Lifetime Cannabis Use and Incident Hypertension- The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: Observational evidence investigating associations between cannabis use and hypertension is inconsistent.

Methods: The association between cumulative lifetime cannabis use (cannabis-years) and incident hypertension was examined over 35 years in a sample of Coronary Artery Risk Development in Young Adults (CARDIA) study participants free of hypertension at baseline. Marginal structural models with inverse probability weighting were employed to adjust for potential time-dependent confounding and censoring. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression. Sensitivity analyses included modeling cannabis-years using restricted cubic-splines, stratifying the primary analyses by sex, race, alcohol and cigarette smoking, and evaluating an additional exposure measure (days of use in the past month).

Results: The analytic sample consisted of 4,328 participants at baseline and 64.9% (n=2,810) at Year 35. Median cannabis-years increased minimally and remained low across visits: 0.0 (Q1,Q3: 0.0, 0.3) at baseline and 0.2 (Q1,Q3: 0.0, 0.7) by Year 35. There were 2,478 cases of incident hypertension over 88,292 person-years (28.1 cases per 1,000 person-years). Cannabis-years were not significantly associated with incident hypertension (aHR: 0.99 (95% CI: 0.97-1.00; p=0.18). The association remained unchanged in sensitivity analyses.

Conclusions: In a cohort of Black and White young adults with 35 years of follow-up, no association was found between cumulative lifetime use of cannabis and risk of incident hypertension. This finding was robust to restricted cubic-spline analyses, analyses stratified by sex, race, alcohol use and tobacco cigarette smoking, and an additional measure of exposure (days of use in the past month).

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Cortico-Accumbal Endocannabinoid Signaling Modulates Cocaine-Seeking

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Background: Global rates of cocaine use reached an all-time high in 2023, with approximately 25 million people worldwide using cocaine. Moreover, as global supply surges, the upward trend of cocaine use is expected to continue increasing. Cocaine and other drugs of abuse lead to profound molecular and physiological changes within the nucleus accumbens (NAc), a key node in the brain's reward circuitry. In the NAc, glutamatergic terminals from the prelimbic (PrL) region of the medial prefrontal cortex (mPFC) synapse onto medium spiny neurons (MSNs) which integrate cortical inputs with dopaminergic signals from the midbrain. Previous studies have implicated the potentiation of these glutamatergic PrL projections to the NAc in promoting cocaineseeking and relapse. Endocannabinoids (eCBs) function as retrograde spatiotemporal "homeostatic regulators" within this cortico-accumbal circuit by decreasing the likelihood of neurotransmitter release onto neurons experiencing extensive levels of activity. Importantly, studies have linked dysfunction of eCB signaling within this reward circuitry to vulnerability to cocaine-seeking and relapse.

Methods: Recent data from our lab has shown that augmenting synaptic levels of the eCB 2-AG in the NAc by inhibition if its degradation enzyme MAGL reduces cue-induced cocaine seeking in mice trained to self-administer cocaine. Our current pilot studies examine spatiotemporal eCB dynamics within cortico-accumbal circuitry by expressing the GRABeCB-2.0 biosensor on PrL terminals in the NAc and imaging in real-time via fiber photometry while mice undergo cue-induced cocaine relapse.

Results: We hypothesize that dysfunctional eCB signaling within this circuit allows for the potentiation of glutamatergic input to the NAc and is critical for the pathogenesis of addiction-related behaviors.

Conclusions: Further, we propose that pharmacologically restoring functional eCB signaling will normalize glutamatergic singaling within the NAc, thereby reducing cocaine-seeking.

Prenatal CBD exposure alters development: A rodent model

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Background: Recently, it has been reported that 20% of pregnant women in the U.S. and Canada use cannabidiol (CBD) during pregnancy. Despite this, the effects of CBD on the developing fetus have not been well studied. Research on effects is hampered by potential polydrug use, difficulty measuring exposure time and dosing, and varying drug administrations. Animal models may increase our understanding of the safety of CBD use during pregnancy.

Methods: The current study exposed pregnant Sprague-Dawley rats to 50 mg/kg/day CBD or control vehicle once daily from gestational day 5-20. CBD was dissolved in honey and delivered via a cookie dough edible; controls received an 'edible' with no CBD.

