

Cannabis: Products, Health Effects, Policies, and Clinical Interventions

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Disclosure Information

Cannabis: Products, Health Effects, Policies, and Clinical Interventions

April 2, 2022 at 11:30 a.m.

Victoria Pham, DO, MBA, FAPA, DFAACAP

- ◆ Dr. Pham is a Chief Medical Officer at Institute for Community Living (ICL)
- ◆ She is a consultant to Office of Mental Health of New York State and grant reviewer of Substance Abuse and Mental Health Services Administration
- ◆ No Financial Conflicts of Interest



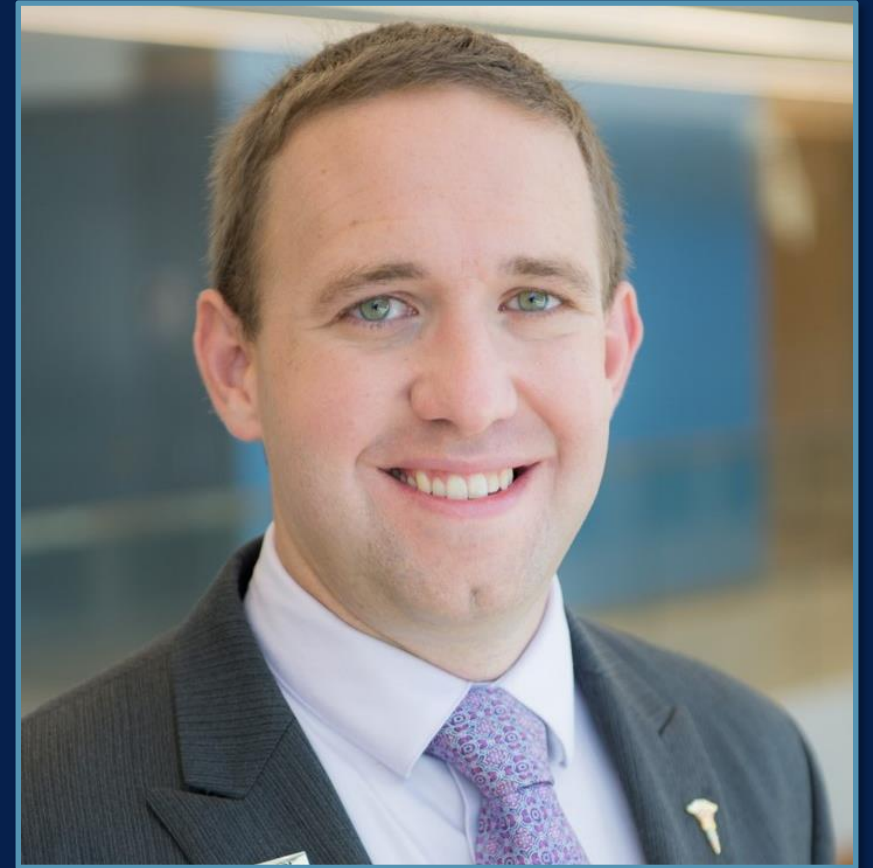
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- ◆ No Financial Conflicts of Interest
- ◆ Dr. Hurley is the President-Elect of the American Society of Addiction Medicine, so comments on topics involving ASAM may be biased towards ASAM



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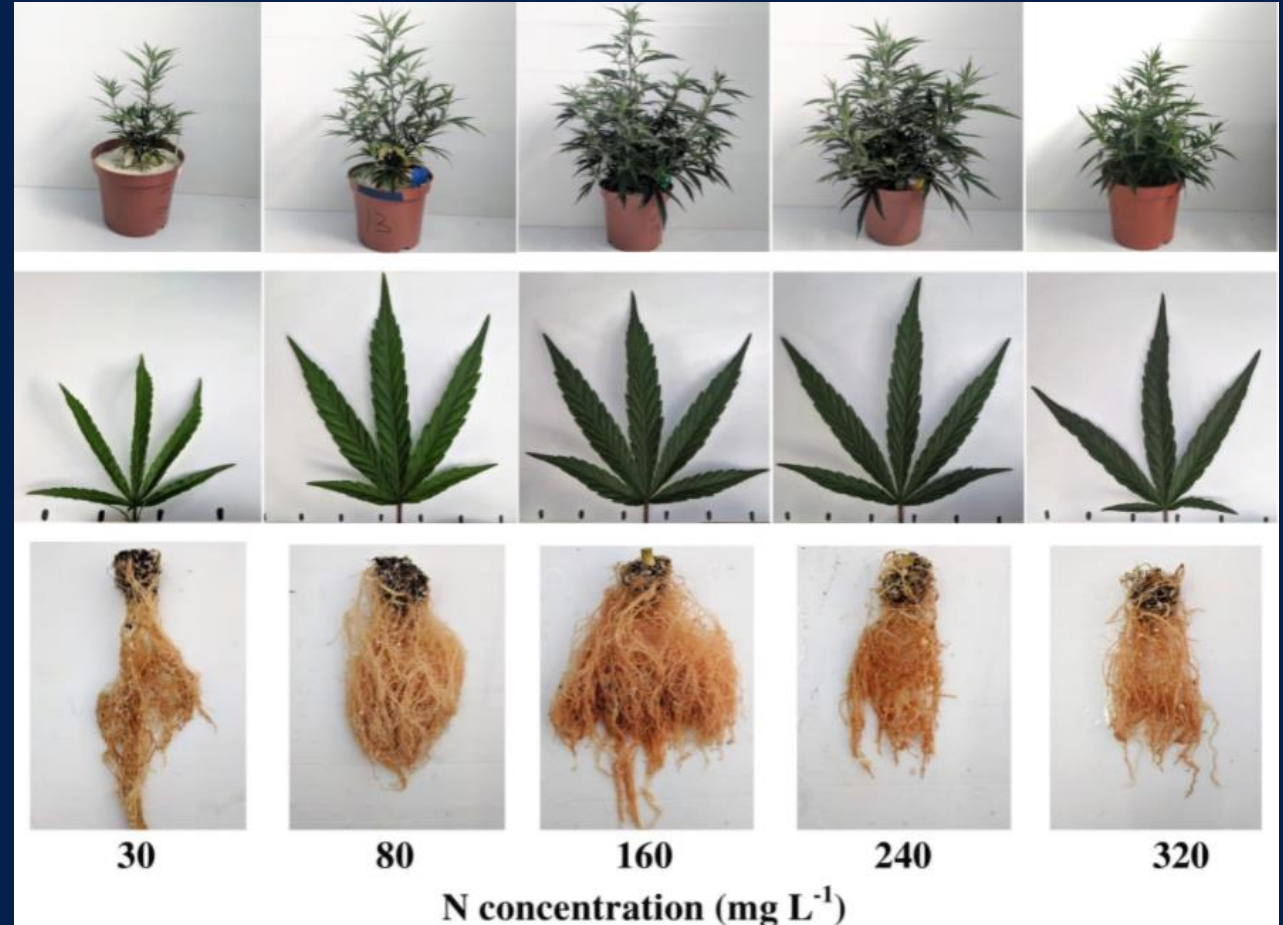
- ◆ Victoria Pham, DO, MBA, FAPA, DFAACAP
 - ◆ Commercial Interests: No financial disclosures
- ◆ Brian Hurley, MD, MBA, DFASAM, FAPA
 - ◆ Commercial Interests: No financial disclosures

Learning Objectives

- ◆ By the conclusion of this learning session, participants will be able to:
 - ◆ Characterize the various types of cannabis products
 - ◆ Describe cannabis use and potency
 - ◆ Explain cannabis' impacts on physical and mental health
 - ◆ Discuss which cannabinoid drugs have FDA approval and which THC/CBD related clinical trials are in the pipeline
 - ◆ Summarize the emerging policies and regulations with regards to Cannabis use in the United States
 - ◆ Identify treatment options available to people with cannabis use disorder

