CCORC 2022 - PROGRAM AND ABSTRACT BOOK

CCORC

CANNABIS CLINICAL OUTCOMES RESEARCH CONFERENCE

May 19-20, 2022

Orlando, FL

Consortium for
Medical Marijuana
Clinical Outcomes Research

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WELCOME FROM THE DIRECTORS

On behalf of the Consortium for Medical Marijuana Clinical Outcomes Research's Scientific Program and Planning Committees, we are delighted to welcome you to our 2nd annual conference: Cannabis Clinical Outcomes Research Conference (CCORC) on May 19th – 20th, 2022 in Orlando, Florida.

CCORC 2021, our inaugural conference, proved to be a central forum for more than 225 researchers, clinicians, policy makers, trainees and other community stakeholders from all over the world to come together virtually to discuss and advance our understanding of the health effects of medical marijuana.

We are very excited to hold CCORC 2022 in-person with virtual options available.

One of the most exciting parts of CCORC 2022 is the opportunity to network, socialize, and get involved with cannabis clinical outcomes research. We expect attendees to be a diverse group of researchers, clinicians, policy makers and more from around the world.

We welcome you to CCORC 2022!

Sincerely,

Almut G. Winterstein, R.Ph, Ph.D, FISPE

Director, Consortium for Medical Marijuana Clinical Outcomes Research

Robert L. Cook, M.D., MPH

Associate Director, Consortium for Medical Marijuana Clinical Outcomes Research

PROGRAM AT A GLANCE

May 19, 2022

TIME EDT	EVENT
9:00-9:30am	**Day 1 Welcome Address Δ** **Dr. Almut Winterstein** Consortium for Medical Marijuana Clinical Outcomes Research University of Florida *Agenda Overview and Introduction to Keynote* **Dr. Amie Goodin** Consortium for Medical Marijuana Clinical Outcomes Research University of Florida
9:30-10:45am	**Keynote: Clarifying Cannabis: Considering the impact of recreational and medical use on cognitive and clinical outcomes* Δ** **Dr. Staci Gruber** McLean Hospital Harvard Medical School
10:45-11:00am	**Exhibitor Hall, Coffee Break**
11:00-12:00pm	**Session: Methods Workshop for Measurement Techniques When Conducting Clinical Cannabis Research** *EMA Assessment Strategies for Medical Marijuana Use and Outcomes* **Dr. Yan Wang** University of Florida Consortium for Medical Marijuana Clinical Outcomes Research *Self-Reported Use Measures and Instruments* **Dr. Catalina Lopez-Quintero** University of Florida *Measuring Doses and Dosing* **Dr. John Markowitz** University of Florida
12:00-1:00pm	**Lunch**
1:00-2:15pm	**Keynote: Effects of THC and CBD: Implications for Future Clinical Trials* Δ** **Dr. Kent Hutchison** Anschutz Medical Campus University of Colorado in Boulder
2:15-2:30pm	**Exhibitor Hall, Coffee Break**
2:30-3:30pm	**Session: Presentations and Q&A of Top Abstracts** Dr. Dinender Singla, University of Central Florida, Moderator **Dr. Karina Villalba** University of Central Florida **Dr. Amie Goodin** University of Florida **Dr. Andrea Cippitelli** Florida Atlantic University

TIME EDT	EVENT
3:30-4:15pm	**Session: IRB Challenges and a Proposed Solution** **Dr. Jeff Konin** Florida International University
4:15-5:00pm	**Workshop: Extending Florida's Adverse Event Reporting System** **Sebastian Jugl** University of Florida
5:00-6:15pm	**Poster Sessions and Exhibitor Hall, Networking Reception**

May 20, 2022

TIME EDT	EVENT
8:00-8:15am	**Day 2 Welcome Address Δ** **Dr. Robert L. Cook** Consortium for Medical Marijuana Clinical Outcomes Research University of Florida
8:15-9:30am	**Keynote: Cannabis Use in Pain and as a Substitute for Opioids* Δ** **Dr. Samer Narouze** Northeast Ohio Medical University Ohio State University College of Medicine American Society of Regional Anesthesia and Pain Medicine American Interventional Headache Society (AIHS)
9:30-10:30am	**Session: Presentations and Q&A of Top Abstracts** Nicole Smolinski, PharmD, University of Florida, Moderator **Erin Berthold** University of Florida **Alexis Cox** Florida State University **Alexandra McMahon** University of Florida
10:30-10:45am	**Exhibitor Hall, Coffee Break**
10:45-11:30am	**Session: Regulatory Challenges in Conducting Cannabis Research in Florida: A Panel Discussion** **Dr. Robert L. Cook** Consortium for Medical Marijuana Clinical Outcomes Research University of Florida *Panel Members:* **Sheila Austin**, MS, ACRP-CP; **Paul A. Borsa**, Ph.D., ATC; **Anthony Ferrari**, Ph.D.; **Paul R. Peluso**, Ph.D.
11:30-12:00pm	**Closing and Reception, Awards Ceremony Δ** **Dr. Ximena Levy** Consortium for Medical Marijuana Clinical Outcomes Research Florida Atlantic University
12:00-1:00pm	**Board Meeting and Invited Lunch Reception**

* Eligible for CME and CPE credits. Please check http://ccorc.mmjoutcomes.org/cme-credit/ and http://ccorc.mmjoutcomes.org/agenda/cpe-credit-2022/ for details.

The University of Florida College of Medicine designates this live activity for a maximum of 3.75 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The University of Florida College of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The University of Florida is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. Each of the Keynote addresses is eligible for 1.25 CPE credits.

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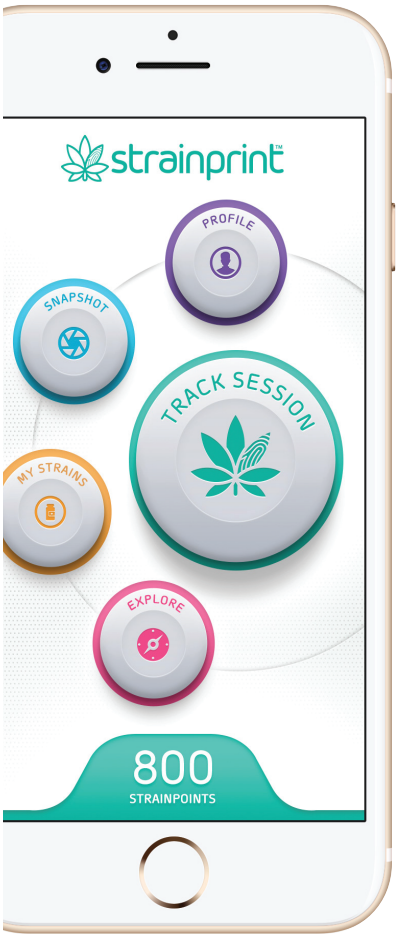

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KEYNOTE SPEAKERS

Staci Gruber, Ph.D.

Clarifying Cannabis: Considering the impact of recreational and medical use on cognitive and clinical outcomes

Director, Cognitive and Clinical Neuroimaging Core, McLean Hospital
Director, Marijuana Investigations for Neuroscience Discovery (MIND), McLean Hospital
Associate Professor of Psychiatry, Harvard Medical School

Staci Gruber, Ph.D. is the Director of the Cognitive and Clinical Neuroimaging Core at McLean Hospital and an Associate Professor of Psychiatry at Harvard Medical School.

Dr. Gruber launched the Marijuana Investigations for Neuroscientific Discovery (MIND) in 2014, which supports numerous projects designed to address the impact of medical cannabis on a number of important variables including cognition, clinical state, pain, sleep, quality of life, brain structure and function and other health-related measures.

She has generated major contributions to the field as the first to assess medical cannabis patients longitudinally, first to acquire neuroimaging data in medical cannabis patients and as Principal Investigator of the first clinical trial of a whole plant-derived, high cannabidiol (CBD) product, which she specifically formulated to treat anxiety.

Research Focus: Impact of medical cannabis use on cognition, clinical state, pain, sleep, quality of life, brain structure and function and other health-related measures.

Kent Hutchison, Ph.D.

Effects of THC and CBD: Implications for Future Clinical Trials

Professor of Psychiatry, Anschutz Medical Campus
Adjunct Professor of Psychology and Neuroscience, University of Colorado in Boulder

Kent Hutchison, Ph.D., is a Professor of Psychiatry at the Anschutz Medical Campus and an Adjunct Professor of Psychology and Neuroscience at the University of Colorado in Boulder. Dr. Hutchison has been an NIH funded scientist for the past 25 years and has published numerous papers related to

substance use research.

Dr. Hutchison has developed and implemented several randomized, placebo controlled, clinical trials to examine the effects of CBD and THC and CBD alone versus a placebo.

Three of his current research projects include the examination of the effects of cannabinoids on opioid use and pain, the study of alcohol use disorder, and the use of hemp-derived CBD in the context of mild cognitive decline and early Alzheimer's disease.

Research Focus: Use of CBD and THC in ratios of CBD only, CBD and THC, and THC only; cognitive outcomes, anxiety, pain and opiate use in relation to cannabis use.

Samer Narouze, M.D., Ph.D.

Cannabis Use in Pain and as a Substitute for Opioid

Associate Professor of Surgery, Northeast Ohio Medical University
Clinical Professor of Anesthesiology and Neurological Surgery, Ohio State University College of Medicine
President, American Society of Regional Anesthesia and Pain Medicine
Chairman, American Interventional Headache Society (AIHS)

Samer Narouze, M.D., Ph.D. (@NarouzeMD) is a Professor of Anesthesiology and Surgery at NEOMED and OUCOM. He is the President of ASRA Pain Medicine Society, the Chairman of the board for the American Interventional Headache Society (AIHS) and the Chairman of the Center for Pain Medicine at Western Reserve Hospital in Cuyahoga Falls, OH.

Dr. Narouze is board certified in anesthesiology, pain medicine, neurology headache medicine and interventional pain management. He serves on many committees for national and international headache and pain organizations.

He has published about 200 research papers, review articles and book chapters. He published few books on Pain and Headache Medicine, interventional ultrasound, and his new book "Cannabinoids and Pain" by Springer was just released in August 2021.

Research Focus: Use of cannabinoids and cannabis in pain medicine, neurology headache medicine and interventional pain management.

SESSION LEADERS AND SPEAKERS

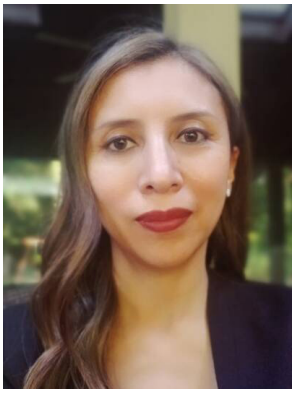
Yan Wang, Ph.D.

EMA Assessment Strategies for Medical Marijuana Use and Outcomes

Assistant Professor, Department of Epidemiology, University of Florida
Faculty Lead - Clinical Core, Consortium for Medical Marijuana Clinical Outcomes Research

Yan Wang is an Assistant Professor of Epidemiology at the University of Florida (UF). Her research interests focus on leveraging advanced technologies and methods (e.g., wearable sensors, ecological momentary assessment/EMA) to improve the understanding of etiology and consequences of substance use (e.g., alcohol, medical marijuana).

Research focus: Leveraging advanced methodology and new technology (e.g., wearable sensor) to improve health behavior monitoring and intervention, marijuana use, alcohol use, mental health and risk behaviors.



