Tribal MAT
A unified response to the opioid crisis in California Indian Country

Project ECHO
University of California Los Angeles
Integrated Substance Abuse Programs

Understanding Cannabis

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Indigenous Land Acknowledgement

- We respectfully acknowledge that we live and work in territories where Indigenous nations and Tribal groups are traditional stewards of the land.
- Please join us in supporting efforts to affirm Tribal sovereignty across what is now known as California and in displaying respect, honor and gratitude for all Indigenous people.

Whose land are you on?

Option 1: Text your zip code to 1-855-917-5263

Option 2: Enter your location at https://native-land.ca

Option 3: Access Native Land website via QR Code:

The use of affirming language inspires hope and advances recovery.

LANGUAGE MATTERS.

Words have power.

PEOPLE FIRST.

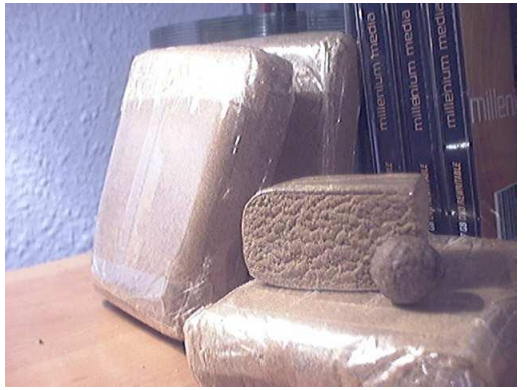
The ATTC Network uses affirming language to promote the promises of recovery by advancing evidence-based and culturally informed practices.

ATTC Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

Disclosures

There are no relevant financial relationships with ACCME-defined commercial interests for anyone who was in control of the content of this activity.

Cannabinoids



History

- Cannabis sativa and indica
  - Indigenous to Central and South Asia
  - Hemp
  - Seeds and seed oils
  - Livestock feed
  - Medicine, religious ceremonies, recreation

Devinsky et al., 2014

Cannabis: Basic facts (1)

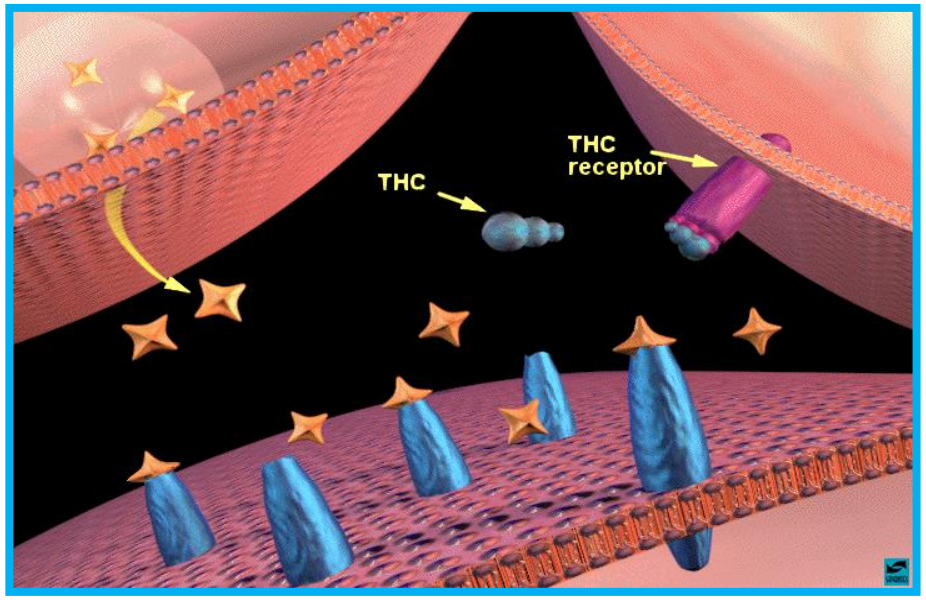
Description: The active ingredients in cannabis are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)

- **Cannabis**: tops and leaves of the plant Cannabis sativa
- **Hashish**: more concentrated resinous form of the plant

Route of administration:

