Marijuana

Discussion slides

Quick review, Brain Health, ED visits & Stroke Risk

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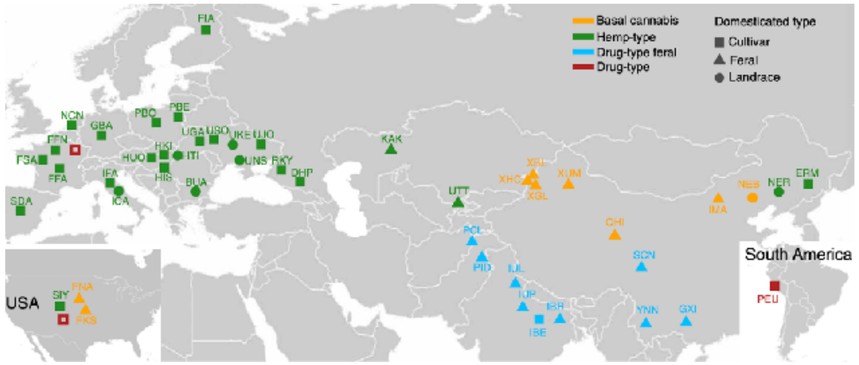
Marijuana

Origins

Archaeological sites with hemp-type Cannabis artifacts are consistently found from 7500 years before present day in China and Japan, and pollen consistent with cultivated Cannabis was found in China more than 5000 years before present day



SCIENCE ADVANCES | RESEARCH ARTICLE

AGRICULTURE

Large-scale whole-genome resequencing unravels the domestication history of *Cannabis sativa*

Guangpeng Ren[1,2*†], Xu Zhang[2†‡], Ying Li[2†], Kate Ridout[1,3], Martha L. Serrano-Serrano[1], Yongzhi Yang[2], Ai Liu[2], Gudasalamani Ravikanth[4], Muhammad Ali Nawaz[5,6], Abdul Samad Mumtaz[7], Nicolas Salamin[8], Luca Fumagalli[1,9*]

Cannabis sativa **has long been an important source of fiber extracted from hemp and both medicinal and recreational drugs based on cannabinoid compounds. Here, we investigated its poorly known domestication history using whole-genome resequencing of 110 accessions from worldwide origins. We show that *C. sativa* was first domesticated in early Neolithic times in East Asia and that all current hemp and drug cultivars diverged from an ancestral gene pool currently represented by feral plants and landraces in China. We identified candidate genes associated with traits differentiating hemp and drug cultivars, including branching pattern and cellulose/lignin biosynthesis. We also found evidence for loss of function of genes involved in the synthesis of the two major biochemically competing cannabinoids during selection for increased fiber production or psychoactive properties. Our results provide a unique global view of the domestication of *C. sativa* and offer valuable genomic resources for ongoing functional and molecular breeding research.**

Author: Guangpeng R et al.

