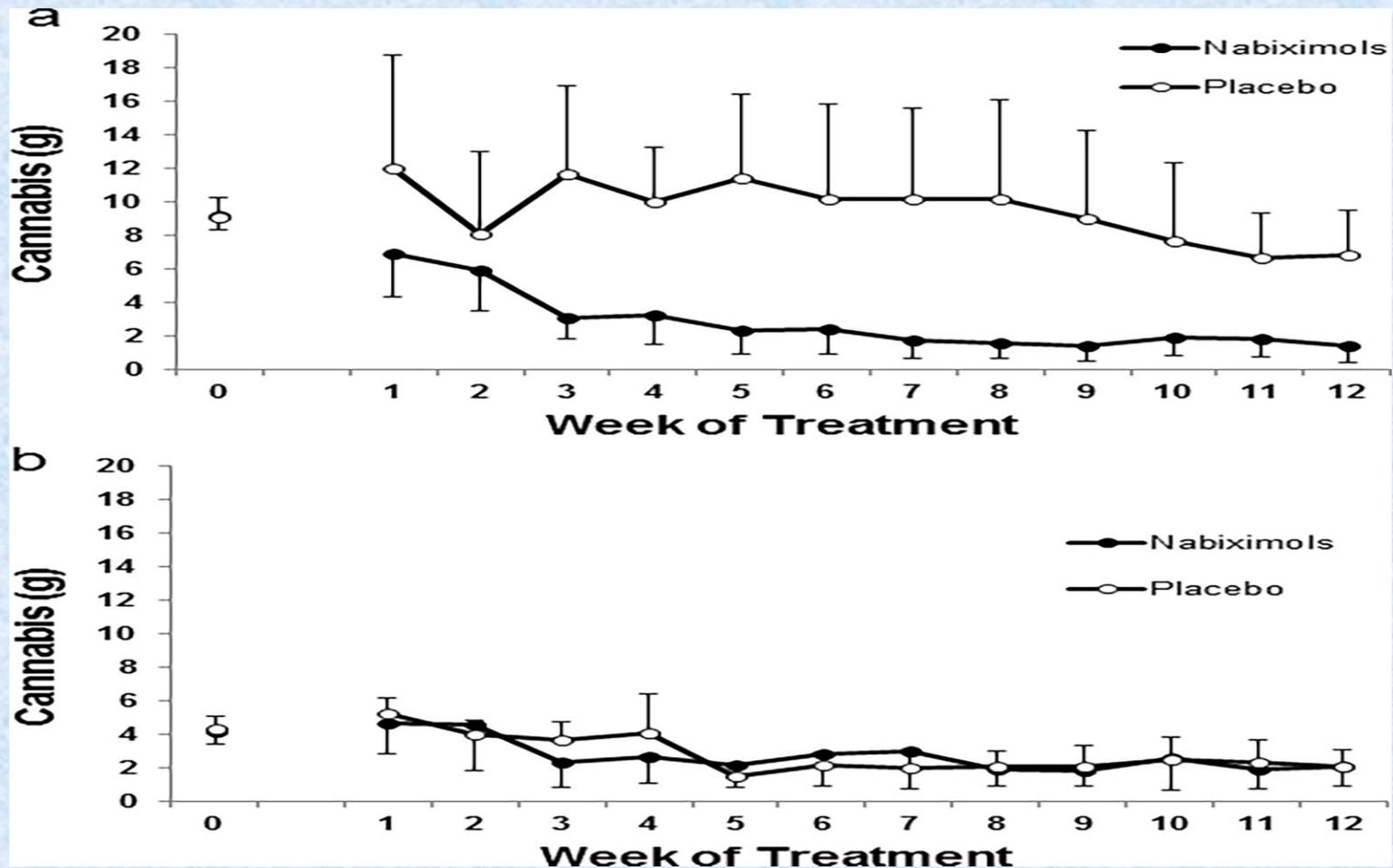
- **Craving and Anxiety in Drug-Abstinent Individuals with Heroin Use Disorder: A Double-Blind Randomized Placebo-Controlled Trial**
- Yasmin L. **Hurd**, et al. AJP, 2019
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- **Objective:** To investigate the potential of CBD to reduce cue-induced craving and anxiety, two critical features of addiction that often contribute to relapse and continued drug use, in drug-abstinent individuals with heroin use disorder.
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- **Methods:** Study type: An exploratory double-blind randomized placebo -controlled trial

- **Subjects:** Heroin abstinent men and women; (35 men, 7 women), 49.8 year old;
- **Dose:** 400 mg and 800 mg CBD once daily for 3 consecutive days or placebo
- **Duration and measures:** Examined for drug cue-induced craving and anxiety at 1, 2, and 24 hr for 3 and 7 days post dosing.
- **Secondary measures:** Participants' positive and negative affect, cognition and physiological status.