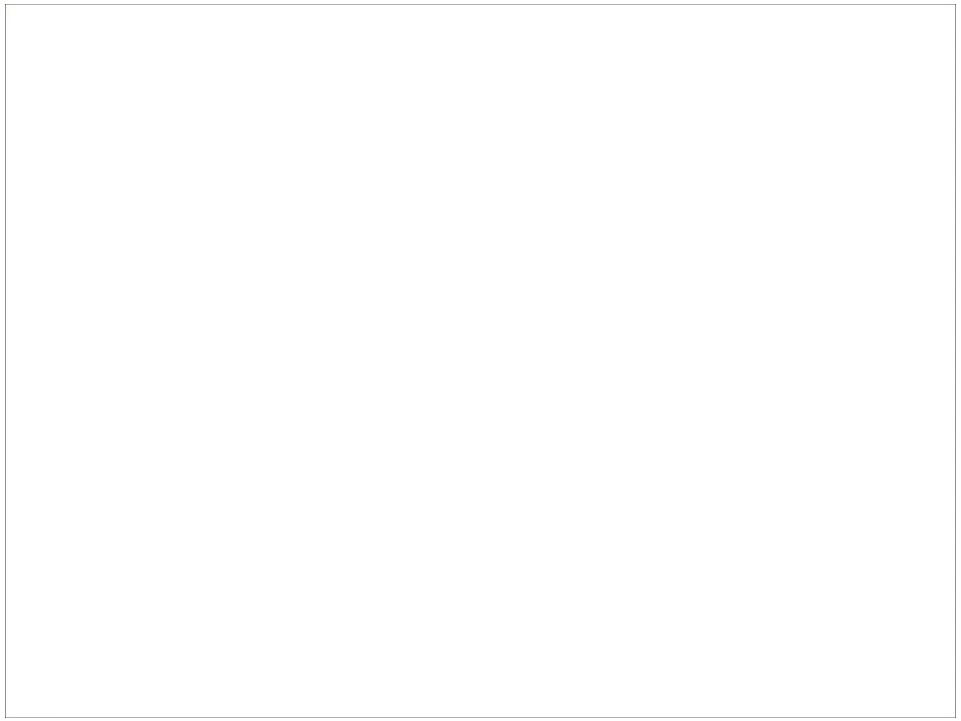
- Smoked as a cigarette or in a pipe
- More recently, "vaping"
- Oral, brewed as a tea or (more recently) made into a food product ("edibles" - cookies, candies, etc)

Cannabis: How Does it Work?



- Contains over 60 cannabinoids: main active chemical is Δ-9-tetrahydrocannabinol (THC)
- Stimulates "high" by triggering receptors in parts of brain that influence pleasure, memory, thinking, concentration, coordination
- THC's molecular structure is similar to that of neurotransmitters that affect cannabinoid receptors (affect pain, appetite, vomiting reflex)
- Effects generally last 1-4 hours

SOURCES: Eddy, 2010; NIDA, 2012a, 2012b (reference list).



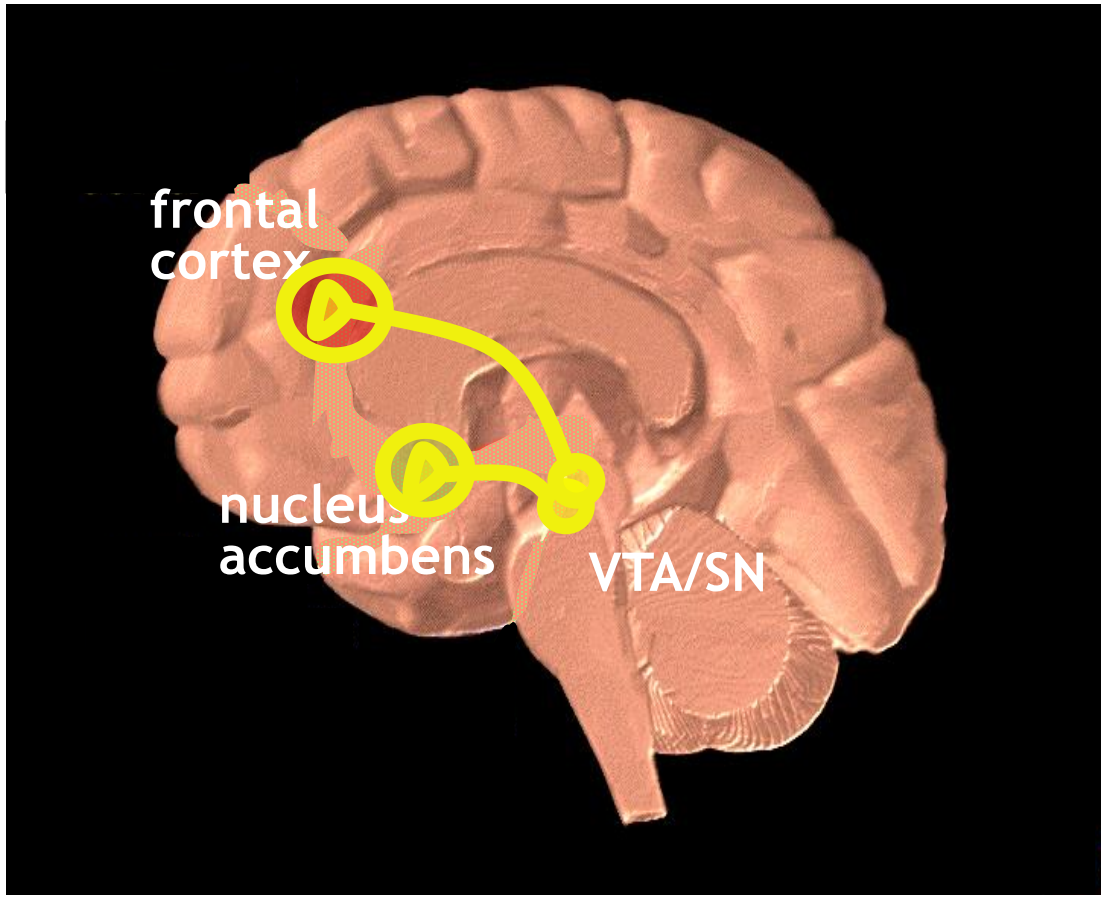
https://www.youtube.com/watch?v=oeF6rFN9org