PMID:34272249

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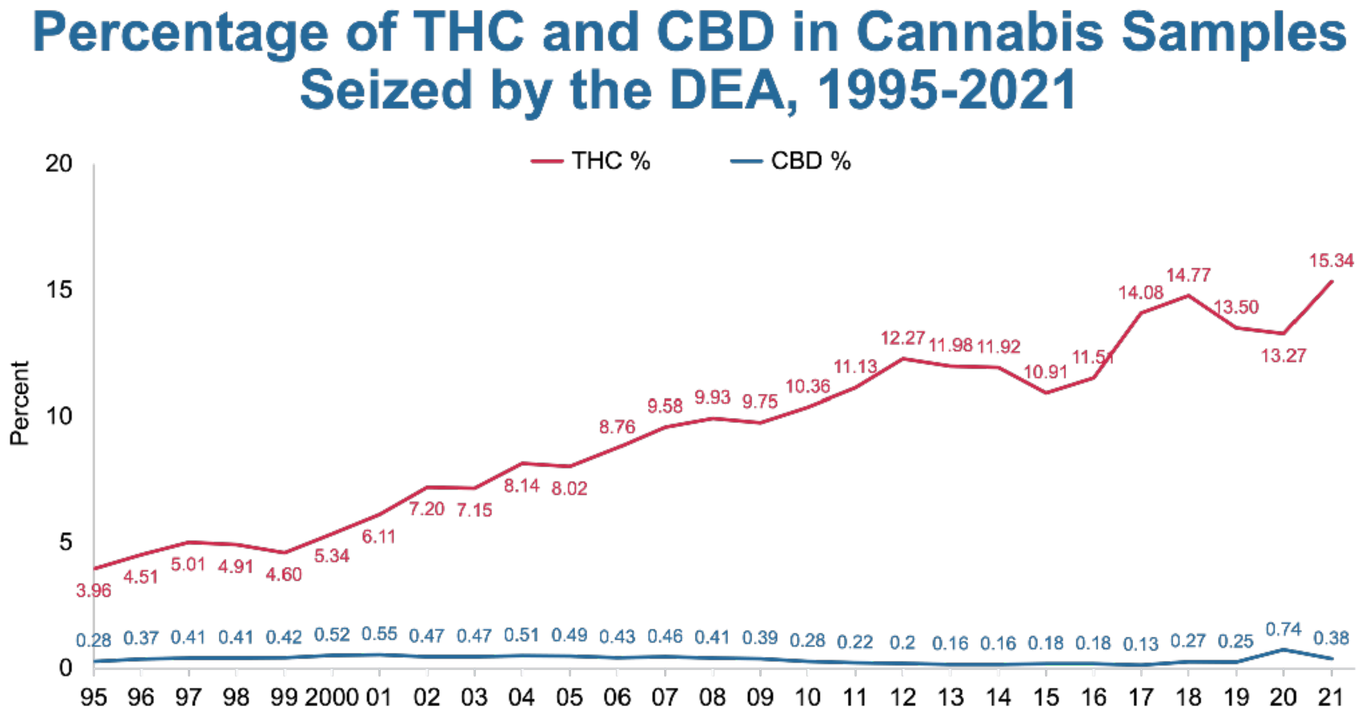
Effects & Potency

The potency of cannabis products in the United States, measured by the concentration of the primary psychoactive constituent of marijuana, Δ9-tetrahydrocannabinol (THC), has gradually increased from ≈4% in 1995 to 15% in 2018.

National Institutes of Health, National Institute on Drug Abuse. Marijuana potency. 2020. Accessed May 23, 2023. https://nida.nih.gov/research-topics/marijuana/cannabis-marijuana-potency



SOURCE: U Miss, Potency Monitoring Project

Author:

PMID:

Global Cannabis use

FIG. 54 Global trends in the number of past-year users of cannabis and the cannabis use perception index, 1998-2014