- **Results:**
- -Acute CBD administration, in contrast to placebo, significantly reduced both craving and anxiety induced by the presentation of salient drug cues compared with neutral cues, 7 days after the final short-term (3-day) CBD exposure.
- -CBD reduced the drug cue–induced physiological measures of heart rate and salivary cortisol levels.
- No differences between 400 mg or 800 mg doses.
- -No effects on cognition, and no serious adverse effects.
- **Conclusions:** CBD’s potential to reduce cue-induced craving and anxiety provides a strong basis for further investigation of CBD as a treatment option for OUD.
- **Need large epi and clinical studies/trials to show that cannabis or CBD can be effectively used to treat OUD**

- **CBD for Treating CUD**
- **Trigo et al. (2018):** In a RDBPC trial of 40 patients (20/treatment arm) were treated with THC+CBD [Sativex] doses of up to 113 mg of THC/105 mg CBD) or placebo for 12 weeks, combined with Motivational Enhancement Therapy and Cognitive Behavioral Therapy (MET/CBT).
- **Results:**
- **Although the amount of cannabis use decreased in both groups, but at higher doses of up to 20 sprays of Sativex, the difference was significant between treatment groups.**
- **Sativex combined with MET/CBT prevented the cannabis withdrawal and craving for cannabis. Sativex was well tolerated without adverse effects.**
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- **Recommendation:** Future trials with combination of doses above 20 sprays per day of nabiximols + MET/CBT should be explored further for its potential as a novel treatment approach for patients with cannabis dependence.



- **Fig 3. High/low study medication effects in cannabis use.** Circles (white placebo, black nabiximols) represent mean (+SEM) for total cannabis intake (g) per week as reported in the timeline follow back (TLFB) (week 0) and smoking diary (weeks 1 ± 12). In a) high medication users' subgroup (> 20 sprays on any treatment day) (n = 5 and 3 for nabiximols and placebo, respectively), in b) low medication users sub-group (< 20 sprays at any treatment day) (n = 8 and 11 for nabiximols and placebo, respectively). (Trigo et al. 2018).

Cannabidiol (CBD)