Cannabis: Basic facts (2)

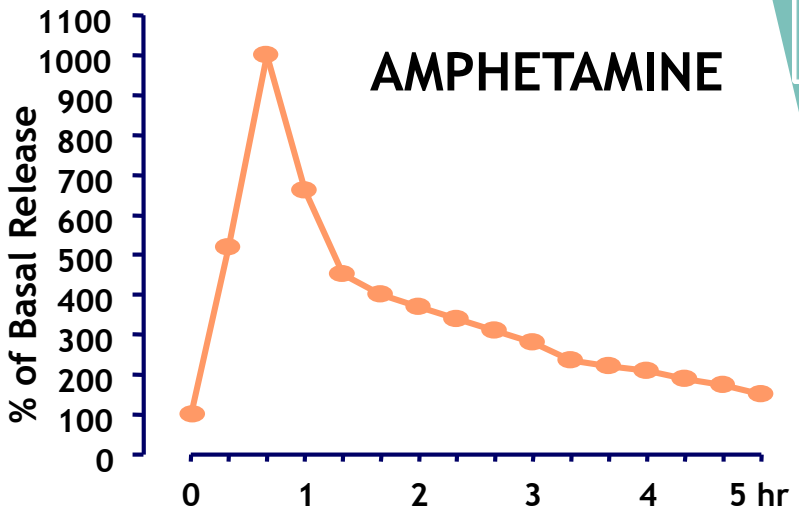
- Effects begin almost immediately when smoked
- Effects of smoked cannabis can last from 1 to 3 hours
- If consumed in foods or beverages, the effects appear later—usually in 30 minutes to 1 hour—but can last up to 4 hours
- Stays in system from a few days to much longer

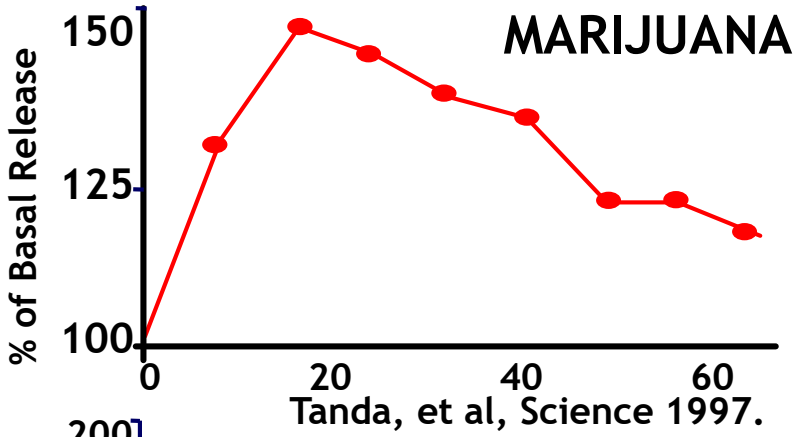
Natural and Drug Reinforcers

Increase Dopamine in NAc

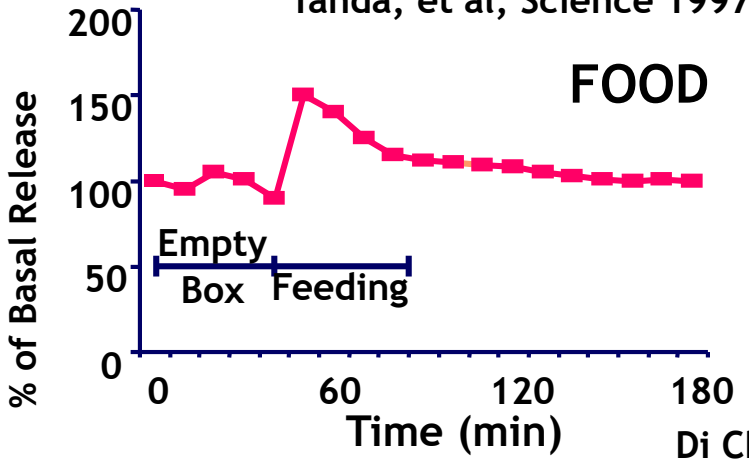


Drugs of abuse increase DA in the Nucleus Accumbens, which is believed to trigger the neuroadaptions that result in addiction





Tanda, et al, Science 1997.



Di Chiara et al.