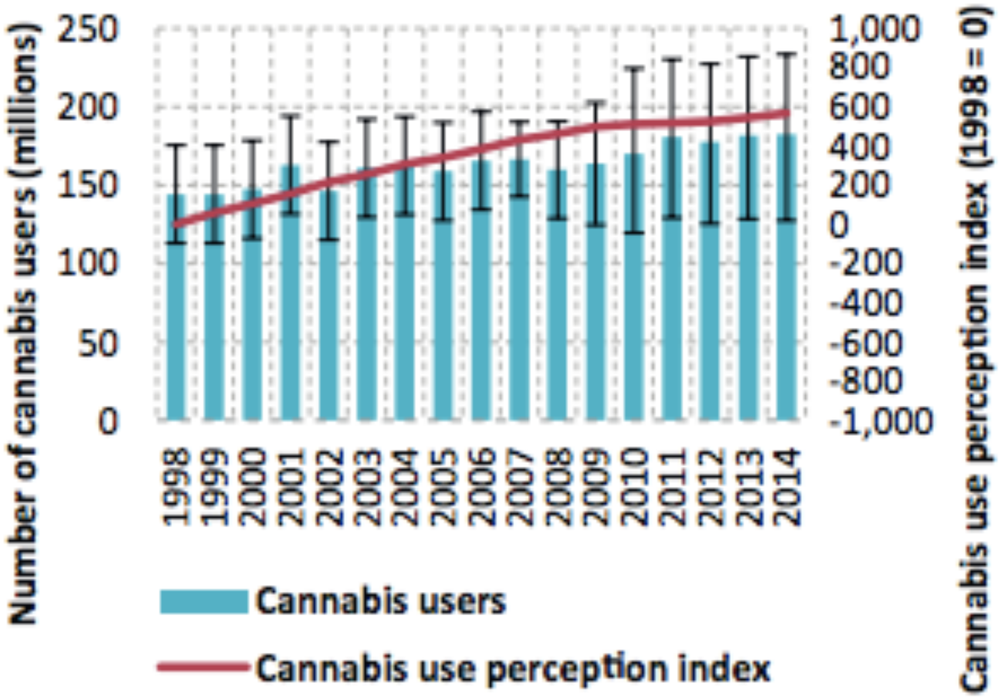
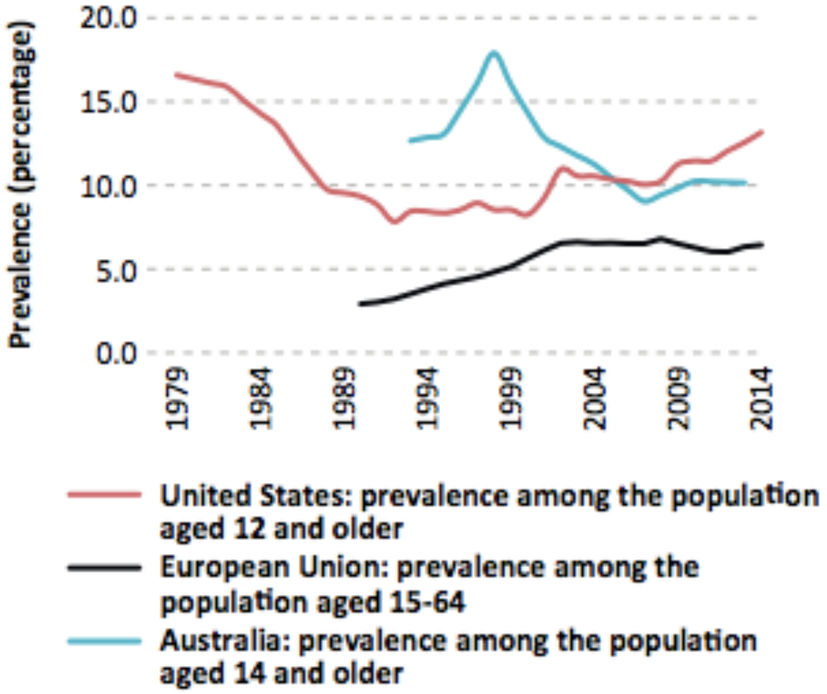


FIG. 55 Prevalence of past-year cannabis use in Australia, the United States and the European Union, 1979-2014



Marijuana

Endo & Exogenous Cannabinoids

Endocannabinoid system ECS is comprised of endogenous cannabinoids (*endocannabinoids*), cannabinoid receptors, and the proteins that transport, synthesize and degrade endocannabinoids.

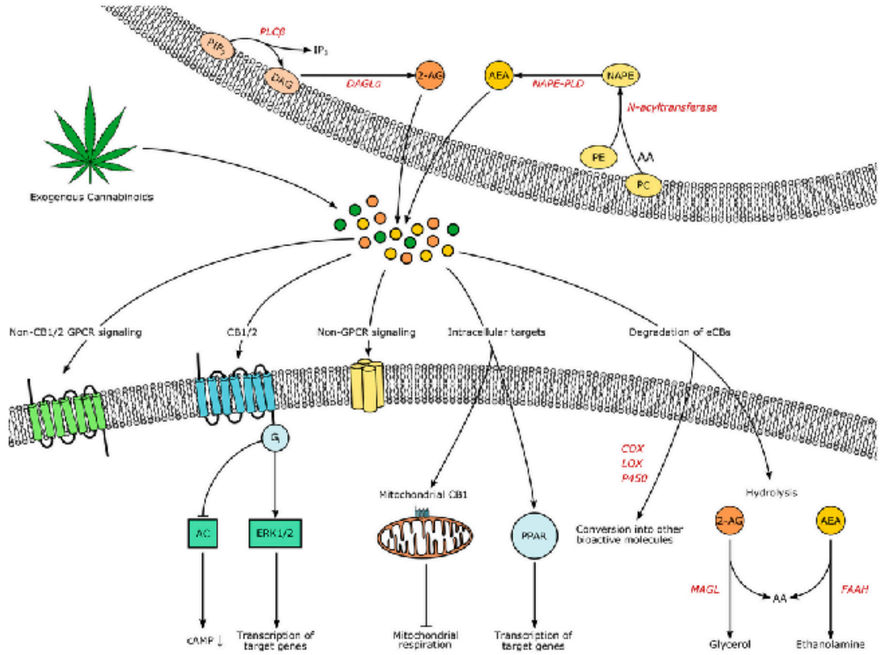
Most components of the ECS are multifunctional.