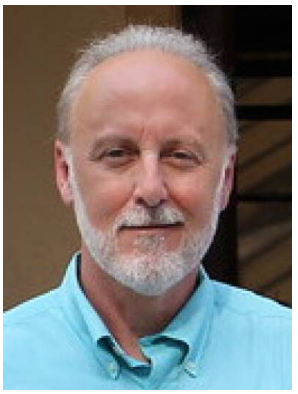
Catalina Lopez-Quintero, Ph.D., MPH

Self-reported Use Measures and Instruments

Assistant Professor, Department of Epidemiology, University of Florida

Dr. Catalina Lopez-Quintero is an assistant professor at the Department of Epidemiology at the University of Florida. Dr. Lopez-Quintero is a Colombian medical doctor with a PhD in public health and post-graduate training and research experience in drug dependence and psychiatric epidemiology, drug use neuropsychology, and drug use and HIV/AIDS disparities.

Research Focus: Disentangling the role that factors at different levels of influence play on the transitions from the early stages of drug use involvement to the development of drug use disorders and other related outcomes.



John Markowitz, Pharm.D., BCPP

Measuring Doses and Dosing

Professor, Department of Pharmacotherapy & Translational Research, University of Florida

Dr. Markowitz's research program has encompassed both in vitro and in vivo investigations including normal volunteer pharmacokinetic studies directed at the assessment of drug-drug interactions in psychiatric pharmacy, botanical-drug

interactions, as well as their associated clinical effects. More recently, the research program has focused on variability in drug metabolism, disposition, and therapeutic response as a consequence of genetic variability influencing both drug transporters and hepatic enzymes.

Research Focus: In vitro and in vivo investigations including normal volunteer pharmacokinetic studies directed at the assessment of drug-drug interactions in psychiatric pharmacy, botanical-drug interactions, as well as their associated clinical effects.

Jeff Konin, Ph.D.

Session Chair

IRB Challenges and a Proposed Solution

Clinical Professor, Department of Athletic Training, Florida International University
Director, DAT Program, Florida International University

Dr. Jeff G. Konin is a Clinical Professor and the Director of the Doctor of Athletic Training program at Florida International University in Miami, Florida. He is a recognized Fellow of the American College of Sports Medicine (ACSM) and the National Athletic Trainers' Association (NATA), and a member of the NATA's Hall of Fame. Dr. Konin's research and scholarship has focused in a number of areas, with an emphasis on preventing, assessing and managing injuries sustained by children playing sports.

Research Focus: sports medicine, physical therapy, athletic related trauma, kinesiology, sports injury pain management

Sebastian Jugl, B.S.Pharm., R.Ph

Session Chair

Introducing, Applying & Assessing an Extension to Existing Adverse Event Reporting Mechanisms in the Floridian Medical Marijuana Program – An Interactive Workshop

Ph.D. Candidate, Department of Pharmaceutical Outcomes & Policy, College of Pharmacy

Sebastian Jugl B.S.Pharm. is a 3rd year PhD student at the Department of Pharmaceutical Outcomes and Policy & the Center for Drug Evaluation, a research assistant at the Consortium for Medical Marijuana clinical outcomes research, a registered pharmacist, and an author for the German pharmaceutical association. Currently his research projects incorporate the use of pharmacoepidemiologic methods to investigate drug utilization, drug safety & effectiveness, and the effects of state and federal laws in medical cannabis research, oncology & women´s health.

Research Focus: Use of pharmacoepidemiologic methods to investigate drug utilization, drug safety & effectiveness, and the effects of state and federal laws in medical cannabis research, oncology & women's health.

Robert L. Cook, M.D., MPH

Session Chair

Regulatory Challenges in Conducting Cannabis Research in Florida: A Panel Discussion

Professor, Department of Epidemiology and College of Medicine, University of Florida
Director, Southern HIV and Alcohol Research Consortium (SHARC)
Associate Director, Consortium for Medical Marijuana Clinical Outcomes Research

Over the past 20 years, Dr. Cook's research has focused on strategies to improve health outcomes related to HIV and sexually transmitted diseases. He is the Director of the Southern HIV Alcohol Research Consortium (SHARC), which supports collaborative research and training related to alcohol and HIV infection across the state of Florida.

Research focus: HIV, sexually transmitted diseases, alcohol, effects of marijuana on HIV-related health and cognition, gut microbiome, neuro-inflammation.

More about this session: A panel consisting of researchers, a university regulatory specialist, and an industry collaborator will discuss their experiences in cannabis-related research. Specifically, the group will discuss their experiences obtaining IRB- and FDA-approvals for a consortium-sponsored pilot clinical trial of CBD. The panel will also discuss potential challenges in extending the research to include THC-containing products, and identify potential resources that could be useful to other researchers seeking to conduct clinical trials of cannabis products.

Session Panelists

Sheila Austin, MS, ACRP-CP
Regulatory Specialist
Clinical and Translational Science Institute
University of Florida

Paul A. Borsa, PhD, ATC
Associate Professor, Department of Applied Physiology & Kinesiology
Director, Sports Medicine Research Laboratory
University of Florida

Anthony Ferrari, PhD
Chief Science Officer
SunFlora, Inc
Palmetto, FL

Paul R. Peluso, Ph.D.
Senior Associate Dean and Professor of Mental Health Counseling
Florida Atlantic University

ORAL PRESENTATIONS OF TOP ABSTRACTS

Andrea Cippitelli, Ph.D.

Abstract: Effects of the non-psychoactive cannabinoid cannabidiol in acute and chronic migraine-like states

Research Assistant Professor, Department of Biomedical Science, Florida Atlantic University

Andrea Cippitelli, Ph.D., is a Research Assistant Professor of Biomedical Science at Charles E. Schmidt College of Medicine at Florida Atlantic University. Dr. Cippitelli's research focuses on the management of substance use disorders through pharmacology and drug discovery. Dr. Cippitelli uses a variety of experimental techniques and rodent models to explore the implications of multiple neurobiological systems in drug abuse and related conditions with the ultimate goal of extending knowledge on these pathological states and finding useful therapies. Dr. Cippitelli's research also focuses in investigating pain disorders including migraine. Migraine is an extremely common but poorly understood nervous system disorder. The development of migraine models and the correct assessment of behavioral measures associated with migraine in laboratory animals is critical to achieve a more adequate management of migraine disorder.

Amie Goodin, Ph.D., M.P.P.

Abstract: Medical Marijuana Treatment Availability in Florida Communities with Higher Proportions of Older Adults

Assistant Professor, Department of Pharamaceutical Outcomes & Policy, University of Florida

Dr. Goodin is an Assistant Professor within the Department of Pharmaceutical Outcomes and Policy (POP) and the Center for Drug Evaluation and Safety (CoDES). She is the lead for Health Services Research track within POP's graduate program as well as the faculty lead for Research Strategy within the Consortium for Medical Marijuana Clinical Outcomes Research. Currently, her research projects incorporate mixed-method approaches to assess the impact of policy changes related to treatment access and utilization for Substance Use Disorders, particularly among persons enrolled in Medicaid and pregnant women.

Research focus: Assess the impact of policy changes related to treatment access and utilization for Substance Use Disorders, particularly among persons enrolled in Medicaid and pregnant women.

Karina Villalba, Ph.D., MPH

Abstract: Cannabis Use and Young Adults in Florida: User Characteristics, Patterns of Use, and its Implications

Assistant Professor, College of Medicine, University of Central Florida

Dr. Villalba is a biobehavioral scientist with a broad understanding and training in basic and behavioral sciences. Dr. Villalba has contributed or led research efforts to adapt and evaluate theoretically and evidence-based interventions for underserved and understudied populations particularly burdened by HIV health disparities, including disproportionate problems with substance use, mental health, and exposure to trauma and violence.

Research focus: intersectionality between violence against women and HIV, substance abuse, and mental health

Erin Berthold

Abstract: Preclinical herb-herb interaction of cannabidiol and kratom in rats

Ph.D. Candidate, Department of Pharmaceutics, University of Florida

Erin Berthold is currently in her final year as a PhD candidate in the Department of Pharmaceutics at the University of Florida College of Pharmacy under the mentorship of Dr. Abhisheak Sharma.

Research Focus: The interaction potential of the major kratom alkaloid, mitragynine, and the major cannabinoid, cannabidiol. Looking to leverage the individual properties of each compound to develop a more readily accessible solution for individuals suffering from substance use disorders. Better understand the risks and prospective benefits of these commonly used natural products in combination by combining preclinical in vivo and in vitro data with translational physiological-based pharmacokinetic models.

Alexandra McMahon, MPH

Abstract: Perceived Effectiveness of Medical Marijuana Among Adults with Chronic Pain: Findings from Interview Data in a Three-Month Pilot Study

Department of Epidemiology, University of Florida

Ms. McMahon is a recent graduate from the Master of

Public Health Program at the University of Florida. She is beginning her PhD in Epidemiology at the University of Miami where she will study genetic epidemiology and health outcomes in chronic disease populations. During her time at UF, she led qualitative analyses on a pilot study funded by UF-CRISP evaluating perceived efficacy of medical marijuana in chronic pain populations. She also served as the Lead Research Assistant in the UF Health Promotion Lab evaluating the integration of technology into weight loss management interventions. She plans to expand her knowledge on alternative medical practices and genetic influences on health outcomes during her PhD studies this fall.

Research Focus: The incorporation of integrative medical practices and genetic epidemiology to improve health outcomes in chronic disease populations.

Alexis Noel Cox, B.Sc.

Abstract: Perinatal Cannabidiol Exposure Decreases Survival in Mice, and Impacts Anxiety-like and Obsessive Compulsive-like Behavior and Object Memory in a Sexually Dimorphic Manner When Raised to Adult

Undergraduate Scholar, Department of Biological Science and Program in Neuroscience, Florida State University

Ms. Cox recently graduated summa cum laude from Florida State University in Biological Science. As a senior undergraduate scholar, she was recognized nationally with the Marion Jewell Hay Award from Phi Beta Kappa. She also served as an undergraduate research leader and successfully acquired a Helen Louis Lee Undergraduate Research Grant. Currently, she and Dr. Debra Ann Fadool lead a team of undergraduate researchers exploring changes in behavior, metabolism, and brain development in adult mice as a result of cannabidiol (CBD) exposure in utero. Ms. Cox has been accepted as a Blazer Graduate Research Fellow to begin her Biomedical Sciences Ph.D. Program at the University of Alabama at Birmingham School of Medicine to study bone development.

Research Focus: Utilizing buried marble, light-dark box, elevated-plus maze, attention task, object memory recognition, and comprehensive laboratory animal monitoring system to phenotype anxiety-like behavior, memory, ADHD-like behavior, obsessive compulsive behavior, ingestive and metabolic parameters in response to acute, chronic, and in utero CBD exposure in mice.

ORAL PRESENTATIONS OF TOP ABSTRACTS

Cannabis Use and Young Adults in Florida: User Characteristics, Patterns of Use, and its Implications

Karina Villalba
University of Central Florida

Co-authors: Jason Ford[1]
[1]University of Central Florida

To our knowledge, there is no research on cannabis use among young adults in Florida. Understanding young adults' attitudes and patterns of use about cannabis can assist healthcare providers, and the State to determine trends in this population. Thus, the overarching aim of this study is to characterize a typical young cannabis user in Florida.

To archive this, we are proposing the following aims, first to compare attitude and demographic characteristics between CBD-dominant and THC-dominant young adults and second, asses the relationship between CBD-dominant use and patterns of use and mental health.