Results: Throughout gestation, maternal body weight and food/water intake were monitored and did not differ between groups. However, exposure to CBD significantly reduced the number of pups born ($p=.025$), and tended to increase the ratio of male-female pups ($p=.069$). These results are alarming and may be indicative of alterations in pregnancy and early hormonal disruptions. Behavior was examined in the offspring on postnatal days 30-34 (early adolescence) in an open field activity chamber during their dark cycle for one hour/day for four days. Interestingly, prenatal CBD exposure significantly increased overall activity levels ($p=.004$). Patterns of activity differed by sex, as males exposed to prenatal CBD were more active during the first ten minutes of the session ($p<.05$), while females exposed to prenatal CBD habituated slower to the open field ($p<.05$). This is particularly interesting, as females exposed to prenatal CBD spent more time in the center of the chamber, indicating risk-taking behavior ($p=.017$). Thus, these data suggest that prenatal CBD may have adverse effects on exposed offspring, leading to hyperactivity, alterations in learning, and increased risk-taking behavior in a sex-dependent manner.

Conclusions: Despite these adverse effects of prenatal CBD exposure, pregnant women remain vulnerable to the perception that CBD use during pregnancy is safe. These data emphasize a critical need for awareness of the risks associated with CBD use during pregnancy, as CBD may alter fetal development. Supported by CMCR P64-07-001.

Influence of smoked cannabis on visuospatial learning and driving performance

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Background: Visuospatial cognition is a critical aspect of driving performance. Acutely, cannabis intoxication was demonstrated to negatively impact verbal learning and memory (Bourque & Potvin, 2021). Studies regarding the impact of cannabis intoxication on visual learning and memory are mixed, with some finding decreased performance relative to non-users and others finding no differences (Wieghorst et al., 2022). Few studies have related post-smoking visuospatial performance to driving performance in healthy cannabis users. The current study therefore examined if use of smoked cannabis produces dysfunction on a novel visuospatial learning test (VSLT) and subsequent driving simulator performance.

Methods: As part of a randomized placebo-controlled clinical trial (Marcotte et al., 2022), 191 cannabis users (using >4 times in the past month) completed a driving simulation 30min post-smoking, immediately followed by a computerized VSLT. The VSLT required participants to view an array of abstract figures on a grid for 10 seconds, and after a delay of either 4, 12, or 24 seconds identify the figures from a list presented at the bottom of the screen and place them in their correct locations. The primary VSLT outcome was the number of correct figures selected and placed in the correct location, across all three trials. The main driving outcome was the Composite Drive Score (CDS), a global measure of driving performance comprising variables including standard deviation of lateral position (SDLP; swerving) and car following.

Results: The cannabis and placebo groups did not differ on the number of correct figures selected and placed in the correct location ($p=.49$). A higher number of correct responses on the VSLT was associated with lower (better) CDS in the entire sample at baseline (rho = -.16), and in the cannabis (rho = -.18) and placebo (rho = .34) groups post-smoking ($ps<.04$). The relationship between post-smoking VSLT performance and CDS did not differ comparing the cannabis and placebo groups ($p=.27$). Within the cannabis group, change in VSLT performance from baseline was unrelated to performance on all CDS subtests post-smoking ($ps>.06$).

Conclusions: The current study examined whether cannabis intoxication produced dysfunction on a novel VSLT and related driving simulator performance. While better VSLT performance was associated with better driving post-smoking in both the cannabis and placebo groups, this relationship did not statistically differ between groups. Future studies may benefit from examination of how cannabis intoxication affects more granular aspects of visuospatial cognition (e.g., perception of angular relationships) and whether any such intoxicating effects predict poorer driving performance.

Surveying Cannabinoid Hyperemesis Syndrome

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Background: Cannabinoid Hyperemesis Syndrome (CHS) is characterized by recurrent nausea, vomiting, and abdominal pain in chronic cannabis users. Despite increasing prevalence in emergency departments, the condition remains underrecognized, in part due to limited data on use patterns and early symptoms. This study sought to characterize cannabis consumption behaviors, symptom timing, and demographic influences among individuals with suspected or diagnosed CHS to support earlier recognition and clinical management.