Cannabidiol (CBD) is another constituent of cannabis, present at variable levels, which interacts with the ECS as well as other neuromodulatory systems.

> **CB1** and **CB2** are the best-characterized cannabinoid receptors. Both are G protein-coupled receptors (GPCRs), primarily coupling to inhibitory G proteins.

While cannabis contains many bioactive compounds, most of the psychoactive effects classically associated with cannabis appear to be mediated through the i**nteraction of Δ9-tetrahydrocannabinol (THC),** the major psychotropic constituent of cannabis, with **cannabinoid receptors.**

Figure 1. The endocannabinoids (eCBs) AEA and 2-AG are produced on demand from lipid precursors and released to the extracellular space. Endogenous and exogenous cannabinoids act through the same signaling systems: Binding to Gi-coupled receptors CB1 or CB2 modulates intracellular cascades and leads for example to the inhibition of adenylyl cyclase (AC) or the regulation of transcription through extracellular signal-regulated kinases (ERKs). Alternative receptors are non-CB1/2 GPCRs, non-GPCRs like TRPV1 and, intracellularly, mitochondrial CB1 (mtCB1) and peroxisome proliferator-activated receptors (PPARs). Signaling is terminated through hydrolysis, but eCBs might also serve as substrates for cyclooxygenases (COXs), lipoxygenases (LOXs) or cytochromes P450 (P450), yielding additional bioactive compounds. Note that all illustrated processes do not have to take place in distinct cells as autocrine eCB signaling has been shown as well. Abbreviations: PIP2 phosphatidylinositol 4,5-bisphosphate, IP3 inositol-1,4,5-trisphosphat, DAG Diacylglycerol, PLC phospholipase C, DAGL diacylglycerol lipase, 2-AG 2-arachidonylglycerol, PC phosphatidylcholine, PE phosphatidylethanolamine, AA arachidonic acid, NAPE *N*-arachidonoyl phosphatidylethanolamine, NAPE-PLD NAPE-specific phospholipase D, MAGL monoacylglycerol lipase, FAAH fatty acid amide hydrolase.



Author: Horn H et al

PMID: 29849009

UPSTATE UNIVERSITY HOSPITAL

Author: Hui-Chen L et al

PMID: 32980261

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Receptors & Effects

Cannabinoid receptors are expressed in high density in areas of the brain involved in **executive function and memory** such as the hippocampus, amygdala, and prefrontal cortex (PFC), particularly during periods of active brain development.

Acute intoxication with cannabinoids can **impair memory and behavioral inhibition**.

