Central East (HHS Region 3)
ATTC
Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

African Americans and Cough Syrup with Codeine Abuse

Benjamin Roy, MD

February 4, 2021

THE DANYA INSTITUTE
SAMHSA
Substance Abuse and Mental Health Services Administration

ATTCs

Funded by SAMHSA

- **Accelerate** the adoption and implementation of evidence-based and promising addiction treatment and recovery-oriented practices and services;
- **Heighten** the awareness, knowledge, and skills of the workforce that addresses the needs of people and substance use and/or other behavioral health disorders; and
- **Foster regional** and national alliances among culturally diverse practitioners, researchers, policy makers, funders, and the recovery community.

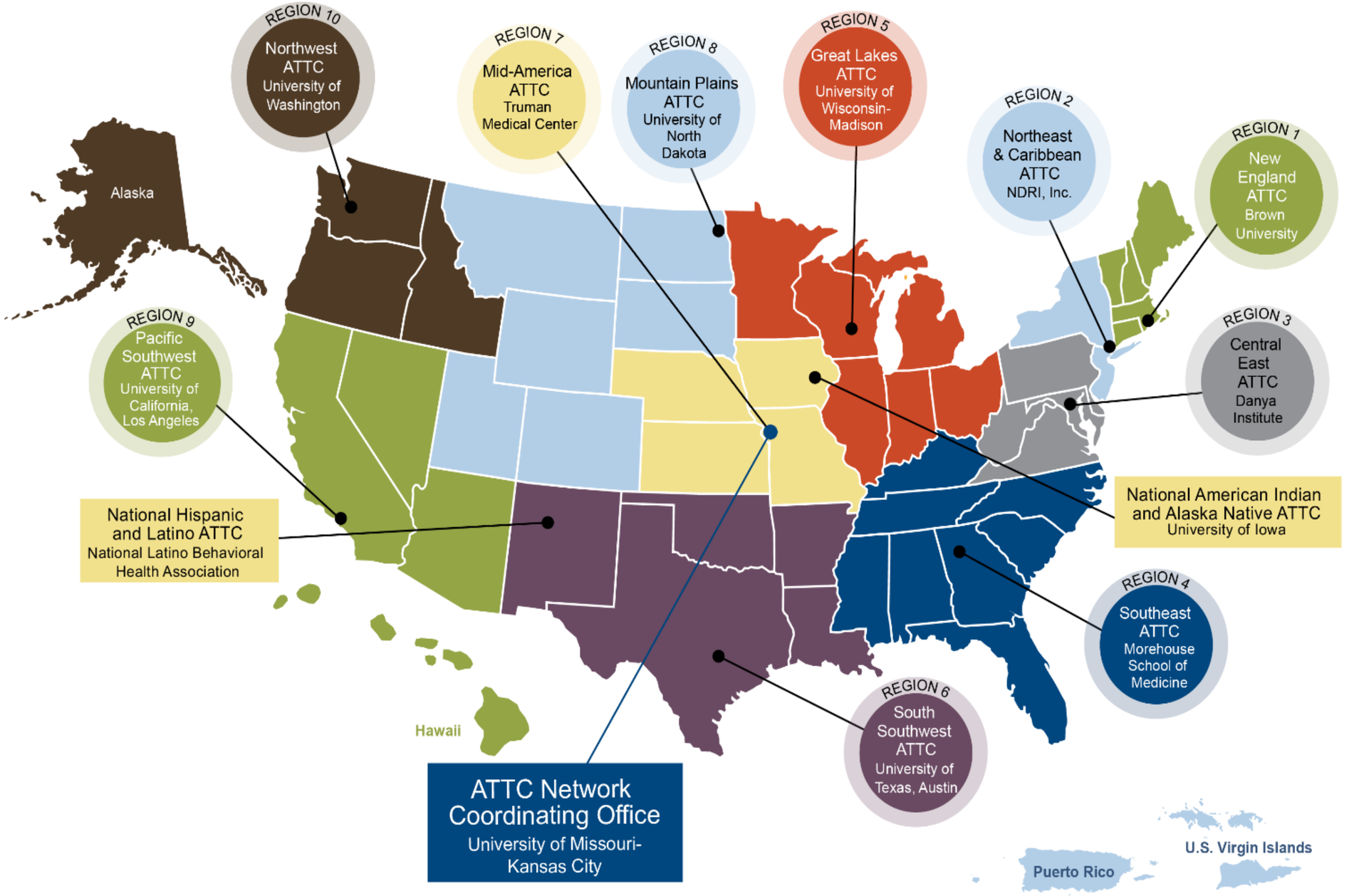
ATTC Purpose

The ATTC Network vision is to unify science, education and service to transform lives through evidence-based and promising treatment and recovery practices in a recovery-oriented system of care.

ATTC Addiction Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

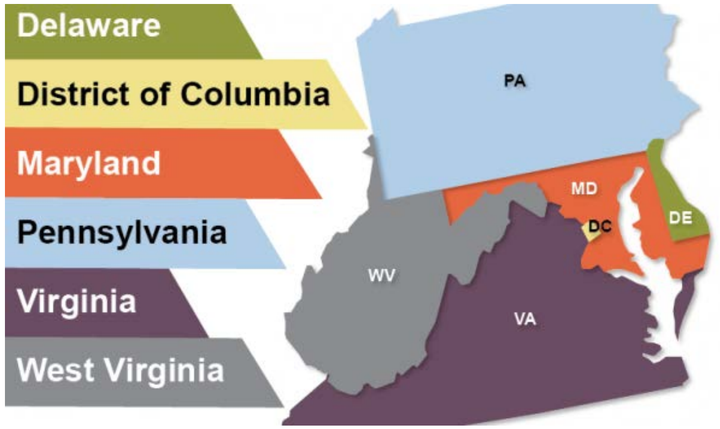
U.S.-based ATTC Network



Central East Focus Areas

- Health Equity and Inclusion
- Evidence-based Practices (EBPs)
  - Motivational Interviewing
  - SBIRT
  - Clinical Supervision
- Medication Assisted Treatment (MAT)
- Opioid Crisis
- Peer Workforce
- Tobacco Cessation

HHS REGION 3



Other Resources in Region 3

Central East (HHS Region 3)

MHTTC Mental Health Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

Central East (HHS Region 3)

PTTC Prevention Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

Central East ATTC Goals

- Collaborate and communicate with key regional stakeholders and develop T/TA responses for the behavioral health and public health workforce
- Increase ongoing implementation of evidence-based SUD interventions, treatment and recovery practices in specialized SUD, HIV, and primary care programs and practices

African Americans and Cough Syrup with Codeine Abuse,
also known as Lean

Benjamin Roy, MD
President, Black Psychiatrists of America

Health Equity Webinar Series

February 4, 2021

Moderator:
Annelle B. Primm, MD, MPH
Black Psychiatrists of America, Council of Elders

COVID-19: Unprecedented Disaster

- Catastrophic impact on Black and other marginalized communities with disparate levels of illness, death, and economic fallout superimposed on layers of pre-existing inequities
- Distancing from loved ones including those who are sick and dying
- Rise in anxiety, depression, and substance use