Methods: We conducted an anonymous, web-based survey distributed via social media between September–December 2024. Participants were eligible if they were ≥18 years of age, reported cannabis use prior to symptom onset, and suspected or had a CHS diagnosis. Of 1,161 respondents, 27 were excluded for prior cyclic vomiting or hyperemesis gravidarum, yielding 1,134 participants. Descriptive and comparative analyse were performed to assess associations between cannabis use characteristics and symptom profiles.

Results: Most participants (96.5%) reported daily cannabis use, with 45% consuming ≥6 times per day. Smoking flower (75.8%) and vaping cartridges (51.2%) were the most common methods. In a single-method subanalysis, exclusive vape cartridge users developed CHS significantly sooner than exclusive smokers (1–2 years vs >10 years) and reported more frequent use (≥6 times/day, $p<0.0001$). Cannabis source—licensed dispensary, unlicensed market, or homegrown—was not associated with differences in symptom presentation. Prodromal symptoms were most often reported in the morning (63.1%) whereas hyperemetic episodes occurred more variably throughout the day. Women reported more symptoms overall, longer hyperemetic episodes (≥3 days vs <1 day for men and 37.8% noted exacerbation during menstruation.

Conclusions: Our findings indicate that CHS is strongly associated with long-term, high-frequency inhalation of Δ9-THC–dominant products. Exclusive vaping was linked to both higher use frequency and significantly shorter latency to CHS onset, suggesting that product type and potency may accelerate disease progression. While cannabis source did not affect presentation, morning-predominant prodromal symptoms and sex-based differences, particularly prolonged episodes in women, represent important diagnostic clues. These data highlight the need for clinicians to ask about cannabis use patterns in detail, including product type, frequency, and symptom timing. Greater awareness of these risk factors may enable earlier recognition, reduce unnecessary emergency visits, and guide harm reduction strategies.

Preparing geriatrics-trained physicians to discuss medical cannabis with their older adult patients

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Background: Older adults are increasingly using cannabis for health conditions such as pain and sleep disorders, but often use it without consultation with a healthcare provider. At the same time, many providers feel unprepared to discuss cannabis use with their patients. This educational intervention aimed to raise geriatrics-trained physician awareness and promote compassionate dialogue about cannabis use with older adults.

Methods: Thirty-one geriatrics and geriatric psychiatry physicians and fellows attended a synchronous, online, didactic series on cannabis divided into four, 30-minute modules on: 1) epidemiology among older adults, 2) history of legalization and stigma associated with use, 3) medical evidence and patient advising, and 4) having compassionate dialogue related to use. Pre- and post-intervention evaluative data were collected (n=22 pre-test, n=13 post-test). Wilcoxon signed-rank tests were performed to assess changes.

Results: Statistically significant (p-value's<.05) increases were seen in the percentage of physicians who reported being: moderately to extremely knowledgeable about medical cannabis (18.2% to 71.4%), somewhat to very comfortable initiating conversations about cannabis (22.7% to 92.9%), very to extremely confident assessing the risks, benefits, and safety of cannabis (<10.0% to 21.2%), and very to extremely confident providing advice to patients about cannabis (0% to 14.2%).

Conclusion: This brief training series was effective in raising physicians' knowledge about and comfort with having conversations about medical cannabis with their older adult patients. Similar training can be easily implemented in pre- and post-doctoral settings. As more older adults turn to cannabis as a form of therapy, physicians will need access to formal training about cannabis.

The Impact of Oral Cannabis Administration and Co-Administration of Alcohol on Impairment

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Background: Concurrent use of oral cannabis products ("edibles") and alcohol is increasingly common. However, controlled research assessing their combined effects is limited. Therefore, this human laboratory study examined the individual and interactive effects of cannabis edibles and alcohol on driving performance, subjective drug effects, and cannabinoid pharmacokinetics.