Background

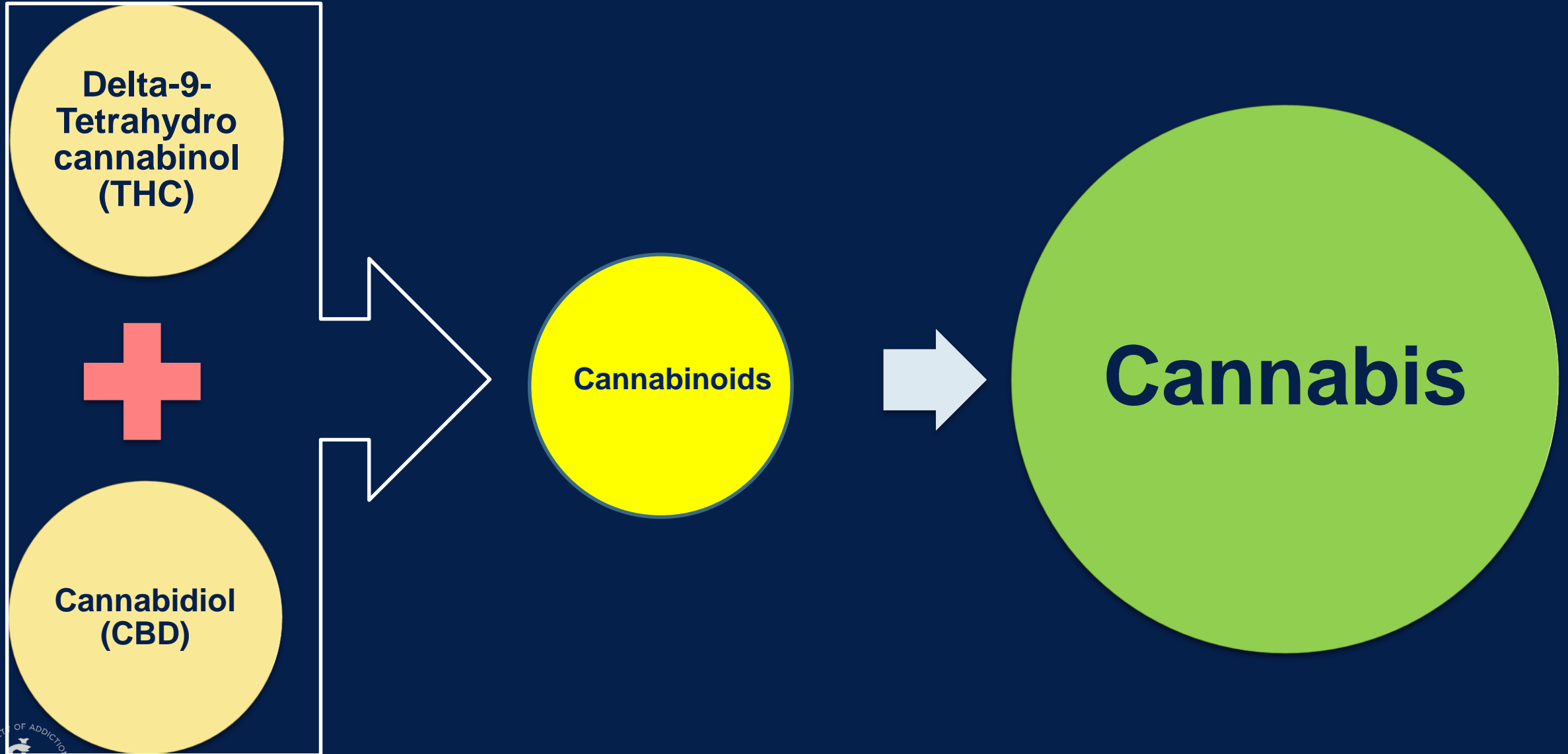
- ◆ ***Cannabis Sativa***: greenish-gray mixture of the dried flowers
- ◆ **Marijuana**: *weed, herb, pot, grass, bud, ganja, Mary Jane, dope, MJ, doobie, hooch, hash, reefers, 'oid', etc*
- ◆ **Stronger form of marijuana**: *sinsemilla, concentrated resin, hash oil, waxy budder, shatter, etc*



113 active cannabinoids identified in cannabis plant



Cannabis Characterization



Hemp



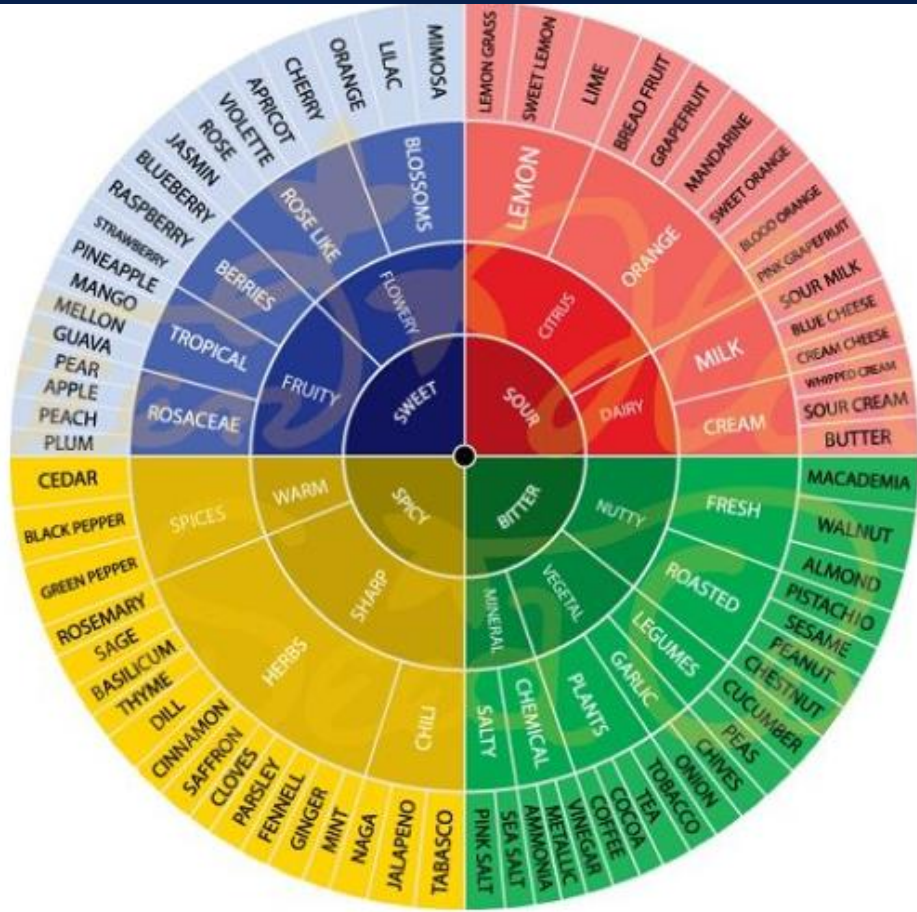
Lower level of THC (<0.3%), Can have high levels of CBD

Marijuana

- ◆ Dried flower tops and leaves of cannabis



Flavored Marijuana



Flavored Marijuana



What is considered flavored cannabis may reflect a variety of use patterns:

- ◆ Flavored rolling papers, as a blunt within a flavored tobacco cigar
- ◆ Cannabis flower that was marketed with flavor descriptors

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Flavored Rolling Papers





General Hydroponics Flora Series Expert Plus Complete Nutrient Kit - Small

★★★★★ (0.0) [Write a review](#)

\$233.49

Qty:

1

Add to cart



Roll over image to zoom in



General Hydroponics GLCMBX0009 Calimagic & Flora Gro, Micro & Bloom Combo, 1 Quart Fertilizer

Brand: General Hydroponics

★★★★★ 194 ratings

Price: \$79.00

Pay ~~\$79.00~~ \$69.00 when you add a new payment method to your Amazon wallet. [Click here to add a Discover card and save.](#) [Terms Apply](#)

Brand	General Hydroponics
Product Dimensions	3.3 x 13.2 x 8.5 inches; 8 Pounds
Liquid Volume	3 Quarts

About this item

- Calimagic is a concentrated blend of readily available calcium and magnesium
- Formulated to Assist fast growing plants by preventing secondary nutrient deficiencies
- Stimulates structural and vegetative growth. Builds strong roots. Provides nitrogen, phosphorous, potassium and secondary minerals.
- Stimulates flower and fruit development. Enhances flavor, aroma and essential oils. Provides high phosphorous, potassium, magnesium and sulfur.