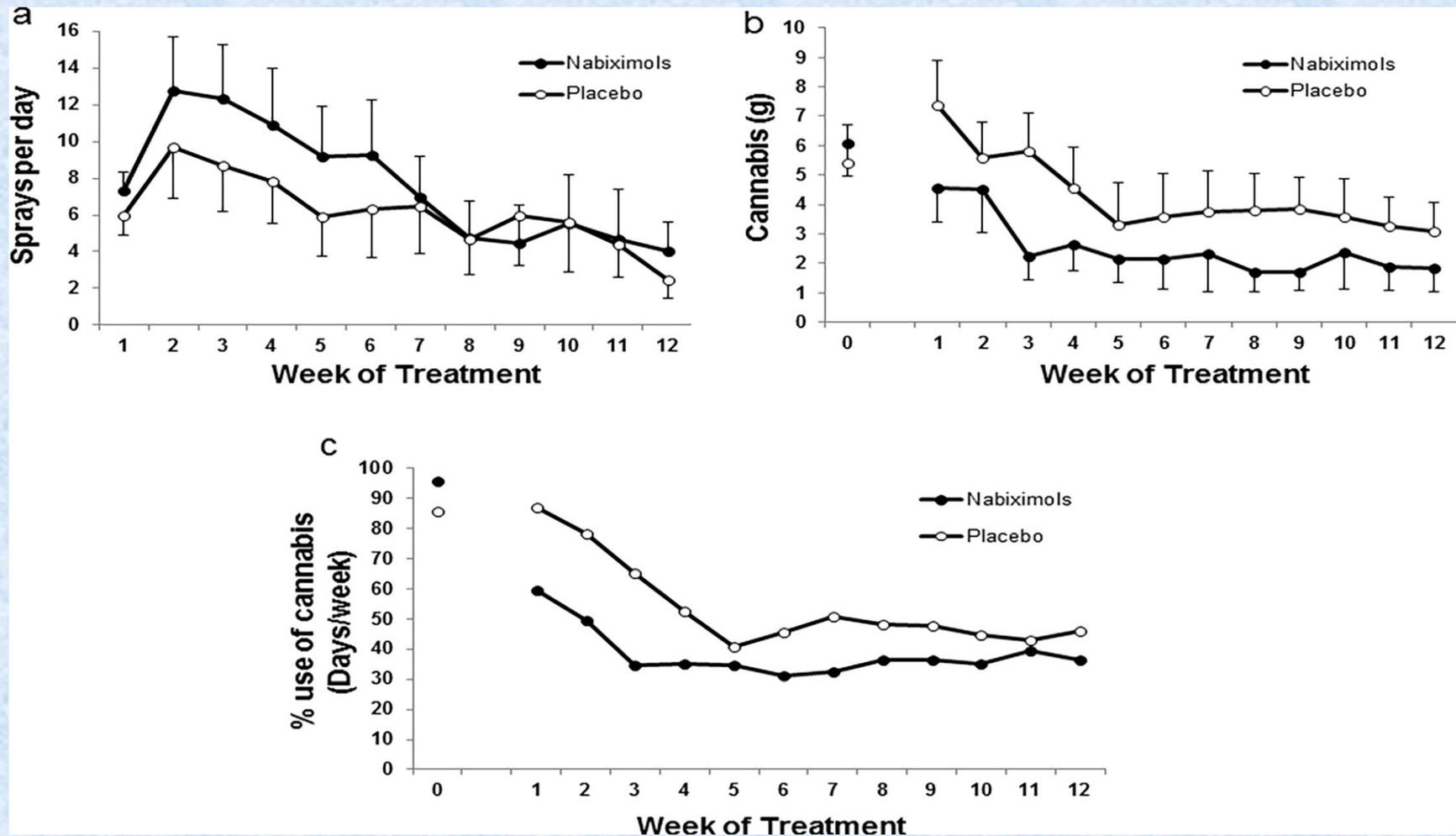
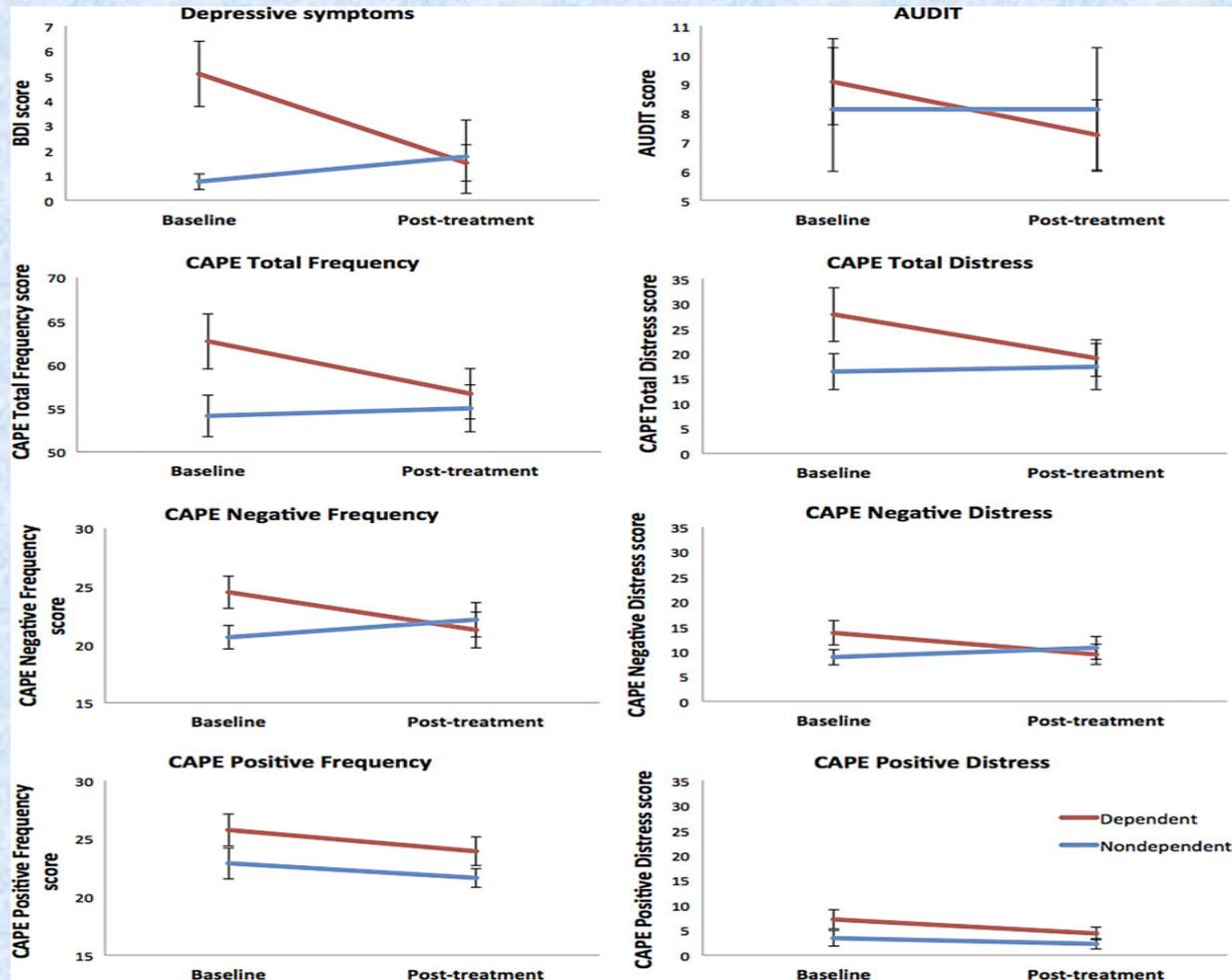