Cannabis: Basic facts (3)

Acute Effects:

- Relaxation
- Increased appetite
- Dry mouth
- Altered time sense
- Mood changes
- Bloodshot eyes
- Impaired memory

Cannabis: Basic facts (4)

Cannabis: Negative Effects on Behavior and Mental Health

- Similar to alcohol/other drugs if misused (impairment)
- Long term use has negative impact on learning and memory
- Long term use reduces motivation ("amotivational syndrome")
- Associated with mental health problems
  - Unclear if cannabis use is cause or effect
  - Heavy use is highly associated with serious mental illness – particularly among those with high risk (e.g., family history)

SOURCES: Ben Amar, 2006; Bostwick, 2012; NIDA, 2012a, 2012b (reference list).

Cannabis and psychosis

- Genetic x environment → schizophrenia
- Cannabis is risk factor – 2x risk
  - Family history, childhood trauma, age of onset of use
  - Common environmental risks
    - Peer victimization, socioeconomic disadvantage
  - But psychotic experiences may drive cannabis use, not common genetic vulnerability
  - 8-14% of cases?
    - But not significant contributor to global burden of disease
- Dopamine associated with neurobiology of schizophrenia

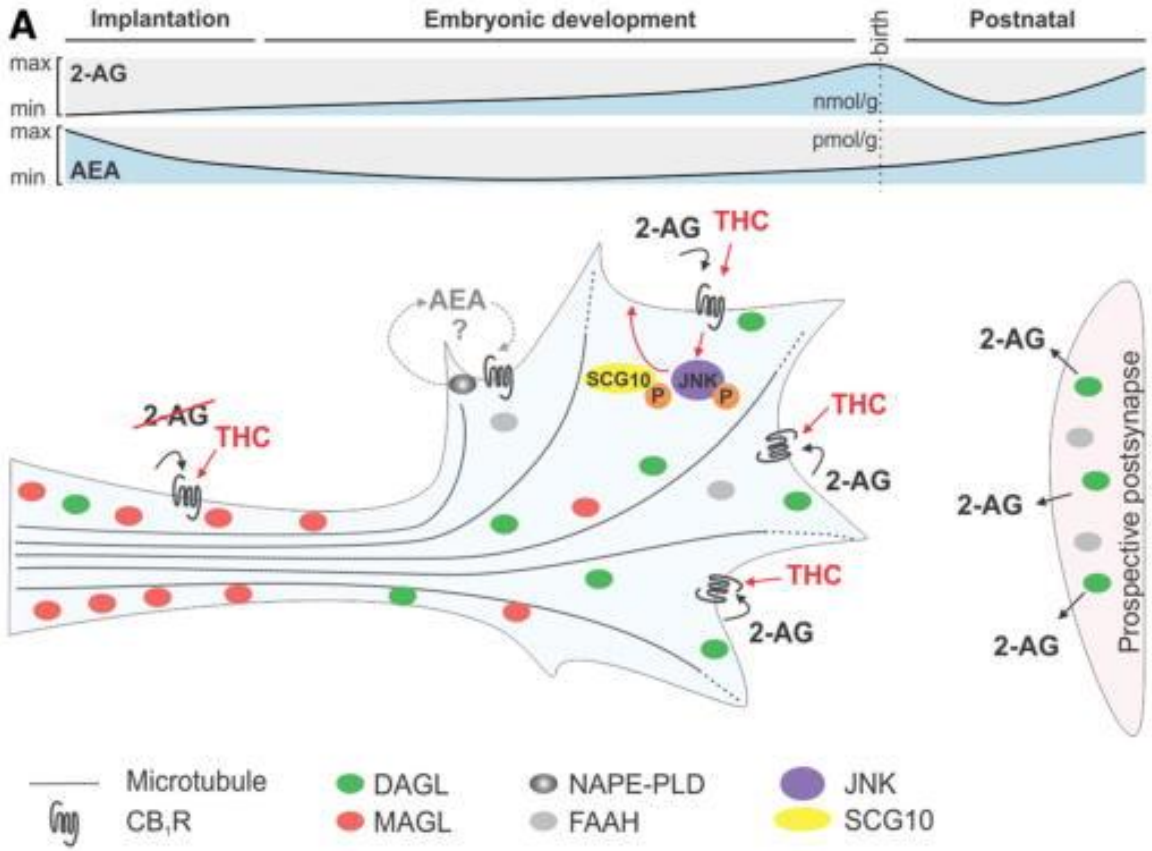
Colizzi et al, 2015; Degenhardt 2013; Radharkrishnan 2014; Shakoor et al 2015.