We used the Florida Young Adult Cannabis Study, which included a total of 415 medical cannabis patients and 485 non-patient cannabis users. Demographic and bivariate association we conducted among the two groups (CBD-dominant and THC-dominant), multivariable logistic regression was used to build three models to identify factors associated with CBD-dominant cannabis use.

Close to 49% of young adults were THC-dominant and 51% were CBD-dominant users. Black young adults (AOR = 1.64, 95% CI = 1.11, 2.41) were more likely to be CBD-dominant users than White young adults. College students/graduates (AOR = 1.75, 95% CI = 1.24, 2.45), young adults with an income over $75,000 (AOR = 1.68, 95% CI = 1.10, 2.57), and medical cannabis patients (AOR = 2.71, 95% CI = 1.99, 3.69) were all more likely to be CBD-dominant users. Young adults who had insurance coverage (AOR = 1.56, 95% CI = 1.06, 2.28) were more likely to be CBD-dominant users. While young adults who self-reported fair or poor overall health (AOR = 0.53, 95% CI = 0.31, 0.90) were less likely to indicate CBD-dominant use, and finally, CBD-dominant cannabis use was also more likely among young adults who indicated having a cannabis use disorder (AOR = 1.87, 95% CI = 1.18, 2.96).

The current research addresses an important gap in the literature by identifying characteristics associated with CBD-dominant use among a sample of young adult cannabis users. This is important given the possible therapeutic effects associated with CBD use.

Medical Marijuana Treatment Availability in Florida Communities with Higher Proportions of Older Adults

Amie Goodin
University of Florida

Co-authors: Michael Maguire[1], Joshua Brown[1]
[1]University of Florida

Objective: Medical marijuana must be dispensed via licensed Medical Marijuana Treatment Centers (MMTCs) and treatment authorization must originate from authorized physicians in Florida. Recent studies have demonstrated that a significant proportion of medical marijuana users are older adults. The purpose of this study was to compare concentration of medical marijuana availability (MMTCs and physicians) with proportion of older adults in Florida counties.

Methods: Two measures of medical marijuana treatment availability were defined for all counties: MMTCs/100,000 older residents and authorized physicians/100,000 older residents. Treatment locations from 2020 were downloaded from Florida Department of Health's Office of Medical Marijuana Use (OMMU) public database. Census Bureau data for the year 2020 was used to calculate the proportion of residents age ≥65 years in each county. Counties comprised of >33% older adults were classified as having a large aging population. Of those with large aging populations, treatment availability measures were calculated as a ratio of physicians or MMTCs per 100,000 older residents. Pearson correlations were calculated for treatment availability measures and proportion of older residents, then measures were mapped using Tableau software.

Results: There were a total of 2,234 authorized physicians and 239 MMTCs in 2020. On average, older adults comprise 23% of the population in Florida counties, with 6 out of 67 counties comprised of a large aging population (>33% older adults). Florida counties had 31 authorized physicians/100k older residents [range: 0 to 102], but correlation was not significant (Pearson R=-0.11; p-value=0.38). The highest concentrations of authorized physicians were in Sarasota (45 per 100k) and Indian River (39 per 100k) counties. Florida counties had 4 MMTCs/100k older residents [range: 0 to 25], but correlation was not significant (Pearson R=-0.16; p-value=0.19). The highest concentrations of MMTCs among aging populations were Sarasota (6 per 100k) and Charlotte (4 per 100k) counties.

Conclusion: Medical marijuana treatment availability, as estimated by MMTC and authorized physician concentration, is widely available in areas with large aging populations in Florida. Risk and benefits of medical marijuana treatment, especially related to potential interactions between marijuana and prescription medications, should be tailored for this population to prevent adverse events.

Effects of the non-psychoactive cannabinoid cannabidiol in acute and chronic migraine-like states

Andrea Cippitelli
Florida Atlantic University

Co-authors: Chiara Sturaro[1], Bianca Fakhouryi[1], Katarzyna Targowska-Duda[1], Gilles Zribi[1], Jennifer Schoch[1], Lawrence Toll[1]
[1]Florida Atlantic University

Objective: Migraine is a debilitating disorder characterized by recurrent headaches accompanied by symptoms of anxiety and abnormal sensory sensitivity, including photophobia. Migraine is often inadequately managed by existing treatments. Thus, additional treatment options with improved efficacy and reduced side effects are a research priority. Surprisingly, despite the extensive historical use of Cannabis in headache disorders, there is limited research on the non-psychoactive cannabidiol (CBD) for migraine and there is no scientific evidence to prove that CBD is an effective treatment. Here, we test the efficacy of CBD in preventing and treating prominent symptoms of acute and chronic, pharmacologically-evoked, migraine-like states in mice.

Methods: We developed and characterized in our laboratory an animal model of acute and chronic migraine that involved measures of periorbital allodynia associated with intraperitoneal (i.p.) administration of the migraine-triggering agent calcitonin-gene related peptide (CGRP, 0.1 mg/kg). Periorbital allodynia was assessed through mechanical stimulation of the mouse periorbital region using von Frey filaments applied according to an up down method. CBD (10 and 30 mg/kg, i.p.) was tested for its ability to decrease this and other CGRP-induced migraine-like symptoms, including facial grimace, photophobia and anxiety in male and female C57BL/6J mice.

Results: A single administration of CGRP induced facial hypersensitivity in both male and female mice. Repeated CGRP treatment produced progressively increased levels of basal hyperalgesia in females, but not male mice. A single CBD administration protected mice from hyperalgesia induced by a single CGRP injection, in both males and females. Repeated CBD administration prevented increased levels of basal hyperalgesia induced by repeated CGRP treatment in female mice. CBD, injected after CGRP, reversed CGRP-evoked allodynia. CBD also reduced spontaneous pain traits induced by CGRP administration in female mice. CBD failed in providing protection from CGRP-induced photophobia. Finally, CBD blocked CGRP-induced anxiety in male mice.

Conclusion: Collectively, these results demonstrate the efficacy of CBD in preventing episodic, as well as chronic headache, particularly in female subjects. Importantly, CBD may serve as an abortive agent for treating migraine attacks. CBD also shows efficacy for headache-related conditions such as anxiety and spontaneous pain, but does not seem to protect from photophobia.

Preclinical herb-herb interaction of cannabidiol and kratom in rats

Erin Berthold
University of Florida

Co-authors: Abhisheak Sharma[1], Michelle A. Kuntz[1], Shyam H. Kamble[1], Siva Rama Raju Kanumuri[1], Alexandria S. Senetra[1], Christopher R. McCurdy[1]
[1]University of Florida

Objective: Consumer use of cannabidiol (CBD) continues to increase. Another natural product, kratom, has also seen increased use in the western world and drawn the attention of regulatory bodies as its abuse liability is not well characterized. The major chemical component of kratom is mitragynine, an atypical opioid agonist that is being investigated as a potential aid to individuals suffering from opioid use disorder, though kratom commercial products contain many additional compounds. Individuals are beginning to combine these products, yet nothing is known about their potential to interact. The goal was to characterize the interaction between CBD and kratom.

Methods: For the oral single-dose study, male Sprague Dawley rats (weight 250 ± 25 g) were dosed with 50 mg/kg CBD and after 30 min, 0.8 mL/kg OPMS. OPMS is a commercially available liquid kratom product with a mitragynine content of 12 mg/mL. For the multiple dose study, rats were pretreated with 25 mg/kg CBD and after 30 min received 0.4 mL/kg OPMS. This dosing schedule was repeated every 12 hr (0900 and 2100) for four days. Plasma samples collected throughout the study were analyzed for content of CBD and kratom alkaloids mitragynine, corynantheidine, speciociliatine, speciogynine, paynantheine, and 7-hydroxymitragynine.

Results: With CBD pretreatment, the maximum concentration of mitragynine increased 2.3-fold and the exposure increased 2.8-fold. After a single oral dose an overall increase in the time to maximum concentration, the maximum concentration, and the exposure was observed for all minor alkaloids. Steady state concentrations of mitragynine and CBD showed similar behaviors as those observed after a single oral dose with an increase in both the maximum concentration achieved and the exposure.

Conclusion: All kratom alkaloids had increased exposure with concomitant CBD administration. These results raise concerns for consumers who are taking kratom products and CBD together. The safety and toxicity of minor kratom alkaloids has not been reported but they have shown activity at a variety of receptor subtypes including adrenergic, dopaminergic, opioid, and serotonergic. Until kratom alkaloids are more widely understood and regulated caution should be taken if used in combination with CBD.

Perinatal Cannabidiol Exposure Decreases Survival in Mice, and Impacts Anxiety-like and Obsessive Compulsive-like Behavior and Object Memory in a Sexually Dimorphic Manner When Raised to Adult

Alexis Cox
Florida State University

Co-authors: Tyla Dolezel[1], Claudia Silver[1], Aidan Carley[1], Alejandro Navarez[1], Destinee Gatlin[1], Ezabelle Franck[1], Ryan Ochoa[1], Debra Ann Fadool[1]
[1]Florida State University

Objective: Anxiety, attention, and memory were examined in adult mice following gestational exposure to cannabidiol (CBD), the non-psychoactive ingredient of cannabis. Administration of oral CBD to the pregnant dam was hypothesized to dampen offspring anxiety behaviors when raised to adult.

Methods: Sexually naïve dams were trained to eat 100 mg of strawberry jam from a dish. Following acclimation and two weeks prior to mating, 100 mg/kg CBD or ethanol vehicle was mixed in the jam and administered daily to provide drug treatment throughout gestation and lactation. Once pups were born, some litters were cross-fostered to vehicle treated dams to separate any effects of CBD-induced changes in maternal behavior. At 3 months of age, offspring were behaviorally phenotyped using the buried marble, light-dark box (LDB), elevated plus maze (EPM), object memory recognition, and object attention tasks.

Results: Pups born to CBD-treated mothers had a reduced survival – 62.2% of pups died before being weaned, whereas only 9.5% of non-drug treated pups died. We did not observe changes in litter size, maternal body weight or pup birth weight (postnatal day 0, P0), however, pups born to CBD-treated mothers weighed significantly greater by P10 and P21. In utero exposure caused mice of both sexes to bury more marbles, and females, not males, lost this behavior if they were cross-fostered to control dams. In utero exposure decreased time spent in the light compartment of an LDB apparatus when females were raised to adults, but had no effect on male mice. In utero exposure did not affect performance in an object attention task or the 1-hour object recognition test but it decreased performance of female mice in the 24-hour object recognition test.

Conclusion: In conclusion, our data showed that gestational CBD decreases survival and may produce long-lasting anxiolytic effects for adult female mice. Gestational CBD increases obsessive compulsive-like behavior in adults, which can be reversed in females by early maternal behaviors. Gestational CBD does not alter ADHD-like behavior but decreases long-term memory in female mice as adults.

Perceived Effectiveness of Medical Marijuana Among Adults with Chronic Pain: Findings from Interview Data in a Three-Month Pilot Study

Alexandra McMahon
University of Florida

Co-authors: Deepthi Varma[1], Hannah Fechtel[1], Kimberly Sibille[1], Zhigang Li[1], Robert L. Cook[1], Yan Wang[1]
[1]University of Florida

Objective: Patient reported outcomes are critical to evaluate effectiveness of medical marijuana (MM) as a potential alternative treatment for chronic pain. The study objective was to examine overall perceived effectiveness of medical marijuana among middle-aged and older adults who were newly initiating MM for chronic pain management.

