Reefer Madness Revisited

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Disclosure

- Consultant/Independent Contractor: Kaleo
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PAINWEEK

Learning Objectives

- Describe the political issues surrounding the legalization of medical marijuana
- Recognize the obstacles to conducting high-quality medical cannabinoid research in the United States
- Discuss how to modify your medical marijuana authorization patterns based on legal realities and empirical data

PAINWEEK

What the Heck is "Medical Marijuana"?!?!?!

- Lots of questions to be asked…
- Lengthy history in the US
  - –California became the first state to legalize MM in 1996
- Currently there are MM laws in 32 states plus DC
- FindLaw. Medical marijuana laws by state. Available at: http://healthcare.findlaw.com/patient-rights/medical-marijuana-laws-by-state.html
- Individual states' medical marijuana laws are incredibly heterogeneous – varying widely in terms of process of obtaining, limits on possession, rules regulating dispensaries, allowable medical conditions, and every other parameter

PAINWEEK

What is Medical Marijuana?

- In the eyes of the pro-marijuana zealots, ALL marijuana is "medical"
- In the eyes of the FDA, NO marijuana is "medical"
- Perhaps the truth falls somewhere in between….
- CSA (1970) made cannabis a Schedule I drug – "drugs with no currently accepted medical use and a high potential for abuse"
- US Drug Enforcement Administration. Drug Scheduling. Available at: http://www.justice.gov/dea/druginfo/ds.shtml
- Remains federally "illegal"

PAINWEEK

What is Medical Marijuana?

- Is it legal or illegal?
- Should it be legal?
- Is it safe?
- Is there an evidence basis for efficacy?
- If it's sold in a dispensary, should it therefore be considered "medical"?
- If it's "medical", can it be abused?

PAINWEEK

So Let's Complicate Things Even More….

- What constitutes "recreational marijuana"?
- Again, to the FDA, legal recreational marijuana doesn't exist
- However, tell this to the good citizens of:
  - Washington
  - Colorado
  - Alaska
  - Oregon
  - California
  - Nevada
  - DC
  - Massachusetts
  - Maine
  - Vermont
  - Michigan

PAINWEEK

The Future of Recreational Pot?

- Predictions for legalization in:
  - Arizona
  - Arkansas
  - Connecticut
  - Delaware
  - Florida
  - Illinois
  - Maryland
  - Minnesota
  - Montana
  - New Hampshire
  - New York
  - Ohio
  - Rhode Island

Stebbins S, et al. USA Today, updated January 5, 2018.

PAINWEEK

Politics

- Only add to the craziness around medical marijuana
- Obama administration: AG Holder, 2009: "[t]he policy is to go after those people who violate both federal and state law"

Associated Press, "Attorney General Signals Marijuana Policy Shift," NBC News, March 18, 2009.

- 2011 – Policy reversal, and the Justice Department began to raid dispensaries in selected states, blaming them for letting the industry get out of control

Onishi N. "Cities Balk as Federal Law on Marijuana Is Enforced," New York Times, June 30, 2012.

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Politics

- 2012 – President Obama announced that cannabis use in states in which it is legal was not a priority for DOJ

Garvey T, Yeh BT. State legalization of recreational marijuana: Selected legal issues. Washington, DC: Congressional Research Service;2014.

- December, 2012 – WA and CO pass recreational MJ laws, Obama administration supported states' rights

Kamin S. Publius J Federalism 2015;45:427-451.

- 2014 – Congress passes the Rohrabacher–Blumenauer amendment, defunding the DOJ from enforcement of federal law in MM states

Lopez G. Vox, May 30, 2014.

PAINWEEK

Politics

- Must be renewed every fiscal year to stay in effect

Sullum J. Reason, January 4, 2016.

- Has been successfully renewed each year – attached to the federal budget bill
- Every time a budget agreement can't be reached, federal protection of states' laws is threatened
- And the DOJ can theoretically run wild….

PAINWEEK

Cannabinoids

- Marijuana contains over 100 cannabinoids

National Institute on Drug Abuse. Drug Facts: Is Marijuana Medicine? Revised April, 2014.