Table 1. Flavored Product Use Among Past 30-Day Users, by Product (N = 1,423), California High School Students, 2019–2020^a

Product	Cigarettes	Moist Snuff	Cigars	E-Cigarettes	Smoked ^b Cannabis	Vaped ^c Cannabis
Past 30-day product use, among total sample	32 (2.2)	20 (1.4)	36 (2.5)	302 (21.2)	160 (11.3)	139 (9.8)
Flavored use, among past 30-day users^d						
Flavored ^e	14 (43.8)	13 (68.4)	29 (80.6)	225 (75.8)	76 (48.1)	80 (58.0)
No flavor or tobacco flavor ^f	15 (46.9)	6 (31.6)	7 (19.4)	27 (9.1)	39 (24.7)	24 (17.4)
Don't know	3 (9.4)	0 (0.0)	0 (0.0)	45 (15.2)	43 (27.2)	34 (24.6)
Missing data ^g						

Table 2. Types of Flavors Used Among Past 30-Day Cannabis Users, California High School Students, 2019–2020

Flavor	No. (Unweighted Percentage) ^a
Smoked cannabis (n = 160)	
No flavor ^b	56 (35.4)
Fruit	48 (30.4)
Candy, dessert, or sweet	38 (24.1)
Alcoholic drink	9 (5.7)
Spice or cinnamon	8 (5.1)
Mint (not menthol)	6 (3.8)
Menthol (cool or frost)	4 (2.5)
Nonalcoholic drink	0 (0.0)
Other flavor	8 (5.1)
Don't know ^c	48 (30.4)
Missing data ^d	2
Vaped cannabis (n = 139)	
Fruit	54 (39.1)
No flavor ^b	43 (31.2)
Candy, dessert, or sweet	38 (27.5)
Alcoholic drink	8 (5.8)
Mint (not menthol)	7 (5.1)
Menthol (cool or frost)	5 (3.6)
Spice or cinnamon	5 (3.6)
Nonalcoholic drink	2 (1.4)
Other flavor	2 (1.4)
Don't know ^c	41 (29.7)
Missing data ^d	1

Hashish

- ◆ Dried extract resin from cannabis flowers compressed into bricks



CANNABIS CONCENTRATES



CRUMBLE

Dried oil with a honey-comb like consistency



BADDER/BUDDER

Concentrates whipped under heat to create a cake-batter like texture



SHATTER

A translucent, brittle, & often golden to amber colored concentrate made with a solvent



DISTILLATE

Refined cannabinoid oil that is typically free of taste, smell & flavor. It is the base of most edibles and vape cartridges



CRYSTALLINE

Isolated cannabinoids in their pure crystal structure



DRY SIFT

Ground cannabis filtered with screens leaving behind complete trichome glands. The end-product is also referred to as kief



ROSIN

End product of cannabis flower being squeezed under heat and pressure



BUBBLE HASH

Uses water, ice, and mesh screens to pull out whole trichomes into a paste-like consistency



Stronger form of marijuana:
*sinsemilla, concentrated resin, hash,
oil, wax, budder, shatter, etc*

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<https://weedhub.delivery/sf-peninsula/concentrates/>. Accessed July 26, 2021

<https://ppaccentral.org/2020/05/13/marijuana-extracts-thc-concentrates/>. Accessed July 26, 2021

Hash Oil

- ◆ Viscous mass of concentrated compounds from cannabis extracted with a solvent



A close-up photograph of a person's mouth and hand using a dabber pen. The person is exhaling a small amount of smoke from the pen's tip. The background is blurred, showing more smoke or a similar environment. The text is overlaid on the left side of the image.

Dabbing delivers high concentrations of cannabinoids to the body quickly. The risks of physical dependence and addiction increase with exposure to high concentrations of THC, and higher doses of THC are more likely to quickly generate its desired (and undesired) effects.

Edibles

◆ Cannabinoids Added to Foods / Products



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Marijuana Infused Foods & Drinks



A collage of various cannabis-infused products. At the top left is a box of 'müv TRANSFERMAL PATCH' with 'LONG-EXTENDED RELEASE' and 'müv' branding. Below it is a black box labeled 'FORIA' and a bottle of 'FORIA' oil. To the right is a cup of coffee with a cannabis leaf on the lid, surrounded by coffee beans. Below the coffee are three cannabis-infused edibles: two round yellow ones and one round purple one, with a cannabis leaf next to them. At the bottom left are two brown cannabis-infused gummies. To their right is a white bag of 'CANNABIS QUEEN ENERGY' from 'ARAPAHO, COLORADO' with a 'THC' logo and 'Royal Spice Marijuana-Inspired' text. On the far right is a green and white box of 'CANNABIS LIP BALM' by 'THE CANNABIS COMPANY'.



