ORAL SESSION: OUCH!!! PASS THE CANNABIS

Cannabidiol (CBD) Co-Administration Alters Delta-9-Tetrahydrocannabinol (THC) Antinociception in the Carrageenan Rat Model of Acute Inflammatory Pain

Bryan Jenkins *[1], Catherine Moore [1], Elise Weerts [1]

[1] *Johns Hopkins University School of Medicine*

Drug Category: Cannabis/Cannabinoids
Topic: Behavioral Pharmacology
Abstract Detail: Preclinical - In Vivo
Abstract Category: Original Research

Aim: Pain relief is the most frequent use for medical cannabis. Some pain patients also substitute cannabis for prescription opioids. Cannabis products being used are delta-9-tetrahydrocannabinol (THC) or cannabidiol (CBD) dominant with variable THC:CBD ratios. Some data suggests that THC and CBD produce analgesia and reduce inflammation. CBD may also augment the therapeutic and/or mitigate the adverse effects of THC. This study tested the anti-nociceptive and anti-inflammatory effects of THC and CBD, alone or combined in different ratios, using a rat model of inflammatory pain.

Methods: Inflammatory pain was induced in adult Sprague Dawley rats via an intraplantar λ-Carrageenan injection in the rat hind paw. Rat treatment dose groups (n = 8-12 per sex/group) were orally administered sesame oil vehicle (control), THC (1, 3 mg/kg) CBD (10, 30 mg/kg), or THC + CBD dose combinations under blinded conditions. Drugs were administered 1 hour prior to λ-Carrageenan. Pain and edema measurements were conducted at baseline, 1, 3 and 5 hours post λ-Carrageenan. Data analysis used repeated-measures ANOVAs with treatment and sex as between-subject factors and time as the within-subject factor.

Results: In controls, λ-Carrageenan reliably increased pain sensitivity to heat (hyperalgesia) and mechanical pressure (allodynia) and produced paw edema. Compared to vehicle, 3 mg/kg THC attenuated λ-Carrageenan-induced hyperalgesia and allodynia (both $p > 0.05$). THC alone at the 1 mg/kg dose, but not 3 mg/kg dose, increased paw edema compared with vehicle ($p > 0.05$). CBD alone did not alter λ-Carrageenan-induced increases in pain-sensitivity or inflammation ($p < 0.05$). Co-administration of 3 mg/kg THC + 10 mg/kg CBD decreased the anti-allodynia observed with 3 mg/kg THC alone. Co-administration of 3 mg/kg THC with 10 or 30 mg/kg CBD increased paw edema compared with 3 mg/kg THC alone (p's > 0.05).

Conclusions: These data demonstrate that a modest THC dose can reduce inflammatory pain, whereas CBD alone had no effect. CBD did not augment THC's effects and some doses of CBD diminished THC's analgesic effects. These findings suggest oral THC isolates are superior to using oral CBD isolates or THC + CBD products for inflammatory pain.

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Acute Pain Sensitivity Varies as a Function of Weekly Delta-9-Tetrahydrocannabinol Exposure

Elisa Pabon *[1], Anna Hilger [1], Nare Arakelian [1], Conor H. Murray [1], Stephanie Lake [1], Ziva Cooper [1]

[1] *University of California, Los Angeles*

Drug Category: Cannabis/Cannabinoids
Topic: Other, Pain and Analgesia
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research

Aim: Pain is one of the most common indications for medical cannabis use. Acute cannabis and cannabinoid administration reduces pain response in healthy volunteers and some patient populations with reported sex differences. However, the extent to which frequent exposure to delta-9-tetrahydrocannabinol (THC), the main psychoactive constituent of cannabis, in the absence of acute administration, influences sensitivity to pain, and how this may differ between males and females, has not been systematically examined. In the present analysis, we investigated the association between self-reported weekly THC exposure, in healthy male and female participants who reported using cannabis ≥ monthly, and behavioral and subjective measures of acute pain using a Cold Pressor Test (CPT), an experimental pain test that has predictive validity for therapeutics used to treat chronic pain.

