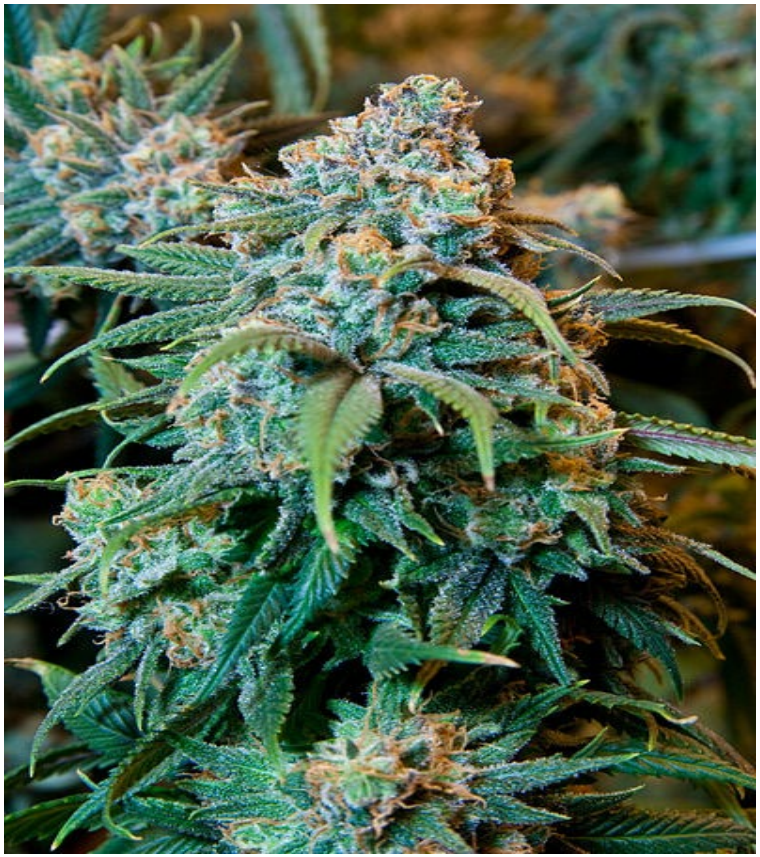
Marijuana: from Medicinal to Adult Recreational: Implications for MH and SUD TX Providers

