The pharmacological and expectancy effects of cannabis on problem behaviors

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Acknowledgments

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Adverse Effects of Marijuana

Marijuana and Psychiatric Disorders: Emotional Dysregulation

Disinhibition and Impulsive Decision-Making: Driving and Marijuana

Marijuana and Alcohol Co-Use

Prezi

Disinhibition and Impulsive Decision-Making: Driving and Marijuana

Driving and Marijuana

- Marijuana doubles the risk of motor vehicle crashes (MVC) and fatalities
- Marijuana-positive drivers involved in fatal MVCs increased after marijuana legalization in CO and in CA
- Marijuana causes impairment of psychomotor skills related to driving
- Marijuana-intoxicated drivers unsuccessfully attempt to compensate for impairment

What Do Marijuana Users Say?

- Most marijuana users have driven after smoking marijuana (83%) or while smoking marijuana (78%)
- Marijuana users endorse low perceived risk, and negligible perceived impairment or even safer driving after marijuana use
- ***"When I drive after smoking, I am more careful (65%) pr as careful (33%) as when driving sober" e.g. more careful not to speed (70%)***
- More positive or permissive driving-related peer norms and attitudes predict greater likelihood of driving under the influence of marijuana and smoking marijuana while driving

Aston, Merrill, McCarthy & Metrik (2016). JSAD, 77, 309-316.

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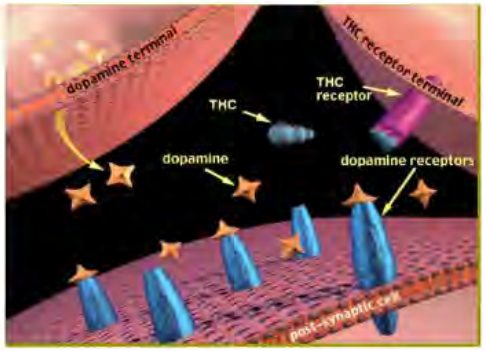
Acute Effects of Marijuana on Inhibitory Control and Impulsive Decision Making

What are the mechanisms whereby
marijuana may influence impulsive and risky decision-making?

Mechanisms of Drug Response



Activation of CB1 receptors modulates the dopamine system by increasing DA in the nucleus accumbens. Increased activity of dopaminergic neurons is implicated in impulsivity.

Drug-related behavior is influenced by **pharmacological action** of a drug and by **associations in memory** that become automatically activated under various conditions

Expectancy Mechanism

Environmental Stimuli → Belief about drug **content** → Belief about drug **effect** → Response

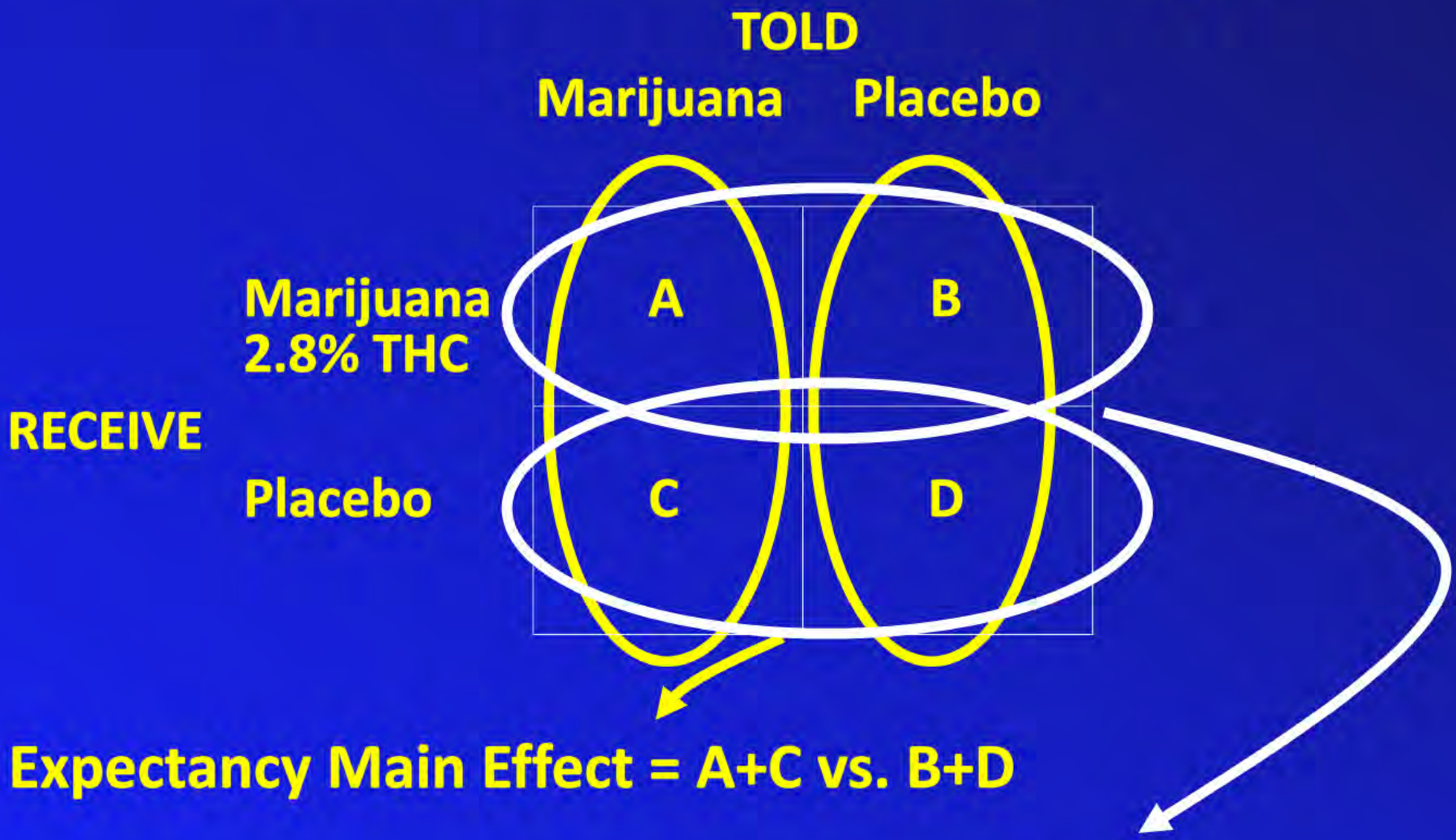
Salient Cues + Instructional Set → Stimulus Expectancy → Response Expectancy → Behavioral Response and Placebo Effect

"I am smoking marijuana"

"I feel relaxed"

"Marijuana helps me relax"