Today's Program

- Special thanks to the Danya Institute for its support of this first of several webinars in the Black Psychiatrists of America Health Equity SME Series
- Today's program features Benjamin Roy, MD, President of the Black Psychiatrists of America

African Americans and Cough Syrup with Codeine Abuse

“Purple Drank” or “Lean”

Learning Objectives

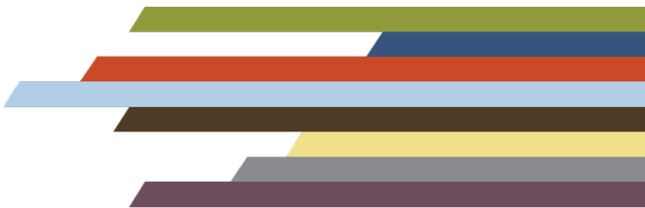
1. Discuss the history of cannabis and stimulant abuse
2. Identify Loud, Dojo, Gas, Lean, Purple Drank, Syrup, Sizzurp, Barre, and Texas Tea abuse
3. Identify the impact of Cannabis and stimulant abuse on cognitive function, lasting mood and psychotic disorders, mortality, and morbidity
4. Disseminate scientific and clinical information on Lean and Loud abuse to the public health community
5. Learn potential susceptibility of Cannabis, Lean abuse to COVID-19
6. Construct a network that provides support, exchanges information, and generates new knowledge to support and improve treatment of Lean, Purple Drank, opiate, and Loud abuse

CANNABIS

The Gateway Drug
“Of the Earth”
“Natural, Not a Chemical”
“God Put it Here”

History of Cannabis

- Bhang (marijuana) introduced into Europe in the 16th century
  - John Huygen van Linschoten (1563 – 8 February 1611), *Voyage ofte schipvaert naer Oost ofte Portugaels Indien, 1579-1592*. Uitgeg. door H. Kern; tweede druk, herzien door H. Terpstra. 3 vols. 's-Gravenhage 1955-1957 (Werken uitgegeven door de Linschoten-Vereeniging, 57, 58 and 60). Transl. *His discours of voyages into ye Easte and West Indies: devided into foure bookes.* London: John Wolfe 1598 —
- Samuel Coleridge Taylor (21 October 1772 – 25 July 1834), “There is a preparation of the Indian Hemp, called Bhang, or àang, or Banghee -- the same Drug, which the Malays take, & under it's influence become most pot-valiant Drawcansirs, run a muck, &c. My friend, T. Wedgewood, is exceedingly desirous to obtain a small specimen of it: from what he has heard of it, he conceives it possible that it may afford some alleviation to his most hopeless malady -- which is a dreadful irritability of the intestinal Canal. Now I know that Sir Joseph Banks has a quantity of it -- and if you should see him shortly, & could procure a small quantity of it.''
    - Letter 485 to Samuel Purkis, February 1803 - he was an opium addict
- Robert Southey (12 August 1774 – 21 March 1843) - a Lake Poet and Poet Laureate of England (*Goldilocks and the Three Bears*)



Intellectual History of Cannabis

- Charles Baudelaire (9 April 1821 – 31 August 1867), “*The Poem of Hashish 1821*“
- Club of Hashishins 1844-1849: Charles Baudelaire, Victor Hugo, Alexandre Dumas, Honore de Balzac, Jacques-Joseph Moreau, Theophile Gautier
- Dr. Jacques-Joseph Moreau, *Du hachisch et del'aliénation mentale: études psychologiques (Hashish and Mental Illness - Psychological Studies)*, 1846
- Charles Baudelaire, “*Les Fleurs du Mal (Flowers of Evil) 1857*”
- Charles Baudelaire, “*Artificial Paradise 1860*”

“Psychonauts”

Geniuses	Academics	Thinking Tools	Comments
Francis Crick	DNA	LSD	Disputed; Nobel Laureate
Timothy Leary	Berkely Psychologist	LSD	
William James	Harvard Psychologist	Mescaline	*The Varieties of Religious Experience*
Steve Jobs	Apple	LSD	
Bill Gates	Microsoft	LSD	Playboy interview 1994
Richard Feynman	Theoretical Physicist	LSD	*Surely You're Joking, Mr. Feynman!*
Paul Erdos	Mathematician	Amphetamine	*The Man Who Loved Only Numbers* by Paul Hoffman
William Halsted	Surgeon - Mastectomy	Cocaine	
Sigmund Freud	Psychoanalyst	Cocaine	“Über Coca” Centrallblatt für die ges. Therapie. 2, 289-314, July 1884
Stephen Jay Gould	Paleontologist	Cannabis	
Kary Mullis	PCR	LSD	California Monthly 9/94; Nobel Laureate Chemistry
Thomas Edison	Electric Light Bulb	Cocaine	Vin Mariani
Carl Sagan	Astronomer	Cannabis	*Marijuana Reconsidered 1971*
John C Lilly	Neurosicentist	LSD/Ketamine	

Pervasive Scientists' Abuse of Stimulants

Sahakian B and Morein-Zamir S. Brain-Boosting Drugs Survey. Nature 2007; 450:1157-1159

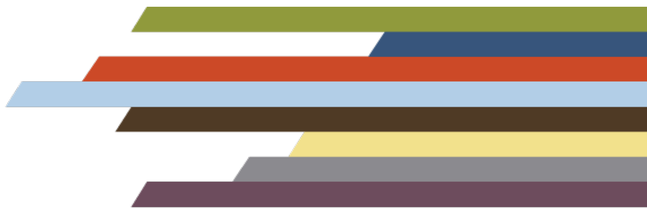
- 1400 Respondents
- 70% in USA
- 70% admitted to use of stimulants for cognitive enhancement
- Drugs of Choice:
  - Methylphenidate (Ritalin) 62%
  - Modafinil (Provigil) 44%

Cannabinoid Chemicals

- There are three groups of cannabinoid chemicals: endocabbinoids, phytocannaabinoids, and synthetic cannabinoids.
- Humans produce natural endogenous cannabinoids.
  - 1. anandamide
  - 2. 2-arachidonoylglycerol
- Endocannabinoids cross lipid membranes but are not water soluble so must be transported through cytoplasm by transport proteins, endocannabinoid transporters (eCBTs). Heat shock proteins (Hsp70s) and fatty acid binding proteins 1,3,5, and 7.

Cannabinoid Receptors

- Endogenous cannabinoids bind to G-coupled membrane cannabinoid receptors.
- CB1 Receptor: CB1 increases nitric oxide synthase (NOS) activity, increases NO production, enhances anandamide transporter activity activity
  - 1. Central and peripheral nervous system
  - 2. Endogenous ligands: anandamide, ajulemic acid, and 2-arachidonoylglycerol
  - 3. THC has high affinity for CB1 receptor.
  - 4. CBD has low to negligible affinity for CB2 receptor.
- CB2 Receptor: inhibits NOS, NO release, and reduces anandamide transporter activity



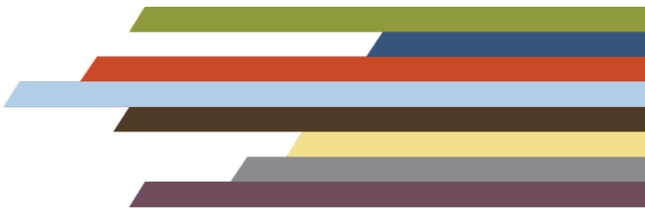
CBD and THC

- The enzyme cannabidiolic synthase converts cannabigerolic acid (CBGA) to cannabidiolic acid (CBDA) which is decaboxylated to cannabidiol (CBD)

- The enzyme tetrahydrocannabinolinic acid synthase converts cannabigerolic acid (CBGA) to tetrahydrocannabinolic acid (THCA) which is decaboxylated to Δ^9-Tetrahydrocannabinol (THC).