Ted Parran MD FACP FASAM

Isabel and Carter Wang Professor and Chair in Medical Education

CWRU School of Medicine

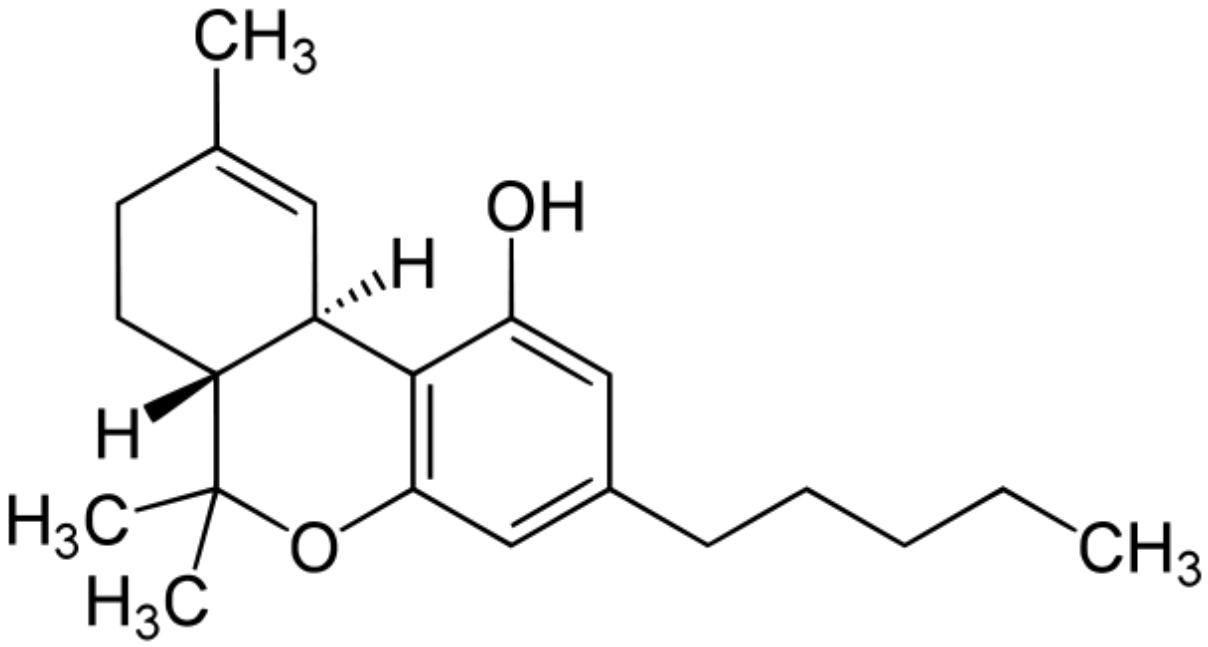
tvp@cwru.edu



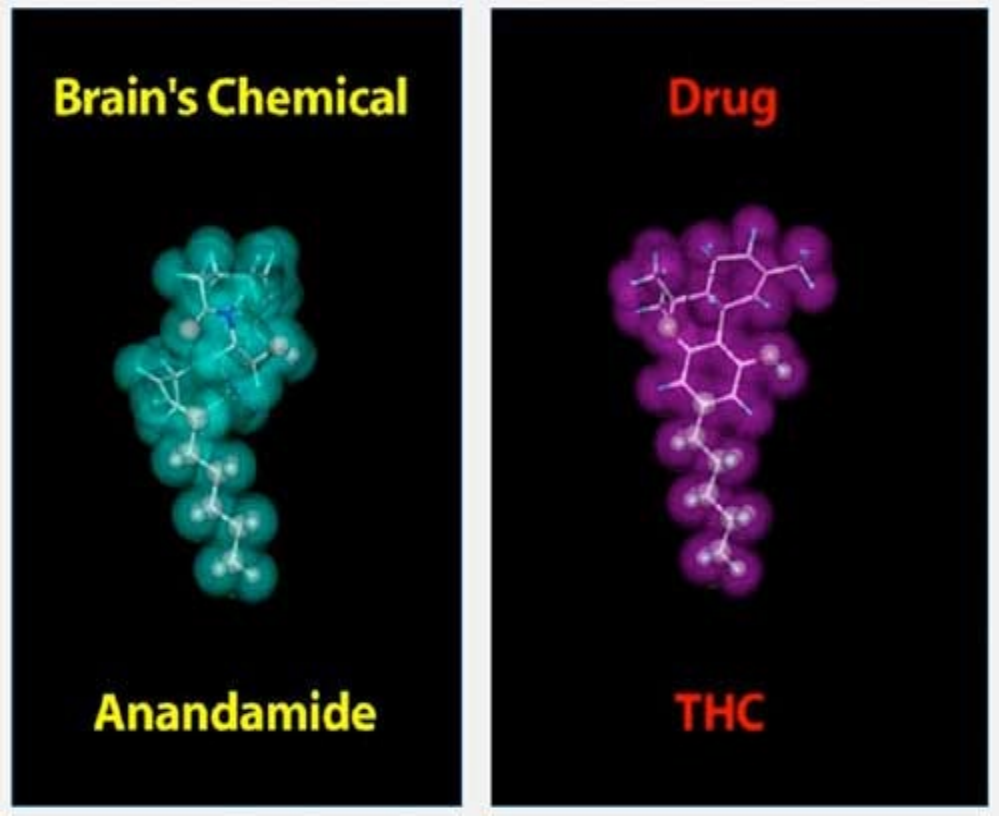
Disclosures

None

Primary Psychoactive Ingredient- *Tetrahydrocannabinol (THC)*

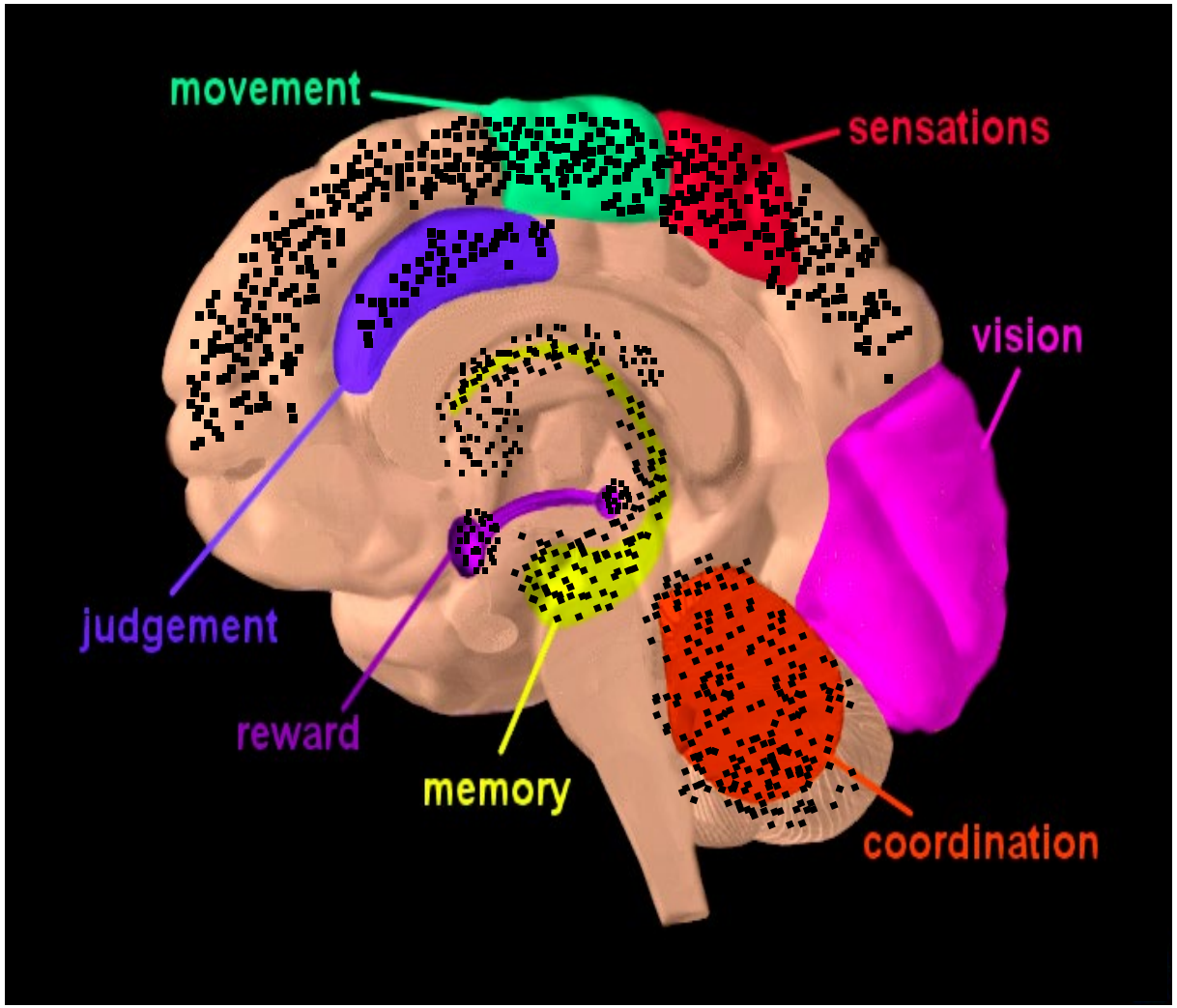