Balanced Placebo Design



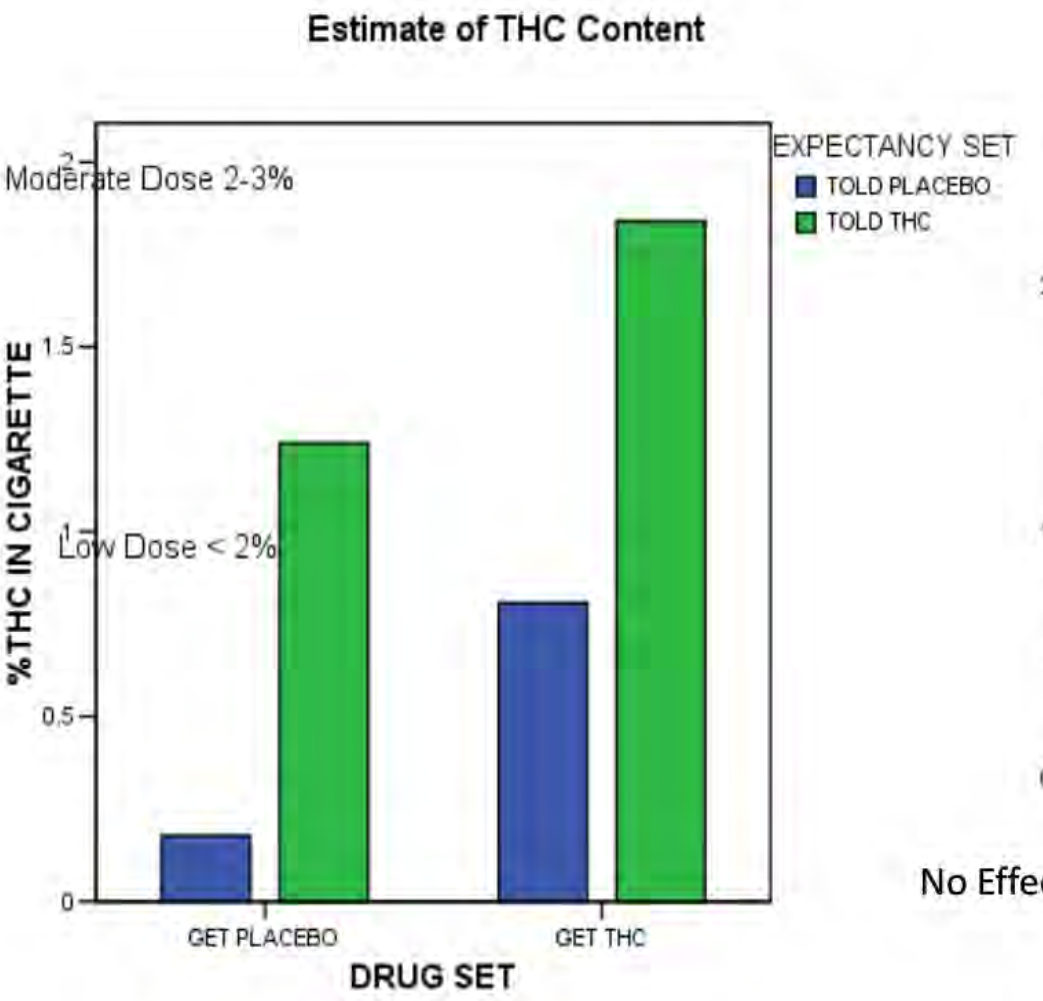
Experimental Smoking Session

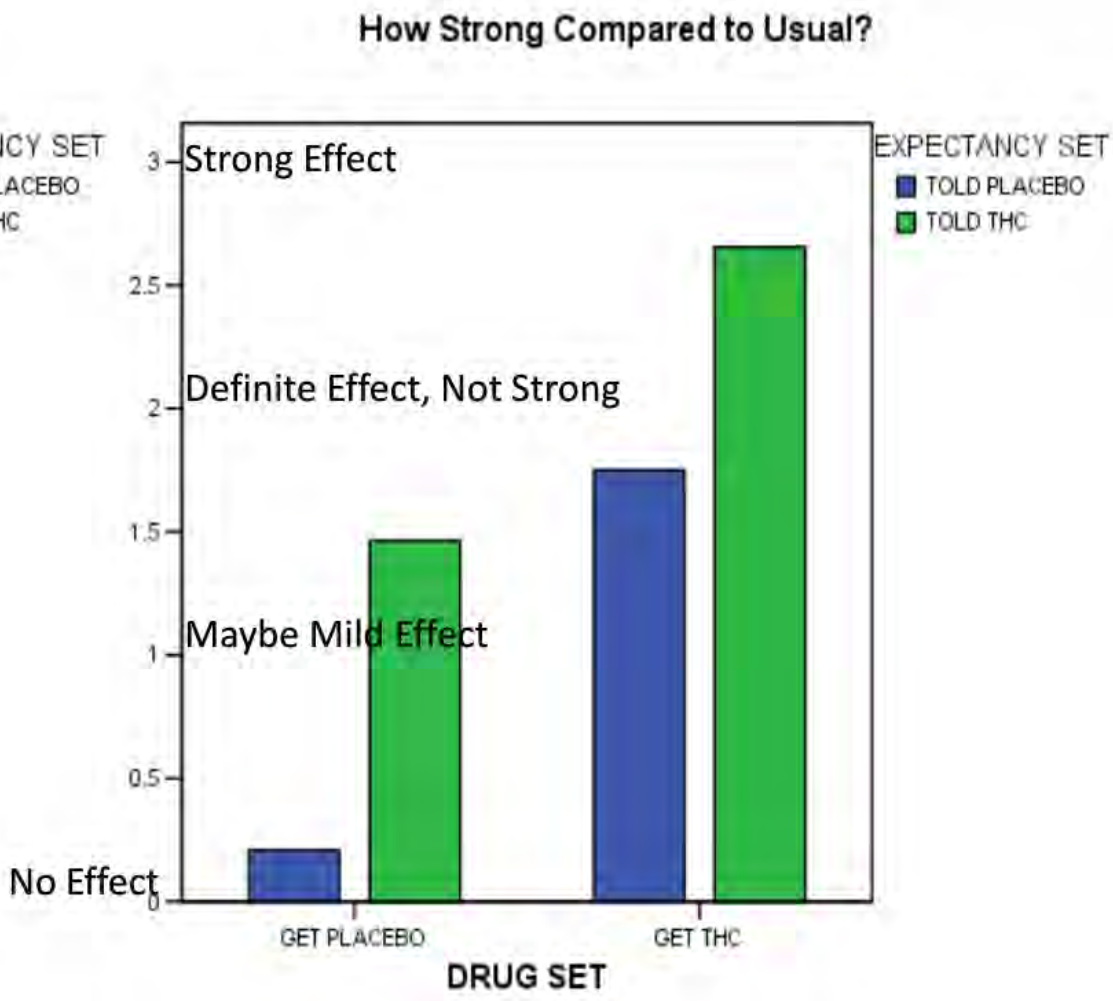
- N = 136 (65% men, mean age 21.4)
- Random assignment to 4 BPD conditions
  - Told THC/Received THC, Told THC/Received Placebo, Told Placebo/Received THC, or Told Placebo/Received Placebo
- Smoking one marijuana cigarette (2.8%THC) or marijuana placebo (0% THC) by paced puffing procedures
- Post-smoking:
  - manipulation checks; subjective drug effects, impulsivity tasks
  - Debriefing (Told Placebo/Received THC)
  - 4 hour wait, sobriety assessment, and taxi transportation

Metrik, J., Rohsenow, D. J., Monti, P. M., McGeary, J., Cook, T. A. R., de Wit, H., Haney, M., and Kahler, C. W. (2009). Effectiveness of a marijuana expectancy manipulation: Piloting the balanced-placebo design for marijuana. *Experimental and Clinical Psychopharmacology, 17*, 217-225.