Capsules

- ◆ Cannabinoids Added to Tabs/Caps



Synthetic Cannabinomimetics

- ◆ Chemical agents sprayed onto plant matter

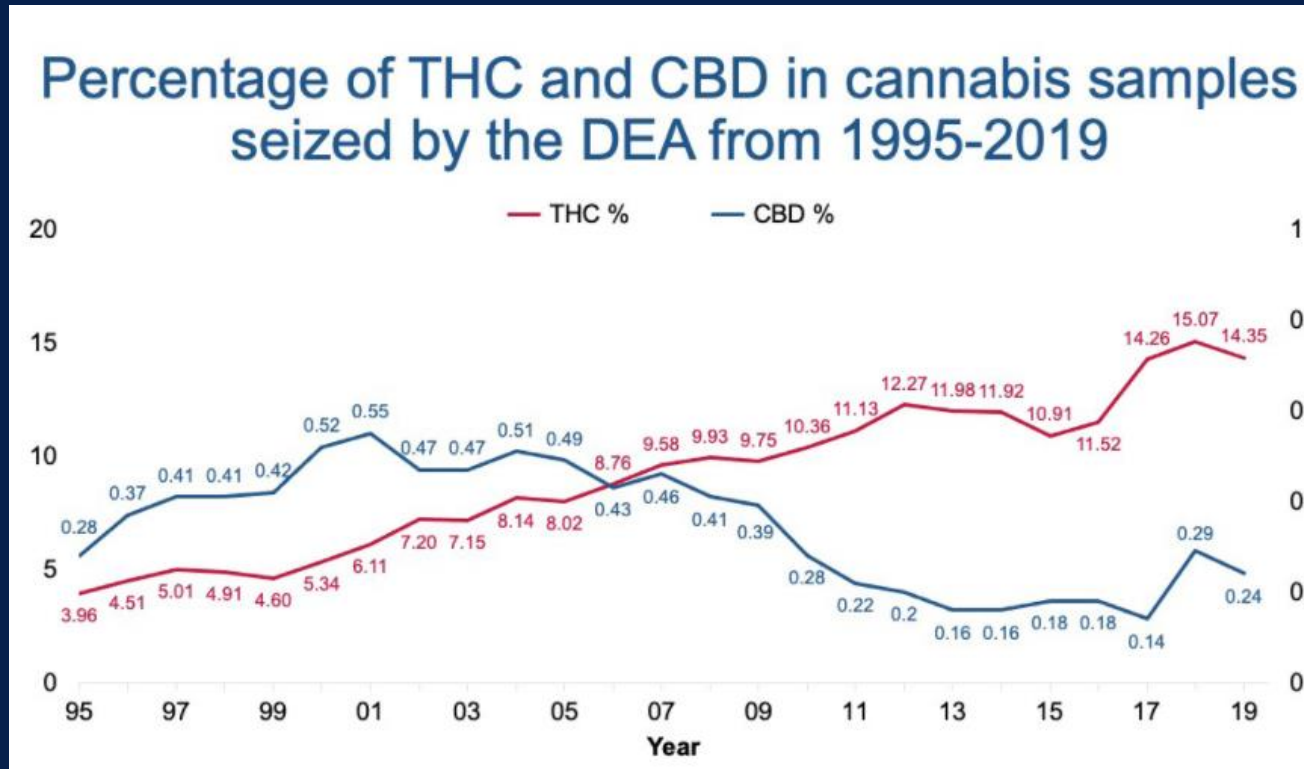


Rising Potency

- ◆ In the early 1990s, the average THC content in confiscated marijuana samples was less than 4%. In 2018, it was more than 15%.



Percent of THC and CBD in Cannabis



Delta-9-tetrahydrocannabinol (THC) and Cannabidiol (CBD) Potency of Cannabis Samples Seized by the Drug Enforcement Administration (DEA), Percent Averages from 1995-2019.

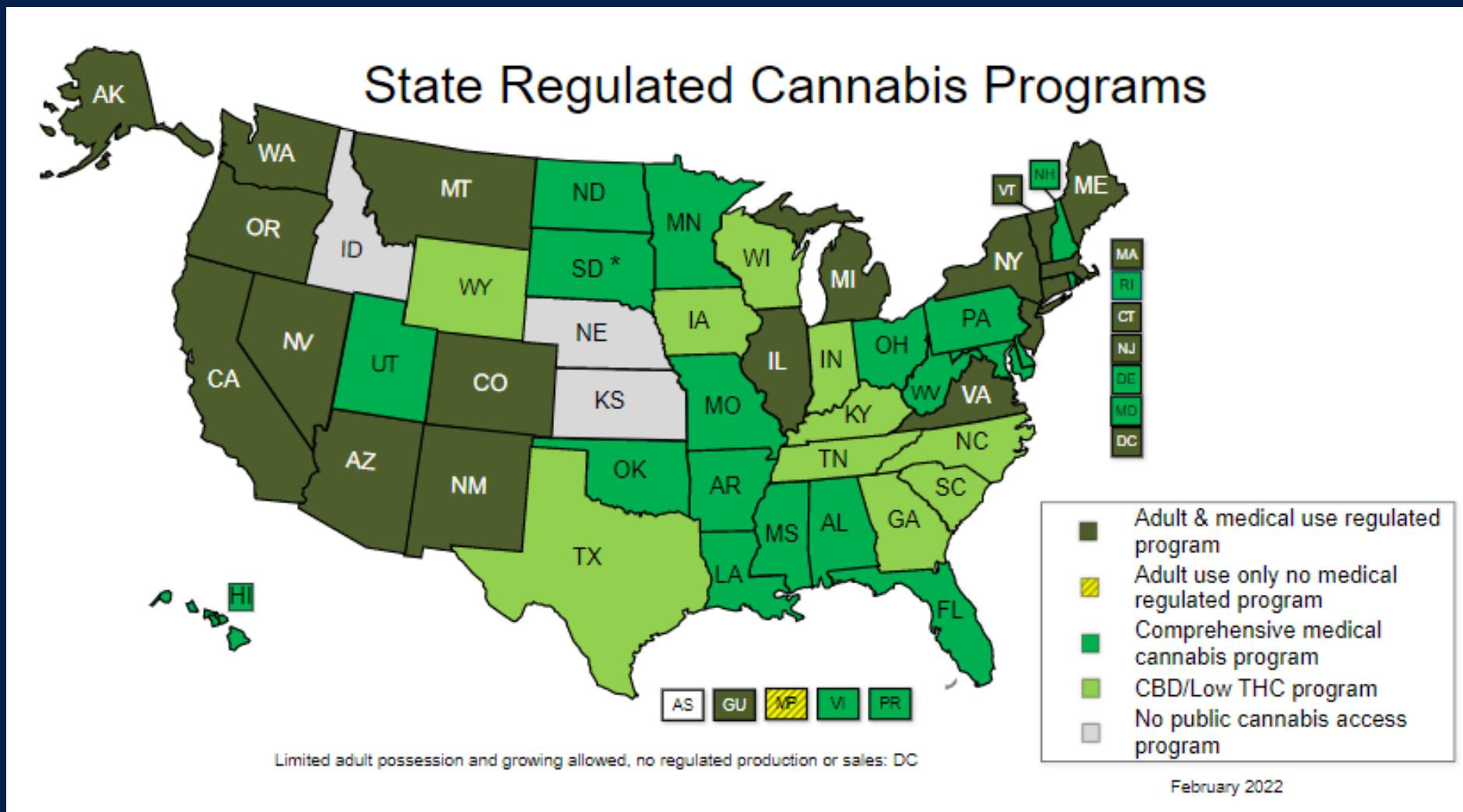
Regulations & Economics



Marijuana Regulation

- ◆ Uruguay and Canada now regulate cannabis as a legally available produce for consumption.
- ◆ At the United States federal level, Cannabis products are classified as Schedule 1, ie, not currently accepted medical use and regulated as a drug with high potential for abuse