Methods: Healthy adults (n=25) completed seven, double-blind, double-dummy sessions lasting 8 hours. In each session, participants consumed a cannabis brownie (10 mg or 25 mg THC) or a placebo brownie. After 45 minutes, they then drank an alcoholic beverage (target breath alcohol concentration [BAC] of 0.0% or 0.05%). A positive control session (0.08% BAC with 0mg THC) was also completed. Study assessments were completed at baseline and repeatedly for 7.5 hours after cannabis use. Outcomes included simulated driving performance (evaluated on several individual tasks and via a global drive score comprised of multiple measures), field sobriety tests, subjective drug effects (positive/negative effects; perceived impairment), DRUID performance (tablet-based cognitive/psychomotor impairment test), and pharmacokinetics of THC/metabolites in blood.

Results: When administered alone, both cannabis and alcohol produced dose-dependent increases in subjective intoxication measures and decreases in driving performance. When combined (0.05% BAC with 10 or 25 mg THC), additive impairment was observed across both subjective and objective measures. Driving impairment from alcohol alone at the legal intoxication limit in the U.S. (0.08%) was similar (or lower) to that of cannabis plus alcohol at .05% BAC. Peak impairment occurred approximately 3.5 hours after cannabis administration (2.5 hours post-alcohol dosing) and was resolved by 7.5 hours. Field sobriety tests consistently detected impairment only at alcohol alone 0.08% BAC and 25mg THC + 0.05% alcohol. DRUID scores differentiated active from placebo sessions but were less dose-responsive than expected. Lastly, alcohol did not significantly alter THC or THC metabolite pharmacokinetics.

Conclusions: These findings demonstrate that cannabis edibles and alcohol produce additive effects on driving impairment and subjective measures. Further, common retail doses of cannabis edibles combined with low doses of alcohol can elicit driving impairment matching or exceeding that of higher doses of alcohol yet may not produce discernable impairment on field sobriety tests. The results from this study highlight the importance of further research to refine roadside impairment detection methods and inform public safety policies in the context of expanding cannabis legalization. Acknowledgements: Funded by the National Institute on Drug Abuse (NIDA) R01-DA052295

Law Enforcement Assessment of Body Tremors during Field Sobriety Tests: An Examination of Acute and Withdrawal Effects of ∆9-tetrahydrocannabinol

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Background: Field Sobriety Test trainings describe body tremors as an indicator of acute cannabis impairment, but tremors may also reflect cannabis withdrawal. We examined whether ∆9-tetrahydrocannabinol (THC) concentration and short-term abstinence predicted detection of body tremors by law enforcement (LE) and assessed whether acute and withdrawal THC effects were moderated by recent cannabis use intensity.

Methods: In a double-blind, parallel clinical trial, cannabis users were assigned randomly to smoke THC or placebo cigarettes *ad libitum*. Approximately 70 minutes post-smoking, LE documented whether participants exhibited body tremors. Mixed effect logistic regression models were estimated to predict the odds of body tremor. Data were limited to participants assessed by LE who evaluated ≥3 individuals in a given arm. Days since last cannabis use (DSLU) and cannabis use intensity (CUI; i.e., six-month total grams) were included in the Placebo Model to assess withdrawal effects (43 participants, 7 LE). Weight-adjusted peak whole blood THC concentration (THC-Peak; ~15 minutes post-smoking) and CUI were included in the THC Model to assess acute effects (101 participants, 12 LE).

Results: Median post-smoking THC concentrations were 0.5ng/mL [0.0, 2.3] and 32.4ng/mL [12.8, 60.9] for the placebo and THC arms, respectively. CUI did not moderate the relationships between body tremor and DSLU (Placebo Model) or THC-Peak (THC Model; *p*s ≥ .268); subsequent results were derived from additive models. In the Placebo Model, neither DSLU nor CUI predicted body tremors (*p*s ≥ .228). In the THC Model, the odds of body tremor increased by a factor of 3.36 for each 1ng/ml/kg increase in THC-Peak, controlling for CUI ($p = .012$). There was no association between CUI and body tremors in the THC Model ($p = .613$). 26% of the placebo arm and 30% of the THC arm were identified as having body tremors. LE explained 79% of the variance in the log-odds of body tremor in the Placebo Model and 28% in the THC Model.

Conclusions: Body tremors were associated with weight-adjusted THC concentration and may be informative in developing a totality of evidence for THC-related driving impairment. However, body tremors alone were not a reliable indicator; a substantial proportion of the variability in body tremor identification was attributable to the LE who conducted the evaluation, and a number of Placebo participants were classified as exhibiting body tremors. Future research should explore physiological mechanisms underlying THC-related body tremors and establish procedures (e.g., electromyography) to accurately differentiate tremor origins (e.g., acute THC use, THC withdrawal, neurodegeneration).