Methods: Interview data from participants in a three-month prospective pilot study on MM's impact on chronic pain and related outcomes were analyzed to assess perceived effectiveness of MM. Participants answered an open-ended question "Overall how effective do you think the MM treatment is for your condition?" in a phone interview approximately one month after baseline, when participants were supposed to find a regimen with a relatively stable dose after self-titration. All responses were transcribed and analyzed using the RADaR (Rigorous and Accelerated Data Reduction) technique.

Results: 51 adults initiating MM for chronic pain were interviewed (52.9% male,
mean age 54.4, SD = 12.0), with the majority (80.3%) identifying as Non-Hispanic White followed by Non-Hispanic Black (13.7%), Multi-racial (3.9%), and Hispanic White (2.0%). Most participants (62.7%) reported MM was effective for pain reduction. The common benefits mentioned included reduction in pain intensity, improved sleep quality, and reduced need for pain and psychiatric medications. Participants also mentioned improvements in mental wellbeing such as better mood, improved focus, and less anxiety, and improvements in physical mobility. Common challenges or concerns mentioned by participants included difficulty finding a suitable product or dose (e.g., could not find the 'sweet spot'), and experiencing side effects such as 'undesired high', 'stomach issues', and a limited 'threshold of pain' treatable by product.

Discussion: Findings suggest a majority of participants perceived MM to be effective overall for chronic pain management, with improved physical and mental functioning and reduction in other medications as commonly cited benefits. However, sides effects and difficulty in identifying proper product and dosage also warrant future investigation as MM becomes a more prevalent treatment option for chronic pain.

BASIC SCIENCE AND TRANSLATIONAL

The Chemistry of Vaping and Dabbing Cannabinoid Acetates

Kaelas Munger
Portland State University

Co-authors: Robert Strongin[1]
[1]Portland State University

Objectives: One of the newer cannabinoid compounds that is being sold to consumers is THC acetate as well as related acetylated products formed from CBN and CBD. During the lung injury outbreak that was first recognized in the summer of 2019, it had been shown that vaping vitamin E acetate led to the formation of ketene. Ketene is a highly reactive poison that was cited as a possible cause of e-cigarette or vaping product use-associated lung injury (EVALI). The objective of this study is to determine if ketene can be produced from vaping cannabinoid acetates.

Methods: Commercial formulations and pure standards of cannabinoid acetates were aerosolized using a temperature-controlled ceramic electronic "nail", a hot surface routinely used for the flash vaporization of cannabinoid concentrate products. The vaporized aerosol was pulled through an impinger containing CDCl3 (NMR solvent) and benzylamine (ketene trapping agent). The ketene-benzylamine product (N-benzylacetamide) was analyzed by quantitative NMR.

Results: N-benzylacetamide formation was observed for all cannabinoids studied. Exposure levels and toxicological thresholds will be presented.

Conclusions: Vaping cannabinoid acetates leads to ketene emissions. Vaping these products thus could be putting users at risk.

Evaluation of chronic combination oxycodone and cannabidiol treatment on pain behavior in an operant pain model

Ariana Brice-Tutt
University of Florida

Co-authors: Wendi Malphurs[1], Robert M. Caudle[1], Marcelo Febo[1], Barry Setlow[1], Niall P Murphy[1], John Neubert[1]
[1]University of Florida

Objective: Investigate the effect of chronic oxycodone and cannabidiol treatment, alone or in combination, on behavior using an operant orofacial reward-pain conflict model.

Methods: Using the orofacial pain assessment device (OPAD) rats were trained to consume a positive reinforcer of a sweetened condensed milk solution under nociceptive (44.5°C) and non-nociceptive (37°C) conditions. We then investigated the effect of chronic oxycodone (0.56 mg/kg, i.p.) and cannabidiol (3.2 and 10 mg/kg, i.p.) treatment, alone or in combination, on operant responding at the different temperatures over 14 days of treatment.

Results: Oxycodone increased responding under both thermal conditions. Neither dose of cannabidiol administered alone altered responding but when combined with oxycodone, cannabidiol dose-dependently increased responding beyond that produced by oxycodone alone. This action was more

efficacious at the higher temperature, suggestive of a largely analgesic effect.

Conclusions: These results suggest that while being devoid of any inherent activity, cannabidiol may potentiate the analgesic effect of oxycodone. As such, cannabidiol may be useful as an opioid-sparing approach to treating pain. Future work will further investigate oxycodone and cannabidiol interactions, particularly in the context of oxycodone reinforcement and reward.

Transcriptomic Analysis of Cannabidiol and Tetrahydrocannabivarin Revealed New Molecular Targets for Treatment of Experimental Diabetic Neuropathy

Anil Kumar Kalvala
Florida A&M University

Co-authors: Arvind Bagde[1], Mandip Singh Sachdeva[1]
[1]Florida A&M University

Purpose: To identify the transcriptomic signatures of Cannabidiol (CBD) and tetrahydrocannabivarin (THCV) in Streptozotocin induced experimental diabetic neuropathy (DN)

Methods: Animals were rendered diabetic using STZ (55 mg/kg, i.p). CBD was administered (10 & 20 mg/kg, i.p) and THCV (15 & 30 mg/kg, i.p) during the last 4 weeks of 12 week diabetic period. The animals' pain perception was assessed using the Hargreaves plantar test, hot and cold plate method, vonfrey aesthesiometer, and Randal Sellito apparatus, and nerve functional assessment using the Laser Doppler oxymeter. After the study, the animals' blood was drawn to measure blood glucose levels and their DRGs were isolated for transcriptomic studies.

Results: Diabetic animals after eight weeks significantly ($P<0.001$) increased hypersensitivity to thermal and mechanical pain and also significantly ($p<0.001$) reduced nerve blood flow when compared to the age matched control animals. CBD and THCV treatment reversed these effects in a dose-dependent manner while having no effect on the animals' body weights or blood glucose levels. Differently expressed genes (transcriptomic analysis) have been discovered in the isolated DRGs of control, diabetic, and treated animals, with 32 genes in the control group, 33 in the THCV group, and 45 in the CBD group, all of which differ from the genes expressed in diabetic animals' DRGs. These genes regulating nerve function by affecting the RAP1 signaling pathway, MAP kinase signaling pathway, neurotrophin signaling pathway, Parkinson's disease, Alzheimer's disease, focal adhesion, insulin signaling pathway, microRNAs in cancer, and others according to KEGG analysis.

Conclusion: Despite the fact that CBD and THCV are non-psychoactive medical marijuana components, they differ in their ability to regulate different genes that contribute to the health of neurons in diabetic condition. More research is needed to understand how these two compounds work together to reduce diabetic pain.

Proteomics and Transcriptomics Uncover the Molecular Targets of CBD and THCV in the Sensitization of Doxorubicin against DOX-resistant MDAMB 231 Xenografts

Mandip Singh Sachdeva
Florida A&M University

Co-authors: Nimma Ramesh[1], Anil Kumar Kalvala[1], Arvind Bagde[1]
[1]Florida A&M University

Purpose: To study the Chemosensitization effects of cannabidiol (CBD) and tetrahydrocannabivarin (THCV) in combination with doxorubicin (DOX) against triple negative breast cancers xenografts.

Methods: The chemo sensitization effect of CBD and THCV in combination with DOX was studied using xenotransplanted DOX resistant MDA-MB-231 cells. After subcutaneous injection of 2.5 million DOX resistant MDA-MB-231 cells in 100 µL matrigel, nude mice were randomized to one of six groups (Control, DOX alone, CBD alone, CBD+DOX, THCV alone and THCV+DOX). In the combination study, CBD (10 mg/kg, i.p.) and THCV (15 mg/kg, i.p.) were given one day before DOX (5 mg/kg, i.p.) to assess the chemo sensitization effect. The treatment was repeated twice a week for 3 weeks until the control group reached 6000 mm3. Using a vernier caliper, the tumor volumes were measured. The animals were euthanized and their blood and tumors collected for further study.

Results: CBD and THCV pre-treatment effectively increased DOX's anticancer potentials, reducing tumor growth and development in mice bearing DOX resistant MDA-MB-231 tumors. Data from RNA sequencing and proteomics revealed that CBD and THCV regulate apoptosis, oxidative stress, and inflammation by targeting the PDL-1 pathway, AMPK pathway, histone proteins, sertonergic pathway, CB1 receptors, and P38-MAPKinase pathway, thereby enhancing the chemosensitization effects of DOX against MDA-MB-231 breast cancers. RT-PCR and westernblot analysis were used to validate the same expression genes and proteins found in RNA sequencing and proteomics. In addition, we discovered significant changes in histone acetylations when CBD/THCV was combined with DOX.

Conclusion: According to the results of RNA sequencing and proteomic studies, CBD and THCV appear to have a chemosensitization effect on DOX by reversing histone modifications and their downstream effectors.

Mechanistic evaluation of combined Cannabis components cannabidiol and β-caryophyllene in reducing chronic pain in a rat SCI model

Amanda Pacheco-Spiewak
University of Miami

Co-authors: Anjalika Eeswara[1], Shirah Aguayo[1], Stanislava Jergova[1], Jacqueline Sagen[1]
[1]University of Miami

Objective: Medical marijuana is often used to relieve pain, but there is a paucity of preclinical studies which

evaluate the effects of cannabis components in a spinal cord injury (SCI) model. Previous studies in our lab have established optimal therapeutic doses of two cannabis components, Cannabidiol (CBD) and β-caryophyllene (BCP), that synergistically or additively attenuate allodynia associated with SCI. To elaborate on our previous findings, 3 aims were pursued in this study: (1) assess for adverse side effects following CBD:BCP coadministration, (2) explore possible mechanisms of action underlying pain reduction, and (3) determine whether long-term CBD:BCP administration reduces opioid-seeking behavior.

Methods: Using male and female Sprague-Dawley rats, spinal cord injuries were induced using a clip compression model at mid-thoracic levels. To assess for adverse side effects, we evaluated disturbances in motor coordination, catalepsy, and body temperature using our highest therapeutic dose. Next, we pretreated with selective CB1, CB2 and opioid antagonists followed by coadministration of CBD:BCP at the pre-determined A50 dose and evaluated for tactile and cold allodynia. Lastly, we used the Conditioned Place Preference (CPP) test with low dose morphine as an analgesic reinforcing agent. CBD:BCP treated or controls were paired with morphine on their non-preferred side and saline on their preferred side, then assessed for CPP.

Results: Coadministration of CBD:BCP did not produce any adverse effects in the behaviors observed. Neither administration of AM630 nor naloxone had any effect on tactile and cold allodynia. However, administration of AM251 reduced or completely blocked the beneficial analgesic effects of CBD:BCP. Furthermore, animals who received CBD:BCP coadministration showed reduced morphine-seeking behavior compared to SCI animals who received morphine only.

Conclusion: These results suggest that CBD:BCP coadministration is both a safe and effective treatment option for SCI-related pain. Further, their use as a supplemental therapeutic agent could potentially reduce opioids needed for effective pain management. Since neither CBD nor BCP are thought to act via the CB1 receptor, our results showing reversal of CBD:BCP analgesic effects by a selective CB1 antagonist suggest potential novel interaction between the 2 components in SCI that may underlie the robust beneficial effects of this combination.

Evaluation of Cannabis constituents in a model of phantom limb pain in rats

Anjalika Eeswara
University of Miami

Co-authors: Amanda Pacheco-Spiewak[1], Stanislava Jergova[1], Jacqueline Sagen[1]
[1]University of Miami

Objective: Phantom Limb Pain (PLP) often results from medically required limb amputation and becomes difficult to manage due to underlying inflammation and other neuropathologies, affecting up to 85% of amputees. Medical marijuana is often used for pain relief and may be beneficial for chronic pain syndromes like PLP due to the wealth of cannabinoid (CB) compounds acting via distinct or synergistic mechanisms. The goal of this study was to evaluate the analgesic potential of delta-9-tetrahydrocannabinol (THC), Cannabidiol (CBD), β-caryophyllene (BCP) and their combination in preventing or reversing PLP-like behavior.