THC Mimics Neurotransmitter *Anandamide* in the Brain's Endocannabinoid System



Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

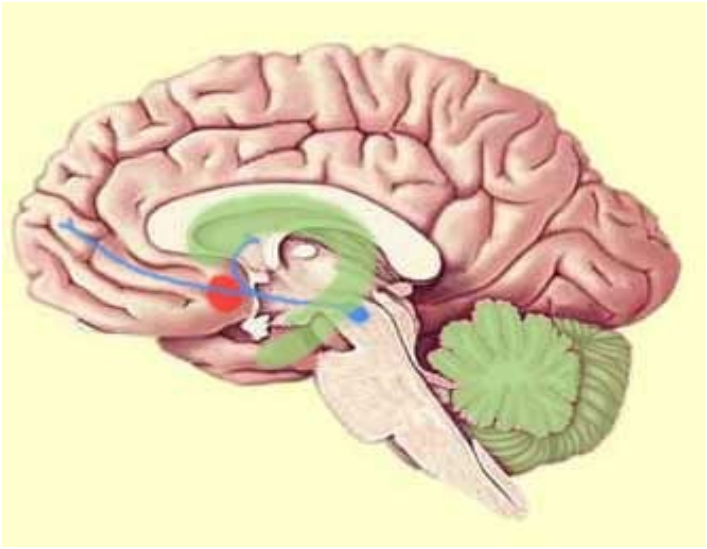
- Brain Development
- Memory and Cognition
- Motivational Systems & Reward (euphoria)
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia



Major cannabinoids found in cannabis (Phytocannabinoids)

- Delta-9-tetrahydrocannabinol (**Δ^9-THC**): most psychoactive, less therapeutic
- Cannabidiol (**CBD**): analgesia; antiseizure moderates effects of THC; healthiest
- Cannabinol (**CBN**): anticonvulsant
- Tetrahydrocannabivarin (**THCV**): ?anti-inflammatory
- Cannabichromene (**CBC**): mixed effects
- Cannabicyclol (**CBL**): analgesic
- Plus **60 or so other cannabinoids**

The Pleasure Centers Affected by Drugs: Cannabis



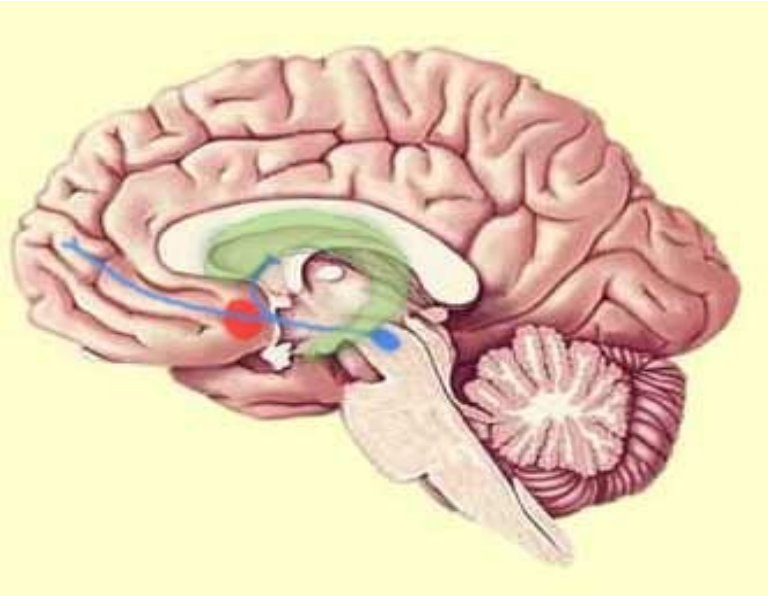
- The most prominent active ingredient in cannabis is THC, which concentrates chiefly in the ventral tegmental area and the nucleus accumbens, but also in the hippocampus, the caudate nucleus, and the cerebellum.
- Movement / coordination / learning and memory / judgement / pleasure
- THC's effects on the hippocampus might explain the memory problems that can develop with the use of cannabis, while its effects on the cerebellum might explain the loss of coordination and balance.

MJ and ADD/ADHD Side Note

- Moderate to heavy MJ use *MIMICS* the signs and symptoms of ADD/ADHD
- MJ use can *NEGATE* the ***therapeutic*** effect of ADD/ADHD medications (especially the scheduled psycho-stimulants), but *potentiates* their **euphoric** effect … or in other words *it limits the "legitimate medical purpose" (LMP) effect and increases the non-LMP effect.*

The Pleasure Centers Affected by Drugs

Cocaine and stimulants – methamphetamine / ecstasy / bath-salts / prescribed stimulants (ADD/ADHD/Obesity/Narcolepsy)



- Cocaine and amphetamines concentrate in the central link of the reward circuit (the ventral tegmental area and the nucleus accumbens). These areas contain especially high concentrations of dopaminergic synapses, which are the preferred target of these drugs.