- Δ9-tetrahydrocannabinol (THC) – the principle psychoactive constituent of cannabis
- Gets all of the press – good and bad
- Recreational marijuana – goal is to maximize THC
- Seems to be the goal of "medical marijuana" as well…….
- Higher THC fetches a higher price in dispensaries

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THC:CBD Ratio

- What kinds of ratios do we see in medical vs. non-medical cannabis?
- Study of over 5000 samples of cannabis seized in CA between 1996-2008:
  - –THC levels increased from 4.56% to 11.75%
  - –CBD levels decreased from 0.24% to 0.08%

Burgdorf JR, et al. Drug Alcohol Depend. 2011;117:59–61.

- THC:CBD ratio – 14:1 in 2001, 80:1 in 2014
  - –Increases in THC thought to be due to shift from traditional strains to sinsemilla

ElSohly MA, et al. Biol Psychiatry 2016;79:613-619.

PAINWEEK

THC:CBD Ratio

- Currently, measurable levels of CBD are rarely found in herbal cannabis
- Niesink RJ, van Laar MW. Front Psychiatry 2013;4:130.
- The THC:CBD ratio is not examined in most studies
  - –Most current data come from toxicology following seizures

Vindenes V, Morland J. Increasing plant concentrations of THC and implications on health related disorders. In: Handbook of Cannabis and Related Pathologies: Biology, Pharmacology, Diagnosis, and Treatment. Academic Press, 2017. pp. 24-32.

- Ability to understand the THC:CBD ratio and the impact of breeding the CBD out of cannabis is essential to understanding its health risks

PAINWEEK

Synthetic THC

- Available as a Schedule III drug (dronabinol/Marinol) since 1985
- Nabilone/Cesamet (Schedule II) –A synthetic THC analogue – also FDA-approved in 1985
- Common side effects include drowsiness, unsteady gait, dizziness, inability to focus thoughts, confusion, mood changes, delusions, and hallucinations

WebMD. Drugs and medications: Marinol oral. http://www.webmd.com/drugs/drug-9308-Marinol+Oral.aspx?drugid=9308&drugname=Marinol+Oral&pagenumber=6.

- Tolerability is dubious
- Consequently, so is clinical utility for pain

Issa MA, et al. Clin J Pain 2014;30:472-478.

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Safety Issues Associated with Marijuana

- The myriad safety concerns identified are thought to be due primarily to THC; more THC means more risks

Rehm J, et al. Int J Health Policy Manag. 2016;5:1–4.

- Can we assume that as the THC levels continue to rise, that safety risks will do the same?
- Smoking remains the most common route of administration

Russell C, et al. Int J Drug Policy. 2018;52:87-96.

- Recent review – pulmonary effects are even worse than we'd thought – "Marijuana Lung"

Leb JS, et al. Chronic Obstr Pulm Dis. 2018;5:81-83.

- Tars from smoked marijuana contain more carcinogens than do those from tobacco

Wu TC, et al. N Engl J Med. 1988;318:347-351.

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Physical Safety Issues

- Insufficient data on safety of vaporization – "Preliminary findings do support the idea that vaporization is an improvement over smoking"

Loflin M, Earleywine M. Can J Respir Ther. 2015;51:7–9.

- Increases rates of acute myocardial infarction and cardiovascular mortality – doubles rate of MI

Hall W. Addiction 2015;110:19-35.

Franz CA, Frishman WH. Cardiol Rev. 2016;24:158-162.

- Predicts heart failure and CVA – whether recreational or medical

Kalla A, et al. J Cardiovasc Med (Hagerstown). 2018;19:480-484.

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Physical Safety Issues

- Associated with higher rates of acute ischemic stroke

Rumalla K, et al. J Neurol Sci. 2016;364:191-196.

- Increased duration of marijuana use is associated with increased risk of death from hypertension

Yankey BA, et al. Eur J Prev Cardiol. 2017;24(17):1833-1840.

- Sexual functioning - THC impairs gonadal function by blocking gonadotropin-releasing hormone (GnRH) release

Harclerode J. NIDA Res Monograph 1984;44:46-64.

- Immunosuppressive – Reduces T-Cell activation

Henriquez JE, et al. J Pharmacol Exp Ther. 2018[Epub ahead of print].

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Physical Safety Issues

- Cannabinoid Hyperemesis Syndrome
  - Characterized by a syndrome of cyclic vomiting, abdominal pain and compulsive showering in some habitual users
  - Symptoms improve with cessation utilization
  - The prevalence of cannabinoid hyperemesis syndrome seen in EDs has doubled since the liberalization of marijuana laws in Colorado

Kim HS, et al. Acad Emerg Med. 2015;22:694-699.