Effects of Prenatal Cannabidiol Exposure on Early Motor Development

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Background: Cannabis is the most commonly used illicit drug among pregnant women. Consumption of cannabidiol (CBD), a non-psychoactive component of cannabis, has increased in popularity among pregnant women, with an estimated 20% reporting use. This popularity is due to the perception that CBD is safe to use during pregnancy, despite a limited literature suggesting CBD may affect the developing fetus. Thus, the purpose of the current study was to examine the effects of prenatal CBD exposure.

Methods: Pregnant rats were given 50 mg/kg of CBD daily during gestational days 5-20 via a honey and cookie dough edible vehicle. On postnatal days (PD) 2-12, offspring were tested on various early motor reflexes, including righting, grasping, geotaxis, and cliff avoidance reflexes, in which success and latency were recorded.

Results: Prenatal CBD exposure led to developmental advancements in reflex development, predominantly among males, although some advancements were seen in females on later motor tasks. We are now examining dose-dependent effects to determine how CBD dose influences outcome. These results indicate that prenatal CBD alters the developmental trajectory of brain areas involved in motor function and that there may be sex-dependent outcomes.

Conclusions: Given that careful control of developmental processes is critical for brain and behavioral function, our findings suggest that CBD use during pregnancy may not necessarily be safe for the developing fetus. Supported by CMCR P64-07-001.

“The Impact of Product Formulation on the Pharmacokinetics and Pharmacodynamics of Cannabis Edibles"

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Wana Brands, Vertosa, iC42 Labs, Anresco Labs, ElSohly Labs

Background: Oral cannabis products (or “edibles”) are among the most popular types of available cannabis products, with gummies, drinks and chocolates being among the most common products purchased in retail cannabis dispensaries. Similar to traditional forms of cannabis, edibles that contain delta-9-tetrahydrocannabinol (Δ9-THC) as the primary constituent have abuse liability and can produce unwanted negative effects. Cannabis users often report that edibles produce highly unpredictable effects, making them prone to eliciting adverse events. Inconsistency in cannabis edible effects likely stems, in part, from the large variety of formulations within this diverse product category. Preclinical research has shown that THC absorption is increased when ingested in lipid or “nanoemulsion” formulations relative to non-lipid or non-nanoemulsion formulations. Thus, formulation characteristics may directly impact the magnitude of THC absorption and related effects in humans. Controlled clinical research on edibles is limited and few studies have evaluated if product formulation influences pharmacokinetic (PK) or pharmacodynamic (PD) outcomes.

Methods: This study will characterize PD and PK outcomes associated with different Δ9-THC infused edibles. Participants will complete 9 double-blind, placebo-controlled outpatient sessions in a randomized order. Participants will self-administer either a placebo or an active Δ9-THC-infused product containing a low or a high dose of Δ9-THC.

Results: This study has many important implications for public health. This project will determine how the formulation impacts the speed or magnitude of Δ9-THC absorption, or variability in absorption across individuals, which would be valuable information for clinical decision making and future research on oral cannabinoid products (e.g., inform product selection in future clinical trials).

Conclusions: This information will be vital for educating the general public on given Δ9-THC-infused products which are often used for medicinal purposes. This project will also provide data that can be used to inform impairment profiles associated with novel Δ9-THC-infused products and help refine how these products may be marketed in the future."

THC alleviates inflammation by modulating immune responses in LPS-induced murine inflammation model

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Background: Δ^9-Tetrahydrocannabinol (THC), the primary psychoactive component of cannabis, modulates multiple immune pathways; however, its precise immunological effects and underlying mechanisms remain incompletely understood. While THC exerts immunomodulatory actions largely through cannabinoid receptor signaling, its influence on immune activation triggered by pathogen-associated molecular patterns (PAMPs) has not been fully elucidated. Lipopolysaccharide (LPS) is a potent endotoxin that activates Toll-like receptor 4 (TLR4). Engagement of TLR4 initiates downstream signaling cascades, including the MyD88- and TRIF-dependent pathways, leading to robust immune activation characterized by the production of pro-inflammatory cytokines and the induction of type I interferon (IFN)–stimulated gene (ISG) responses. Cannabinoids modulate innate immune signaling in both the brain and periphery, in part by targeting TLR4-mediated pathways critical for host defense and neuroinflammatory processes.