MJ Use in ADD/ADHD patients

- It may well not be possible to truly accurately DX ADD/ADHD in a relatively heavy MJ user
- A heavy MJ user who might have ADD should abstain
  - TO BETTER CONFIRM THE DX
  - TO ENABLE THE PHARMACOTHERAPY TO BE MORE EFFECTIVE
  - TO ASSIST IN RULING OUT A SUD-mod-severe DX
- MJ users who can not (will not) stop MJ should be considered as likely to have MJ SUD-mod-severe
  - Treatment with controlled drugs is problematic in SUD patients
  - Controlled stimulants lose efficacy and increase euphoria
  - Best treated with non-controlled drug ADD alternatives

Marijuana Has Been Used As Medicine Throughout History

- Ancient History
  - Used in *Chinese* medicine dating back 10,000 years; still a basic herbal in Traditional Chinese Medicine
  - Ancient *Egypt* - hemorrhoids and other inflammatory conditions
  - *India* - used for insomnia, pain, digestive problems
  - Ancient *Greece* - extensive veterinary uses, also in humans (nosebleeds, tapeworms, etc.)
  - **Middle East** - used as antiemetic, diuretic, antiepileptic, anti-inflammatory

Marijuana Has Been Used As Medicine Throughout History

- Early Western Medicine 1800-1900s
  - Europe - used for muscle spasms, stomach cramps
  - America - widespread use in "patent medicines"
- Modern times- Advocates Support Use for Many Conditions
  - Insomnia
  - Pain
  - Nausea and vomiting
  - Decreased appetite with weight loss
  - Muscle spasms
  - Epilepsy
  - Glaucoma

American Patent Medicines

In Recent Times, Medications Are Subject to Scientific Standards

- Purity
- Indications
- Dosage
- Dose / response relationship
- *Prospective randomized reasonable scale research* to determine the medication's:
  - Efficacy / Safety / Adverse effects / Special populations (children/adol/pregnancy/elderly)
- Medicinal MJ does NOT meet these criteria

FDA- Approved Cannabinoids Are Already Available in U.S.

- Dronabinol (Marinol®) - **Purified THC**, Schedule III, approved for CINV, wasting syndrome in AIDS
- Nabilone (Cesamet®) - Synthetic cannabinoid resembling THC, Schedule II, approved for CINV
- Nabiximols (Sativex®) - CBD>THC, oral mucosal spray, not approved in U.S., used in Canada and Europe. Currently in Phase III trials in US for MS, cancer pain, CINV
- CBD (Epidiolex®) – **Purified CBD,** Schedule V, approved for severe childhood epilepsy (Dravet syndrome)

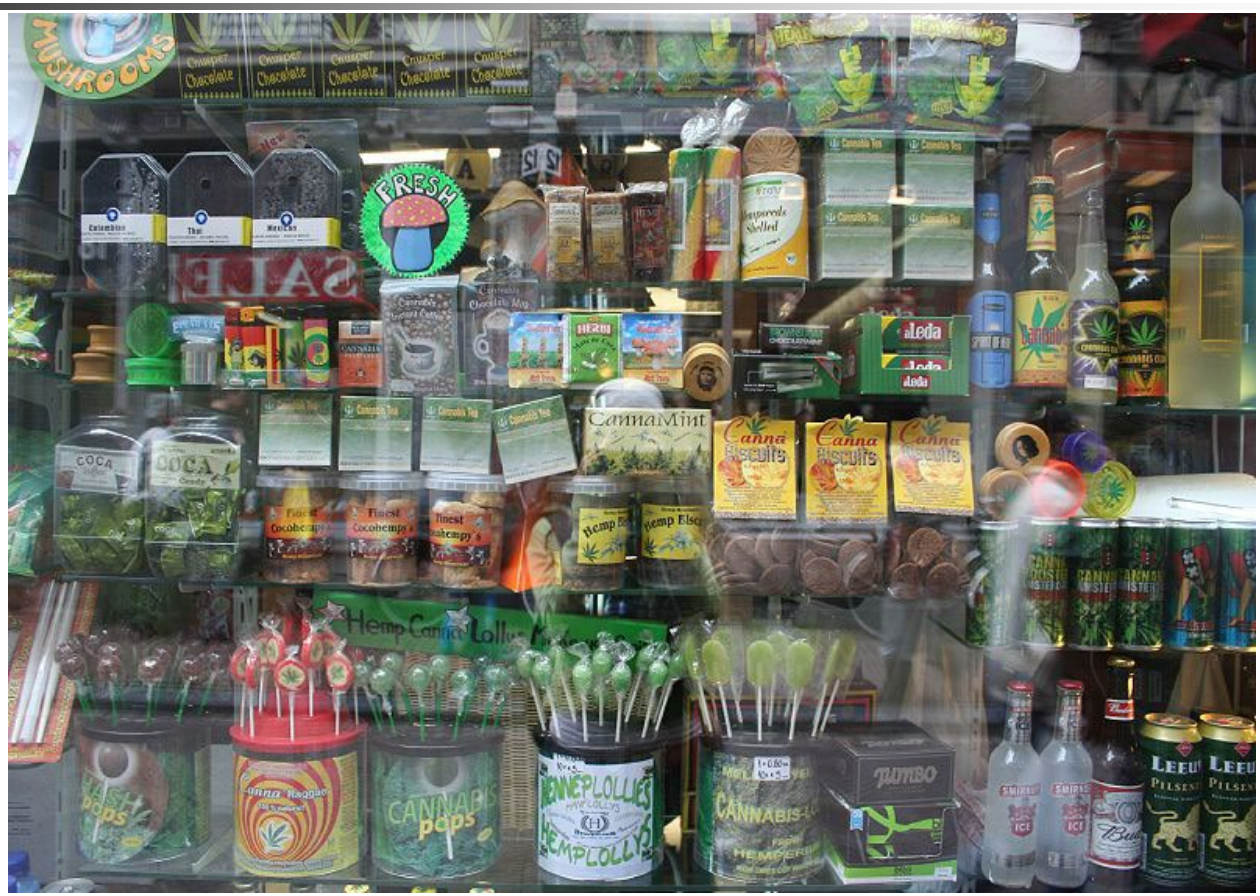
Cannabis Is a Plant (and really not a medicine … sorry!!!!!)