  - Can masquerade as an eating disorder

Brewerton TD, Anderson O. Int J Eat Disord. 2016;49:826-829.

  - Estimated 2.75 million cases in the US annually

Habboushe J, et al. Basic Clin Pharmacol Toxicol. 2018;122:660-662.

  - Fatal cases now being reported

Nourbakhsh M, et al. J Forensic Sci. 2018[Epub ahead of print].

PAINWEEK

Physical Safety Issues

- Cannabis use is associated with higher rates of occupational injuries, injury severity, and prolonged lost workdays among construction workers

Khashaba E, et al. Toxicol Ind Health 2018;34:83-90.

- Drugged driving – 96% of cases involve cannabis

Bonar EE, et al. Addict Behav. 2018;78:80-84.

- Drugged driving continues to increase, with increases associated with more traffic fatalities

Rogeberg O, Elvik R. Addiction 2016;111:1348-1359.
Robertson RD, et al. Accid Anal Prev. 2017;99(Pt A):236-241.

PAINWEEK

Physical Safety Issues

- French study: One in two drivers in fatal accidents under the influence of ETOH were also under the influence of cannabis

Martin JL, et al. PLoS One 2017 8;12(11):e0187320.

- High-risk drinking behavior recently found to be related to medical cannabis utilization

Davis AK, et al. Addict Behav. 2018;77:166-171.

- Older adults – Cannabis use associated with greater physical injury risk and ED visits

Choi NG, et al. Am J Drug Alcohol Abuse. 2018;44:215-223.

- Increases the likelihood of fatal two-vehicle crashes

Li G, et al. Ann Epidemiol. 2017;27(5):342-347.

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Physical Safety Issues

Perhaps the issue is that users of MJ have been found to have greater perceived safety than those who don't

Sartor CE, et al. Addict Behav. 2017;66:114-117.

- Pregnancy – Use of marijuana among pregnant women increased by 69% between 2009 and 2016

Young-Wolf KC, et al. JAMA 2017;318(24):2490-2491.

- Currently at 22%

Oga EA, et al. Matern Child Health J. 2018[Epub ahead of print].

- Cannabis use associated with preterm birth

Prunet C, et al. J Gynecol Obstet Hum Reprod. 2017;46(1):19-28.

- Likelihood of stillbirth or miscarriage 12 times higher among women using MJ during pregnancy

Coleman-Cowger VH, et al. Neurotoxicol Teratol. 2018;68:84-90.

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Physical Safety Issues

- Addiction
  - Not as severe as opioid or benzo addiction
  - Abrupt cessation results in irritability, insomnia, anorexia

Haney M, et al. Neuropsychopharmacology 2013;38:1557-1565.

- Perceived barrier to quitting MJ – fear of severe withdrawal symptoms

Zvolensky MJ, et al. Addict Behav. 2018;76:45-51.

- When used hs, withdrawal's impact on sleep is particularly problematic

Cranford JA, et al. Drug Alcohol Depend. 2017;180:227-233.

- Reduced MJ use associate with improved sleep quality

Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.

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Cognitive Safety Issues

- We've known about chronic MJ use and its impact on diminution of grey matter in the brain for years

Block RI, et al. Neuroreport 2000;11:491-496.

- Of particular concern in the developing brain
- Executive functioning deficits associated with MJ use

Clark DB, et al. Front Behav Neurosci. 2017;11:223.

- Myriad studies and review indicate that chronic MJ use results in cognitive deficits
  - Long-term and short-term

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Cognitive Safety Issues

- Long-term deficits ("residual cannabis effect") include (from a meta-analysis):
  - Learning
  - Forgetting/Retrieval
  - Abstraction/Executive Functioning
  - Attention
  - Motor Skills
  - Verbal/Language

Schreiner AM, Dunn ME. Exp Clin Psychopharmacol. 2012;20(5):420-429.

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Mental Health Risks

- Clearly are going to overlap with cognitive risk data, although no consensus regarding the extent of such
- Most studied issue has been early-onset psychosis and recovery from it in marijuana users
- MJ-Psychosis association recognized back to the 1950s

Ames F. J Ment Sci. 1958;104(437):972-999.

- High THC cannabis increases the risk of psychosis 3-fold compared to non-users, and 5-fold among daily users

Di Forti M, et al. Lancet Psychiatry 2015;2(3):233-238.