Methods: Using male Sprague-Dawley

rats, complete sciatic nerve transection was used to replicate limb amputation. To model complex limb injuries leading to medically-indication amputation, first chronic constriction injury (CCI) was induced using chromic gut ligatures placed around the sciatic nerve. One week later intraplantar formalin was injected 2 hours prior to performing complete axotomy. To assess for PLP, animals were observed daily using a scale designed to capture and distinguish overall autotomy severity. Based on previous studies in our lab that established optimal synergistic CBD:BCP doses, animals were injected twice daily with either THC, CBD:BCP or THC:CBD:BCP at the following doses: 0.04 mg/kg THC, 2.0 mg/kg CBD and 16.0 mg/kg BCP. Animals were sacrificed when proximal injury appeared, with the day of termination recorded, or by 72 days post-axotomy.

Results: Administration of all of the tested cannabis combinations showed attenuation in the severity and onset of PLP-like behaviors compared to the vehicle controls. Comparison between experimental groups showed that animals treated with either THC alone or CBD:BCP combination displayed lower autotomy scores compared to animals receiving all three together (THC:CBD:BCP). This may be due to competing partial agonist effects of one or more of the components, and will be further investigated. No overt side effects were observed following any treatments.

Conclusion: These findings further support the novel use of cannabis constituents as therapeutic agents for the management of neuropathic pain syndromes. In particular, identification of effective combinations of mechanistically distinct cannabis components may be beneficial in preventing the development of debilitating and difficult-to-treat phantom limb pain.

Extracellular Vesicles from Human Umbilical Cord Mesenchymal Stem Cells Loaded with Cannabidiol Alleviate Paclitaxel Induced Peripheral Neuropathy

Mandip Singh Sachdeva
Florida A&M University

Co-authors: Peggy Arthur[1], Arvin Badge[1], Anil Kumar Kalvala[1]
[1]Florida A&M University

Purpose: Chronic paclitaxel (PTX) treatment causes excruciating pain in cancer patients, limiting its use in cancer chemotherapy. Herein, neuroprotective potential of synthetic cannabidiol (CBD) and CBD formulated in extracellular vesicles (CBD-EVs) isolated from human umbilical cord derived mesenchymal stem cells were studied against PTX-induced neuropathic pain (PIPN) in C57BL/6J mice.

Methods: PTX (8 mg/kg, i.p,) was injected every other day (four doses) to induce neuropathy in C57BL/6J mice. CBD and CBD-EVs was administered (5 mg/kg, i.p) for 6 weeks with twice a week frequency. At the end of study, behavior of the animals towards pain perception were measured using Hargreaves plantar apparatus, hot and cold tail immersion test, vonfrey aesthesiometer and randalsellito apparatus. Dorsal root ganglions (DRGs) were isolated from animals for molecular studies. Further, invitro studies were conducted in DRG primary cultures to study the mitochondrial effects of CBD and CBD-EVs against PTX insult.

Results: EVs and CBD-EVs particle size, surface roughness, nanomechanical attributes, stability, and release studies were investigated. CBD-EVs treatment significantly improved mechanical and thermal hypersensitivity ($P<0.001$) as compared to EVs or CBD alone. PTX-treated mice's dorsal root ganglions and spinal homogenates had mitochondrial dysfunction which was significantly improved by CBD and CBD-EVs by regulating the AMPK pathway ($P<0.001$). Blocking studies with 5HT1A receptors and AMPK demonstrated that CBD had no effect on PIPN neurobehavioral or mitochondrial function.

Conclusion: Our results suggest that CBD-EVs can be a novel therapeutic option for the treatment of PIPN and CBD treatment activates AMPK axis in regulating PIPN.

Clinical Drug Interaction Assessment of Cannabidiol and Methylphenidate

John S. Markowitz
University of Florida

Co-authors: Brandon Klee[1], Ludmila De Faria[1], Qingchen Zhang[1], Philip W. Melchert[1], Reginald Frye[1], Yuli Qian[1]
[1]University of Florida

Medical cannabis (MC) refers to cannabis or cannabis-based products recommended to alleviate or reduce symptoms of a medical condition or a disease. The two primary cannabinoids utilized for their therapeutic properties are cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC). MC may consist of purified single agents (e.g. CBD or THC), or complex mixtures within multiple which may be administered via a range of dosing routes. Drug-drug interactions (DDIs) are a significant cause of ED visits, hospital admissions and increased morbidity and mortality. Importantly, MC is frequently used by complex medical patients taking conventional prescription medications and the DDI potential of MC remains only partially understood. In vitro data indicate that THC and CBD can potently inhibit the drug metabolizing enzyme, carboxylesterase (CES1). This finding may be significant since functional CES1 is required for both detoxification and metabolic activation of prodrugs.

Objective: An open-label, placebo-controlled, crossover study in healthy subjects (n=12) assessed the influence of 4-days of either 750 mg CBD oral solution (Epidiolex®) twice daily vs placebo on a 10 mg dose of the CES1 substrate methylphenidate (MPH; Ritalin®).

Methods: Following a run-in of CBD or placebo, an additional dose of CBD or placebo, and 10 mg of MPH was administered. Serial blood samples were collected over 8 hrs and concentrations of MPH and CBD were measured by LC-MS/MS. Pharmacokinetic parameters were summarized by noncompartmental analyses.

Results: The MPH maximum plasma concentration (Cmax) was reached within 0.5-3 h and CBD (1-6 hours). Co-administration of CBD led to a numerical increase in the exposure to MPH. The ratio (90% CI) of AUCinf and Cmax central values when MPH was administered with CBD versus alone were 1.09 (0.98, 1.22) and 1.08 (0.87, 1.35), respectively. The geometric mean AUC0-8 and Cmax of CBD were 1470 ng·hr/mL and 360 ng/mL, respectively. There was a trend of increased MPH exposure with CBD co-administration.

Conclusion: CBD at the dose evaluated, produced only weak and clinically insignificant effects on MPH exposure. However, given the positive trend observed between MPH and

CBD exposure, some vigilance is warranted when CBD is administered at higher doses or with CES1 substrate medications.

Endocannabinoid modulation of the mouse Insular Cortex

Mariela Marques
Florida State University

Co-authors: Cecilia G. Bouaichi[1], Vincis Roberto[1]
[1]Florida State University

In recent years, the endocannabinoid system (ECS) has emerged as one of the most important neuromodulatory systems involved in the regulation of food intake. It has gathered significant attention as a promising therapeutic target in eating disorders. Stimulation of cannabinoid receptors with exogenous ligands has been shown to increase appetite and food intake towards food with high palatability.

In addition, the ECS has been shown to play a role in neural processing of salient stimuli important for food-seeking and eating initiation. While animal studies have indicated that these effects result in part from ECS modulation of the mesolimbic reward system, less information is available on endocannabinoid influences on cortical regions important for eating behaviors.

For all these reasons, we believe that understanding the neuromodulatory effect of endocannabinoids on neural processing of food-predicting cues within the mouse Insular Cortex (IC) will increase our knowledge of the neurobiological mechanisms of cannabinoid actions and provide crucial information for the development of cannabinoid-based pharmacotherapies.

Here we will present two parts of this research. First, we are going we present neural data using a new novel genetically encoded cannabinoid indicator that allowed us to record the endocannabinoid modulation within the IC while the animals perform a taste-related task. Second, we are going to present behavioral data of male and female mice engaged in a taste-related task, measured before and after pharmacological manipulation of the ECS in the IC.

An Exogenous Cannabinoid Decreases Olfactory Sensitivity in Non-fasted Mice

Chloe E Johnson
Florida State University

Co-authors: Douglas A. Storace[1], Adam K. Dewan[1]
[1]Florida State University

The endocannabinoid system is a widespread neuromodulatory network that influences numerous aspects of sensory perception including olfactory processes. Previous research in rodents has suggested that endocannabinoids may regulate food intake through an olfactory-dependent mechanism (Soria-Gómez & Bellocchio et al. 2014). Specifically, cannabinoid type-1 (CB1) receptors within the granule cell layer of the main olfactory bulb (MOB) were proposed to stimulate ingestion in fasted mice by enhancing their olfactory sensitivity.

To further explore this phenomenon, we used an operant conditioning go/no-go assay with highly reproducible odor stimulus delivery to measure olfactory thresholds in mice. Infusions of the CB1 agonist, WIN 55,212-2, (WIN) directly into the granule cell layer (GCL) of the MOB in these animals, yielded a significant decrease in behavioral

sensitivity as compared to vehicle or no manipulation ($p = 0.001$). Intrabulb infusions of the CB1 antagonist, AM251, into the GCL did not have a significant effect on olfactory sensitivity compared to vehicle ($p = 0.35$).

Further, peripheral injections of WIN also did not influence odor detection ($p = 0.76$), contrary to previous findings utilizing this manipulation. These results indicate that exogenous cannabinoids acting on granule cells, blunt rather than enhance olfactory sensitivity, at least in non-fasted mice. Additional research is needed to uncover how metabolic state (e.g., fasting) influences cannabinoid signaling within the olfactory bulb and ultimately odor perception.

Synthetic cannabinoids as a host-targeting approach to reduce inflammation and clear intracellular infection

Hailey Barker
University of Florida

Co-authors: Mariola J. Edelmann[1]
[1]University of Florida

Salmonella Typhimurium is a Gram-negative intracellular bacterium that causes foodborne illness, characterized by robust inflammation of the gastrointestinal tract. Salmonella infects a variety of cells, including antigen-presenting cells such as macrophages. Our laboratory discovered that host lipid metabolism is a critical process targeted by this pathogen. Specifically, Salmonella affects the host endocannabinoid (eCB) metabolism involved in the cell's anti-inflammatory status.

Upon the highly proinflammatory infection with Salmonella that causes damage to the epithelial cells of the small intestine, there is a critical need for the host macrophage to shift from an M1 phenotype to M2. M2 phenotype is associated with resolving inflammation and improvement in tissue healing. Our study has demonstrated that eCBs and synthetic cannabinoids (CBs) prime macrophages towards a more phagocytic and less inflammatory M2 phenotype. Hence, the CBs are expected to help with bacterial clearance and reduce inflammation.

This study aimed to determine if synthetic CBs can modify innate immune responses directed against Salmonella and help maintain homeostasis during this highly inflammatory infection. Towards this goal, we infected RAW264.7 or bone marrow-derived primary macrophages (BMDMs) with S. Typhimurium, followed by exposure to such CBs as noladin ether and WIN55,212-2. The cytokine analysis was done at 2- and 24-hours post-infection, revealing that WIN55,212-2 can completely block proinflammatory TNF-alpha responses. Additionally, we evaluated the effect of CBs on bacterial clearance, where WIN55,212-2 was shown to increase bacterial clearance.

Overall, our results suggest that CBs can be used to decrease inflammation and promote host pro-phagocytic functions during Salmonella infection.