- **484** known biological compounds
- Flowers, seeds, leaves and stems are consumed
  - Smoking
  - Vaporization
  - Concentrated oils
  - Infused "teas"
  - Edibles, plant usually cooked into foods
- At least **84** brain-active cannabinoids
  - THC = primary euphoriant
  - Cannabidiol (**CBD**) = little euphoria, little effect on learning / memory
  - Cannabinol (**CBN**) = intermediate euphoria, perhaps some alalgesia
  - Many others with unclear or unknown effects


OPEN
BOULDER
MM
DISPENSARY
ADT


$5.00

Edibles


MUSHROOMS
FRESH
SALE
CannaMint
Canna Biscuits
Canna Biscuits
Canna Biscuits
Hemp Cannabis Lollipops
HEMPLOLLIES
CANNABIS pops
Hash pops
Canna Reggae
JUMBO


TASTE GOOD BUT...
I CAN'T FEEL
MY WHISKERS!!!

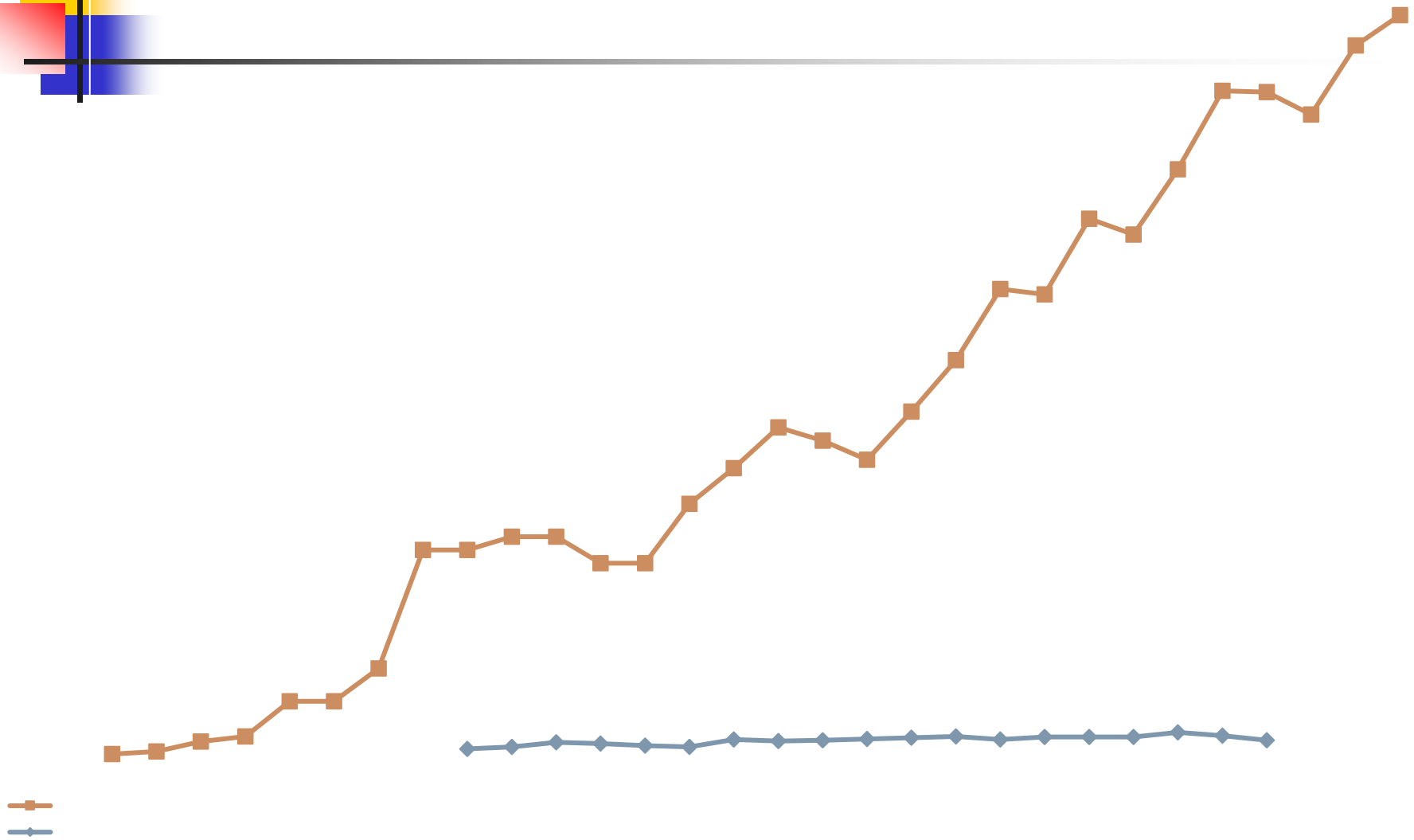
More Potent Pot

Marijuana Potency Monitoring Project University of Mississippi

Average Potency of THC in US *street* marijuana

- 1976 – 2% THC
- 1983 – 4% THC
- 2005 – 5.2% THC
- 2007 – 7.3% THC
- 2008 – 10.1% THC
- 2015 – to present 15%**+** THC
- More potent formulations proliferating

Average THC and CBD Levels in the US: 1960 - 2011



What Are Risks, Adverse Effects

- Side effects (common in medicinal users)
- Addiction (8-12% of users activate MJ SUD mod-severe)
- Impaired:
  - Motor skills (musical / sports performance, OVI)
  - Cognitive skills
  - Motivational skills
  - Judgement
- Risks associated with method of consumption
- Special risks for adolescentsa and perhaps pregnancy
  - Impact on brain development
  - Psychotic syndromes