  – Particularly problematic in patients using ultra-high-THC wax dabs

Pierre JM, et al. Schizophr Res. 2016;172(1-3):211-212.

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Mental Health Risks – Psychosis

- Cannabis use in first episode psychosis is associated with failure of anti-psychotic medications

Patel R, et al. BMJ Open. 2016;6(3):e009888.

  – As well as is adherence to anti-psychotic medications

Schoeler T, et al. Lancet Psychiatry 2017;4(8):627-633.

- Extended abstinence from MJ doesn't seem to reverse symptoms in cannabis-dependent schizophrenics

Rabin RA, et al. Schizophr Res. 2018r;194:55-61.

- A risk factor for violent behavior in early phase psychosis

Moulin V, et al. Front Psychiatry. 2018;9:294.

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Mental Health Risks – Bipolar Disorder

- Cannabis using patients with bipolar disease demonstrate poorer treatment adherence

Van Rossum I, et al. J Nerv Ment Dis. 2009;197(1):35-40.

- Cannabis predicts earlier age of bipolar disorder onset

De Hert M, et al. Schizophr Res. 2011;126(1-3):270-276.

  - The heavier the use, the earlier the onset

Lagerberg TV, et al. Eur Arch Psychiatry Clin Neurosci. 2011;261(6):397-405.

- Continued MJ use following diagnosis is associated with higher risk of recurrence and poorer functioning

Zorrilla I, et al. Acta Psychiatr Scand. 2015;131(2):100-110.

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Mental Health Risks – Bipolar Disorder

- MJ use has been associated with lower remission rates in patients with Bipolar Disorders

Kim SW, et al. Psychiatry Investig. 2015;12(3):349-355.

- A significant correlation between MJ use and suicide attempts in patients with bipolar disorders

Carrà G, et al. Bipolar Disord. 2015;17(1):113-114.

- Cannabinoid hyperemesis syndrome is associated with manic episodes due to lowering of serum mood stabilizer levels

Gregoire P, et al. BMJ Case Rep. 2016;pii: bcr2016215129.

PAINWEEK

Mental Health Risks - Anxiety

- The acute induction of anxiety associated with THC cannot be ignored
- Early studies found an anti-anxiety effect of MJ

Sethi BB, et al. Biol Psychiatry 1986;21:3-10.

- Recent meta-analysis concludes that THC's impact on anxiety is not necessarily impressive
- Turna J, et al. Depress Anxiety. 2017;34:1006-1017.
  - –However, that may have much to do with Indica vs. Sativa strain
- Recent study found that longitudinally, reduction of MJ use was associated with decreased anxiety
- Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.

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Mental Health Risks - Anxiety

- PTSD – Once thought to be "treatable" with cannabis
- However chronic MJ use has been found to impair fear extinction

Papini S, et al. J Abnorm Psychol. 2017;126:117-124.

- MJ use after initiating tx associated with worse PTSD symptoms, more violent behavior, and alcohol use

Wilkinson ST, et al. Curr Addict Rep. 2014;1:115-128.

- Indicas may be helpful, activating sativas likely to exacerbate
- Good news: Dispensary employees found to be more likely to recommend an indica or a hybrid for PTDS than a sativa

Haug NA, et al. Cannabis Cannabinoid Res. 2016;1:244-251.

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Cannabidiol (CBD)

- Contrary to popular belief, THC is not the most relevant cannabinoid for medical application

Campos AC, et al. Philos Trans R Soc Lond B Biol Sci. 2012;367:3364–3378.

- CBD was first isolated in 1934

Robson P. Br J Psychiatry 2001;178:107-115.

- First synthesized in 1967, first easily useable form in 1985

Baek SH, et al. Tetrahedron Lett. 1985;26:1083-1086.

- Ignored for many years
- Seen as something limiting the amount of THC marijuana could potentially contain

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CBD

- Of no interest to recreational users….and tragically, for many medical users
- Initially described as “nonpsychotropic”
- However, produces anxiolysis through increasing serotonergic transmission

Espejo-Porras F, et al. Neuropharmacology 2013;75:155-163.

- Appears to have a mild antidepressant effect with those with low levels of serotonin

Sales AJ, et al. Prog Neuropsychopharmacol Biol Psychiatry. 2018;86:255-261.

- More appropriately called “noneuphoriant”

Russo EB. Ther Clin Risk Manag. 2008;4:245-259.