Cannabis Legal History

- Cannabis acquired the name ''marihuana'' after 1910 as its use was attached to Mexican immigrating into the United States to escape the Mexican Revolution
- Mexicans were denigrated as vagrants smoking ''locoweed,'' cast them a threat to security.
- Politicians blamed the drug for loose morals, crime, and orgies.
- Marihuana Tax Act 1927
- Controlled Substance Act of 1970
- Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970 classified THC and CBD as Schedule I drugs. Marijuana and hemp were classified
- Agricultural Act of 2018 (2018 Farm Bill)
- President Donald Trump's 2018 farm bill defined hemp as containing less than 0.3% THC and explicitly legalized ''hemp and hemp-derived products,'' removing them from Schedule I and regulation by the Controlled Substance Act of 1970. This encouraged cultivation of cannabis-based hemp crops generating a mass market for cannabidiol (CBD) derived from hemp. However, marijuana-derived CBD remains a controlled substance regulated by the Food and Drug Administration and Drug Enforcement Administration, despite there is no difference in the CBD molecule derived from either variant.



Cannabis Species

- There are three species of cannabis: sativa, indica, and ruderalis.
- Marijuana differs by ratio of Sativa:Indica
  - 1. Cannabis sativa
    - a. Destroyer: 100:0 Sativa: Indica
    - b. Kwazulu: 100:0 Sativa: Indica; 20% THC
    - c. Kilimanjaro: 100:0 Sativa: Indica; 20% THC
    - d. Thai: 100:0 Sativa: Indica; 22% THC
  - 2. Cannabis indica
    - a. Afghan Kush: 0:100 Sativa: Indica
    - b. Purple Kush: 0:100 Sativa: Indica; 15.5% THC
    - c. Hindu Kush: 0:100Sativa: Indica
    - c. Northern Lights: 0:100 Sativa: Indica}
  - 3. Cannabis ruderalis

Cannabis Species

- 4. Selected Breeds (This not an exhaustive list)
  - a. Loud Dream: has a high THC content 26%
    - $1000 an ounce
    - However, "Loud" is also slang for any marijuana that is strong or has a strong oder
    - Street "Loud" may be laced with gasoline or other chemicals to give the strong kick; its other street nickname is "Gas." This is a common tactic; in the past "Love Boat" was marijuana laced with formaldehyde or antifreeze (ethylene glycol)
  - b. Sour Diesel: 80:20 Sativa:Indica; 19% THC
  - c. Cannabis Caviar: $1400 an ounce; 20% THC
  - d. Green Crack: 60:40 Sativa: Indica; 20% THC
  - e. Chernobyl: 80:20 Sativa: Indica; 22% THC; $130 an ounce
  - f. Amnesia: 90:10 Sativa:Indica; 25% THC; $125 an ounce
- Cannabis effect on innate immunity: THC, CBD, CBG, and CBN are anti-inflammatory but antagonize the anti-inflammatory action of steroids
- Benz[a]anthracene and benzo[a]pyrene are polycyclic aromatic hydrocarbons metabolized to intermediates that disrupt DNA leading to cancer and are up to twofold higher in marijuana tar