Metrik, J., Kahler, C. W., Reynolds, B., McGeary, J.E., Monti, P.M., Haney, M., de Wit, H., and Rohsenow, D.J. (2012). Balanced-placebo design with marijuana: pharmacological and expectancy effects on impulsivity and risk taking. *Psychopharmacology, 223* (4), 489-499.

Cigarette Potency

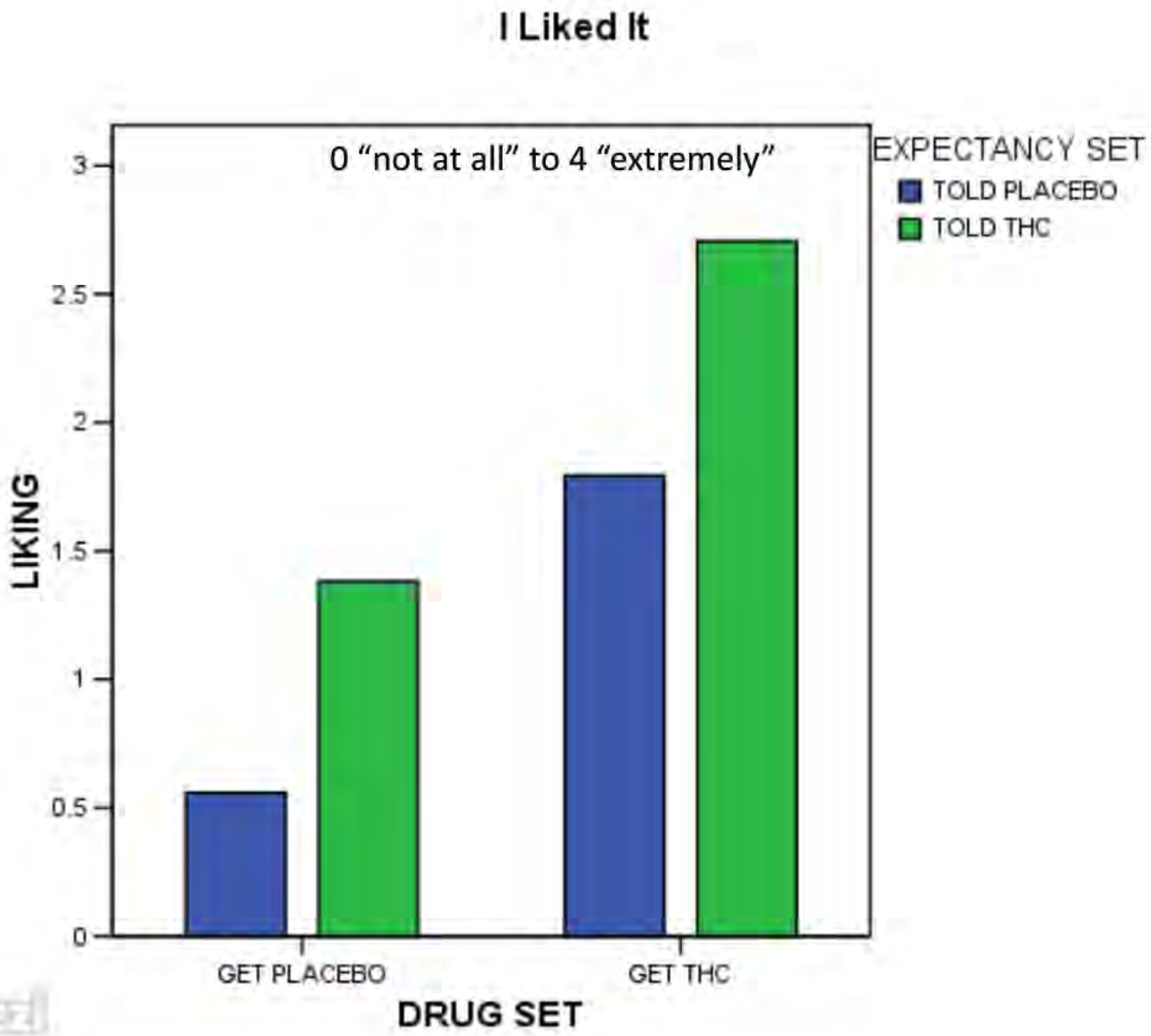




Expectancy Main Effects: η^2 = .31-.38, $p < .001$

Drug Main Effects: η^2 = .19-41, $p < .001$

Liked the Cigarette



Expectancy main effect: $\eta^2 = .14$, $p < .001$

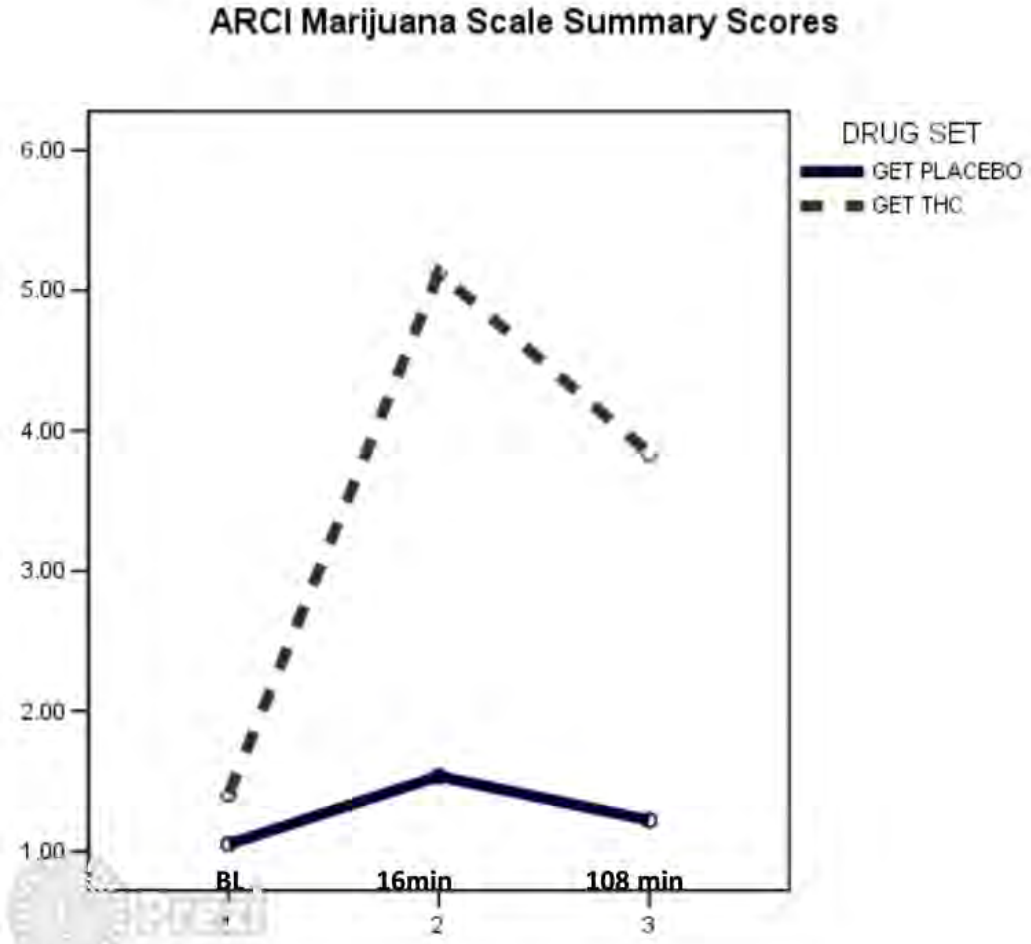
Drug main effect: $\eta^2 = .20$, $p < .001$