Cannabinoids also regulate anxiety and can produce psychosis-like effects

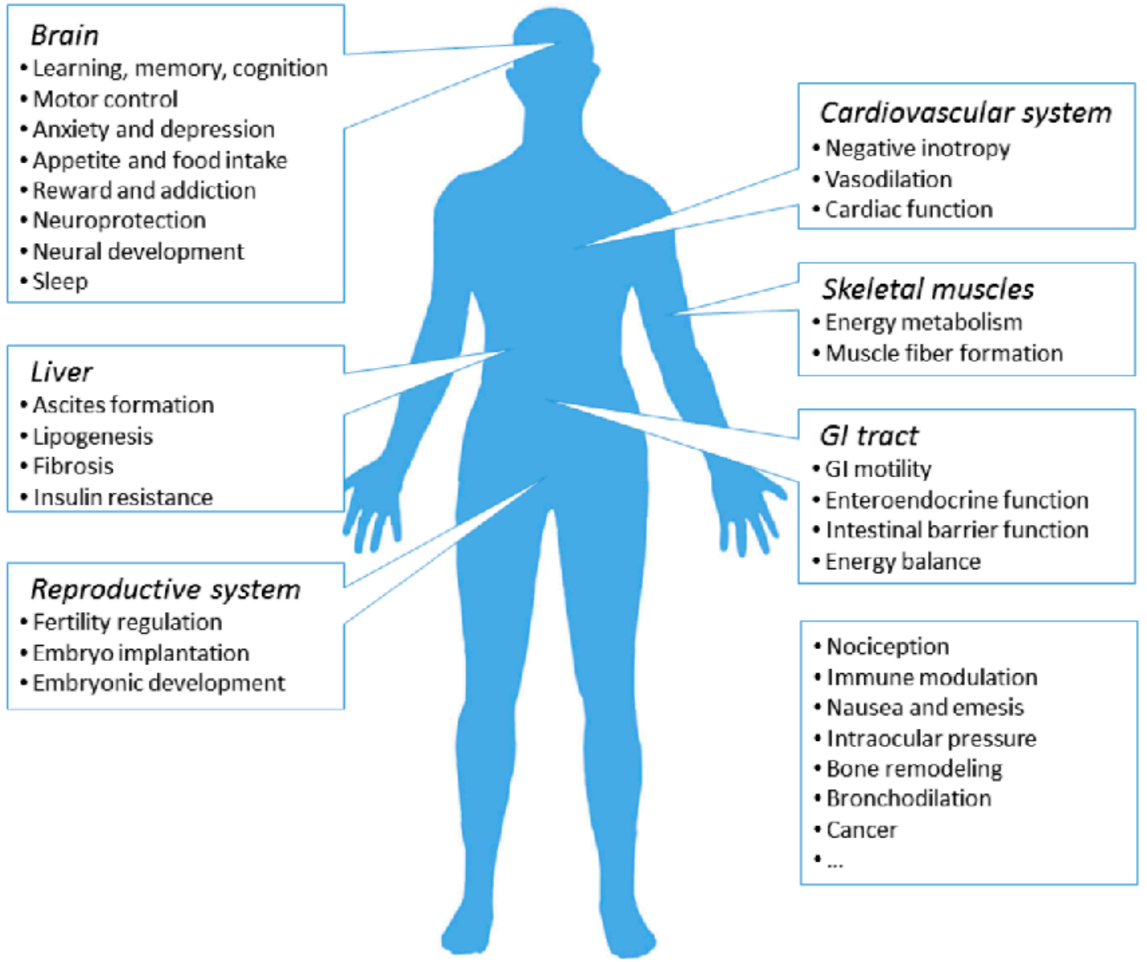
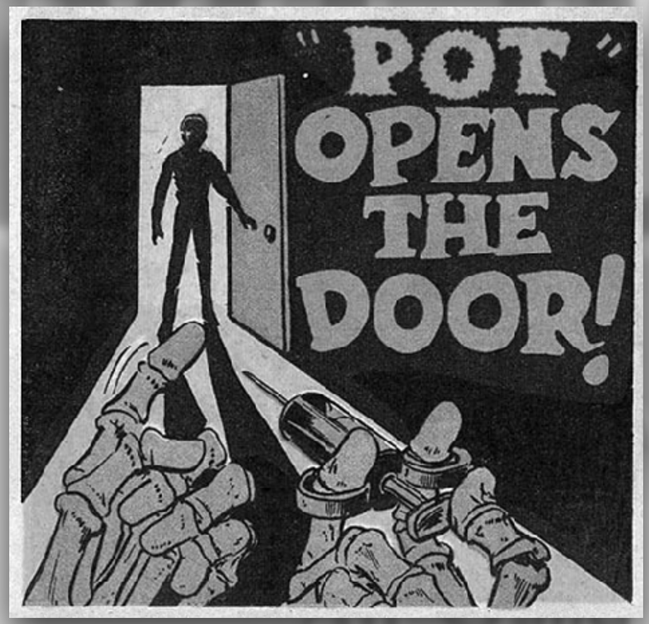


Figure 2. Major localization sites and associated functions of the CB1R in the human body. The majority of CB1Rs expressed in human body is found in the brain, where it is involved in various neurological activities. CB1Rs on the peripheral sites, although to a lesser extent, participates in the regulation of local tissue functions.

Author: Zou S & Kumar U

PMID: 29533978

Harmful effects



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Users experience

A convenience sample of cannabis users (n = 179) was surveyed via Amazon Mechanical Turk (mTurk).