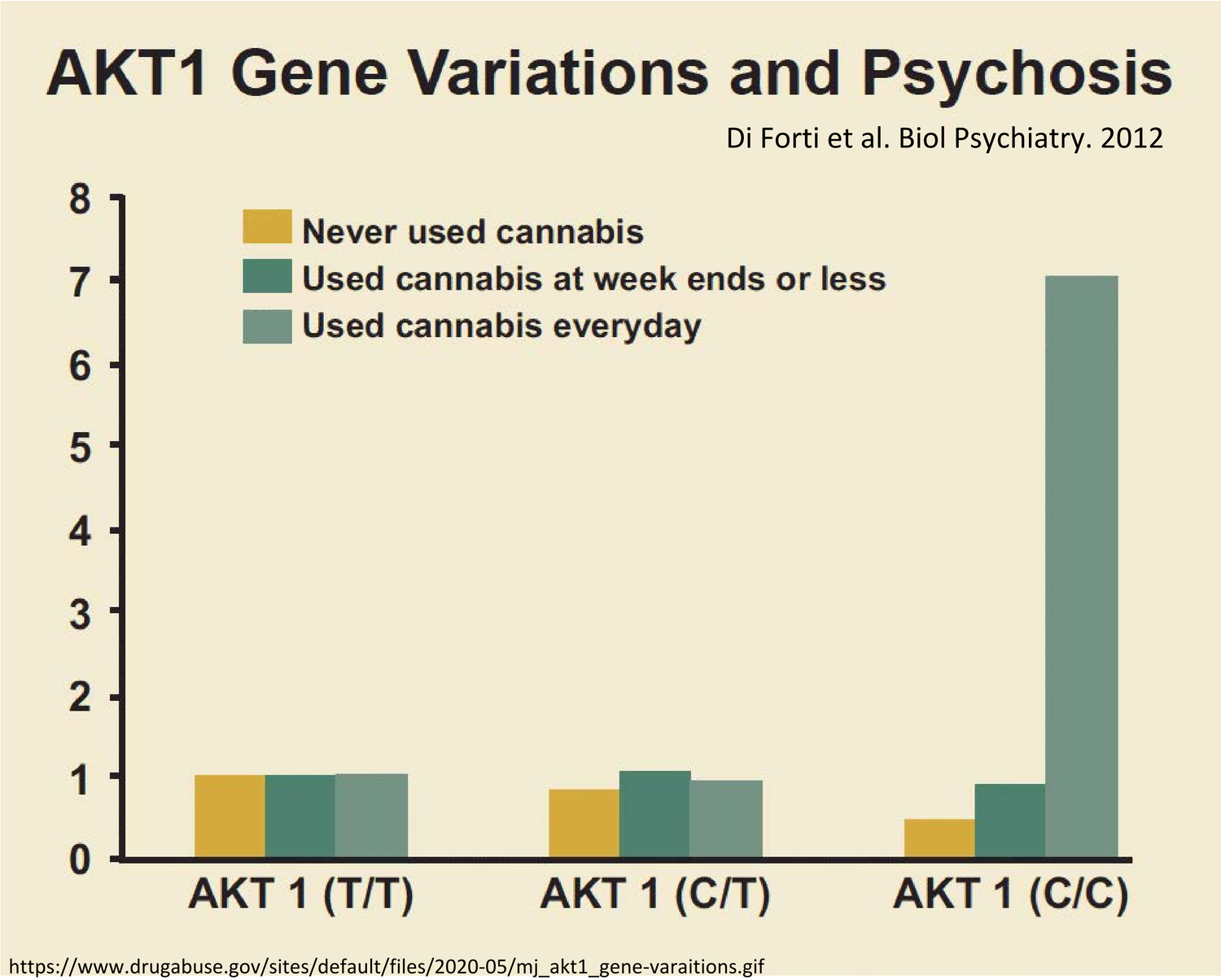
Epidemiology

- Legal Cannabis Vaping
  - In states where marijuana is legal (Oregon, Washington, Colorado, California, Massachusetts, Nevada, and Alaska) 27% vape; demographically they are age 39, 40% are college of higher degree graduates, 50% are employed, and two-thirds are male
- Vaping
  - The concentration of THC reaches 60%. Counterfeit CaliPiffs measure 7,000 times the allowable level of myclobutanil, a pesticides that when heated in the vaping apparatus emits hydrogen cyanide. Other contaminants include mercury, lead, and arsenic.
- Teen Vaping: 8% consider themselves addicted
  - 21% of 12th graders
  - 19% of 10th graders
  - 7% of 8th graders

Cannabis Cognitive Effects

- Impaired short-term memory
- Attention deficit
- Anxiety
- Paranoia
- Psychosis

Cannabis Genetic Susceptibility Psychosis



https://www.drugabuse.gov/sites/default/files/2020-05/mj_akt1_gene-varaitions.gif

PURPLE DRANK/LEAN

Promethazine-Codeine
Dextromethorphan

History of Cough Suppressants

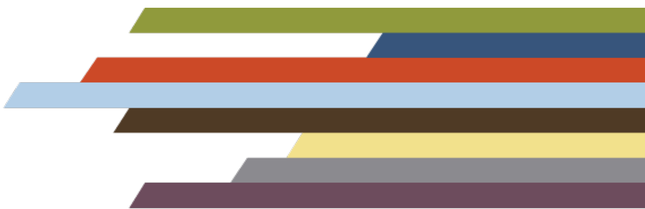
- Laudanum
  - Paracelsus (1493 – 1541)
  - Thomas Sydenham (1624 – 1689) - improved laudanum
- Thomas DeQuincey, *Confessions of an English Opium Eater 1822*
- Laudanum - American West
  - The Cowboys - a drug cartel, identified by red bandannas
  - Wyatt Earp

History of Cough Syrups

- Pulmonary Tuberculosis was a worldwide plague
- Codeine was invented in 1832
- Mrs. Winslow's Soothing Syrup 1849 - morphine
- 1898 - Bayer modified morphine to create Heroin, a cough suppressant
- circa 1910 heroin was a recreational drug so widespread it provoked the Harrison Anti-Narcotics Act of 1914

Codeine Abuse

- Codeine is an opiate drug obtained by legal prescriptions both as a cough syrup but also as Tylenol No. 3, i.e., acetaminophen and codeine
- Codeine is a $10b per year business
- Promethazine-codeine abuse is an opiate addiction
- Statistics for codeine abuse and deaths are obscured by the focus on fentanyl, heroin
- Prescriptions for codeine doubled from 23,985 in 2014 to 40,409 in 2016 as a direct consequence of codeine addiction
- Actavis stopped manufacturing the drug. Prescriptions dropped to 20,072 in 2018, which dried up supplies and forced switch to dextromethorphan



Purple Drank

- ''Purple Drank'' is the name used in Houston, Texas for a concoction of promethazine-codeine cough syrup, which is purple colored.
- Promethazine-codeine cough syrup is added to Sprite soda and dressed with Jolly Rancher candy - it may also be referred to as ‘'Syrup'' or “Lean.”
- In Atlanta and other areas of the Southern United States over-the-counter liquid cold medicines containing dextromethorphan, an antihistamine (chlorpheniramine or doxylamine), and acetaminophen replace codeine and is also referred to a ''Lean.''
- Children as early as the 6th grade in middle school abuse the drug.

Purple Drank Pharmacology

- Promethazine ($C_{17}H_{20}N_2S$) is 93% protein bound and metabolized by CYP2D6 but it also is a weak inhibits CYP2D6. The major metabolite is promethazine sulfoxide, and small percentage desmethylpromethazine

- Codeine ($C_{18}H_{21}NO_3$) is 25% protein bound. CYP2D6 converts codeine to morphine ($C_{17}H_{19}NO_3$; 35% protein bound) and CYP3A4 converts it to norcodeine. UDP-glucuronosyltransferase (UGT) 2B7 and 2B4 glucuronidate codeine to codeine-6 glucuronide (C6G), and morphine to morphine-3-glucuronide (M3G), morphine-6-glucuronide (M6G)

		μOR Ki nm	δ pKi	κ pKi	%	CYP2D6	CYP3A4	CYP2C9	CYP2C19	CYP1A2	UGT
Promethazine	$C_{17}H_{20}N_2S$	H1R antag			93	+	+				
Codeine	$C_{18}H_{21}NO_3$	734			25	+					
Morphine	$C_{17}H_{19}NO_3$	1.14	6.9		35						2B7
Dextromethorphan	$C_{18}H_{25}NO_3$	NMDA		6.7	70	+	+	+			
Acetaminophen	$C_8H_9NO_2$	COX			25						
Oxycodone	$C_{18}H_{21}NO_4$	25.9			45	+	+				
Hydrocodone	$C_{18}H_{21}NO_3$	41.8		6.6	36	+	+				
Hydromorphone	$C_{17}H_{19}NO_3$	0.365	7.4	8.6	20						
Meperidine	$C_{15}H_{21}NO_2$	450			75						
Fentanyl	$C_{22}H_{28}N_2O$	1.35			85		+				
Carfentanil	$C_{24}H_{30}N_2O_3$	0.024		7.4							
Methadone	$C_{21}H_{27}NO$	3.38	6.9		90	+	+			+	
Tramadol	$C_{16}H_{25}NO_2$	12,500	8.0	7.8	20	+	+				+
Heroin	$C_{21}H_{23}NO_5$				0						
Buprenorphine	$C_{29}H_{41}NO_4$	0.216			96						
Propoxyphene	$C_{22}H_{29}NO_2$	120.4			78		+				
Cocaine	$C_{17}H_{21}NO_4$	σ1; DAT					+				
Alcohol	C_2H_6O										
Cocaethylene	$C_{18}H_{23}NO_4$										
Δ^9-THC	$C_{21}H_{30}O_2$	CB1 receptor			97		+	+			
Methamphetamine	$C_{10}H_{15}N$	TARR1				+					

%: protein binding; DAT = dopamine transporter; TARR! = trace amine associated receptor 1; CYP = cytochrome P450 enzyme; UGT: UDP-glucuronosyltransferase

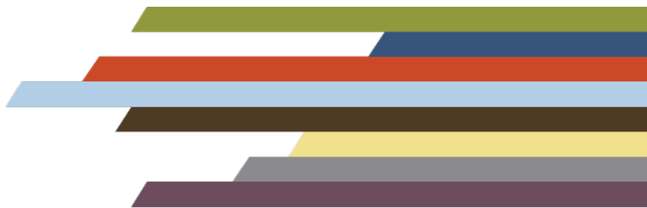
Opioid Mechanism

The opioid receptor is a G-protein coupled receptor. An opioid binds the opiate receptor and activates dephosphorylation of guanosine triphosphate (GTP) to guanine diphosphate (GDP). Activation inhibits adneylate cyclase leading to a reduction of cyclic 3',5'-adenosine monophosphate (cAMP). The consequence is activation of the voltage gated potassium channel, which hyper polarizes neurons and downregulates their excitation. The opiate receptor inhibits Ca^{2+} channel, which also downregulates neuron excitation by inhibition of the release of excitatory neurotransmitters.