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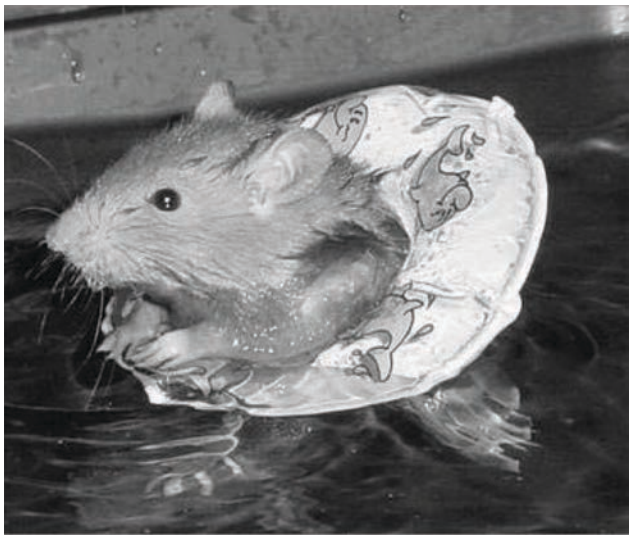
Rat Cheating on a Forced-Swim Test



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CBD Safety Profile

- Safety has been well-established
  - Cunha JM, et al. Pharmacol. 1980;21:175-185.
  - Consroe P, et al. Pharmacol Biochem Behav. 1991;40:701-708.
  - Zuardi AW, et al. J Psychopharmacol. 2006;20:683-686.
  - Zuardi AW, et al. J Psychopharmacol. 2009;23:979-983.
  - Zuardi AW, et al. J Psychopharmacol. 2010;24:135-137.
  - Bergamaschi MM, et al. Curr Drug Saf. 2011;6:237-239.
  - Devinsky O, et al. Lancet Neurol. 2016;15:270–278.
  - McGuire P, et al. Am J Psychiatry 2018;175:225-231.
- Attenuates the "high" caused by THC at 8:1 CBD:THC ratio
  - Kim PS, Fishman M. Curr Pain Headache Rep. 2017;21(4):19.
- The Director of NIDA wrote, "CBD appears to be a safe drug"
  - Volkow N. Huffington Post July 23, 2015.

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CBD Availability

- Despite its safety profile and the impossibility of abusing it, CBD from whole plant MJ is still considered a Schedule I drug
- Other than recently FDA-approved Epidiolex

Traynor K. Am J Health Syst Pharm. 2018;75:1088-1089.

- Has been available in all medical marijuana states
- 13 states had the wisdom to legalize it without MM legalization
- New changes in the law allow for CBD from the hemp plant

Knight R. DEA clarifies marijuana extract rule and CBD legality. Available at: http://kightoncannabis.com/dea-clarifies-marijuana-extract-rule-and-cbd-legality/

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CBD Legal Status

- Hemp plant is in the same genus as MJ, but contains, by definition and law, <0.3% THC content

Yang Y, et al. Cannabis Cannabinoid Res. 2017;2:274-281.

- THC will not show up in standard UDT immunoassays
- Now most commonly used for pain, anxiety, depression, and sleep disorders

Corroon J, Phillips JA. Cannabis Cannabinoid Res. 2018;3:152-161.

- Due to lack of regulation, CBD products online are often mislabeled regarding constituents

Freedman DA, Patel AD. Pediatr Neurol Briefs. 2018;32:3.

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CBD and Pain

- Much of the existing supportive data is preclinical
- CBD is anti-inflammatory

Thapa D, et al. FASEB J. 2017;31(Suppl 1):Abstract 811.7.

- Anti-inflammatory, analgesic in arthritis

Hammell DC, et al. Eur J Pain 2016;20:936-938.

- Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in osteoarthritis

Philpott HT, et al. Pain 2017; 158:2442-2451.

PAINWEEK

CBD and Pain

- Found to be anti-inflammatory in human cell lines

Petrosino S, et al. J Pharmacol Exp Ther. 2018;365:652-663.

- Relevance for back pain: CBD has anti-inflammatory effects on rat nucleus pulposus cells

Chen J, et al. Mol Med Rep. 2016;14:2321-2327.

- Reduces chemotherapy-related peripheral neuropathy without diminishing nervous system function or chemotherapy efficacy

Ward SJ, et al. Br J Pharmacol. 2014;171:636-645.