State Regulation of Cannabis



Cannabis Taxes and State Revenue

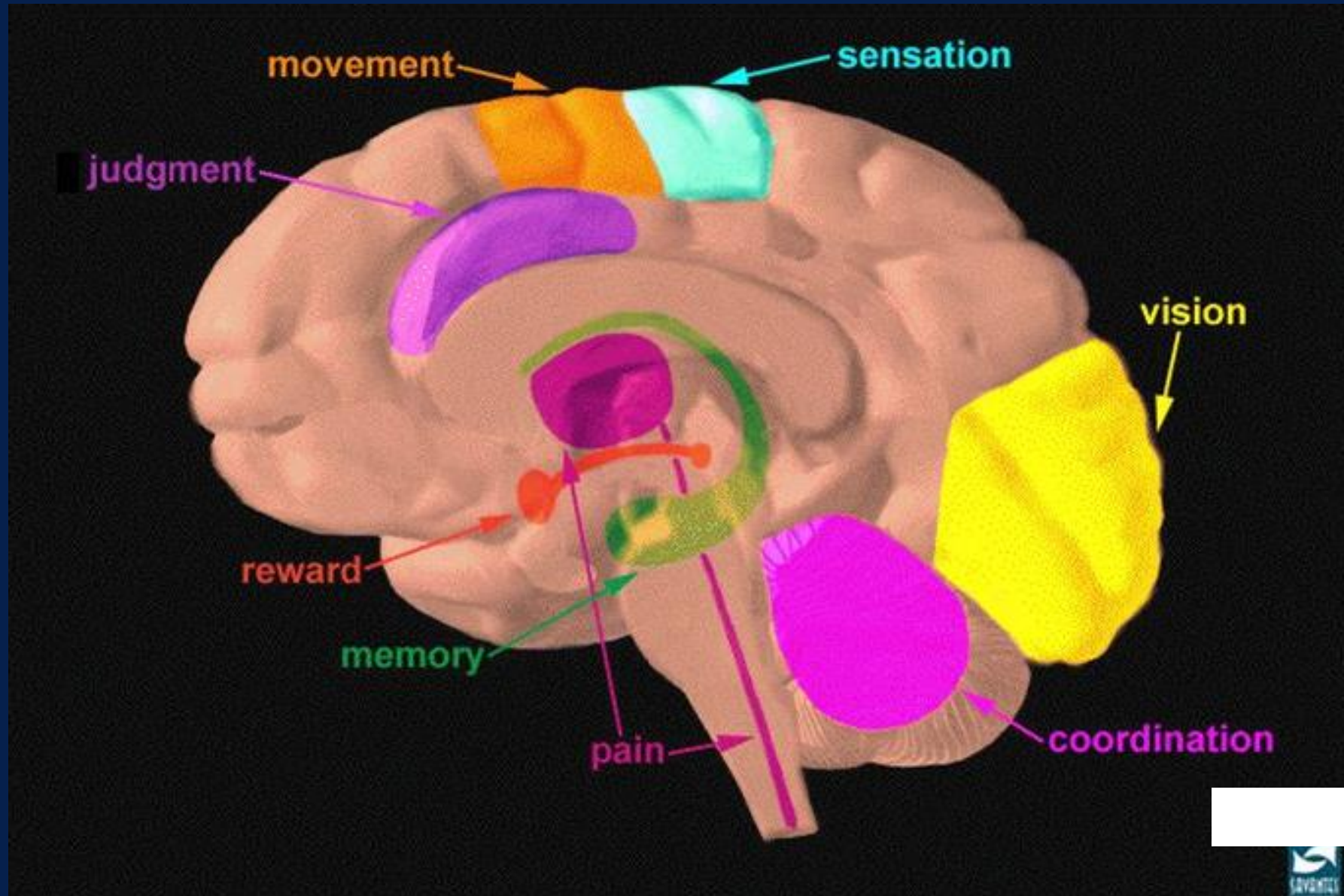
- ◆ **CO:** 2.9 % tax for both medical and recreational sales, but 15% excise tax when marijuana moves from grower to seller
 - ◆ In 2019, Colorado collected more than \$302 million in taxes and fees on medical and recreational marijuana. Sales in the state totaled over \$1.7 billion
 - ◆ It took the state 3.5 yrs to get to \$500 million mark in total state revenue from marijuana sales
- ◆ **NV:** An RCG Economics and Marijuana Policy Group study on Nevada projected:
 - ◆ Legalizing recreational marijuana in the state could support over 41,000 jobs until 2024 and generate over \$1.7 billion in labor income.
- ◆ **CA:** The ICF study estimates at least 81,000 additional direct, indirect, and induced jobs in California as a result of legalized marijuana sales. It also projects an increase in total labor income by at least \$3.5 billion.



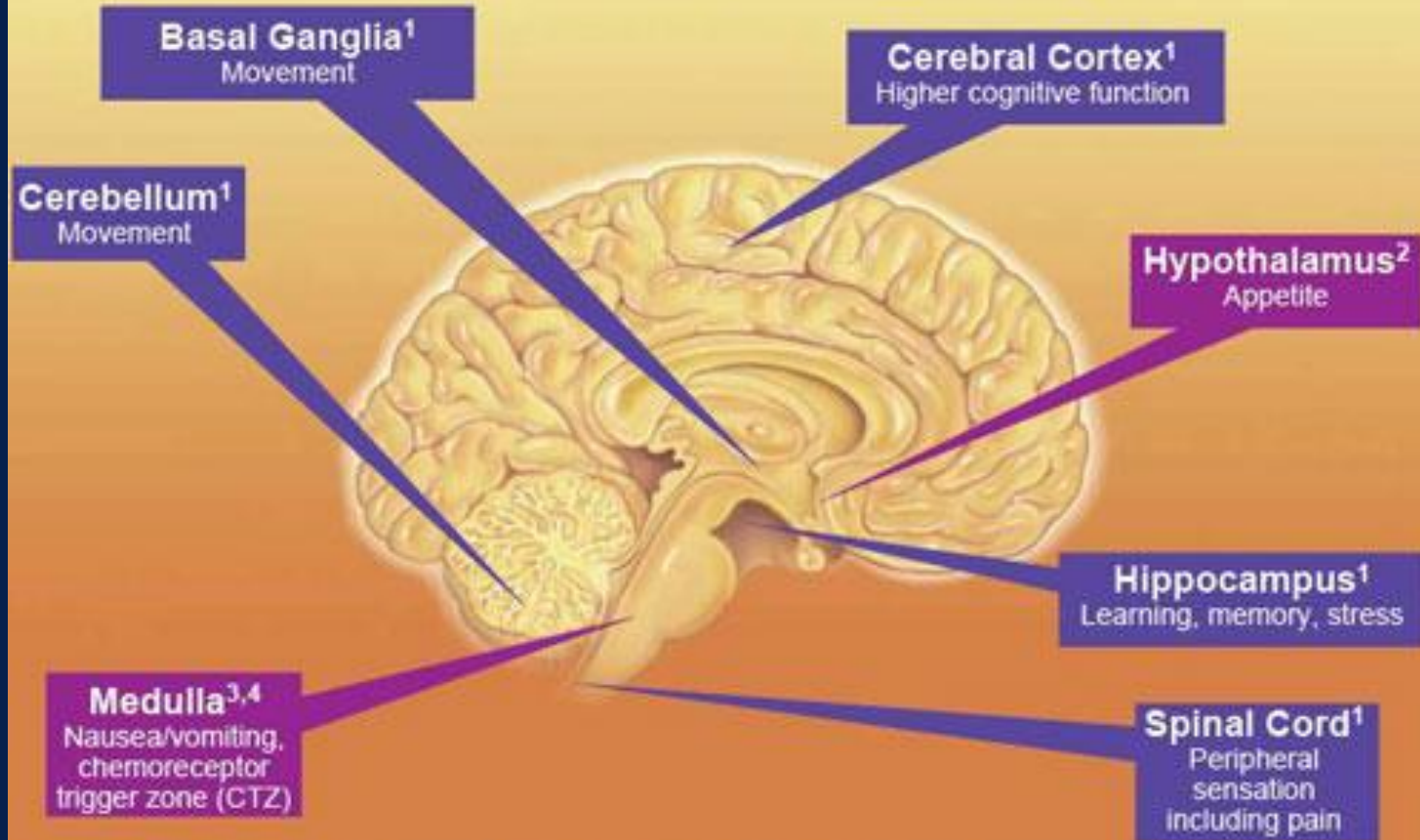
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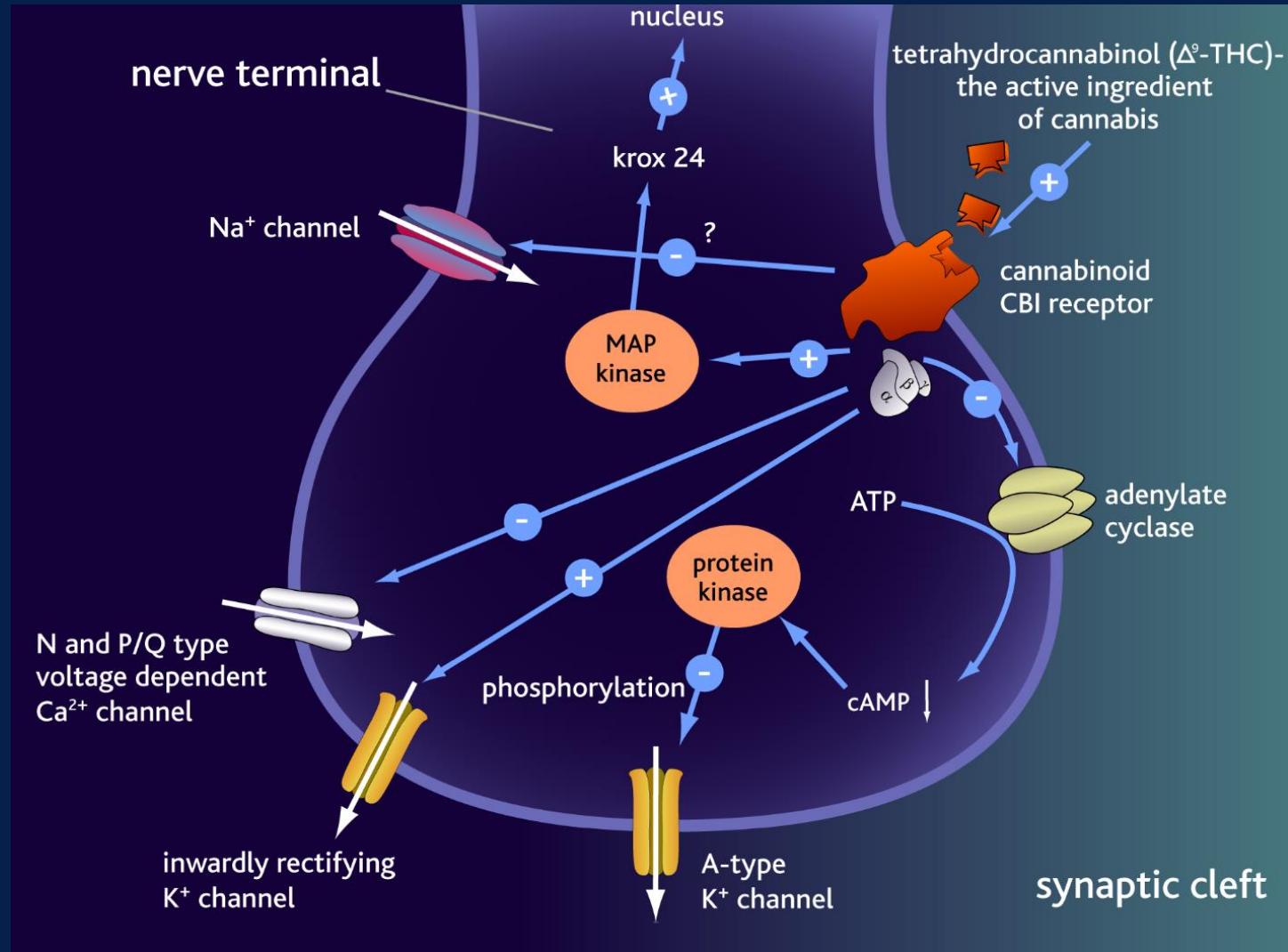