Subjective Intoxication

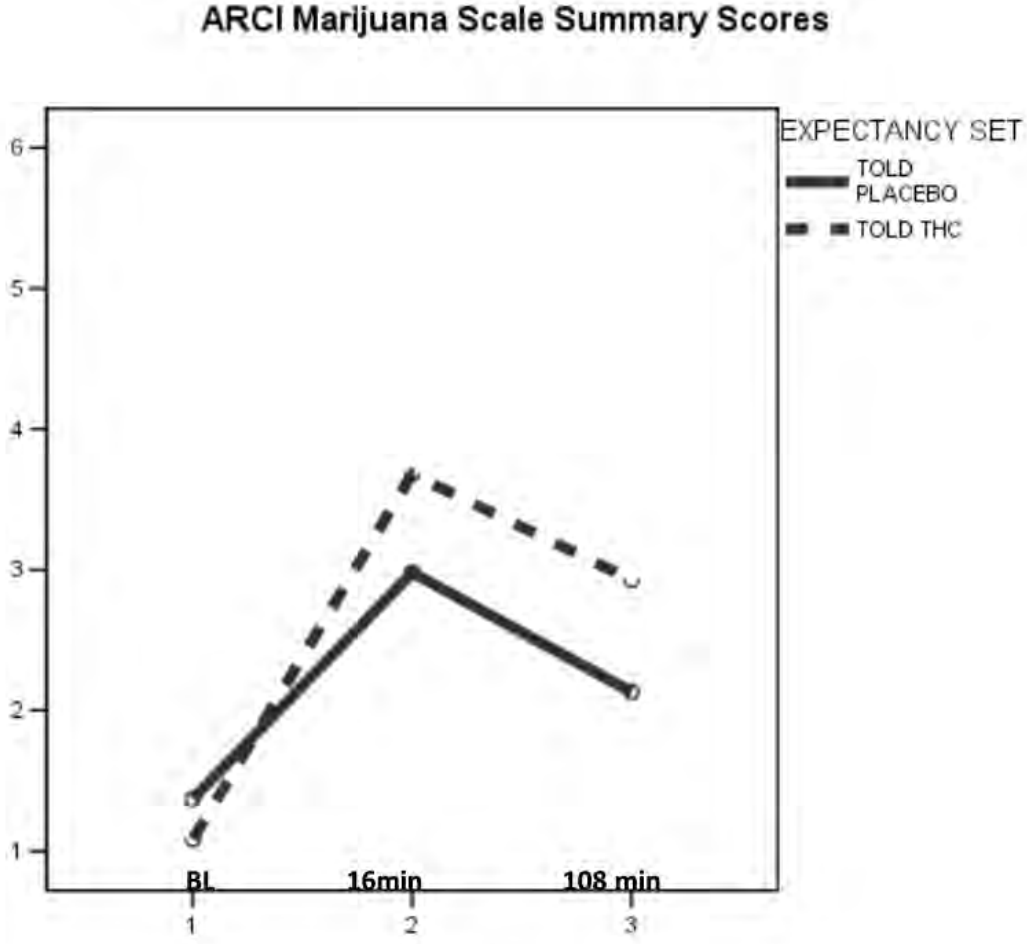
Drug Main Effect, F (1, 125) = 77.23, $p < .001$