Methods: Here, we investigated the effects of THC on LPS-induced inflammatory and interferon responses in human monocytic cells, primary monocytes, and a murine model.

Results: In THP-1 cells treated with and without THC in the presence and absence of LPS, THC markedly reduced LPS-induced expression of multiple ISGs and pro-inflammatory cytokines such as IL1b and TNFa, which was further supported by RNA sequencing, which revealed downregulation of type I IFN signaling and inflammatory gene pathways. In primary human monocytes stimulated with LPS and treated with and without THC at different doses, THC decreased surface expression of activation markers CD80, CD83, CD209, and HLA-DR in a dose-independent manner. In vivo, when wild type immunocompetent mice were fed with control diet or THC supplemented diet followed by LPS challenge, THC resulted in the reduction of the frequency of activation marker $CD80^+$ among CD11b myeloid cells in blood and spleen, as well as $CD38^+$ and $CD69^+$ on T cells. Brain RNA-seq analysis further demonstrated attenuated expression of MX1, OAS1, ISG15, IL1B, and TNFa in THC-treated mice compared to controls.

Conclusions: Collectively, these findings demonstrate that THC selectively dampens LPS-induced immune activation and inflammatory gene expression, providing mechanistic insight into its potential role in modulating excessive inflammatory responses.

Cannabis and “Psychosis?”

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Background: “Psychosis” is a general umbrella term used in medicine and psychiatry. It is a dynamic and heterogeneous description which may be a symptom, part of a syndrome essential to a diagnosis or condition like Cannabis-Induced Psychotic Disorder. What is labeled as “psychosis” in medical cannabis literature, however, is often not well-defined. In addition, a similar median age of onset of schizophrenia and cannabis use disorder, as well as shared genetic loci of these disorders complicates this particular relationship. Seemingly contradictory findings relating cannabis and cannabinoids to “psychosis” has affected trust in their use as therapeutics. We discovered that part of the reason may be the nomenclature itself.

Methods: A systematic literature search of published cannabis articles was completed using three databases (PubMed, Google Scholar, PsycINFO) between 2017-2025. Cannabis studies were closely examined, and several hundred terms referred to as “psychosis” were identified by significant statements, codes, key words and phrases in the texts. Thematic analysis was used to analyze the results.

Results: There were many more descriptions of “psychosis” in cannabis publications that were a lower likelihood compared to terms that were a higher likelihood of representing psychosis defined in the psychiatry medical specialty. Some examples include phrases (*self-reported psychotic-like experiences*), descriptions (*at risk of psychosis*), stand-alone definitions (*psychosis proneness*), words taken out of context (anhedonia), less accurate descriptions rather than more accurate alternatives (pareidolia and apophenia, semantic hyper-priming), mislabeling psychosis (pathogenic belief, teleological or divergent thinking), inventing new words (*spiceophrenia*), obsolete diagnosis (*Psychosis, NOS* deemed a "catch-all" diagnosis that does not offer enough specific diagnostic information), non-psychotic disorders and syndromes (culture bound syndromes like Koro, dissociative disorders, some types of catatonia, and delirium), narrow cause and effect reports (cannabis induced Capgras syndrome), symptoms not considered psychotic (perceptual disturbances such as illusions without delirium and hallucinations with intact reality testing), loose interchangeability of labels (psychosis, psychotic disorder and schizophrenia) and counting prescribed antipsychotics for non-psychotic disorders.

Conclusion: An understanding of this circumstance lessens the stigma and may advance cannabis research with respect to psychosis. It is intended to clarify for cannabis clinicians who use the term, “psychosis” in designing and reporting results of clinical trials, developing clinical treatment guidelines and standards of care, and reporting clinical outcomes during the care of cannabis patients.