- High-dose CBD appears to be hypnotic – increasing sleep, while low-dose CBD has been associated with increased wakefulness
- Babson KA, et al. Curr Psychiatry Rep. 2017;19:23.

PAINWEEK

More Recent CBD Research

- Safety established when co-administered with fentanyl

Manini AF, et al. J Addict Med. 2015;9:204-210.

- Enhances fracture healing

Kogan NM, et al. J Bone Miner Res. 2015;30:1905-1913.

- Animal model - Protective effects on lesion-induced intervertebral disc degeneration

Silveira JW, et al. PLoS One 2014;9:e113161.

- Animal model – synergistic with morphine for certain pain conditions

Neelakantan H, et al. Behav Pharmacol. 2015;26:304-314.

- Clinical research – Effective for reducing chronic pain in kidney transplant patients (small study)

Cuñetti L, et al. Transplant Proc. 2018;50:461-464.

PAINWEEK

Marijuana and Pain Research

- Extremely difficult to do in the US
- All federally-funded MM research currently must use low-grade MJ grown at the U of Mississippi for NIDA
- 3 dose strengths available
  - Low potency (1.29% THC)
  - Moderate potency (3.53%)
  - High potency (7%)

Wilsey B, et al. J Pain 2013;14:136-148.

- Why is this a problem?

PAINWEEK

Marijuana and Pain Research

- Oil or wax dabs available at some dispensaries have THC contents as high as 90%!!!!

Loflin M, Earleywine M. Addict Behav. 2014;39:1430–1433.

  - Now being used regularly by 36.5% of cannabis users

Sagar KA, et al. Drug Alcohol Depend. 2018;190:133-142.

- Medical marijuana sold in dispensaries is higher in THC than that sold on the streets

Sevigny EL, et al. Int J Drug Pol. 2014;25:308-319.

- Recent breakthrough – NIDA has approved a 13.4% THC MJ for research

PAINWEEK

Edibles

- THC dosing in edibles has been described as “insane” by toxicologists

Gussow L. Emerg Med News 2014;36:24.

- Edibles are infused with almost pure THC
- They typically take 30-90 minutes to take effect, reach their peak in 2-3 hours, and can last for 4-12 hours

Grotenhermen F. Clin Pharmacokinet. 2003;42:327-360.

- Thus, they don’t allow for titration due to a lack of immediate effect
- Labeling of constituents’ content is often inaccurate

Vandrey R, et al. JAMA 2015;313:2491-2493.

PAINWEEK

Edibles

- This inability to titrate effectively has led to increases in ER visits due to THC intoxication

Kim HS, Monte AA. Ann Emerg Med. 2016;68:71-75.
Vo KT, et al. Ann Emerg Med. 2018;71:306-313.

- And multiple deaths

Hancock-Allen JB, et al. MMWR Morbidity and Mortality Weekly Report 2015; 64: pp. 771-772.

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Science vs. "Religion"

- Medical marijuana advocates tend not to let the data get in the way of their opinions
- Try discussing potential harms of MM on Twitter….
- "There is none so blind as those who will not see…"

PAINWEEK

MM and Pain Research – What DO We Know?

- Is it effective for chronic pain?
- Depends on the properties of the marijuana being used and one's definition of "effective"
- It also depends upon goals of treatment
  - Is analgesia sufficient, even if it incapacitates the patient?
- It also depends on the medical indication
- E.g., opioids are effective for many types of pain, but not for neuropathic pain

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MM and Pain Research

- Neuropathic pain – first methodologically-robust study conducted in 2008 – found efficacy
  - Higher doses (7% THC) resulted in cognitive deficits

Wilsey B, et al. J Pain 2008;9:506–521.

- Similar findings in a 2009 study on neuropathic pain in HIV

Ellis RJ, et al. Neuropsychopharmacology 2009;34:672-680.

- 2010 Canadian study using 9.4% THC MJ – efficacy for neuropathic pain

Ware MA, et al. CMAJ 2010;182:E694-701.

PAINWEEK

MM and Pain Research

- 2013 study using low-dose (1.29% THC) MJ – efficacy for neuropathic pain, without significant cognitive effects

Wilsey B, et al. J Pain 2013;14:136-148.

- 2015 study on MJ for pain diabetic neuropathy – higher dose (7% THC) more effective than lower dose (1.29%)…but with more cognitive effects

Wallace MS, et al. J Pain 2015;16:616-627.