Expectancy Main Effect, F (1, 125) = 6.32, $p = .01$

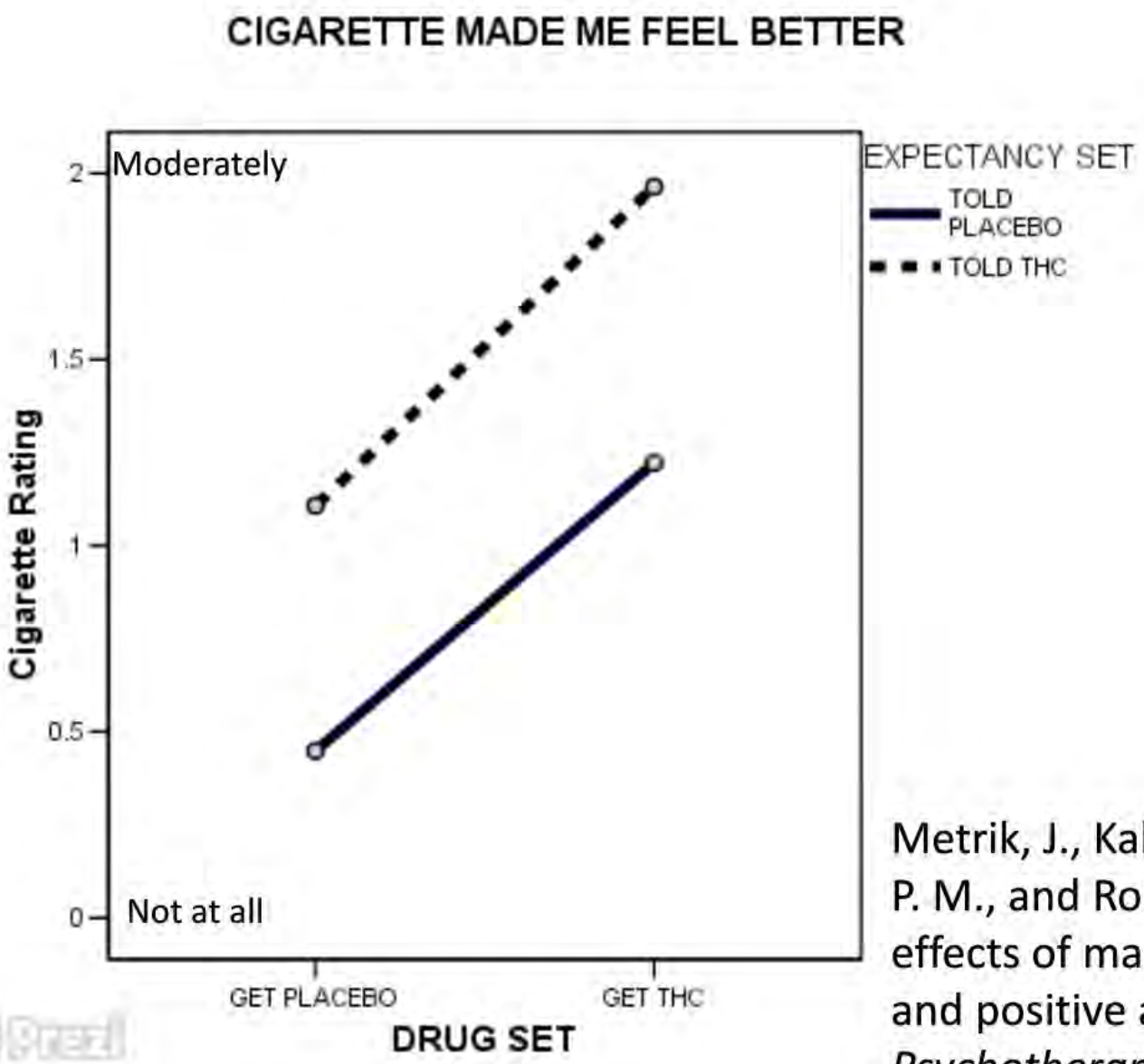
DRUG



EXPECTANCY



Cigarette Made Me Feel Better



Expectancy

(sr^2 = .12, p < .001)

Drug

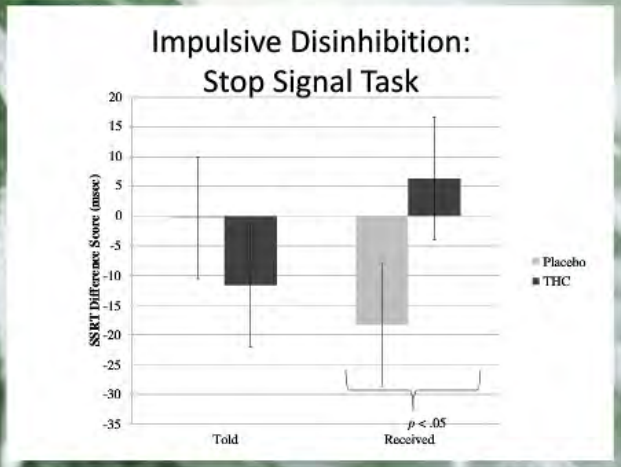
(sr^2 = .14, p < .01)

Metrik, J., Kahler, C.W., McGeary, J. E., Monti, P. M., and Rohsenow, D. J. (2011). Acute effects of marijuana smoking on negative and positive affect. *Journal of Cognitive Psychotherapy, 25*, 1-16.

Acute Effects of Marijuana on Inhibitory Control

Pharmacologic effect of THC on inhibitory control:
Relative to placebo, THC (2.8%) impaired inhibition on the Stop Signal task (SSRT: B = 19.76, SE = 9.72, sr2 =.03, *p* = .04) and reduced correct answers on color-incongruent trials on the Stroop Color-Word task (B = -1.28, SE = .57, sr2 =.02, *p* = .03)
No effect of stimulus expectancy on inhibitory control measures.

Metrik, Kahler, Reynolds, McGeary, Monti, Haney, de Wit, Rohsenow (2012) Psychopharmacology.



Expectancy of Marijuana Increases Awareness of Risks

Expectancy effect on impulsive decision-making (Experiential Discounting):
Relative to those Told Placebo, those Told THC discounted delayed rewards *less*
(B = .09, SE = .04, sr2 =.03, *p* = .02)
No pharmacologic effect of THC on the EDT.

Expectancy effect on increased perception of sexual risk among women (no pharmacologic effect of THC) and on perceived likelihood of alcohol-related risk behaviors such as drunk driving and riding in a car with someone who has consumed alcohol

Metrik, Kahler, Reynolds, McGeary, Monti, Haney, de Wit, Rohsenow (2012) Psychopharmacology.

Expectancies of greater cognitive and behavioral marijuana impairment were associated with lower risk taking on the Balloon Analogue Risk Task among those who received THC but not those who received Placebo (B = −0.19, SE = 0.08, p= 0.02, sr2= 0.04).

Gunn, Skalski, Metrik (2017). Drug and Alcohol Dependence.

BPD Study Findings

- Active drug and expectancy independently increase subjective intoxication and positive affect
- Small THC effects on measures of impulsive disinhibition (Stop Signal and Color-Word Stroop tasks)
- Expectancy alters decision-making responses to marijuana tempering the expression of disinhibited behaviors = increased awareness of risk
- Findings suggest that expectancy of impairment and intoxication may actually change behavior (e.g., driving behavior by slowing down) in an effort to decrease risk. However, because of the predominant perception of low risk and "safer" driving under the influence of marijuana, this expectancy might increase the likelihood of engaging in driving when under the influence of marijuana.

Marijuana and Psychiatric Disorders: Emotional Dysregulation

- **Comorbidity between PTSD/MDD with CUD (36%) is explained by coping-oriented cannabis use motives**

  Metrik, Jackson, Bassett, Zvolensky, Seal, Borsari (2016). Psychology of Addictive Behaviors.