Purple Drank Marketing

- DJ Screw: “Sippin Codeine” from *3 ’n the Mornin’: Part Two* (1995)
  - "I sip codeine It makes a southside playa lean (makes me leeeaaaan) Stackin green (yeeea) Steady stackin green, steady sippin' codeine (codeine)"

- Big Moe: “Purple Stuff” from *City of Syrup* (2000)
  - “It was hard momma saw me with a case of codeine And promethazine now I'm the codeine fiend … Now I got the whole world sippin drank with me”

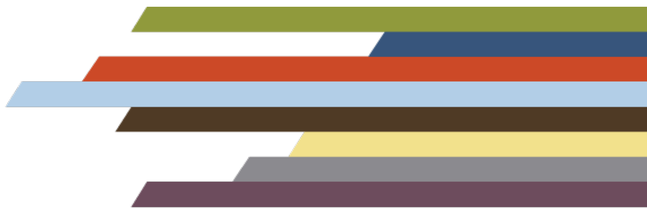


Purple Drank Marketing

- Z-Ro: “Can’t Leave that Drank Alone” from *Cocaine* (2010)
  - “Yall would think that with 3 felony cases I would leave drank alone I'm still out on bond And ima keep dranking till all the drank is gone … Woot woot dam HPD right behind me I got a little weed and a pint and a half … And since my doctor wrote me this prescription Ain't no body got to bail my ass out … And I'm in love with mary jane and codeine … I can remember my first cup, oh I was so in love So when I wake up in the morning Before I brush my teeth I'm pouring up”
- 2 Chainz: “Gasolean” from *Codeine Cowboy* (2011):
  - “ Yeah, I'm on that gas, and yeah, I'm on that lean”
- Future: “Dirty Sprite” from *Dirty Sprite* (2011):
  - “I wake up leaning from last night I drink my lean for breakfast … I'm trued up With two cups They shook up with dirty sprite Promethazine can't get enough Till I O.D you know whats up … I'm moving slow the lights ain't bright as they supposed to be … I think I lost my heartbeat for a second in a half”

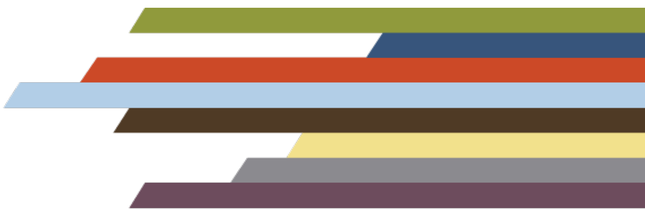
Rappers are not the Only Ones

- James Taylor - his songs were odes to his heroin addiction vs. explicit rap songs to come
- Mark Ribowsky (2016). *Sweet Dreams and Flying Machines: The Life and Music of James Taylor*
- Elvis Presley - codeine plus others overdose
- Hank Williams - morphine overdose
- Janis Joplin - heroin overdose
- Phillip Seymour Hoffman - actor died of overdose
- Corey Haim - deceased
- River Phoenix - deceased
- Heath Ledger - deceased
- Robert Downey, Jr.
- Mathew Perry of *Friends*
- Bradley Cooper
- Gerard Butler
- Macklemore



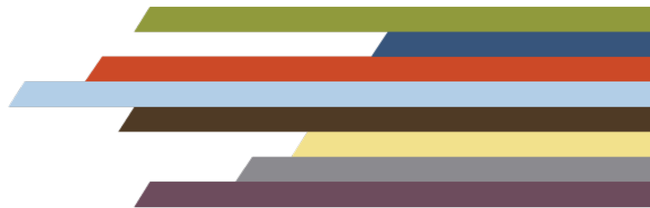
Promethazine/Codeine Deaths

- DJ Screw (Robert Earl Davis Jr.: July 20, 1971 – November 16, 2000) codeine overdose combined with PCP and diazepam
- Big Moe (Kenneth Doniell Moore:[21] August 20, 1974 – October 14, 2007) of a myocardial infarction
- Pimp C (Chad Lamont Butler: December 29, 1973 – December 4, 2007)
- Mac Miller (Malcolm James McCormick: January 19, 1992 – September 7, 2018)
- Fredo Santana: (Derrick Coleman: July 4, 1990 – January 19, 2018) - liver failure
- Chris Penn (October 10, 1965 – January 24, 2006) - actor



Purple Drank and Celebrities

- Lil Wayne hospitalized for seizures
- Justin Bieber
- Gucci Mane
- T.I.
- Beanie Siegel
- Terrence Kiel (San Diego Chargers)
- Johnny Jolly (Green Bay Packers)
- Jamarcus Russell