- Similar findings in 2016 study on neuropathic pain due to spinal cord injury or disease

Wilsey B, et al. J Pain 2016;17:982-1000.

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MM and Pain Research

- Conclusions of MJ for neuropathic pain:
  - Weak evidence as effective in terms of analgesia at higher doses

Murff HJ. Ann Intern Med. 2017;167:JC62.

  - Cognitive side effects are dose-related
  - Never studied head-to-head against gabapentinoids
  - Gabapentinoids also have dose-related cognitive side effects
  - Research needed on MM with significant CBD content as well
  - Research needed on the types of MJ actually carried in dispensaries (25%+ THC)
- Recommendation: Consider as a last option for neuropathic pain
- Recent Australian review suggests that CBD may be better

Casey SL, Vaughan CW. Medicines (Basel). 20185(3). pii: E67.

PAINWEEK

MM and Pain Research

- Musculoskeletal pain and arthritis – "Evidence is Needed"

Perrot S, Trouvin AP. Joint Bone Spine. 2018[Epub ahead of print].

- Rheumatic conditions – no evidence for efficacy
- Experts recommend against it until more research is available

Häuser W, et al. Dtsch Arztebl Int. 2017;114:627-634.

- Fibromyalgia – No empirical evidence for efficacy

Fitzcharles MA, et al. Schmerz 2016;30:47-61.

- Headache – very limited evidence for efficacy

Lochte BC, et al. Cannabis Cannabinoid Res. 2017;2:61-71.

- Cancer pain – May have "potential use" – although human studies are of poor quality, limited size, and outdated

Wilkie G, et al. JAMA Oncol. 2016;2:670-675.

PAINWEEK

MM and Opioids

- The most compelling evidence basis for MJ in treating chronic pain was for its opioid-sparing effect
  - Boehnke KF, et al. J Pain 2016;17:739-744.
  - Vigil JM, et al. PLoS One. 2017;12:e0187795.
- Medical cannabis laws were associated with lower opioid overdose mortality rates
  - Bachhuber MA, et al. JAMA Intern Med. 2014;174:1668-1673.
- Less so, however, as laws on dispensaries have become tougher
  - Powell D, et al. J Health Econ. 2018;58:29-42.
- Synergistic with opioids? Likely urban myth…
- Not associated with lower prescription rates and dosages of Schedule II opioids
  - Liang D, et al. Addiction. 2018[Epub ahead of print].

PAINWEEK

MM and Opioids

- Perioperative opioid use is significantly higher in MJ-users despite lower subjective pain scores

Bauer FL, et al. Perm J. 2018 Jul 19;22.

- MJ use recently found to be predictive of opioid dependence

Butelman ER, et al. Front Psychiatry. 2018;9:283.

- Predictive of a 2.5 fold increase in the rate of opioid aberrancy

DiBenedetto DJ,…Schatman ME, et al. Pain Med. 2017[Epub ahead of print].

- Medical marijuana users more likely to use prescription drugs – including opioids – non-medically

Caputi TL, Humphreys K. J Addict Med. 2018[Epub ahead of print].

PAINWEEK

"Watcha Smoking, Dude?"

- To talk about "medical marijuana" as a single entity is ridiculous
- We need to be discussing "medical marijuanas"
- Indica or sativa? – 2 separate species, usually in a hybrid form
- Indicas empirically established as preferable for pain management, but cause more sedation than sativas

Cohen NL, et al. J Stud Alcohol Drugs 2016;77(3):515-520.

PAINWEEK

"Watcha Smoking, Dude?"

- Sativas are more of a euphoriant, but also more likely to cause anxiety and paranoia

Baconi DL, et al. J Mind Med Sci. 2014;1:28-39.

- Do we know which strain is more effective for pain management?
- Head-to-head research is needed