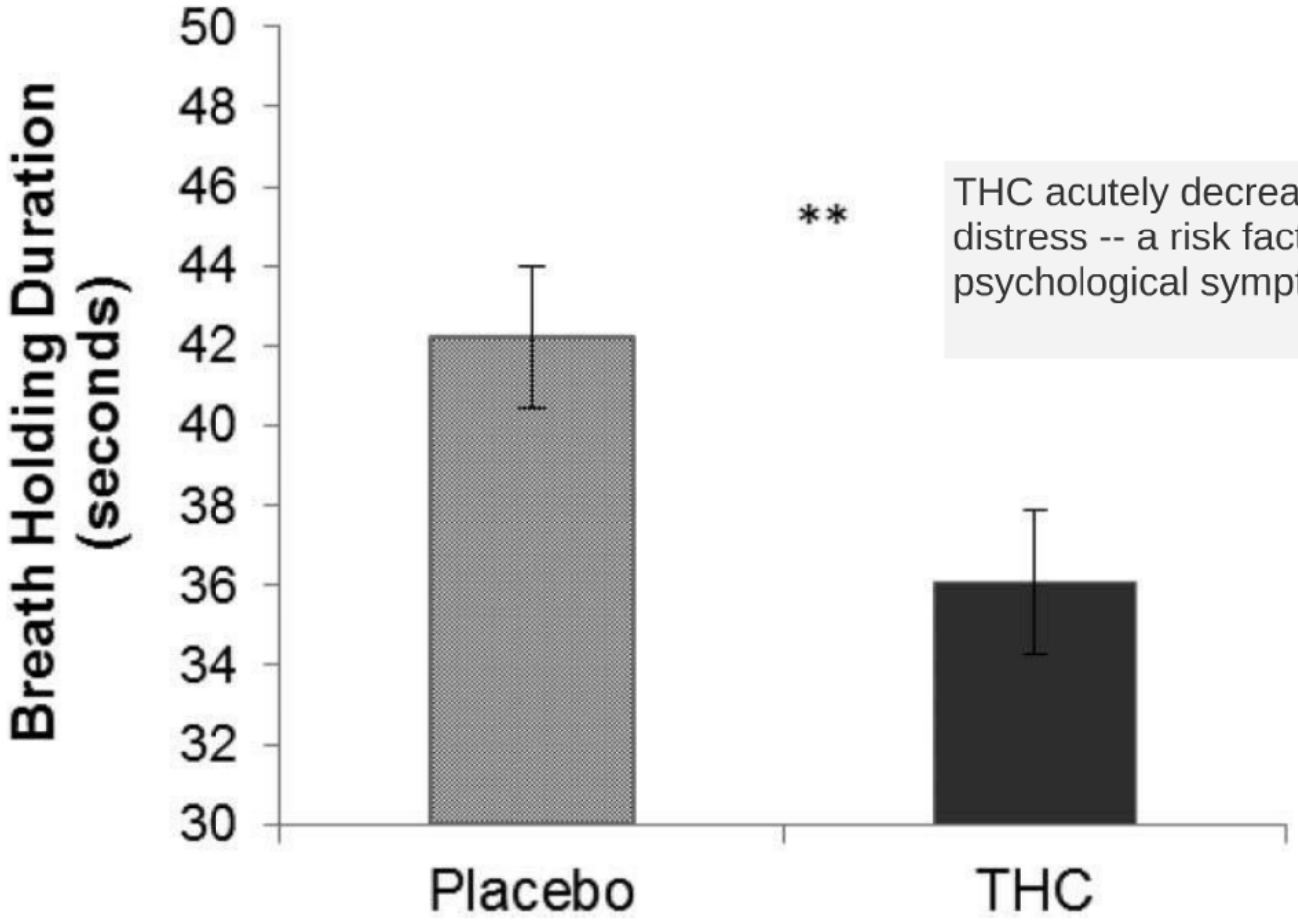
- **Emotionally vulnerable individuals (high anxiety sensitivity and distress intolerance) use marijuana to cope with distress, which maintains CUD, greater severity of craving, greater number of problems**

  Farris, S.G., Metrik, J., Bonn-Miller, M.O., Kahler, C.W., Zvolensky, M.J. (2016). Anxiety sensitivity and distress intolerance as predictors of cannabis dependence symptoms, problems, and craving: the mediating role of coping motives. Journal of Studies on Alcohol and Drugs, 77, 889-897.

- **Laboratory study: Marijuana's acute effects on distress intolerance and attentional processing (bias in selective attention) of rewarding and negative affective stimuli**

- **Within-subjects placebo-controlled study (n = 89), THC 3.0%**

Acute Effects of Marijuana on Breath-Holding Duration



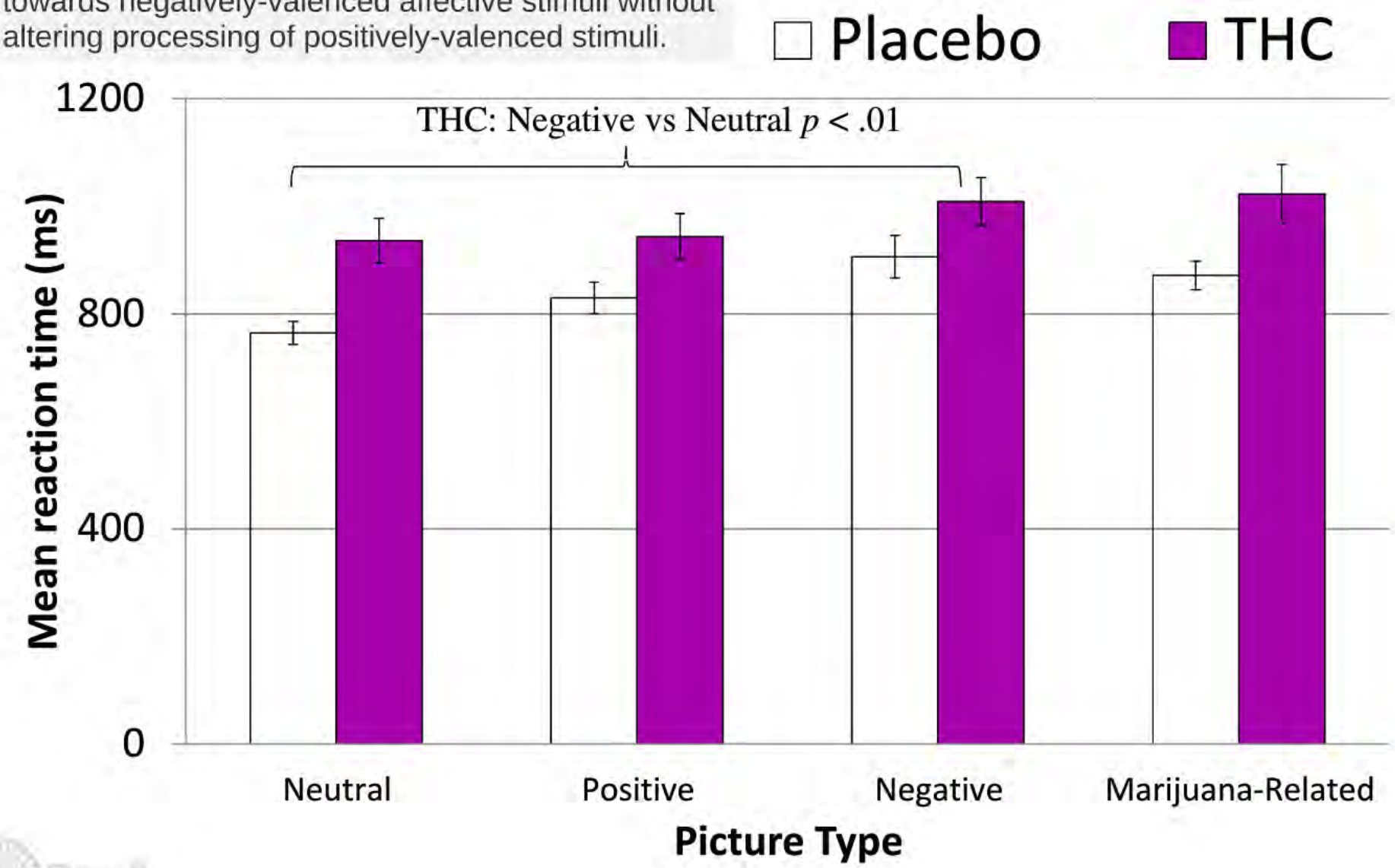
THC acutely decreases ability to tolerate physical distress -- a risk factor associated with psychological symptoms and disorders.