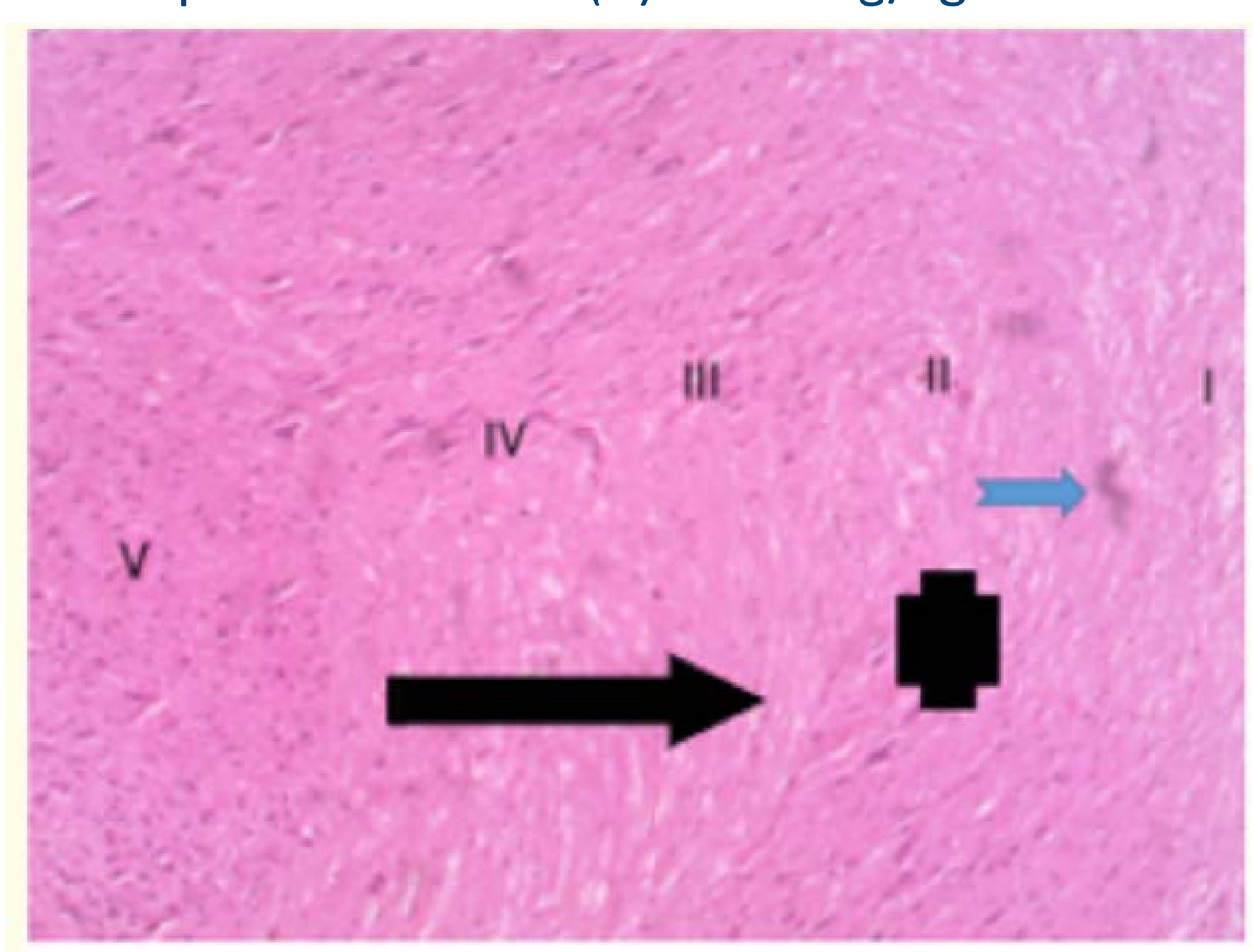
Purple Drank/Lean Abuse

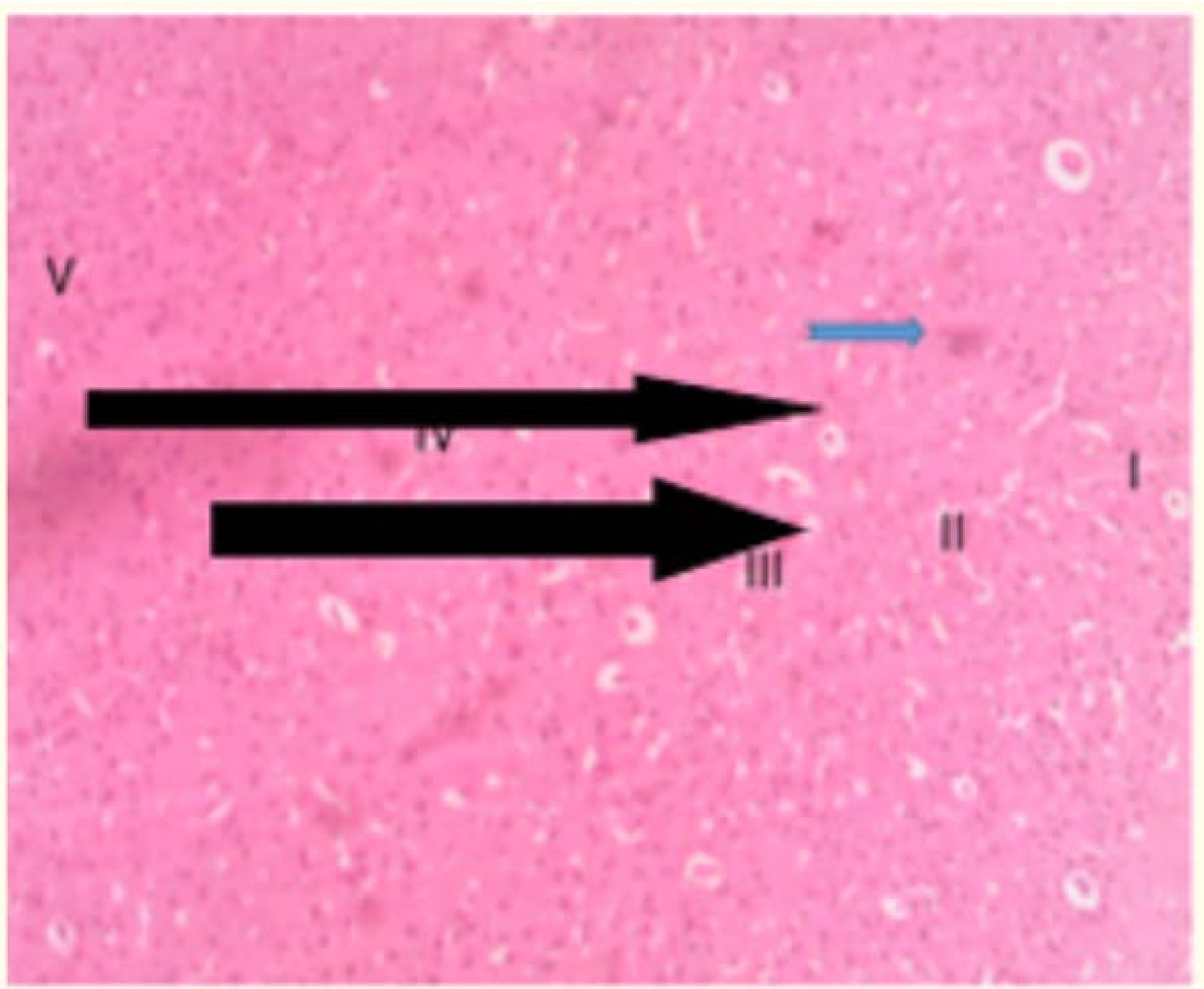
- The entire bottle of cough medicine is used in a single glass. Users consume several a day.
- Promethazine-Codeine 240 ml bottle: 6.25 mg/10 mg per 5 ml - total dose 300 mg promethazine and 480 mg codeine.
- Nyquil Cold and Flu 236 ml bottle: dextromethorphan 30 mg, doxylamine 12.5 mg, and acetaminophen 650 mg per 30 ml - total dose for a bottle is 236 mg dextromethorphan, 98.33 mg doxylamine, and 5.11 grams acetaminophen.