Concentrations of CB₁ receptors



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Intoxication Features

◆ Desired Effects

- ◆ Euphoria
- ◆ Relaxation
- ◆ Enhanced sensations
- ◆ Slowed time

• Physical Signs

- Conjunctival injection
- Dry mouth
- Raised heart rate & blood pressure
- Orthostatic hypotension
- Impaired motor coordination

◆ Undesired Effects

- ◆ Social withdrawal
- ◆ Impaired judgment
- ◆ Short-term memory loss
- ◆ Anxiety, Paranoia, Psychosis



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Potential Benefits

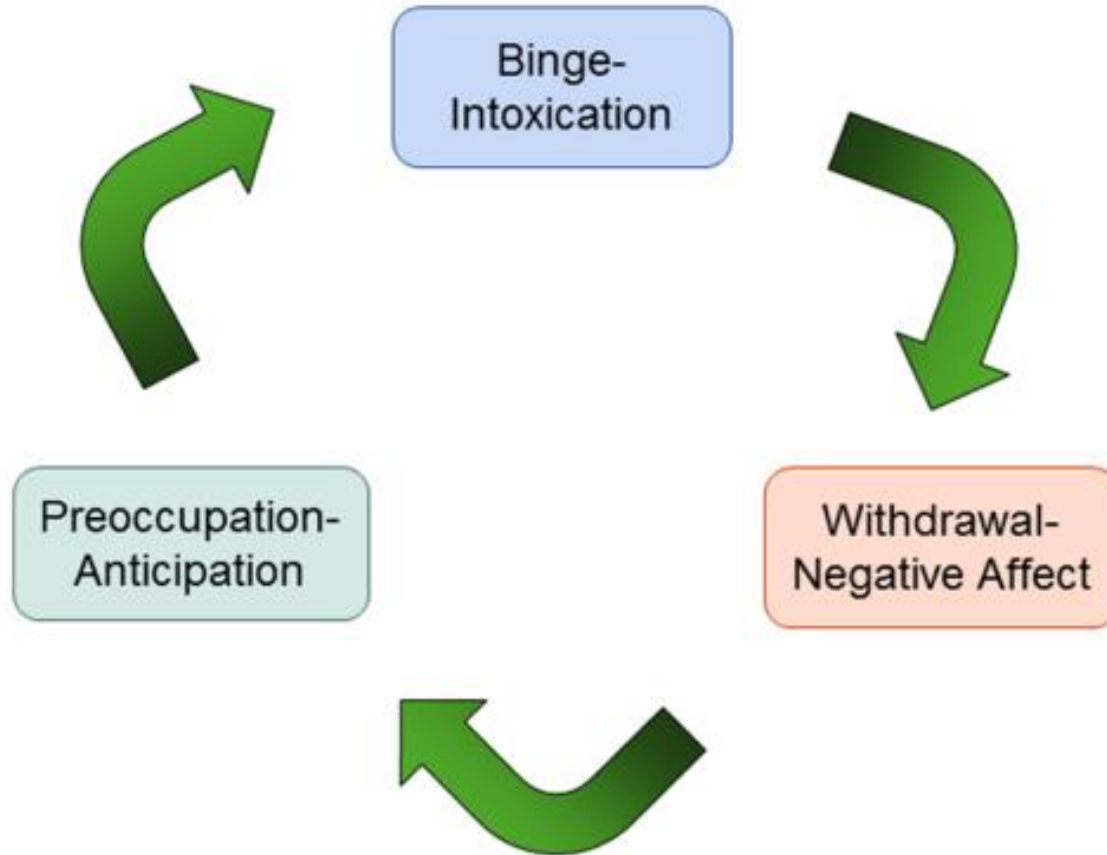
- ◆ Stimulate appetite – severe weight loss in AIDS
- ◆ Suppress nausea & vomiting – chemotherapy
- ◆ Alleviate spasticity – multiple sclerosis
- ◆ Decrease eye pressure – glaucoma
- ◆ Suppress seizures – epilepsy in children



A

Behavior Impaired salience processing	Neurophysiological Adaptations THC-induced DA release Blunted stimulant-induced dopamine release	Imaging Correlates Changes in striatal activation during reward processing	Therapies Direct CB1 Receptor Antagonists Cannabidiol
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Behavior Potential impairments in executive function domains of short-term verbal memory and IQ
Neurophysiological Adaptations Disrupted glutamate signaling: Increased glutamate transmission during abstinence, correlated with craving and relapse
Imaging Correlates Enhanced cue-reactivity of mesocorticolimbic-reward system and insula to cannabis-related cues
Therapies N-acetylcysteine as anticraving agent



Behavior Presence of withdrawal syndrome Increase in negative affect Amotivational state
Neurophysiological Adaptations Increase in CRF in central nucleus of amygdala in rodents HPA axis dysfunction
Imaging Correlates Decreased stimulant-induced DA reactivity - associated with greater negative emotionality Affect dysregulation related to amygdala functioning
Therapies Greatest withdrawal symptom reduction: oral THC, nabixmol, nabilone Lowest relapse: naltrexone, gabapentin, N-acetylcysteine