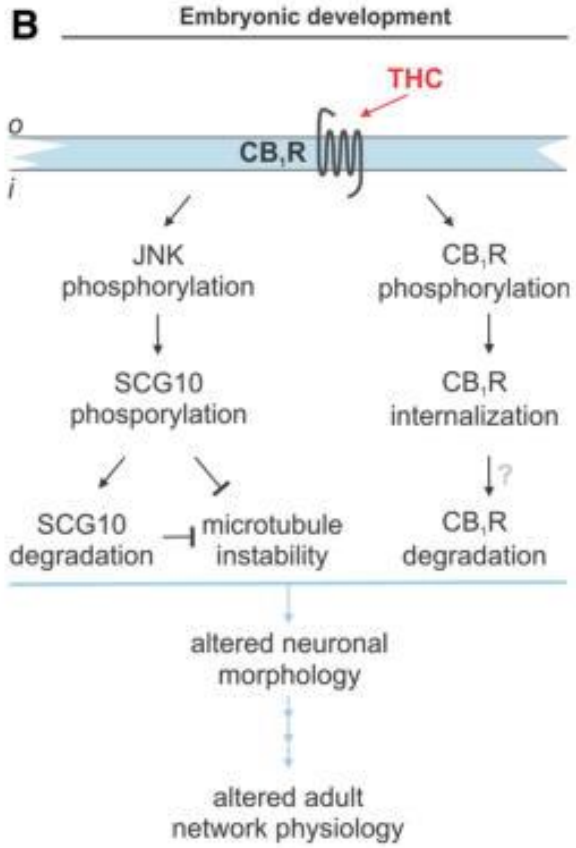
Cannabis and development

- Risk factor for maladjustment/conduct problems
- Reduced affective response
- Association between frequent cannabis use and problematic substance use, delinquency, and poor functional well being at age 20
- In UK, association with mental ill health, mental health related Rx

Thompson et al 2021; Shanahan 2021; Keerthy et al 2021

THC in developing neurons



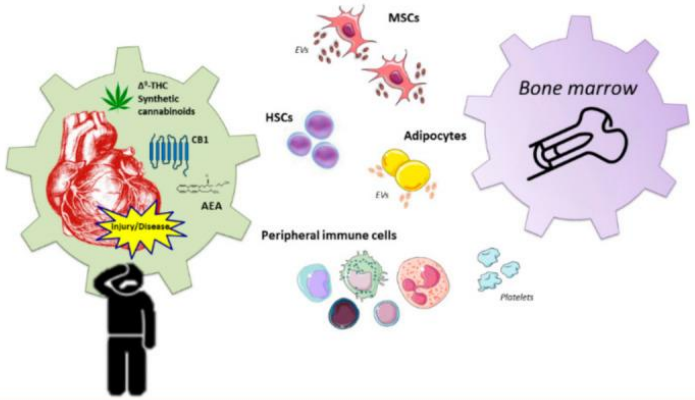


Potential medical uses/complications of cannabis

- Dementia – insufficient data
- 0.6% of HF patients had CUD
  - Higher cost admissions
- Epilepsy
- Headaches
- MS spasticity
- Dravet syndrome
- Neuropathic pain
- Dental health
- CVD – pathophysiology and protection
- Fibromyalgia