Figure 1. Breath-holding duration after THC versus placebo. Covariate adjusted mean breath-holding duration following administration of THC and placebo. Error bars represent standard error of the mean. ***p* < .001.

Farris & Metrik (2016). Experimental and Clinical Psychopharmacology.

Pleasantness Rating Task

THC increases allocation of attentional resources towards negatively-valenced affective stimuli without altering processing of positively-valenced stimuli.



Marijuana and Alcohol

- Comorbidity: 68% of individuals with current CUD meet criteria for AUD
- Combined use increases cognitive and psychomotor impairment; significantly higher THC blood levels when used with alcohol
- Marijuana use is associated with increased risk of AUD onset and persistence over the course of three years (NESARC data) Weinberger, Platt, Goodwin, 2016
- Marijuana use during treatment for AUD is associated with lower abstinence post-treatment and at 1 year (Project COMBINE data) Subbaraman, Metrik, Patterson, Swift, 2017, *Addiction*
- Medical marijuana users drink less often and have less alcohol problems than recreational marijuana users

Metrik, Bassett, Aston, Jackson, Borsari (in press). Translational Issues in Psychological Science.

Daily Patterns of Marijuana and Alcohol Co-Use

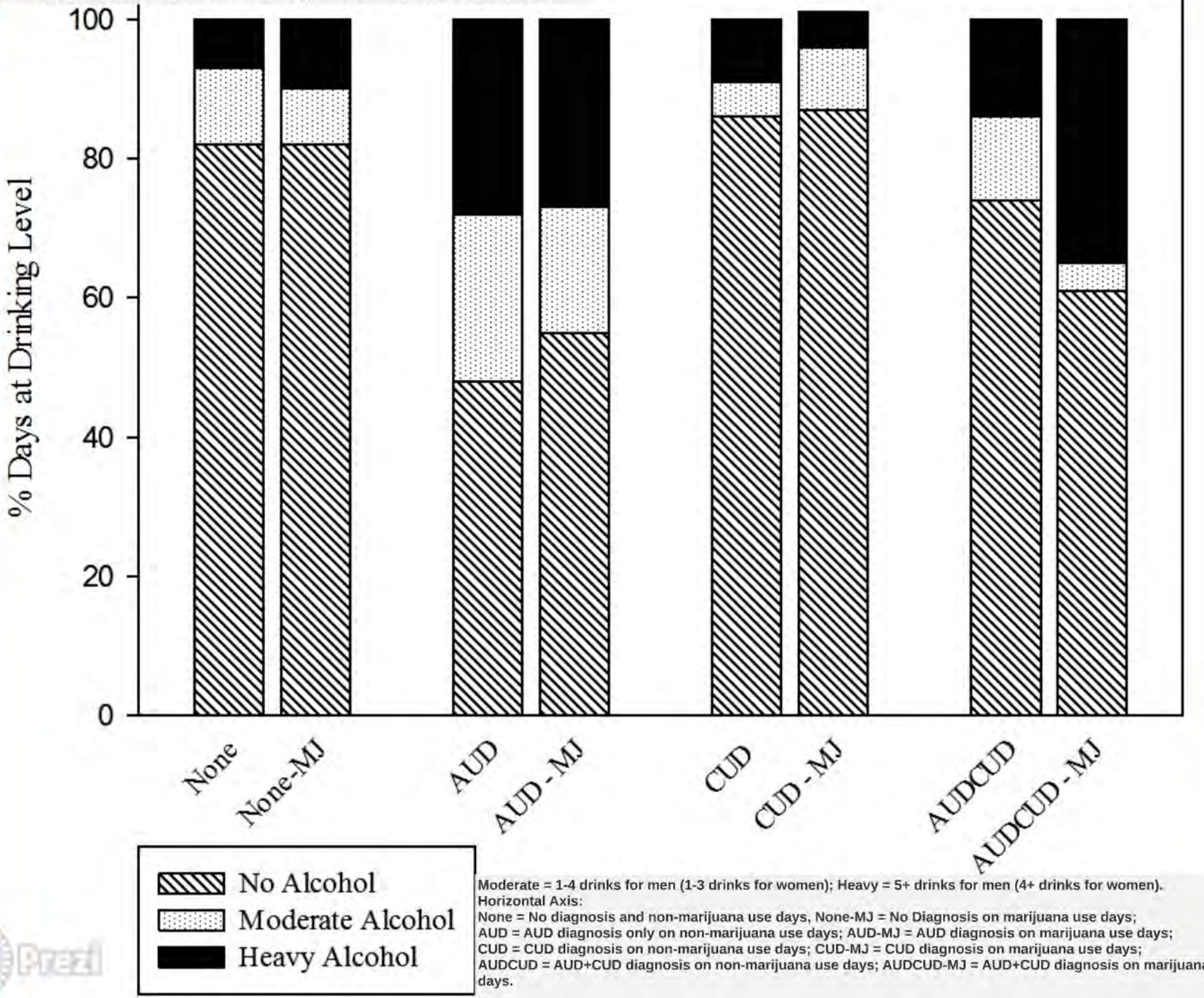
Examined daily associations between marijuana and alcohol use and how these differed by CUD and AUD diagnosis
TLFB interview of 127 Veterans over 180 days (22,860 observations)

37% with DSM-5 CUD
40% with DSM-5 AUD
15% both CUD + AUD

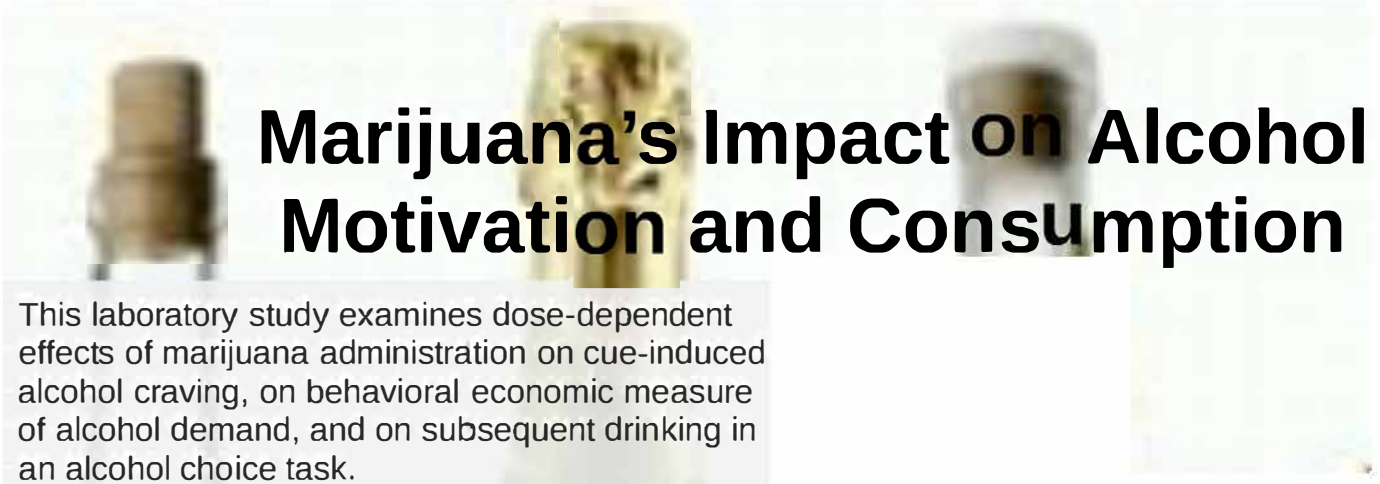
Multilevel modeling analysis showed that participants were more likely to drink heavily (>5/4 drinks) vs moderately (OR = 2.29) and moderately vs not drinking (OR=1.57) on marijuana use days relative to non-use days.