Codeine Cognitive Effects

- Inattention
- Concentration difficulties
- Memory deficits
- Psychomotor dysfunction
- Perceptual distortions
- Executive dysfunction
- Somnolence
- Sleep disorders

Codeine-Induced neuronal cell disorganization, increased apoptotic cells (arrow)and extensive neuropil vacuolization (V): 5-10 mg/kg



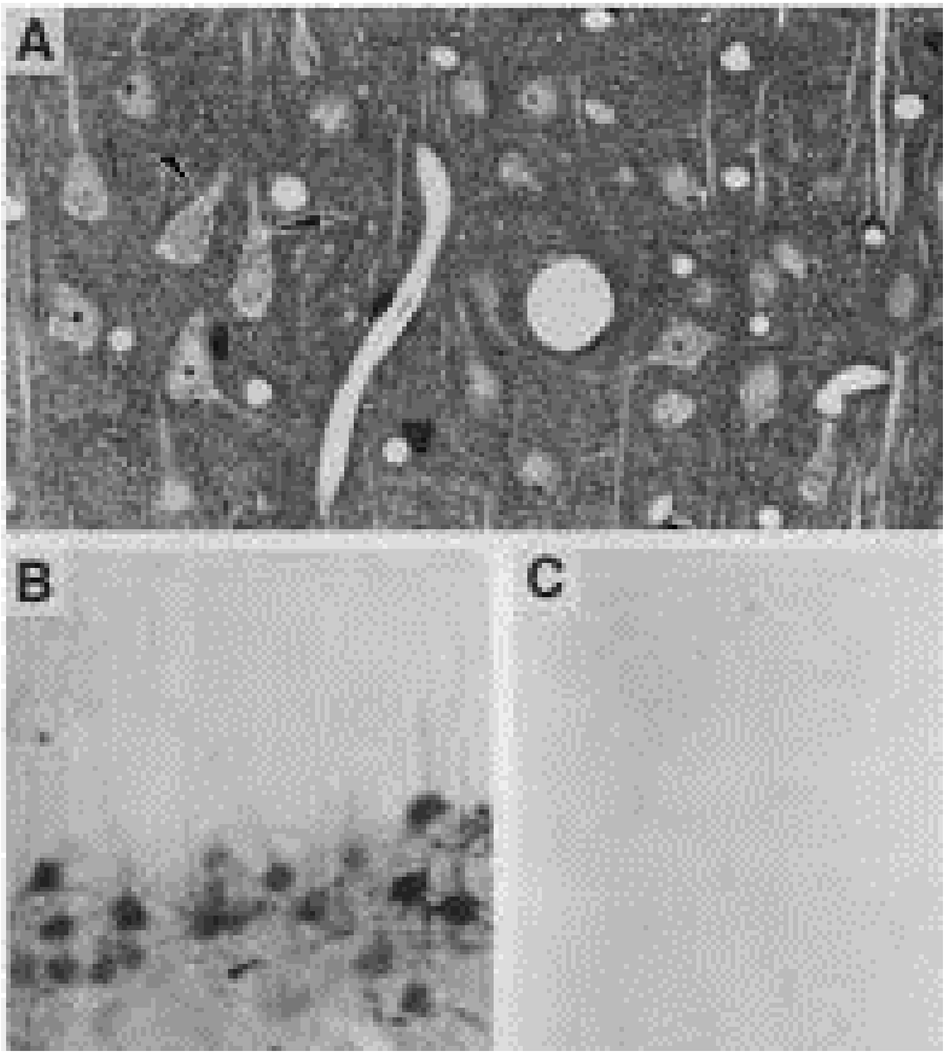


Achukwu PU et al. Codeine and its Histopathological Effect on Brain of Albino Rats: An Experimental Study. ACTA SCIENTIFIC NUTRITIONAL HEALTH 2019; 3(2):125-133.

Dextromethorphan Cognitive Effects

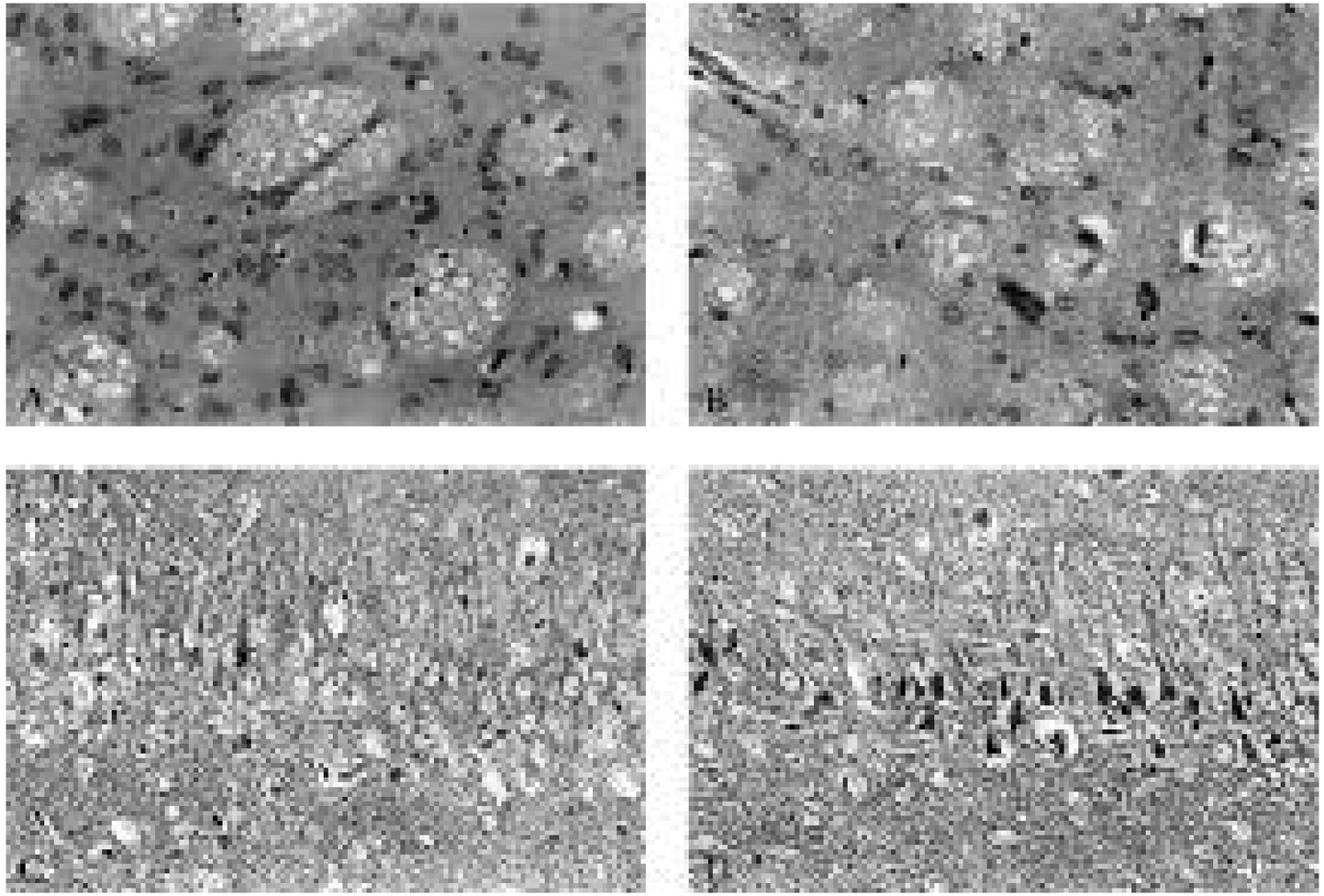
- Dextromethorphan 100–300 mg/70 kg:
  - Abbreviated attention span
  - Impaired working memory
  - Impaired episodic memory
  - Impaired metacognition
  - 10–30 times the therapeutic induce psychosis that persists after stopping use
    - Dissociation
    - Euphoria
    - Body hallucinations
    - Time distortion

Olney JW et al. NMDA Antagonist Neurotoxicity: Mechanism and Prevention. Science 1991; 254(No. 5037):1515-1518.