Erku 2021; Poudel et al 2021

ECS and CVD



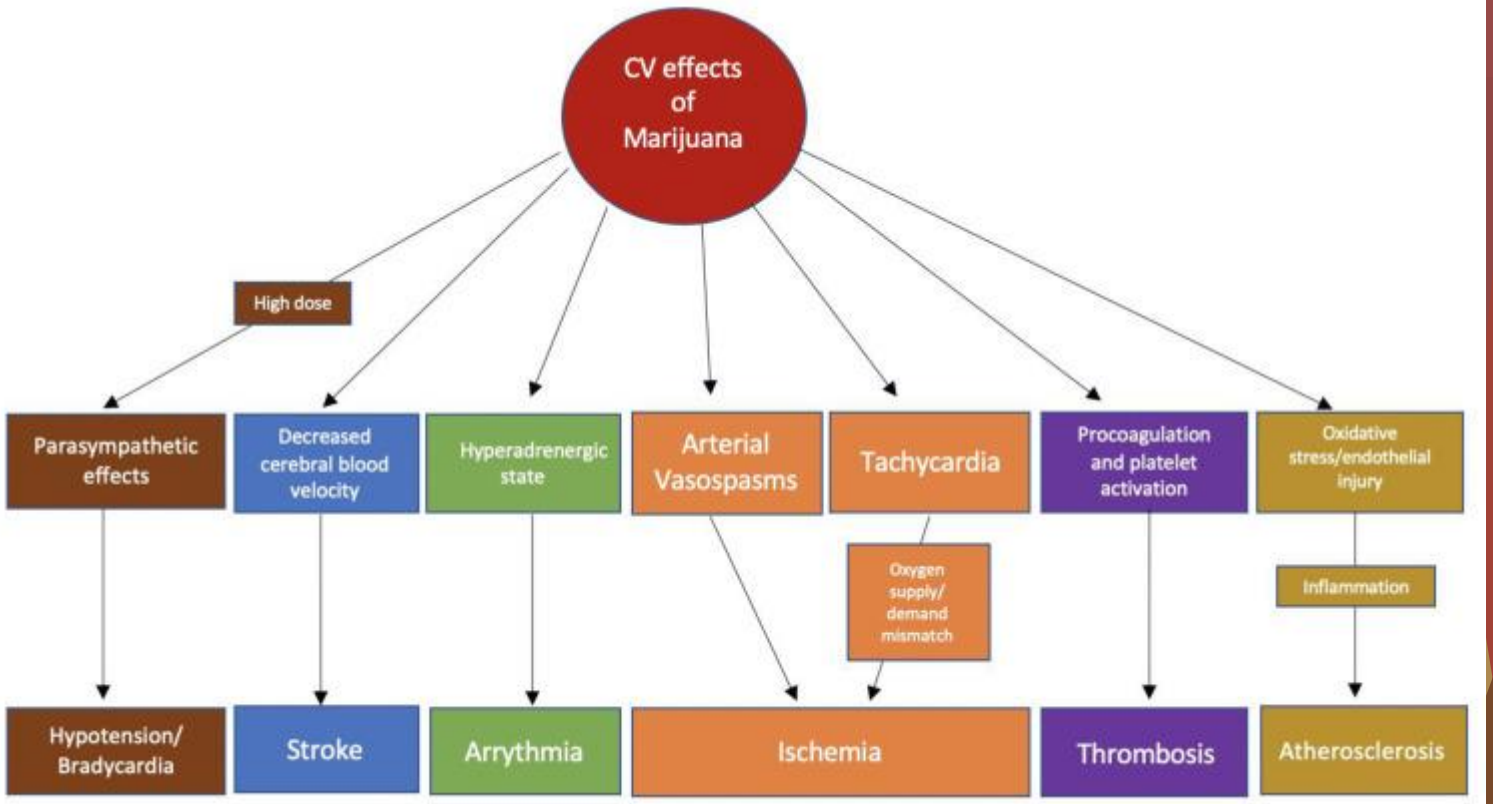
The Endocannabinoid system

Pathophysiology

- ECS is minimally expressed in healthy hearts
- Dysregulation of the ECS associated with several CVDs
- Increased eCB tone drives oxidative strees, inflammation and fibrosis

Cardioprotection

- The ECS controls cell proliferation, migration and immune cell functions
- Potential novel strategy of targeting the ECS to support cardioprotection
- Unknown impact of cannabinoid-use on cardiac therapy

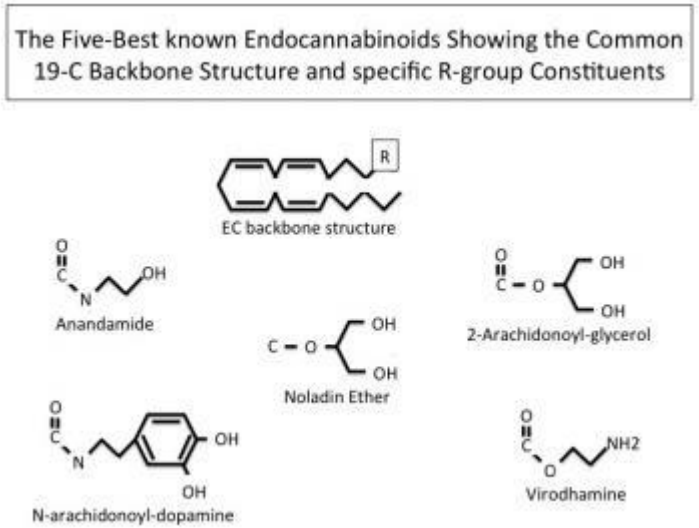


Endocannabinoid system

- EC system plays important role in early neurodevelopment and neurodegenerative diseases
  - Regulation of neurotransmission
  - Synaptic plasticity?
  - CB1 and CB2 couple to inhibitory G protein receptors

Endocannabinoid system

- Cell signaling
- Retrograde transmission
- Very short half life
- CB1-R and CB2-R
  - G protein coupled receptors
- Roles
  - Inflammation
  - Insulin sensitivity
  - Energy and fat metabolism
  - Memory
  - Mood
  - Reward systems
  - Use disorders
  - Stress
    - Mediates stress response
    - Release of norepinephrine and cortisol
  - Cancer – anti-inflammatory, antiproliverative, antiinvasive, antimetastatic, proapoptotic



Griffing, 2015

THC (delta 9 tetrahydrocannabinol)

- Psychoactive
- Higher concentrations of THC associated with addiction, psychosis, cognitive impairment
- Schizophrenia – exacerbate psychosis, anxiety, memory impairment
- Neurotoxic and neuroprotective effects
- Affected areas
  - Striatum
  - Anterior cingulate/medial prefrontal cortex
  - Lateral prefrontol cortex
  - Parahippocampal gyrus
  - Amygdala
  - Temporal and occipital cortices

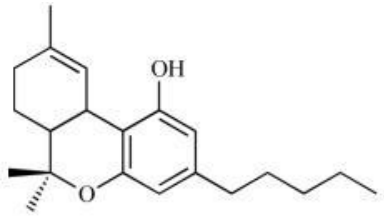
Englund et al., 2017; Bhattacharyya et al., 2010