EDUCATION, QUALITY, AND SAFETY

Evaluation of administrators' and clinicians' knowledge of, attitudes about, and barriers to medical marijuana (MMJ) utilization in Florida's long-term care settings

Jennifer Attonito
Florida Atlantic University

Co-authors: Katherine Freeman[1], Ximena Levy[1], George Luck[1], Bernardo Reyes[1], Melanie Bone[12]
[1]Florida Atlantic University
[2]Dr. Melanie Bone

Objective: to evaluate administrators' and clinicians' knowledge of, attitudes about, and barriers to medical marijuana (MMJ) utilization in Florida's long-term care settings.

Methods: A survey was developed, peer-reviewed, and delivered to clinicians and administrators in nursing homes and assisted living facilities throughout the state mainly via email. From November 2021 through February 2022, data on respondents' age, sex, race/ethnicity, and title, as well as type and size of facility were collected. Questions were grouped to reflect 1) attitudes; 2) knowledge; 3) barriers. Frequencies of respondent characteristics were described, and correlations were calculated between factors.

Results: During this period, 117 responses were collected: 21.1% were physicians, 36.8% were nurses, and 42.1% were other professionals; 52% reported having an administrative role. The mean age of respondents was 47.2 years (SD=13.5); 74.4% identified as female, with 5.4% identifying as Black or African American and 73% as Caucasian/White. Regarding ethnicity, 17.6% identified as Hispanic, Spanish or Latinx. About half of the facilities had under 150 beds, with the median number of residents at 150. Significant ($p<0.05$) correlations were found between belief that MMJ is a viable therapy and a) having received adequate training on MMJ, b) understanding differences between MMJ and CBD, c) awareness of different routes of MMJ administration and d) knowing how to obtain an MMJ card in FL. Older respondents were more likely to indicate that MMJ was not helpful for managing certain symptoms (e.g. insomnia). Females were more likely to have reported receiving inadequate MMJ training and inexperience discussing MMJ with patients; however, males were more likely to disagree that healthcare professionals should receive MMJ training. Latinx respondents were more likely to disagree that providers should recommend MMJ for some conditions and that MMJ could have concerning interactions with other therapies. The most frequently selected barriers to recommending MMJ for patients were not having enough training and lack of clinical guidelines.

Conclusion: These observations indicate substantial need for training and clinical guidelines for clinicians in residential, long-term care in Florida. Given the prevalence of symptoms known to respond to MMJ among older adults,1-3 facilitating access to MMJ would be helpful.

Performance Assessment Measures: Florida A&M University (FAMU) Medical Marijuana Education and Research Initiative (MMERI) Public Education Plan

Patricia Green-Powell
Florida A&M University

Co-authors: Michelle M. Wilson[1], Marixcia Chrishon-Jones[1], G.P. Mendie[1], Bagnama V. King[1]
[1]Florida A&M University

Objective: Florida A&M University (FAMU) established the Medical Marijuana Education and Research Initiative (MMERI) to educate minorities about marijuana for medical use and the impact of the unlawful use of marijuana on minority communities, pursuant to Section 381.986 Florida Statutes (F.S.). This presentation provides an overview and update on ongoing assessment measures of how MMERI's Public Education Plan (Education, Community Engagement, and Communication) has educated and engaged individuals using education courses, print and broadcast media, public service announcements, virtual technologies, including e-Newsletters and virtual forums. This presentation also presents the evaluation of the statewide impact of MMERI's engagements, programs, courses, and activities. In July, 2020, the FAMU MMERI launched an integrated Public Education Plan for the fiscal year 2020-2021 and 2021-2022. It includes results-based approaches to Educate, Learn and Talk about marijuana with minority and diverse audiences statewide.

Methods: Assessment measures, such as, descriptive statistics with comparative analyses using quantitative and qualitative data, are used to organize, summarize and report on selected activities. These data are extracted from formative and summative data results and reported in the required legislative Quarterly Reports. The FAMU MMERI Core Metrics for the three key components of the Public Education Plan, include material downloads; consumer E-newsletter signups; requests for information, digital and social media analytics, including reach, impressions, click-through rate, downloads, and user engagement; estimated listenership and circulation of print, radio, and outdoor advertising; audience attendance at events, programs, and activities (virtual and in-person); responses to pre- and post-activity surveys and questionnaires, and audience sentiment, share of voice, and public commentary. It includes results-based approaches to Educate, Learn and Talk about marijuana with audiences statewide.

Results: FAMU's MMERI educated minorities about marijuana for medical use and the impact of the unlawful use of marijuana, pursuant to Section 381.986 Florida Statutes. However, the invaluable data extracted from assessment and surveys, provided critical insight showing participants not only moved from one level of competency to a higher one in the cognitive domain, but in the affective domain as well.

Institutional Review Board Challenges Associated with Contemporary Cannabis-based Proposals

Jeff Konin
Florida International University

The primary purpose of an institutional review board (IRB) is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. (Grady 2015) As noted by Grady, the research landscape has grown and evolved since the inception of the IRBs in 1974 and is likely one of the reasons inconsistencies in the IRB review and in the application of federal regulations has led to the dissatisfaction of investigators.

In Florida, the Consortium for Medical Marijuana Clinical Outcomes Research (CMMCOR) was established in 2019 for the purpose of conducting, sharing, and supporting research on the effects of medical marijuana on health conditions and symptoms. The CMMCOR is comprised of selected Universities across the state and works to contribute to the understanding of medical marijuana. In accordance with the US regulatory requirements, each institution board must include a scientific member amongst the diverse make-up of at least 5 in total, whose responsibilities include evaluating research acceptability related to laws, regulations, institutional commitments, and professional standards. This includes determining the levels of risk and anticipated benefits of a proposed study Given the recent financially supported cannabis research initiatives in Florida and the complexity of the regulations surrounding marijuana laws in addition to the limited expertise of institutional faculty, it is proposed to establish a centralized review model where the combined Florida institutions form an alliance a create a new central IRB for the sole purposes most accurately reviewing cannabis-based research proposals.

Federal regulations permit such centralized review boards for the primary purposes of minimizing redundant reviews, alleviating the overall burden, reducing delays in reviews, and facilitating member expertise for a given research focus area. Resistance to adopting a central review have been based on the importance of local context, local accountability, liability, discomfort with relinquishing control over the review, uncertainty of the quality of the review, and logistical concerns of cost-sharing. It is proposed that for the purposes of effectively studying medical marijuana under one state program that a centralized IRB would serve the initiative well.

R/THCO: A Rapid Netnographic Examination of THC-O-Acetate

Carlton Bone
Portland State University

Co-authors: Upward Hemp Kitchen, LLC

The use of rapid online ethnographic assessment represents a novel exploration into the growing phenomenon of semi-synthetic cannabinoids. This research outlines the emergence of an online community dedicated to the consumption and distribution of the substance, THC-O-Acetate.

The role of prosumers of these products as mediators of knowledge and substances is explored, to

contextualize the nature of the broader growth of semi-synthetic cannabinoid markets. Observations about the perceived safety and potency of these substances are noted in the context of the overarching regulatory landscape in which these substances are emerging, with implications for their regulation discussed in the conclusion.

While the use of rapid ethnographic methodologies has been explored in design processes [Heinonen and Medberg 2018] and medical settings [Ackerman et al 2015], the utilization of online field sites and social media networks as subject communities reflect the more integrated technological approach known as netnography [Kozinets 2010]. As rapid ethnographic engagement is usually limited temporally, the utilization of digital networks of information and community allows for a more elaborate picture, especially when combined with other methods of "Time Deepening" [Millen 2000].

An important distinction between more traditional ethnography and the methods utilized for this research is that the researcher did not use data collected from personal engagements, interviews, or focus groups in order to avoid ethical complications that may arise from the author's own embedded position as a cannabis industry stakeholder. The remainder of this section will explain the motivations behind site choice, and the background of the community is explored.

POPULATION HEALTH AND CLINICAL

Factors Associated with the Perceived Effectiveness of Marijuana for Anxiety Among People Living with HIV

Karina Villalba
University of Central Florida

Co-authors: Ruba Sajdeya[1], Li Yancheng[1], Stella Seeger[1], Christa Cook[2], Jocelyn Mueller, Jason Ford[2], Robert L. Cook1[1]
[1]University of Florida
[2]Unviersity of Central Florida

Among people living with HIV (PLWH), the prevalence rates of marijuana use range between 20 to 60%, with more than half using marijuana to manage anxiety symptoms. However, not all PLWH perceive marijuana as an effective treatment for anxiety. Understanding which factors are associated with perceived marijuana effectiveness has the potential to improve therapeutic recommendations for PLWH.

Thus, this study aimed to identify specific characteristics (i.e., demographic and health conditions) associated with perceived marijuana effectiveness for anxiety among PLWH. This was a cross-sectional study using baseline data from the Marijuana and Potential Long-term Effects (MAPLE) Study. Demographic characteristics included age, sex, sexual orientation, and health conditions (e.g., physical, mental). The effectiveness score was dichotomized into two categories, not very effective (0-8) and very effective (9-10). The descriptive analysis was done using Chi-Square and Fisher's exact tests for categorical variables (N %) and the Mann-Whitney test for numerical variables (Median IQR). The multivariate logistic regression analyses were performed to identify characteristics associated with perceived effectiveness using the backward elimination method.

A total of 187 participants who self-reported anxiety (Yes/No) or had a GAD-7 score ≥ 10, or those who reported using cannabis for anxiety/ stress were included in the analysis. The median (IQR) age was 50 (39, 57), 62% were males, 62% were African Americans, and 57% were heterosexual. In the bivariate analysis, perceived marijuana effectiveness for anxiety was significantly greater in women, LGBTQ, and self-report schizophrenia, cancer, and chronic lung disease ($p \leq 0.05$).

In the adjusted analysis, PLWH who were LGBTQ (OR 0.26, 95% CI .10 - .67) or reported diabetes (OR 0.14, 95% CI .02 -.95), depression (OR 0.37, 95% CI .14-.97), or schizophrenia (OR 0.12, 95% CI .02-.64) were less likely to report marijuana as very effective; whereas those with PTSD (OR 3.7, 95% CI 1.10-12.6) and cancer (OR 11.7, 95% CI 1.1 – 128.5) were more likely to report marijuana as very effective for anxiety. No other variables were significant in the bivariate or multivariate analyses.

The current research addressed an important gap in the literature by identifying characteristics associated with perceived marijuana effectiveness among PLWH who reported anxiety.

The co-presence of opioids in Cannabinoid-related mortality during the COVID-19 pandemic in Florida

Armiel Suriaga
Florida Atlantic University

Background: As more Americans died from opioid overdoses (more than half a million opioid deaths in the US since 1999 and 75 673 during the COVID-19 pandemic's initial year), medication-assisted treatment (MAT) to curb opioid overdoses was one of the top priorities. The MAT treatment includes methadone, buprenorphine, and cannabinoids. Some studies implicate the role of cannabinoids in opioid use disorder or its analgesic properties to reduce opioid use. However, research on the co-use of opioids in cannabinoid-related mortality (CRM) is limited.

Purpose: This study reports the co-presence of opioids in cannabinoids as a cause of death during the COVID-19 pandemic in Florida. (A drug is considered the cause of death when it plays a causal role in the death of a person through autopsy and toxicology results).

Methods: We used retrospective analysis of people who died from cannabinoids as a cause of death with the co-presence of opioids in their system. We used descriptive statistics in describing the co-presence of opioids in CRM using the Florida Department of Law Enforcement data in 2020.