Fig 1: Study medication rates/effects in cannabis use. Circles (white placebo, black nabiximols) represent mean (+SEM). In a) self-titrated medication (sprays/day) as reported in the smoking diary. In b) total average cannabis intake (g) per week as reported in the timeline follow back (TLFB) (week 0) and smoking diary (weeks 1±12). In c) mean percentage of days using cannabis (nabiximols $n = 20 \pm 13$, placebo $n = 20 \pm 14$). (Trigo et al.)

- **Slowij et al. (2018):** CBD was also tested in 20 subjects (10/arm of CBD at 200 mg/day or placebo [miglyol 812 and softisan 378]) for 10 weeks to see if CBD would treat psychological symptoms and cognitive function in chronic cannabis users.
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- **Results:**
- **CBD was well-tolerated with no side effects or impact on psychological and cognitive functions during the treatment or 30-day follow-up periods.**
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- **Participants reported significantly fewer depressive and psychotic-like symptoms at post-treatment relative to base-line, and exhibited improvements in attentional switching, verbal learning, and memory.**
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- **The participants retrospectively reported reduced euphoria when smoking cannabis.**
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- FIG. 3. Psychological symptom changes from baseline to PT in dependent and nondependent cannabis users. Group-by-time interactions for BDI scores ($F_{1,18} = 8.29$, $p = 0.010$); Alcohol Use Disorders Identification Test scores ($F_{1,18} = 3.10$, $p = 0.095$); CAPE Total Symptom Frequency score ($F_{1,18} = 6.82$, $p = 0.018$); CAPE Total Symptom Distress scores ($F_{1,18} = 7.03$, $p = 0.016$); CAPE-negative symptom frequency scores ($F_{1,18} = 12.64$, $p = 0.002$); CAPE-negative symptom distress scores ($F_{1,18} = 12.83$, $p = 0.002$), and CAPE-positive symptom frequency scores ($F_{1,18} = 0.21$, $p = 0.649$). Wilcoxon signed-rank Test for CAPE-positive symptom distress scores: dependent users $Z = 2.11$, $p = 0.035$; nondependent users $Z = 0.92$, $p = 0.356$. (Slowij et al.)

- Solowij et al.
- **Increased plasma CBD concentrations were associated with improvements in attentional control and beneficial changes in psychological symptoms.**
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- **Greater benefits were observed in dependent than in nondependent cannabis users.**
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- **Conclusions:** Prolonged tx with CBD appeared to have promising therapeutic effects for improving psychological symptoms and cognition in regular cannabis users.
- **CBD may be a useful adjunct treatment for cannabis dependence.**

- **Beale et al. (2018):**
- **CBD was tested in chronic cannabis users to see if CBD treatment would protect against brain structural harms conferred by chronic cannabis use.**
- **CBD showed restorative effect on the subicular and CA1 subfields in current cannabis users, especially those with greater lifetime exposure to cannabis.**
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- **CBD for Treating TUD**
- **In a randomized, double-blind, placebo controlled cross-over study (Hindocha et al.2018):**
- **A single dose of 800 mg oral dose of CBD, reduced the salience and pleasantness of cigarette cues, compared with placebo, after overnight cigarette abstinence in dependent smokers.**
- **But CBD did not influence tobacco craving or withdrawal or any subjectively rated side effects.**

- **CBD for Treating TUD**

- **In a study by Morgan et al. (2013), 24 tobacco smokers were randomized to receive an inhaler of CBD or placebo for one week.**
- **They were instructed to use the inhaler whenever they felt a craving to smoke.**
- **Over the course of one week, those taking the CBD inhaler reduced their number of cigarettes smoked by 40% while those receiving the placebo inhaler did not decrease the number of cigarettes they smoked.**

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SUMMARY:

- *Limited evidence rom to suggest that would support the use of CBD as medicine for the treatment of substance use disorders such as OUD, CUD and TUD.*
- *Well-designed RDB-placebo controlled trials are needed to obtain the FDA approval to use CBD for the treatment of SUDs.*

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