Methods: Weekly THC exposure was calculated using average cannabis use days per week in the past month multiplied by estimated daily THC consumption. After biochemical confirmation of cannabis abstinence for at least twelve hours, 57 healthy adults (21F, 36M; 30.7 +/- 7.6 years) who reported using cannabis an average of 4.7 +/- 2.3 days per week in the past month completed a CPT. During the CPT, participants immersed their hand in cold water (4°C) and time to report pain (pain threshold) and time to withdraw hand (pain tolerance) were recorded. Subjective pain ratings of the cold-water stimulus were measured using the Short-Form McGill Pain Questionnaire (SF-MPQ) and the 'Painfulness' and 'Bothersomeness' scale. Mixed effects models were used to predict the effects of weekly THC exposure, sex, and their potential interaction on all outcome measures (alpha = 0.05).

Results: Greater weekly THC exposure was associated with lower pain threshold ($F_{threshold} = 6.7$, $p > 0.001$) and tolerance ($F_{tolerance} = 6.4$, $p > 0.001$), as well as greater subjective ratings of pain ($F_{SF\text{-}MPQ} = 4.2$, $p > 0.001$; $F_{Painful} = 10.6$, $p > 0.001$, $F_{Bothersome} = 5.9$, $p > 0.001$). There was no significant effect of sex, or interaction between weekly THC exposure and sex, on any of the outcome measures.

Conclusions: Overall, greater THC exposure in healthy, recently abstinent individuals who use cannabis ≥ monthly was related to decreased pain threshold and tolerance, and increased subjective ratings of pain, and did not vary by sex. These findings suggest frequent THC exposure may impact sensitivity to painful stimuli, a factor that should be considered in the clinical use, and study of, cannabinoids as potential analgesic therapies.

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Pain and Sociodemographic Correlates of Cannabis Use Among Patients With Insomnia in the 'All of Us' Research Program

Liva LaMontagne *[1], Kaitlyn Swacil [1], Linda Cottler [1], Roger Fillingim [1], John Williamson [1], Yan Wang [1], Catalina Lopez-Quintero [1]

[1] *University of Florida*

Drug Category: Cannabis/Cannabinoids
Topic: Epidemiology
Abstract Detail: Clinical - Epidemiology
Abstract Category: Original Research

Aim: More than half of patients with insomnia report chronic pain, leading to potential self-medication with cannabis and addiction. Insomnia data from electronic health records (EHR) can add valuable information above self-report assessments. Accordingly, we

analyzed EHR and self-report data from the NIH All of Us research program to investigate associations of past 3-month cannabis use with pain and socio-demographic factors.

Methods: The sample included 2000 individuals with insomnia, M (SD) age 58.2 (14.2), 63.8% female. Median pain intensity for cannabis users was 5 (IQR: 2-7), compared to 3 (IQR: 1-6) for non-users on a 10-point scale. We used Chi-square tests and logistic regression in R to examine associations of cannabis use with pain and sociodemographic factors.

Results: Thirty percent reported cannabis use in the past 3 months. Adjusted logistic regression indicated that a unit increase in pain intensity increased the odds of cannabis use by 6% (ORa = 1.06, CI [1.02; 1.11], p = 0.003). Black/African American and Latino participants were more likely than White participants to use cannabis (ORa = 2.24, CI [1.69; 2.96], p > 0.001 and ORa = 1.53, CI [1.03; 2.28], p > 0.05, respectively). Participants with $50,000–75,000 and < $75,000 income were less likely to use cannabis compared to participants with > $25,000 (ORa = .55, CI [0.38; 0.79], p > 0.01 and ORa = .63, CI [0.47; 0.86], p > 0.01, respectively). While age had a negative association, tobacco and alcohol use showed a positive association with cannabis use.

Conclusions: Thirty percent of insomnia patients used cannabis in the past 3 months, compared to 9% in the general population. Increased pain levels were associated with cannabis use, indicating potential self-medication for pain relief. More research is needed to develop efficacious and accessible treatments for pain and insomnia, especially among underrepresented groups.