Results: 42 decedents died from cannabinoids as a cause of death in Florida in 2020. Age range from 17-74 years, mean age of 39.52 (SD=14.829). Most decedents were male (83.3%), non-Hispanic whites (n=33 or 78.6%). All 42 decedents died in accidents, 16 of 42 from vehicular motor accidents and, 21 of 42 from polysubstance use while under the influence of cannabis, 17 of 42 active tetrahydrocannabinol or THC (no dosage reported). Twelve cases involved morphine, 11 cases with fentanyl, 6 cases with heroin, 3 cases with codeine, 2 cases with oxycodone and buprenorphine, and a case with hydrocodone. Heroin involvement accounts for 6 cases.

Implications: Cannabinoid-related mortality is indeed a serious problem. The co-presence of opioids such as morphine and fentanyl is notable, warrants further study. Until a safety level of the analgesic effect of cannabinoids is proven safe, the public is warned about the potential adverse effects of using the drugs concurrently.

Cannabis use among young adults in the state of Florida: A comparison of medical cannabis patients and non-patient cannabis users

Jason Ford
University of Central Florida

Co-authors: Stephen Lankenau[1]
[1]Drexel University

Objective: As state laws regulating cannabis use have changed in recent years that has been a corresponding increase in the prevalence of cannabis use, particularly among young adults. Since the repeal of a ban on smoking medical cannabis in 2019, the state of Florida has seen a dramatic increase in both the number of treatment centers and qualified patients. The primary goal of the current research is to compare medical cannabis patients (MCP) to

non-patient cannabis users (NPCU) along demographic characteristics, characteristics of cannabis use, and health-related conditions.

Methods: The Florida Young Adult Cannabis Study included respondents aged 18 to 34, who had used cannabis products at least three times in the past 90-days and were residents of the state of Florida during the previous 12-months. Participants were recruited during the winter of 2020 via an online survey panel program, Qualtrics Inc. Participants included 900 individuals who submitted complete survey data, including 415 MCP and 485 NPCU.

Results: A sizeable portion of the sample reported motives for cannabis use that were inconsistent with their "patient" status, as 13% of MCP endorsed primarily/exclusively recreational motives, while 31% of NPCU endorsed primarily/exclusively self-treatment motives. Regarding demographic characteristics, MCP were more likely to be male, college graduates, employed, and have health insurance compared to NPCU. Additionally, MCP were more likely to report several different forms of cannabis (e.g., edibles, concentrates), to microdose, and be CBD-dominant users compared to NPCU. However, NPCU initiated regular cannabis at a younger age and reported more daily use than MCP. Regarding social characteristics of cannabis use, MCP reported more sources of cannabis, used cannabis with different groups of people, and identified more sources of information about cannabis compared to NPCU. Finally, MCP were more likely to report pain interferes with daily activities, suicidal ideation, symptoms associated with PTSD, and COVID-19 related medical issues than NPCU.

Conclusion: The current research identified several significant differences between MCP and NPCU and informs state-level policy. Relative to NPCU, MCP used for self-treatment motives, used safer forms of cannabis, initiated regular cannabis use at an older age, and used cannabis less frequently.

Tracking real-time changes in anxiety/ depression among Florida cannabis consumers using Releaf App and exploring user demographics connected to relief outcome.

Tyler Dautrich
Releaf App

Co-authors: Nathan Pipitone[1], Martha Rosenthal[1], Kelly L. Schuller[1], Benjamin Banai, Jessica Walters
[1]Florida Gulf Coast University

In recent years, scientific attention has increasingly focused on the therapeutic effectiveness of cannabis use for a wide variety of physical and mental ailments. One-third of Americans will suffer from an anxiety disorder at some point in their lives, and over 20% will suffer from major depressive disorder. Traditional pharmaceutical treatments for depression and anxiety may be problematic, due to their relatively low efficacy as well as their potential for abuse.

As such, medical cannabis—now legal in some form in over 70% of U.S. states—has attracted interest due to its potential to alleviate symptoms of both conditions. Surveys of medical cannabis users across the United States have shown that relief from symptoms of anxiety and depression are among the most common reasons cited by patients for using medical cannabis.

Recently, smartphone technology has facilitated the collection of large amounts of data from cannabis users. One popular smartphone app—Releaf App™ technologies—has been used worldwide by researchers, healthcare professionals, and cannabis product manufacturers to collect data on the performance of legal cannabis and hemp-derived CBD products.

The present study used the Releaf App to review the self-reported experiences of cannabis users in Florida, with a focus on understanding how cannabis may impact anxiety and depression symptomology. Over the last three years, several hundred Releaf App users from the state of Florida provided anonymous, real-time reports of their symptoms of anxiety and/or depression immediately before and after a cannabis use session.

Changes in symptomology, gender, age, method of consumption, and dose amount were analyzed. Multilevel modeling was used to analyze the data. After controlling for symptom levels before sessions, cannabis consumption significantly reduced anxiety/depression symptomology for the majority of participants, with higher relief for depressive symptoms. Doses and method of consumption also significantly predicted symptom reduction, but gender and age did not impact findings. We also explore user demographics among those who reported positive relief (70%), no relief (25%), and negative relief (5%) outcomes.

Medical Marijuana & Me (M3): A New Combined Cohort/Cross-sectional Study of Medical Marijuana Users in Florida

Ruba Sajdeya
University of Florida

Co-authors: Yan Wang[1], Hannah Fechtel[1], Gabe Spandau[1], Sebastian Jugl[1], Nicole E Smolinski[1], Amie Goodin[1], Joshua Brown[1], Almut G. Winterstein[1], Robert L. Cook[1]
[1]University of Florida

Background: Significant knowledge gaps regarding the effectiveness and safety profile of medical marijuana (MMJ) impose challenges for MMJ-certifying clinicians who make treatment recommendations. The Medical Marijuana & Me (M3) study is proposed to collect patient-centered data from Florida MMJ users.

Objectives:

- Quantify MMJ use persistence and identify reasons for discontinuation.
- Describe outcome trajectories for primary reasons for MMJ use and determine factors associated with different trajectories among MMJ initiators.
- Describe MMJ use patterns, including consumption modes, dosing, and use frequency that patients report as “most effective,” and identify characteristics associated with such use patterns.
- Describe changes in products, consumption modes, and dosing over time.
- Characterize adverse effects,

including cannabis use disorder, and identify associated products and patient characteristics.

- Track alcohol, tobacco, and other substance use among MMJ initiators.
- Describe concurrent prescription medications use, and factors associated with changes in medications after initiating MMJ.
- Identify concomitant medication use with potential drug-MMJ interactions risk

Protocol Summary: The M3 databank will house: 1) data from a prospective cohort of MMJ initiators who complete surveys at enrollment, three months, and nine months after MMJ initiation, and 2) data from a cross-sectional sample of current MMJ users. A multidisciplinary committee including researchers, physicians, pharmacists, patients, and dispensary personnel planned study protocols. We plan to recruit 1000 participants aged ≥18 years with ~50% new and ~50% current MMJ patients from clinics and dispensaries. Consented participants will be compensated with a gift card for each survey completion. Survey domains include sociodemographic characteristics, physical and mental health, marijuana use history, reasons for MMJ use and discontinuation, MMJ products and use patterns, concurrent use of prescription medications and other substances, and side effects. We pilot-tested the questionnaires on 20 randomly selected participants from the Marijuana Center Contact Registry. We established a concept system to facilitate sharing and analysis of deidentified M3 data. Linkages with other databases are planned as well. Enrollment begins in May 2022.

Conclusion: The M3 databank will provide data to investigators affiliated with the consortium to enhance research to inform policy, clinical practice, and improvements in patient outcomes.

Efficacy and Safety of Older Adults with Chronic Pain using Medical Marijuana

Lenny Chiang-Hanisko
Florida Atlantic University

Co-authors: David Newman[1], Deborah D'Avolio[1]
[1]Florida Atlantic University

Objective: The purpose of this study is to identify if Medical Marijuana (MMJ) is effective and safe for older adults with chronic pain, to develop an understanding of what educational materials are required to facilitate access to appropriate products at medical marijuana treatment centers (MMTC), and to provide evidence to guide policy for clinical practice.

Method: This study utilized an explanatory sequential mixed methods design. The quantitative phase was descriptive correlational and investigated the preparation to use MMJ, patterns of use and effects on pain relief including potential side effects. The qualitative phase used content analysis to identify emergent themes from the interview data.

Results: Data was collected using REDCap online survey tools. 131 participants met inclusion criteria with 124 completing the questions. Thirty participants were purposely invited to the interviews with seven interviews completed and analyzed. The analysis revealed the occurrence of several common side-effects of MMJ use. The largest side effect was an increased appetite (22.3%), followed by change

in lethargy (14.0%). There were also elevated levels reported in mood changes (12.4%), lack of concentration (11.6%) and dizziness (9.1%). 3 (2.5%) participants reported that they did not receive any MMJ education prior to filling their prescription, with 52.5% reporting the education was less than 20 minutes. MMJ was considered effective in reduction of overall chronic pain on a visual analog scale ranging from 0 to 100 with a decrease in average pain from 70.9 prior to MMJ use to 33.8 after use [$t(79)=16.29$, $p<.001$, $d=1.82$]. Six themes were identified from the qualitative interviews included: 1) reasons for using marijuana, 2) side effects of MMJ, 3) benefits, 4) lack of education about the safe use of MMJ, 5) dispensary challenges, and 6) the cost burden of obtaining the MMJ license and renewal. All seven participants confirmed their difficulty with seeking out information about MMJ on their own.

Conclusion: These themes, in combination with the quantitative findings, suggest that state legislative bodies understand the importance of implementing mandatory MMJ education among dispensary site personnel to help address any gaps of MMJ education.

CONVERSATIONS ON CANNABIS

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KNOWING FLORIDA'S MEDICAL MARIJUANA LAWS CAN KEEP YOU OUT OF TROUBLE

Sharing your medical marijuana with others is illegal and can get you in trouble.

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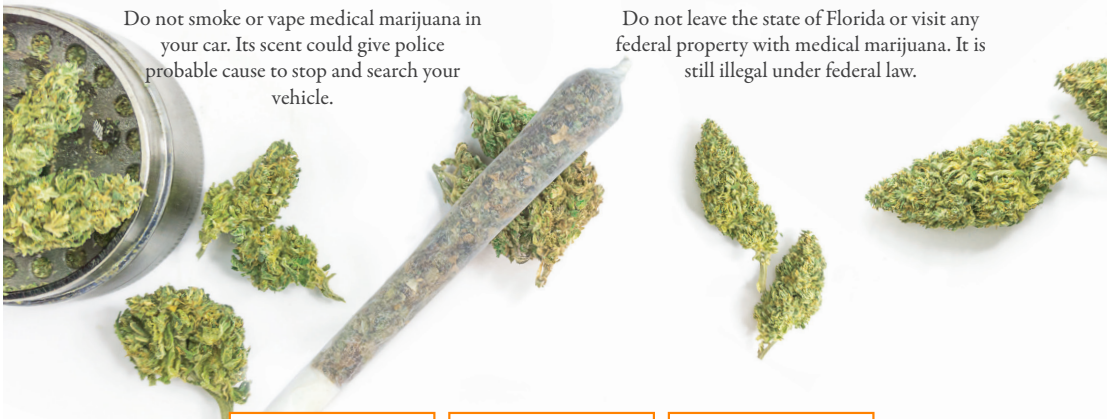
Do not leave the state of Florida or visit any federal property with medical marijuana. It is still illegal under federal law.