Cannabis Use Disorder

- ◆ Cannabis dependence occurs when the brain adapts to large amounts of the drug by reducing production of and sensitivity to its own endocannabinoid neurotransmitters
- ◆ 30% of those who use marijuana may have some degree of Cannabis Use Disorder (CUD)
- ◆ People who begin using marijuana before the age of 18 are **4-7x** more likely to develop a CUD than adults
- ◆ People who use marijuana frequently often report irritability, mood and sleep difficulties, decreased appetite, cravings, restlessness, and/or various forms of physical discomfort that peak within the first week after quitting and last up to 2 weeks



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Cannabis Withdrawal: DSM-5

- ◆ Cessation of cannabis use that has been heavy and prolonged (ie, usually daily or almost daily use over a period of at least a few months).
- ◆ **Three or more** of the following signs and symptoms that develop **within 1 week after abrupt reduction or the cessation of prolonged cannabis use**:
 1. Irritability, anger, or aggression
 2. Nervousness or anxiety
 3. Sleep difficulty (eg, insomnia or vivid dreaming)
 4. Decreased appetite or weight loss
 5. Restlessness
 6. Depressed mood
 7. At least one of the following physical symptoms that causes discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache
- ◆ The signs or symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

First-Episode Psychosis: Co-occurring Conditions



- ◆ Cannabis is a risk factor for developing or exacerbating psychosis. Some studies suggested early cannabis use is a causal factor in developing Schizophrenia
- ◆ Retroactive study of 404 youths with first break psychosis:
 - ◆ 50% had any life-time SUD use
 - ◆ 34.7% used Cannabis, vs. 11% in general population



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Cannabinoids with FDA approval

Pharmaceutical Cannabinoids

- ◆ Cannabinoids with FDA approval are:
 - ◆ **Dronabinol (Marinol, Syndros)**
 - ◆ **Nabilone (Cesamet)**
 - ◆ **Cannabidiol (Epidiolex)**
- ◆ **Nabiximols (Sativex)** is approved for use in UK, other European markets, and in Canada
 - ◆ In Phase III trials in the US for oncology pain
- ◆ For non-prescription use, cannabidiol derived from industrial hemp is legal at the federal level, but legality and enforcement varies by state

Dronabinol

- ◆ **Indications in adults:** Anorexia in patients with AIDS, Chemotherapy-induced nausea and vomiting refractory, Obstructive sleep apnea (off-label use for moderate/severe sxS)
- ◆ **Mechanism of Action:** Synthetic delta-9-THC. Activates cannabinoid receptors CB1 and CB2
 - ◆ CB1 produces marijuana like effects on psych and circulation

Nabilone

- ◆ **Indications for adults:** Nausea and vomiting (refractory) associated with cancer chemotherapy
- ◆ **Mechanism of Action:** Antiemetic activity may be due to effect on cannabinoid receptors (CB1) within the central nervous system

Cannabidiol (Epidiolex)

◆ Indications in adults:

- ◆ Seizures associated with Dravet Syndrome
- ◆ Seizures associated with Lennox-Gastaut Syndrome
- ◆ Seizures associated with Tuberous Sclerosis Complex

◆ Monitoring Parameters:

- ◆ ALT/AST/total bilirubin to be checked at baseline, 1mo, 3mo, 6mo, then periodically

◆ Mechanism of Action: unknown



Nabiximols

- ◆ Approved in Canada and various European Markets under brand name Sativex. Not approved in the US.
- ◆ Approved for Spasticity associated with multiple sclerosis
- ◆ Buccal spray
- ◆ Mechanism of action: Stimulates cannabinoid receptors CB1 and CB2 in the CNS and dorsal root ganglia as well as other sites in the body. Cannabinoid receptors in the pain pathways of the brain and spinal cord mediate cannabinoid-induced analgesia. Peripheral CB2 receptors modulate immune function through cytokine release

THC & CBD Drugs in the Pipeline

THC & CBD Drug Products in the Pipeline

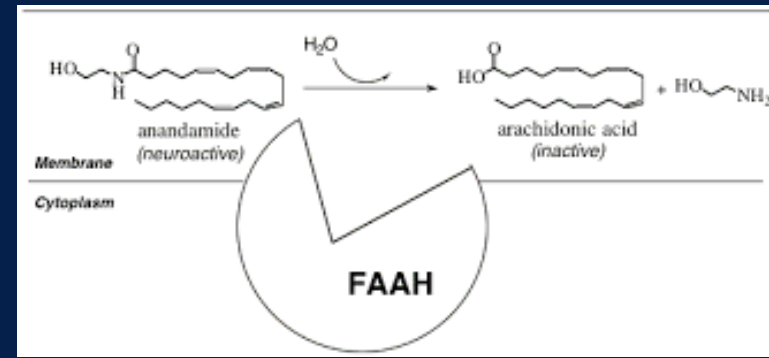
Over 100 trials:

- ◆ Cannabidiol 133mg + Cannabigerol 66mg + Tetrahydrocannabinol 4mg vs. Placebo as Adjuvant Treatment in **Chronic Migraine**
- ◆ **Oral or Oral spray** of THC and CBD
- ◆ THC and CBD in **osteoarthritis of the knee**
- ◆ Does Cannabidiol attenuate the acute effects of THC intoxication in individuals diagnosed with **Schizophrenia**?
- ◆ Effect of THC and CBD on Human **Episodic Memory** Function
- ◆ Comparing CBD to THC and Alprazolam
- ◆ **“Do adolescents and adults differ in their acute response to Cannabis?”**

THC & CBD Drug Products in the Pipeline

- ◆ Studies in **Bipolar, Schizophrenia, Anxiety Disorders, ADHD, PTSD**, etc
- ◆ THC & CBD oil in adults with **chronic back/neck pain**
- ◆ THC & CBD in **Crohn's Disease**
- ◆ Effects of THC-free CBD oil on **agitation in patients with Alzheimer's Disease**
- ◆ THC & CBD in **Multiple Sclerosis**
- ◆ THC and CBD combination with Temozolomide and radiotherapy in patients with newly diagnosed **Glioblastoma**
- ◆ A double-blinded, randomized, placebo control experimental study
- ◆ Inhaled cannabis for **acute migraine** treatment
- ◆ THC & CBD in **advanced cancer and associated cachexia**
- ◆ Medical Cannabis in patients with **spasticity with severe forms of cerebral palsy**
- ◆ Cannabis for **essential tremor**

FAAH Inhibitors



- ◆ There are trials of an FAAH-Inhibitor PF-04457845 to treat cannabis withdrawal.
 - ◆ Study description: Blocking the degradation of Anandamide by fatty acid amide hydrolase following discontinuation of cannabis could reduce withdrawal symptoms by increasing the brain's capacity to make its own endocannabinoids.
- ◆ In a Phase II placebo-controlled trial involving 46 male participants, there was reduced withdrawal symptoms, reduced self-reported cannabis use, and reduced urine THC concentration over a four-week treatment trial.

Psychotherapy & Cannabis Use Disorder (CUD)

Evidenced-based psychotherapies demonstrated effectiveness in reducing frequency and quantity of cannabis use.