- Cyclic vomiting syndrome

Non-SUD Risks

- Altered brain development & impaired cognition:
  - Impaired neuronal connectivity
  - Depressed activity prefrontal cortex (judgement/memory)
  - Less volume in hypocampus (reward)
- Associated with:
  - presentation of psychotic SX & prevalence of psych DO
  - Decreased school performance and increased drop-outs
  - Increased use and lower educational attainment
  - MJ use associated with non-medical stimulant use and lower grades
  - Increased use and lower work productivity

Non-SUD Risks (cont)

- Edibles (~45% of market)
  - Particularly attractive to children & adolescents
  - Wide ranges of THC content, slower onset of euphoria, risk of accumulated onset = more ODs
  - Impairment of driving – data pending

One last thing: the delivery system or "route of delivery"

- Speed of onset
- Intensity of effect
- Duration of action
- Some routes are more medical … some are ***not***
  - Which routes are typically associated with medication use?
    - PO
    - Mucosal
    - Topical (dermal)
    - PR (suppository)
    - Inhaled (inhaler)
    - Smoked – *faster and more intense than IV, short duration*

More about the "route of delivery"

- What happens when a substance is smoked? **Hint: think smoking cigarettes, or cocaine carbonate ("crack")**
  - VAPORIZES
  - REACHES THE LUNG ALVEOLI (huge absorption area)
  - INSTANT ABSORPTION
  - 3RD HEART BEAT = 20% UNDILUTED BOLUS TO BRAIN
- Faster than IV
- More INITIAL kick than IV
- INCREDIBLY HIGHLY RE-ENFORCING