State of Medical Cannabis in California

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Background: Medical cannabis in California has come a long way since it originally was medically legalized in 1996. In 2018, with the passage of adult-use laws, the landscape has evolved significantly, and questions have been raised about the role and practice of medical cannabis within the clinical setting. To more thoroughly understand this, we have secured a grant from the Department of Cannabis Control DCC to evaluate the state of medical cannabis through the lens of four independent cannabis physicians and their patients.

Methods: A survey was created to evaluate the following aspects of a medical cannabis patient: 1) Age, gender, caregiver involvement, 2) Specific types and amounts of cannabis used (including hemp) and associated costs, 3) Duration of medical cannabis use and approval Length of medical usage/approval, 4) Patient-reported improvements, side effects, and ER visits as a result of medical cannabis.

Results: To date, we have accumulated over 500 active patient surveys that provide insights into the health profiles of medically supervised cannabis patients. Patients range in age from infants and teenagers, whose care is always managed by their parents/guardians, to seniors, some of whom have dementia or mild cognitive impairment and are supported by caregivers. Diagnoses ranged from Autism Spectrum Disorder, cerebral palsy, cancer, dementia, Parkinson's, to chronic and neuropathic pain management. Notably, there have been no emergency room visits reported as a direct result of cannabis use among our patients.

Conclusions: We are in the midst of the data analysis at this time and more detailed findings will be presented at the upcoming UCSD conference. Preliminary results indicate the demographic profile of medical cannabis patients is broader than that suggested by existing studies, which tend to depict cannabis users as males between ages 20 to 40. Our findings reveal that patients who seek medical care include both pediatric, and senior populations. Patients under physician-guided care tend experience better short- and long-term outcomes, reduce their reliance on other medications and avoid emergency room visits. We observed little to no side effects from physician-managed cannabis use. In contrast, individuals who self-administer cannabis appear more likely to have side effects necessitating ER visits. Overall, physician-supervised cannabis use overall has a positive impact on patient outcomes, even amidst the change in legal and policy landscapes that have increased access.

Contribution of genetic factors to individual differences in anxiety in response to the cannabinoids THC and CBD

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Background: Responses to cannabis and cannabinoids vary dramatically among individuals, ranging from euphoria and anxiolysis to anxiety, panic, memory impairment, and in rare cases, psychosis. Twin studies and GWAS suggest a strong genetic contribution to these differences, but human studies are confounded by heterogeneous exposures, environmental influences, lifestyle factors, and reliance on self-reported data. As a result, the genetic basis of complex host responses to cannabinoids remains poorly defined. Leveraging mouse genetics provides an opportunity to overcome these challenges, allowing precise control of cannabinoid exposures, standardized environmental conditions, and comprehensive phenotyping in a population-based model system. We are using the Collaborative Cross (CC) mouse resource, a panel of fully genotyped, genetically diverse strains that captures human-like phenotypic variation, to investigate how genetic background shapes behavioral and molecular responses to cannabinoids. We previously performed an unbiased genetic screen across 30 CC strains, identifying significant strain-to-strain variability in baseline anxiety-like behavior using the light/dark box assay.

Methods: Building on this foundation, we are now examining how acute exposure to delta-9tetrahydrocannabinol (THC), cannabidiol (CBD), or their combination modifies anxiety phenotypes in genetically defined high-, intermediate-, and low-anxiety strains. Mice are tested using light/dark box and elevated plus maze assays 30 minutes after exposure, followed by collection of hippocampal and liver tissues. This systems genetics approach will enable us to identify quantitative trait loci and candidate genes that modulate susceptibility or resilience to cannabinoid-induced changes in anxiety. Transcriptomic profiling of hippocampus and liver will reveal molecular pathways engaged by THC and CBD, including strain-specific differences in cannabinoid metabolism and neural signaling.

Results: Together, these data will define gene–cannabinoid interactions that underlie adverse and beneficial behavioral responses. At the CMCR Symposium, we will present preliminary behavioral analysis from our CC screen, highlighting variability in anxiety phenotypes across strains and early insights into how THC and CBD modulate these responses.

Conclusions: By integrating genetic mapping with behavioral and transcriptomic outcomes, this work will provide mechanistic insight into the biological basis of individual variability in cannabinoid response and inform precision approaches to cannabinoidbased therapeutics.