Cannabidiol

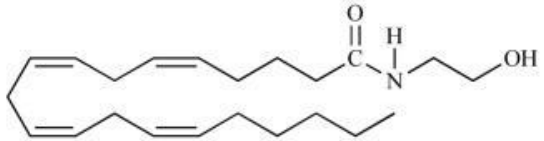
- Neuroprotective effects in neonatal hypoxic-ischemic encephalopathy
- Modulates mesolimbic system
  - May have anti-psychotic and affective effects
    - Limbic and neocortical areas affected
  - Anxiolytic affects
    - Limbic and paralimbic systems
- Addiction
  - Reducing drug seeking behavior
  - Normalizes drug-induced changes (AMPA and CB1 receptors) in nucleus accumbens

Devinsky et al., 2014; Renard et al., 2017

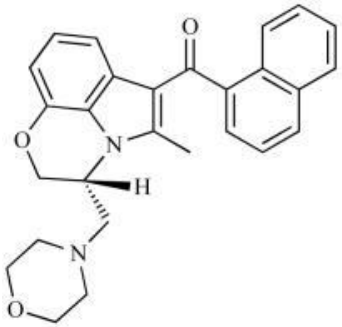
Neurobiology of EC system



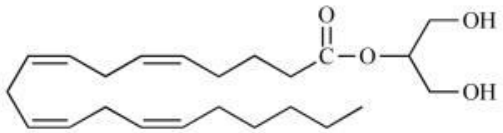
Δ^9-Tetrahyrocannabinol



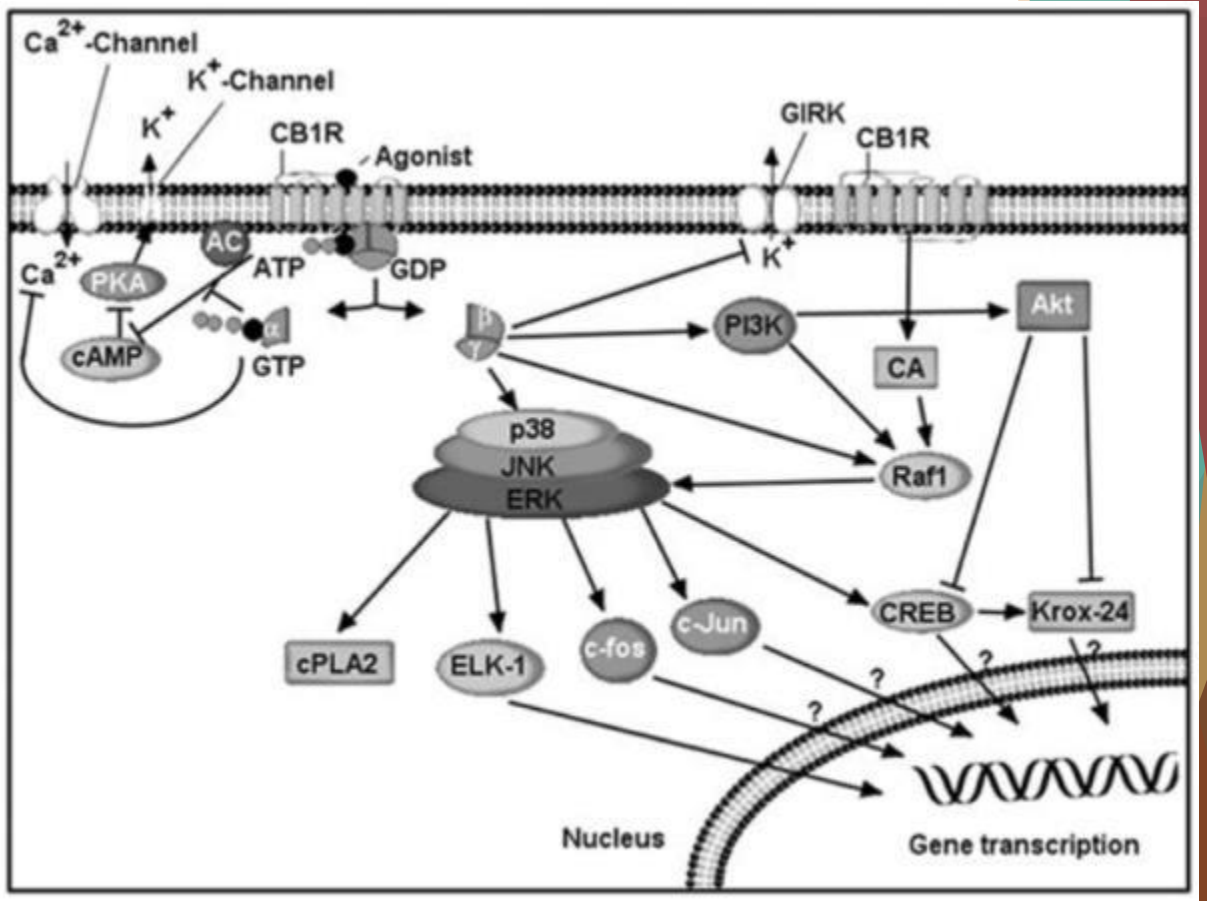
Anandamide



R(+)-WIN 55,212-2 mesylate



2-Arachidonoylglycerol



Basavarjappa 2016

Cannabidiol

- Neuroprotective effects in neonatal hypoxic-ischemic encephalopathy
- Modulates mesolimbic system
  - May have anti-psychotic and affective effects
    - Limbic and neocortical areas affected
  - Anxiolytic affects
    - Limbic and paralimbic systems
- Addiction
  - Reducing drug seeking behavior
  - Normalizes drug-induced changes (AMPA and CB1 receptors) in nucleus accumbens