- ◆ **Motivational Enhancement Treatment (MET):** Effective at engaging people who are ambivalent about treatment
- ◆ **Cognitive Behavioral Therapy (CBT):** Enhance abstinence following treatment (preventing relapse)
- ◆ **Contingency Management (CM):** Lead to longer periods of abstinence during treatment by incentivizing abstinence
 - ◆ Including financial based incentives or vouchers

Access to psychotherapy and compliance are main issues



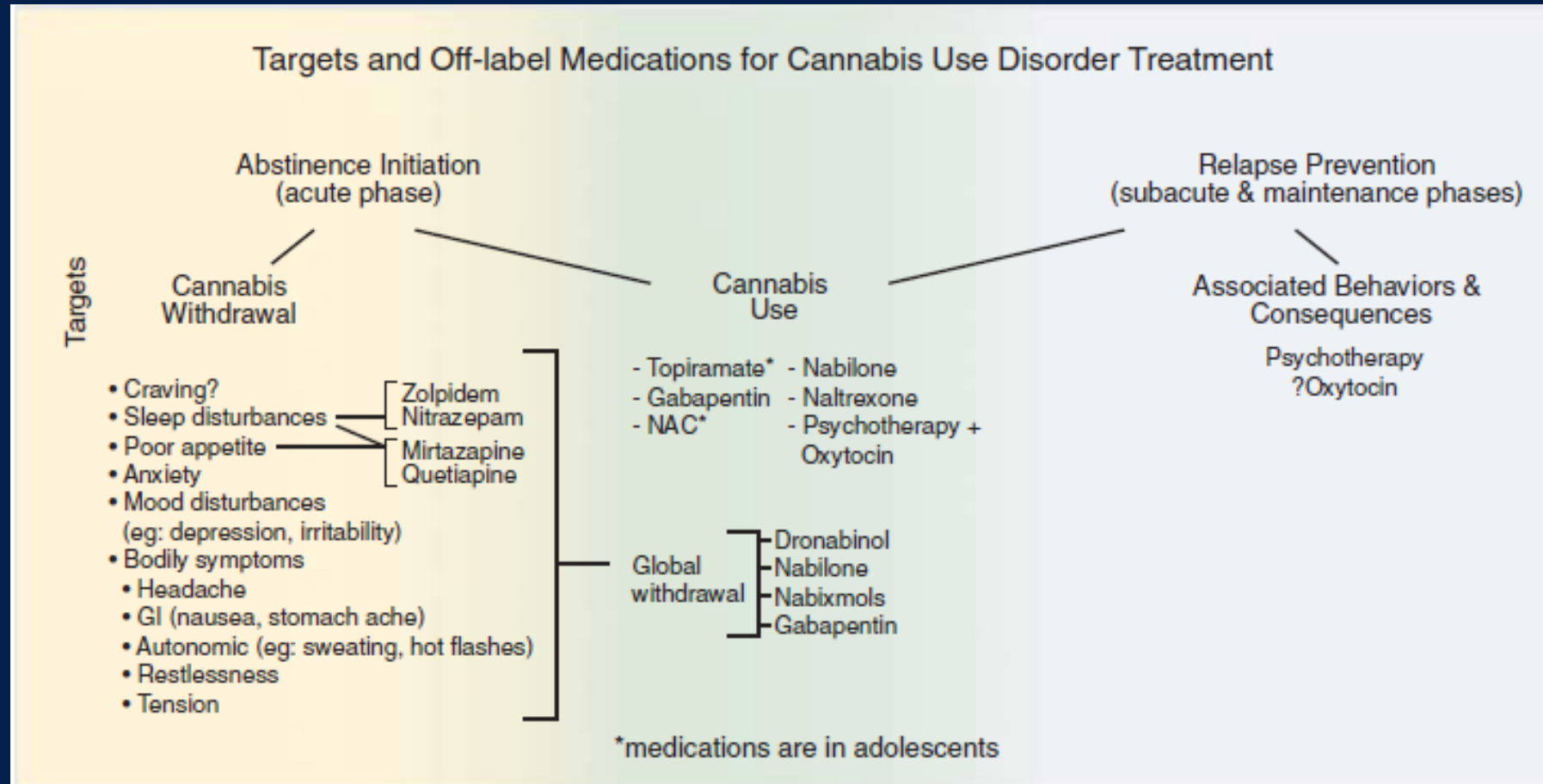
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Medications for Cannabis Use Disorder

To date, there are no FDA-approved medication treatments for CUD

Medications for Cannabis Use Disorder



Medications for Cannabis Use Disorder

- ◆ **Mirtazepine** and **Quetiapine** reduce some symptoms of cannabis withdrawal, though these medications do not affect cannabis use
- ◆ **Zolpidem** and possibly **benzodiazepines**, like nitrazepam, may be useful in short term reduction in sleep disturbances as a result of cannabis withdrawal in adults
- ◆ **Oral THC**, such as **nabixmols**, and **nabilone**, have evidence for targeting global cannabis withdrawal
- ◆ **Topiramate** (though poorly tolerated in adolescents), **Gabapentin**, **NAC**, and **Naltrexone** have demonstrated reductions in cannabis use and extension in abstinence in small (eg **Gabapentin**) or age-specific patient samples (eg, **NAC** in adolescents) but **NAC** has not yet shown efficacy in larger trials involving adults

Medications for Cannabis Use Disorder

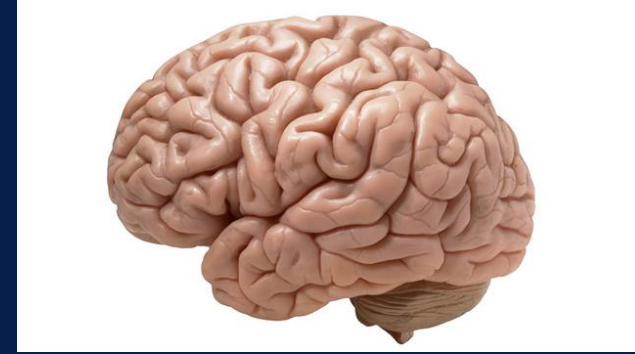
◆ Dronabinol: Oral THC

- ◆ Has FDA indications for the treatment of 1) anorexia associated with AIDS and 2) second line treatment for nausea/vomiting associated with cancer chemotherapy (20mg/daily)
- ◆ At dose 80mg/daily, decrease withdrawal symptoms, including craving, appetite suppression, mood disturbance
- ◆ Failed to separate from placebo for cannabis abstinence

Medications for Cannabis Use Disorder

- ◆ GABA-A agonist sleep agents and other medications with GABA-A activity, such as **Gabapentin** and **Topiramate**, show promise in the treatment of CUD to target difficulties with sleep as a result of withdrawal and/or maintenance treatment of CUD by decreasing cannabis use, respectively.
- ◆ Larger, fully powered placebo-controlled trials need to be completed

Rimonabant



- ◆ Cannabinoid antagonist with inverse agonist properties.
- ◆ Removed from the global market, and no longer under development following two deaths by suicide were reported in patients taking Rimonabant for obesity.
- ◆ Associated with dangerous psychological side effects, including anxiety, depression, and suicidality (Sam, 2011).

Cannabidiol Versus Risperidone For Recent-Onset Psychosis with Cannabis Use

- ◆ **Ongoing study:** N=130 patients. Age: 18-64.
 - ◆ Recent diagnosis of psychosis, comorbid cannabis use and currently not treated with antipsychotics.
 - ◆ Randomized to 7 weeks of treatment. Either Cannabidiol (CBD) 300mg BID or Risperidone 2mg BID.
 - ◆ Primary measures: cessation of cannabis use and psychotic symptom severity
 - ◆ Outcomes: PENDING

Final Takeaways/Summary

- ◆ There is increasing availability of regulated cannabis in a widely proliferating variety of formats across the United States.
- ◆ Cannabis regulations vary from state to state.
- ◆ Chronic cannabis use is associated with cannabis use disorder and withdrawal, and cannabis use increased the risk for developing a psychotic disorder.
- ◆ Psychotherapy is a mainstay of CUD treatment, and there are medications which can help patients, off-label, with cannabis withdrawal and cannabis use disorder

Questions?

Thank you!

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