  (think about it)

MJ (THC) Physical Dep & W/D

- Long half-life = high rate of P.D. & W/D
  - PD & W/D in low-risk brains (Med-MJ data)
    - DAILY USE FOR > 8-12 WEEKS = P.D. AND W/D
  - PD/WD with cravings in SUD patients
- THC W/D: intensity = dose & duration
  - Onset 2-4 days
  - Sx irritability / anxiety /depressive sx / insomnia
  - Peak day 7-14 / Duration 21+ days

MJ (THC) W/D TX

- Little longitudinal data
- No clear recommendations
- “Low-risk” patients = taper over 6-12 weeks
- SUD / High Risk Patients = discontinuation
- Followed by “Symptomatic treatment” & close follow-up (IOP / PHP and 1-2Xweek MAT visits to monitor and treat symptoms

"Symptomatic" THC W/D TX

- Insomnia:
  - OTCs (melatonin / Benadryl)
  - Mirtazapine 15-30 mg/hs
  - Amitriptyline or Doxepin 25-50 mg/hs
  - Trazodone 25-50 mg/hs (for women, not in men)

"Symptomatic" THC W/D TX

- Anxiety:
  - Topiramate 25-50 BID – TID PRN
  - Avoid the gabapentinoids
  - Lamictal / Trileptal / Depakote
  - SSRIs (start low, go slow for anxiety)
  - Buspirone (pretty high doses)
  - Hydroxyzine PRN
  - Clonidine or beta blockers PRN

"Symptomatic" THC W/D TX

- Depressive Sx:
  - Assess with validated screening / assessment
  - Periodically assess for S/H-I
  - Individual and group counseling (CBT)
  - SSRIs >>> SNRIs

Who develops MJ SUD?

- Overall risk 8-12%
- Initiation of use in adolescence 17%
- Daily users 25+%
- Past year use by adults 4-6%
- If + past month use then 25 - 36% risk SUD
  - This has increased ... ?due to higher THC content
-

MJ SUD: risk factors

- H/O or current other SUD
- Age of experimentation
- Daily or more frequent use
- Positive FH SUD
- Additional Axis 1 (DSM IV) MH DX

MJ SUD Mod-Severe

MJ use recommendations

- Preliminary ("developing" per SAMHSA)
  - Adults (over 24y/o) with no SUD / MH HX:
    - 3X/week or less
    - Quantity unclear
  - Elderly with no SUD/MH HX:
    - Unclear if there is a low risk level (falls/memory/etc.)
  - Under 25 y/o / or + SUD or MH HX or Pregnant:
    - No use

ASAM / AMA Legal MJ Best Practices

a. Prohibit the legal sale of marijuana products to anyone younger than 25 y/o

b. Prohibit marketing and advertising to youth, akin to the current restrictions on tobacco product advertising.

c. Require that products made available for retail sale be tested for potency and clearly labeled with THC content.

d. Require rotating warning labels to be placed on all marijuana and marijuana products not approved by the U.S. Food and Drug Administration (FDA) which are offered for sale in retail outlets, stating, *"Marijuana use increases the risk of serious problems with mental and physical health, including addiction,"* or *"Marijuana should not be used by pregnant women or persons under age 25,"* or *"Marijuana should not be used by persons prior to operating motor vehicles and heavy machinery."*

ASAM / AMA Legal MJ Best Practices

e. Require that marijuana products (such as edibles and beverages) be sold only in child-proof packaging and be accompanied by the mandatory education re: the risks of overdose and poisoning

f. Earmark taxes placed on marijuana and marijuana product sales, wholesale or retail, such that a majority of tax revenues are required to be devoted to public education about addiction, prevention of addiction or initiation of cannabis and cannabinoid use by youth, and SUD / MH treatment services

g. Limit marijuana and marijuana product sales to state-operated outlets, akin to Alcohol Beverage Control regulations existing in several states and Canadian provinces, which preserve both public access and the potential for governmental revenues linked to sales, while limiting the broad commercialization.

h. Implement public awareness campaigns which highlight the risks of marijuana use to discourage *vulnerable populations*, including youth (i.e., adolescents and young adults), individuals with mental illness, and those with a history of addiction involving alcohol or other drugs, from using marijuana products.

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