Devinsky et al., 2014; Renard et al., 2017

Cannabis and use disorder

A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least 2 of the following, occurring within a 12-month period:	Cannabis is often taken in larger amounts or over a longer period than was intended.	There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.	A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
Craving, or a strong desire or urge to use cannabis.	Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.	Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.	Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
Recurrent cannabis use in situations in which it is physically hazardous.	Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.	Tolerance, as defined by either a (1) need for markedly increased cannabis to achieve intoxication or desired effect or (2) markedly diminished effect with continued use of the same amount of the substance.	Withdrawal, as manifested by either (1) the characteristic withdrawal syndrome for cannabis or (2) cannabis is taken to relieve or avoid withdrawal symptoms

Copeland et al, 2017

Cannabis use in AI/AN populations

Some traditional use

Some tribes moving to grow/sell

Highest use among US ethnic groups

- Adolescents 52.8 vs 16.4% for having ever used
- 10th graders 14% vs 3.6% for daily use
- Earlier and heavier use
- ¼ users progressed to CUD at some point

Association of CUD with MSUD

Stanley et al 2018; Spillane et al 2021; Copeland 2017

Cannabis use among AI/AN

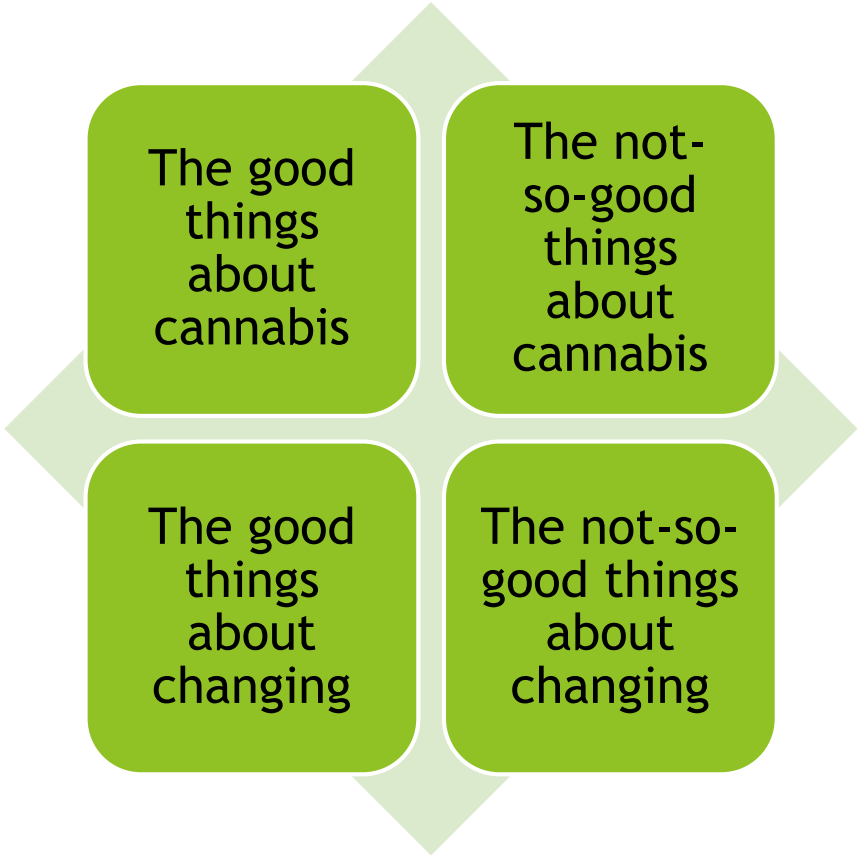
- Family injunctive norms (prescriptive) important for adolescent use
  - Spending time with family and elders
  - Descriptive norms (actual thoughts, feelings, actions) also important
- Indigenous youth more likely to endorse coping model than white youth
  - EtOH use – coping + conformity

Three Steps to Start the Conversation about Cannabis Use

1. Decisional Balance
2. Feedback Sandwich
3. Explore options

1. Decisional Balance

Have patient explore what they perceive to be the benefits/costs of using medical cannabis



2. Feedback Sandwich

- Ask permission to give patient feedback on how cannabis may be affecting his/her health
- Give feedback
  - Acknowledge pros/cons patients mentioned
  - Mention concerns about cannabis' effects as they pertain to the patient (physical/behavioral health issues, regulatory/legal issues)
  - Present information in a non-judgmental manner
- Ask for patient response to feedback

3. Explore Options

- If Steps 1 and 2 show that reducing cannabis use would benefit patient, explore additional strategies to achieve symptom relief
  - Behavioral interventions
  - Pharmacological interventions
  - FDA-approved THC medication (Marinol ®)

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