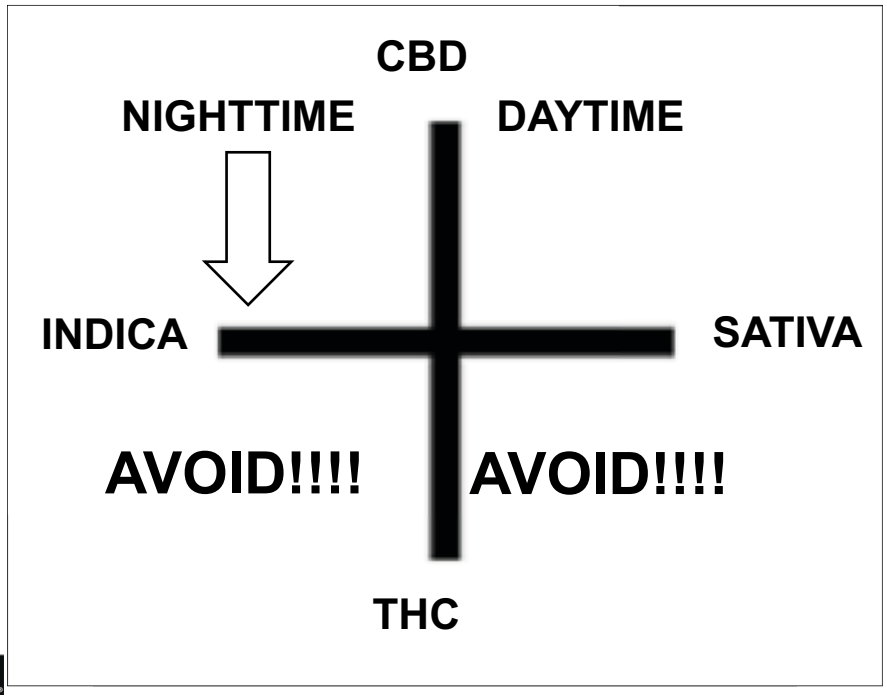
PAINWEEK

Indica vs. Sativa – Street Reputations

- Indicas
  - Relaxing and calming
  - Body buzz or 'couch lock'
  - Best suited for night use
- Sativas
  - Uplifting and energetic
  - Cerebral, spacey or hallucinogenic
  - Best suited for day use

Leaf Science, 2014. Indica vs. Sativa: Understanding The Differences. Available at: http://www.leafscience.com/2014/06/19/indica-vs-sativa-understanding-differences/.

PAINWEEK



PaiNweek

Treatment Recommendation

- "The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients via a Written Document"

B Wilsey, et al. Clin J Pain 2015;31:1087-1096.

- Absolutely brilliant!!!!
- "Medical marijuana" is heavily abused

Wen H, et al. J Health Econ. 2015;42:64-80.

- "….physicians would seem to have an obligation to understand and inform their patients on key issues of the evidence base on cannabinoid therapeutics"

PaiNweek

Medical Cannabis Agreement

- Covers reduction of diversion – particularly to vulnerable children and adolescents
- Addresses inappropriate utilization by the authorized patient
  - We must not lose sight of the data indicating that marijuana is indeed addictive
- Discusses the risks of marijuana generally and to specific populations
- Recommends vaporization over smoking

PAINWEEK

Medical Cannabis Agreement

- Warns against driving a car or operating machinery
- Emphasizes "start low, go slow" when dosing – particularly with new strains
- Covers potential benefits of FDA-approved cannabinoids over smoked marijuana
  - Based on empirical evidence…and clinical experience, I disagree
- Recommends withdrawing slowly if a patient wants to stop
- Addresses the need to evaluate the efficacy and appropriateness of therapy on an ongoing basis
- Covers not using MM in public places

PAINWEEK

Medical Cannabis Agreement

- Warns that medical authorization will NOT protect a patient's job
- Gives the physician the right to discontinue MM treatment
- Respect for patient autonomy is contingent upon the doctrine of informed consent

Dalla-Vorgia P, et al. J Med Ethics 2001;27:59-61.

- This is exactly what these agreements are providing
- Thus – they constitute ethical pain medicine practice
- And perhaps even protect the physician as well as the patient

PAINWEEK

Closing Thoughts

- The future of medical cannabinoids in the US is uncertain
- To assume that marijuana is safe because it's "natural" is neuromysticism
- As is assuming that anecdotal evidence of efficacy provides us with "the truth"
- Improving the quality and quantity of MM research is imperative if MJ is ever to become "medicine"
- CBD, not THC, promises to be the most medically-relevant cannabinoid

PAINWEEK

Closing Thoughts

- If you're going to use MM in your practice, educate yourself and your patient – and do it right
- Take marijuana as a drug seriously – irrespective of what you smoked as a youth
- If you use an opioid agreement, consider using a medical cannabis agreement
- Practicing cannabinoid medicine is challenging when we know so little
- Better data are hopefully just around the corner

PAINWEEK

THANK YOU

PAINWEEK