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REVIEWS

Doses of cannabis and cannabinoid products in clinical trials - A rapid review

Sebastian Jugl
University of Florida

Co-authors: Nicole E. Smolinski[1], Almut G. Winterstein[1]
[1]University of Florida

Introduction: Cannabis and cannabinoid (CaC) products are increasingly used for various medical conditions. Identifying evidence that supports safe and effective dosing is important to guide policy and clinical practice. The objective of this rapid review was to summarize doses of CaC in randomized clinical trials (RCT) investigating the effectiveness and safety of CaC products.

Methods: To retrieve RCTs that assessed the effectiveness and safety of CaC in clinical settings we identified relevant studies from previously published reviews and updated this information with a new literature search in PubMed, Embase, and Web of Science, to retrieve recently published RCTs between November 2019 and October 2021. We excluded articles that were inaccessible or not written in English. Two reviewers (NES, SJ) extracted information about indication, route of administration (RoA), products used (e.g., tablet), agents used (e.g., cannabidiol (CBD)), doses, and publication year. We conducted a qualitative synthesis of included studies.

Results: We identified 81 RCTs. Doses where either defined by content of delta-9-Tetrahydrocannabinol (THC) (17), CBD(8), THC and CBD(28), Dronabinol(12), Nabilone(13), Levonantradol(2), or CT3(1). Minimum and maximum daily doses as defined per protocols were 1.2–216, 20-800, 2.7/2.5–142/145.8 mg, for THC, CBD, and THC/CBD defined products respectively. The consumed daily mean dose was reported in only 9 publications, and out of those the highest was 82.8, 74.8, and 30.8 /31.6 mg for THC, CBD, and THC /CBD defined products respectively. Investigated doses differed widely across products, RoA and indication. For, THC and THC/CBD defined products, the maximum daily dose (216 mg , 142 /145.8 mg) was found in a trial that evaluated inhalation in patients with posttraumatic stress disorder. For CBD defined products the maximum allowed daily dose was in patients with psychosis.

Conclusion: CaC RCT protocols included a wide range of doses, which differed by indication, product, and RoA. However, the consumed dose was often uncertain. Investigated doses appeared generally lower than those certified for medical marijuana patients in Florida. In selected conditions, for specific RoAs and products, evidence exists to guide safe and effective dosing, but more evidence is needed for the majority of CaC products across medical conditions.

Three theories explore why women who use cannabis regularly are twice as likely to orgasm

Suzanne Mulvehill
International Institute of Clinical Sexology

Co-authors: Jordan Tishler[1]
[1]inhaleMD, Inc.

Objective: Research reveals that up to 41% of women have difficulty orgasming (Laumann et al., 2005). Research also

suggests that women who regularly use cannabis are twice as likely to orgasm (Lynn et al., 2019). Women, more than men report cannabis' sexual faciliatory effects (Gorzalka et al., 2010). The objective of this literature review is to explore three different theories that point to why cannabis may enhance women's ability to orgasm. If data collection supports these theories, it follows that female orgasmic disorder (FOD) could become a condition of treatment for medical cannabis.

Method: Literature Review

Findings: The psychoactive chemical in cannabis, THC, alters consciousness. Altered states of consciousness were found to be strongly related to higher sexual responsiveness in women, and to a lesser extent in men (Costa et al., 2016). Altered State of Consciousness Theory proposes that women who learn to induce altered states of consciousness with cannabis are more likely to orgasm.

Women, more than men, need to be in a state of absorption to orgasm (Swartz, 1994). A state of absorption can be created with an intense focus on bodily sensations and/or the imagination, both of which are stimulated by cannabis. The State of Absorption Theory proposes that a state of "absorption" is essential for high sexual arousal and orgasm in many, if not all, women.

Cannabis reduces the activity in the amygdala, a part of the brain associated with hypervigilance and anxiety (Rabinak et al., 2020). A reduction in anxiety associated with a sexual encounter could improve experiences and lead to improved orgasm and satisfaction in women (Kosiba et al., 2019). The Amygdala Reduction Theory proposes that reduced amygdala activity can positively affect female orgasmic disorder.

Conclusion: It can be hypothesized that women who use cannabis more regularly may be more comfortable with altered states of consciousness that allow deeper bodily sensations. This altered state of consciousness may lead to enhanced ability to orgasm. The researcher is collecting data to explore how and whether the use of cannabis has any impact on women's orgasmic difficulty.

Medical Cannabis for Chronic Nonmalignant Pain Management

Samir Ruxmohan
Larkin Community Hospital

Co-authors: Jonathan Quinonez[12], Amean Amra[1], Esha Jain[1], Ahmad Oleimat[1], Maha Hameed[1], Saloni Mitra[1], Joel Stein[13], Trevine Albert[13], Steven Licata[13]
[1]Larkin Community Hospital
[2]CannaMD
[3]Institute of Non-Surgical Orthopedics

Cannabis has been used since ancient times for medical and recreational research. Current cannabis research has shown that medical cannabis is indicated for symptom management for a myriad of conditions not limited to cancer, chronic pain, headaches, migraines, and psychological disorders (anxiety, post-traumatic stress disorder).

Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are active ingredients in cannabis that modulate a patient's symptoms. These compounds work to decrease nocireception and symptom frequency via the endocannabinoid system. Research regarding pain management is limited within the United States as the Drug Enforcement Agency (DEA) classifies it as a schedule one drug.

Few studies have found a limited

relationship between chronic pain and medical cannabis use. This review article will document the validity of how medical cannabis can be utilized for chronic non-malignant pain management. 77 articles were selected after a thorough screening process using PubMed and Google Scholar.

The following keywords were used: “Cannabis,” “Medical Marijuana,” and “Chronic Non-Malignant Pain.” This paper demonstrates that medical cannabis use provides adequate pain management. Patients suffering from chronic nonmalignant pain may benefit from medical cannabis use due to its convenience and efficacy.

Medical Cannabis, Headaches, and Migraines: A Review of the Current Literature

Jonathan Quinonez
Larkin Community Hospital, CannaMD

Co-authors: Sujan Poudel[1], Samir Ruxmohan[1], Jinal Choudhari[1], Zachary Au[1], Armond Theiss[1], Mobashir Hosameddin[1], Geraldo Ferrer[1], Jack Michel[1]
[1]Larkin Community Hospital

Cannabis has been long used since ancient times for both medical and recreational use. Past research has shown that cannabis can be indicated for symptom management disorders, including cancer, chronic pain, headaches, migraines, and psychological disorders (anxiety, depression, and post-traumatic stress disorder).

Active ingredients in cannabis that modulate patients’ perceptions of their conditions include Δ9-tetrahydrocannabinol (THC), cannabidiol (CBD), flavonoids, and terpenes. These compounds work to produce effects within the endocannabinoid system to decrease nociception and decrease symptom frequency. Research within the United States of America is limited to date due to cannabis being classified as a schedule one drug per the Drug Enforcement Agency. Few anecdotal studies have found a limited relationship between cannabis use and migraine frequency.

The purpose of the review article is to document the validity of how medical cannabis can be utilized as an alternative therapy for migraine management.

Thirty-four relevant articles were selected after a thorough screening process using PubMed and Google Scholar databases. The following keywords were used: “Cannabis,” “Medical Marijuana,” “Headache,” “Cannabis and Migraine,” “Cannabis and Headache.” This literature study demonstrates that medical cannabis use decreases migraine duration and frequency and headaches of unknown origin. Patients suffering from migraines and related conditions may benefit from medical cannabis therapy due to its convenience and efficacy.

A Review of Recent Changes to DEA Cannabis Regulations and What It Means For Medical Cannabis Research

Joseph A. Grzyb
Groff North America

After years of delay, the Drug Enforcement Administration is promulgating new regulations that change the way researchers can

investigate cannabis. Although still a Schedule 1 narcotic requiring registration with the DEA, changes in regulations mean that it is easier for researchers and clinicians to access and work with federally-legal cannabis flower, extracts and customized cannabis preparation (THC, CBD and other cannabinoid mixtures) that are more representative of what is available state-legal programs. Although navigating DEA regulations and applications is still a challenge, there has never been a better time to pursue medical research and pharmaceutical development.

In this talk, we will review recent changes in federal regulations and what the implications are for medicinal cannabis research in the US. We will review an example of a successful application to the DEA and FDA for investigation of the antimicrobial properties of THC and other cannabinoids, and also review how recent regulatory changes influence the availability of high quality, pharma grade cannabis, extracts, isolates and custom preparations for research.

EXHIBITORS

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CannaMD is committed to providing compassionate care to Florida patients through evidence-based application of medical cannabis research. Centered around education, empathy, and exceptional customer service, CannaMD offers an unparalleled patient experience – empowering Florida residents to pursue a better quality of life. Learn more.

Every day, the OMMU works to provide qualified patients, caregivers and physicians the information and resources they need to access Florida's medical marijuana program.

The mission of the Medical Marijuana Education and Research Initiative is to educate and inform Florida's diverse minority communities about medical marijuana and the potential consequence to health and well-being from recreational use. Learn more.

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The Consortium for Medical Marijuana Clinical Outcomes Research, founded by the state of Florida legislature, conducts, disseminates and supports research on the clinical effects of medical use of marijuana.

Composed of nine universities in the state of Florida, the Consortium works to enhance the evidence on the safe and effective use of medical marijuana to inform clinical decision-making and guide policy.

Learn more at mmjoutcomes.org.

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MEDICAL CANNABIS AND CANNABINOIDS JOURNAL

As the official journal of the Consortium, Medical Cannabis & Cannabinoids will publish the Consortium's conference proceedings, guidelines, and position statements.

For CCORC 2022, selected abstracts will be published in the Medical Cannabis & Cannabinoids. Read more about Medical Cannabis and Cannabinoids.

THANK YOU

On behalf of the Consortium for Medical Marijuana Clinical Outcomes Research's Scientific Program and Planning Committees, we would like to express our gratitude to all involved in organizing and conducting CCORC 2022, including: keynote speakers, session members, board members, exhibitors, and volunteers. We thank the Creative Works and LifeLong Learning Team as well as the Office of Events at the University of Florida College of Pharmacy for technical support and event coordination. We hope to see you again at CCORC 2023!

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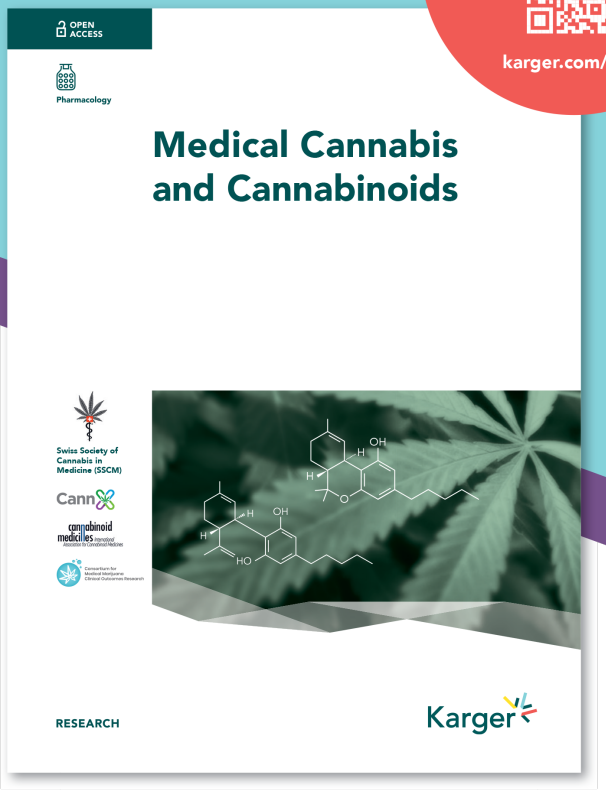

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