Metrik, Gunn, Jackson, Sokolovsky, Borsari, under review.

Metrik, Gunn, Jackson, Sokolovsky, Borsari, under review.



Moderate = 1-4 drinks for men (1-3 drinks for women); Heavy = 5+ drinks for men (4+ drinks for women).
Horizontal Axis:
None = No diagnosis and non-marijuana use days, None-MJ = No Diagnosis on marijuana use days;
AUD = AUD diagnosis only on non-marijuana use days; AUD-MJ = AUD diagnosis on marijuana use days;
CUD = CUD diagnosis on non-marijuana use days; CUD-MJ = CUD diagnosis on marijuana use days;
AUDCUD = AUD+CUD diagnosis on non-marijuana use days; AUDCUD-MJ = AUD+CUD diagnosis on marijuana use days.



Marijuana's Impact on Alcohol Motivation and Consumption

This laboratory study examines dose-dependent effects of marijuana administration on cue-induced alcohol craving, on behavioral economic measure of alcohol demand, and on subsequent drinking in an alcohol choice task.

ClinicalTrials.gov Identifier: NCT02983773
R01AA024091 (PI Metrik)

Double blind crossover design:

3 doses: 7.2% THC, 3.0% THC, placebo

PROJECT M.A.R.S.

Looking for volunteers between the ages of 21 and 44 who are current **alcohol** and **marijuana** users to participate in a confidential research study on the effects of alcohol and marijuana

Participants will receive up to **$407** for completing the study

For more information:

call: 401-863-6688

e-mail: **ProjectMARS@brown.edu**

This study has been approved by:
Brown University Institutional Review Board

Study Eligibility

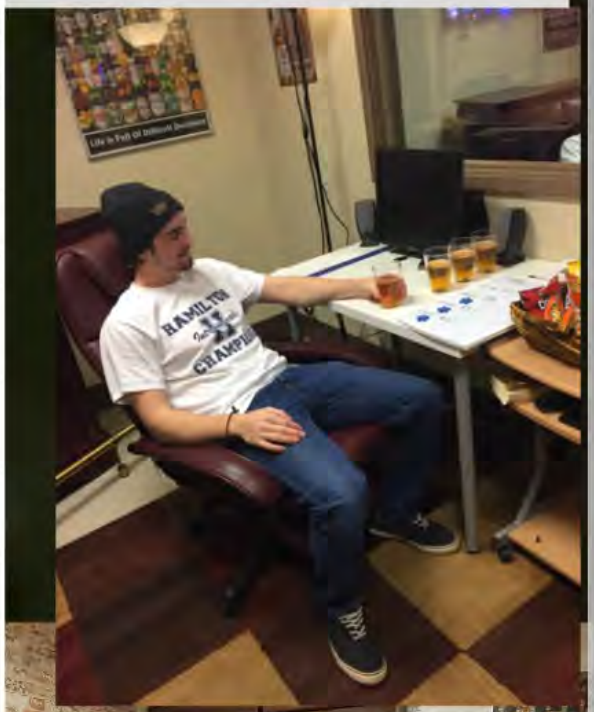
Inclusion Criteria:
Age 21 to 44
Marijuana smoking at least 2x in past month/weekly past 6 months, confirmed by positive THC screen
Current heavy episodic (binge) drinking
In good physical health and weighing < 250 lbs

Exclusion Criteria:
Positive pregnancy test/nursing
Positive urine toxicology screen for drugs other than cannabis
Interest to quit or receive treatment for marijuana or alcohol use
Meeting criteria for a current affective disorder (depression, or mania, panic disorder, and having psychotic symptoms as assessed by the SCID)

Sample characteristics (N = 25)
Mean age = 25.9, *SD*=5.6
28% Female
16% African-American
4% Asian
60% Caucasian
20% Other
24% Hispanic/Latino ethnicity
DSM-5 current AUD 44%
DSM-5 current CUD 56%

Time course of sessions

Time	Event	Time	Event
-90	Arrival	**38**	**Alcohol CR: neutral**
	BrAC, CO (< 8 ppm)	45	BP/HR, ACQ, VAS, APT-state
	Urine drug/pregnancy screen, CIWA, Behavior Checklist Diary BP/HR	**52**	**Alcohol CR: alcohol**
	Blood draw 1	60	BP/HR, ACQ, VAS, APT-state, BAES
	Standardized lunch meal	**67**	**Alcohol choice Task Block 1**
	Pre-smoke assessment battery	112	BP/HR, Blood draw 4 ACQ, SIE, BAES, ARCI, VAS, APT-state, BrAC
	MPT, APT, ARCI-M, SIE,BAES, VAS, MCQ, ACQ, BP/HR	**127**	**Alcohol choice Task Block 2**
0	**Smoke marijuana**	172	BP/HR, Blood draw 5 ACQ, SIE, BAES, ARCI, VAS, APT-state, BrAC
10	Blood draw 2, BP/HR	187	Rest period with BrACs, field sobriety, meal
12	ARCI-M, VAS, MCQ, ACQ, BP/HR		
18	Cognitive impairment tasks		
35	Blood draw 3, BP/HR		



High Priorities for the Next 5 Years

- Rigorous research combining laboratory marijuana administration and ecological momentary assessment (EMA) methods to examine how drug state-dependent processes (e.g, inhibitory control, sensitivity to marijuana impairment) and contextual factors impact decisions to drive after using marijuana and driving behavior.
- Innovative technology to improve reliable detection of marijuana impairment.
- Randomized clinical trials and balanced-placebo studies to derive more precise estimates of pure pharmacologic effect of THC and other cannabinoids separate from the confound of expectancy (pain, anxiety, etc)
- Increased access by researchers to a variety of marijuana products currently on the market to better characterize the safety/risk profile (e.g., vaping highly concentrated THC oils)
- Leveraging behavioral economics approaches to better understand cross drug reinforcement (co-use of marijuana and tobacco; marijuana and alcohol)

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