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Effects of Repeatedly Administered Cannabis With THC and CBD on Experimental Pain and Abuse-Related Outcomes in Humans

Caroline Arout [*1], Hannah Harris [2], Stephanie Reed [3], Tonisha Kearney-Ramos [4], Richard Foltin [1], Margaret Haney [1]

[1] *Columbia University Irving Medical Center*
[2] *Columbia University, New York State Psychiatric Institute*
[3] *Columbia University*
[4] *Columbia University Medical Center*

Drug Category: Cannabis/Cannabinoids
Topic: Tolerance/Dependence
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research

Aim: Though most medical cannabis patients cite pain relief as their primary indication, little is known about how (1) cannabis effects on pain and abuse liability change with daily administration and abrupt cessation, and (2) the relative concentrations of tetrahydrocannabinol (THC) and cannabidiol (CBD) affect these outcomes. Herein we present preliminary human laboratory investigations addressing these questions.

Methods: Nontreatment-seeking daily cannabis users (N = 10) were enrolled in one of two 15-day inpatient conditions varying in type of cannabis administered (THC or CBD:THC). Each day, participants smoked cannabis cigarettes 3x/day, with strength varying across days: Day 1: active cannabis (THC condition: ~78 mg; CBD:THC condition: ~30mg CBD + ~18mg THC); Day 2-8: placebo cannabis; Day 9-15: active cannabis. We assessed the effects of repeated cannabis use and abstinence from active cannabis on cold pressor experimental pain and intoxication ('high'). Data collection is ongoing.

Results: In the THC condition, active cannabis administration following 7 days of abstinence (placebo cannabis) produced a 63% increase in analgesic effects and an 84% increase in ratings of 'high' relative to baseline (Day 1). Tolerance developed to both the analgesic and intoxicating effects following 7 days of active cannabis administration (Day 9 vs. Day 15). The CBD:THC condition produced minimal changes in pain response vs. placebo. However, following 7 days of abstinence, CBD:THC produced a 111% increase in ratings of intoxication relative to baseline; this effect did not change with repeated administration.

Conclusions: Understanding the impact of daily cannabis use and abrupt abstinence is a public health necessity. Our findings suggest that cannabis differing in THC:CBD produces distinct effects: 1) analgesic tolerance develops to high-THC cannabis; (2) tolerance develops to THC cannabis' abuse-related effects, and is reversible with abstinence. These patterns are not seen with CBD cannabis with lower THC content.

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ORAL SESSION: INTERSECTING PERSPECTIVES ON SUICIDALITY AND SUBSTANCE USE

Trauma and Suicide Screening Outcomes Among Hospitalized Adults With Opioid Use Disorder and Serious Injection Related infections: Baseline Characteristics From an Ongoing Randomized Clinical Trial

Michelle Lofwall [*1], Shelby Montgomery [1], Paul Nuzzo [1], Connor Vanmeter [1], Sharon Walsh [1], Loui Chang [1], Wyatt Kunzelman [1], Laura Fanucchi [1]

[1] *University of Kentucky, College of Medicine*

Drug Category: Opiates/Opioids
Topic: Comorbidities, Substance Use Disorder
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research

Aim: Persons with an opioid use disorder (OUD) have increased risk for medical hospitalization, trauma experiences, and prior suicide attempts. The aim is to describe the prevalence and types of traumatic experiences and suicide screening outcomes among persons with an OUD currently hospitalized with a serious injection-related infection (SIRI).

Methods: The Outpatient Parenteral Antimicrobial Therapy Plus Buprenorphine for OUD and SIRI study (NCT04677114) is a randomized, 2-arm clinical trial enrolling adults while hospitalized for SIRI. Participants are randomized 1:1 to either discharge once medically stable to an integrated buprenorphine and infectious disease outpatient care model or to treatment as usual. Preliminary baseline responses to the Brief Trauma Questionnaire (BTQ), Primary Care Posttraumatic Stress Disorder screen for DSM-5 (PC-PTSD-5), Mini International Neuropsychiatric Interview from the DSM-5 (MINI), and Columbia Suicide Severity Rating Scale (C-SSRS) are reported.

Results: The first 55 participants randomized are included herein. Trauma screening assessments showed 31 (56%) experienced