NMDA Receptor Antagonist Induced Olney Lesions (Neuronal Vacuolation)

Ikinimidou C et al. Neuronal death enhanced by N-methyl-Daspartate antagonists. PNAS 2000; 97(23):12885-12890

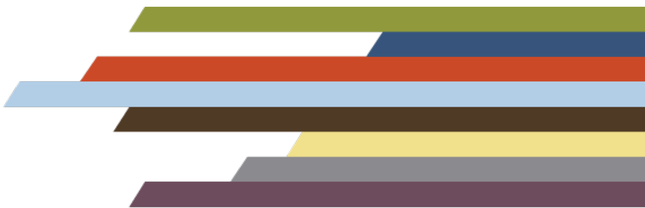


OTC Cold Medicine Based Lean

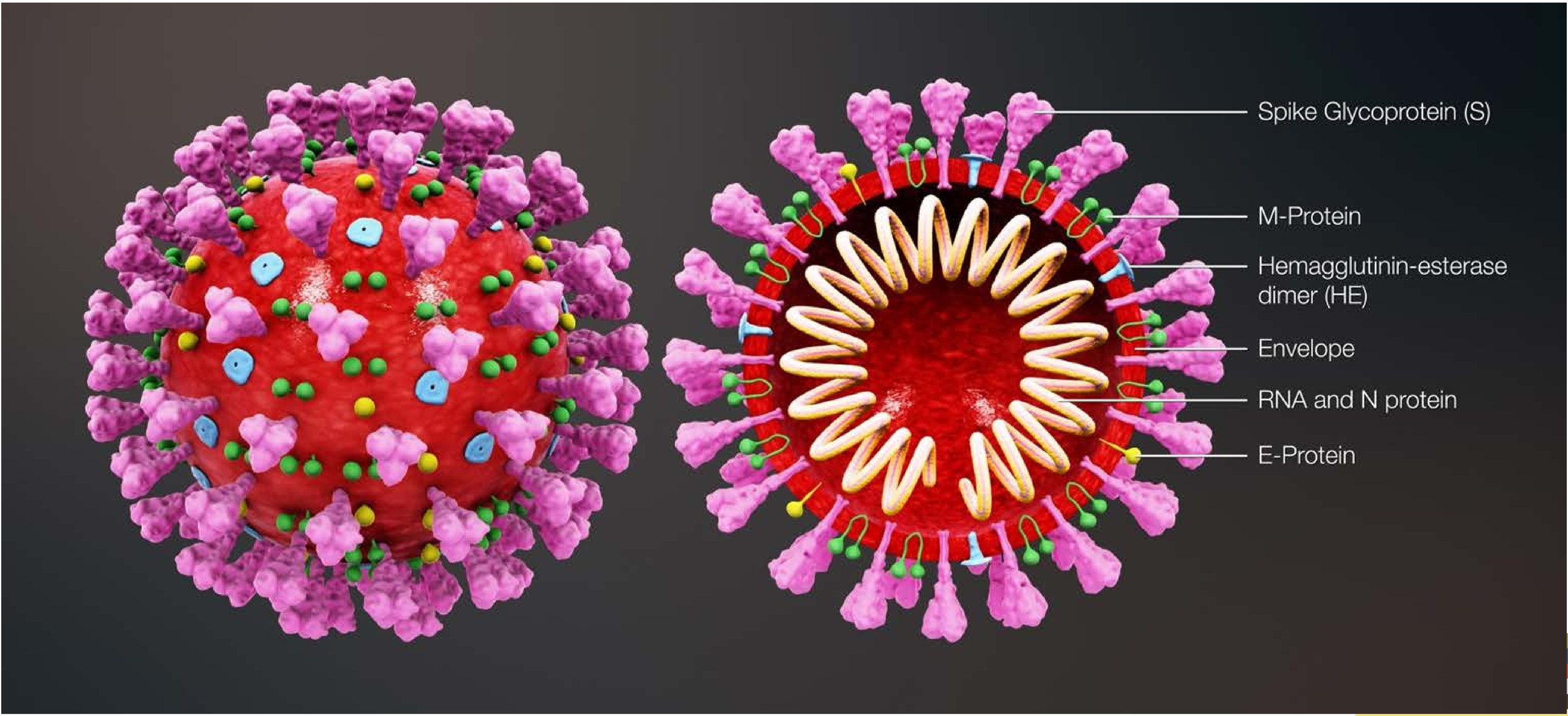
- Mental health practitioners focus on the psychoactive effects.
- However, there are life threatening outcomes unrelated to the CNS that demand more attention.
- Acetaminophen is hepatotoxic and more than 4 grams is sufficient to induce acute liver failure and death.

Sigma-1Receptor Agonists

- Fluoxetine
- Escitalopram
- Fluvoxamine (Luvox)
- Imipramine (Tofranil)
- Lamotrigine
- Methylphenidate
- Cocaine
- Methamphetamine
- Dextromethorphan
- Dehydroepiandrosterone (DHEA)
- Pregnenolone
- Buprenorphine
- NN-Dimethyltryptamine
- Siramesine
- Ketamine
- Memantine
- Phencyclidine
- Pentazocine



Structure of SARS-CoV-2

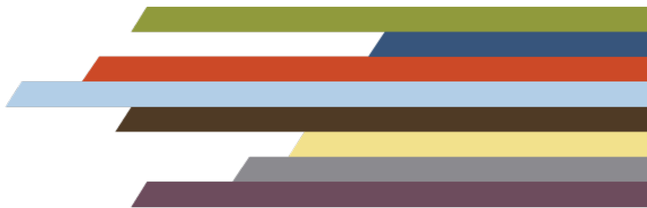


Neuropharmacology of COVID-19

- Spike protein binds ACE2 to enter cells
- ACE2 is not the only receptor it binds
- SARS-CoV-2 genome
- Nonstructural proteins (nsp) and open reading frames (ORF)
- nsp6 and ORF9c bind the sigma receptor

Cannabis, Opioids, and COVID-19

- Cannabis effect on innate immunity: THC, CBD, CBG, and CBN are anti-inflammatory but antagonize the anti-inflammatory action of steroids
- Opioids are immunosuppressive: fentanyl > morphine >> oxycodone
- Opioid abusers' risk for COVID-19 is 10.244, with high death rate (9.6%) and high rate of hospitalization (41.0%)
- New kid on the block: Isotonitazene, aka "iso," is a synthetic derivative of Etonitazene



Questions?

Thank You


danke
謝謝
ngiyabonga
teşekkür ederim
спасибо
dank je
thank you
gracias
tapadh leat
mochchakkeram
bedankt
hvala
mauruuru
dziękuję
go raibh maith agat
sagolun
sukriya
kop khun krap
arigato
takk
dakujem
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