Participants were asked about their prior use of, subjective experiences with, and opinions on indica versus sativa cannabis and completed hypothetical purchasing tasks for both cannabis subtypes.

Participants reported a greater preference to use indica in the evening and sativa in the morning and afternoon. Participants were more likely to perceive feeling “sleepy/tired” or “relaxed” after using indica and “alert,” “energized,” and “motivated” after using sativa.

Respondents were more likely to endorse wanting to use indica if they were going to sleep soon but more likely to use sativa at a party.

Author: Sholler DJ et al.

PMID: 33856822

Marijuana

Edibles and ED visits

Four-hundred and thirty calls were reported (**2013-2015);** Colorado (N = 166, 1.05/100,000 population/year) and Washington (96, 0.46) yielded the highest number of exposures.

Three hundred and eighty-one (91%) calls occurred in states with decriminalized medical/ recreational marijuana. The **number of calls increased every year of the study.** The most common age groups were: ≤ 5 years (N = 109, 0.15/100,000 population/year) and 13-19 (78, 0.09).

The most frequent clinical effects were **drowsiness/lethargy** (N = 118, percentage = 43%), tachycardia (84, 31%), agitated/irritable (37, 14%), and confusion (37, 14%).

Children ≤5 years have more drowsiness/lethargy, ataxia, and red eye/conjunctivitis. No deaths were reported.

The most common therapies administered were intravenous fluids (85, 20%), dilute/irrigate/ wash (48, 11 %), and benzodiazepines (47, 11%).

Three patients (ages 4, 10, and 57 years) received intubation.

97 (23%), 217 (50%), and 12 (3%) calls were managed at home, treated/released, admitted to a critical care unit, respectively.

Author: Cao D et al.

PMID: 27418198

Marijuana

Table 1. Synthetic and Semisynthetic Cannabinoids

Cannabinoid type	Active ingredient	Indication
Medical[15,16]		
Cesamet	Nabilone (synthetic THC analog)	Treatment of refractory cancer chemotherapy–associated nausea and vomiting*†
Marinol (pill)	Dronabinol (synthetic THC)	Anorexia with weight loss in patients with AIDS or cancer*†
Syndros (solution)	Dronabinol (synthetic THC)	Treatment of refractory cancer chemotherapy–associated nausea and vomiting*†
Epidiolex	Purified CBD	Seizures associated with Lennox-Gastaut syndrome and Dravet syndrome in patients >1 y of age* Seizures associated with tuberous sclerosis complex in patients >1 y of age*
Sativex	Nabiximols (extract of THC, CBD, and other minor cannabinoids, terpenoids, and flavonoids)	Adjunctive therapy for symptomatic treatment of refractory spasticity in adult patients with multiple sclerosis indication† Adjunctive treatment for symptomatic neuropathy in adult patients with multiple sclerosis indication† Adjunctive treatment for patients with advanced cancer with refractory severe pain indication†
Illicit[17]		
K2, Spice, Kronic, Kaos		Originally synthesized to study the endocannabinoid system Bind cannabinoid receptors with high affinity and can cause hallucinations, agitation, psychosis, short-term memory loss, seizures, coagulopathy, and myocardial infarction

CBD indicates cannabidiol; and THC, Δ^9-tetrahydrocannabinol.
*Approved by the US Food and Drug Administration.
†Approved by the Health Products and Food Branch of Health Canada.

AHA SCIENTIFIC STATEMENT

Use of Marijuana: Effect on Brain Health: A Scientific Statement From the American Heart Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Fernando D. Testai, MD, PhD, Chair; Philip B. Gorelick, MD, MPH, Vice Chair; Hugo J. Aparicio, MD, MPH; Francesca M. Filbey, PhD; Raul Gonzalez, PhD; Rebecca F. Gottesman, MD, PhD; Miriam Melis, PhD; Mariann R. Piano, RN, PhD; Tiziana Rubino, PhD; Sarah Y. Song, MD; on behalf of the American Heart Association Stroke Brain Health Science Subcommittee of the Stroke Council; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; Council on Lifestyle and Cardiometabolic Health; and Council on Peripheral Vascular Disease

ABSTRACT: Marijuana is perceived as a harmless drug, and its recreational use has gained popularity among young individuals. The concentration of active ingredients in recreational formulations has gradually increased over time, and high-potency illicit cannabinomimetics have become available. Thus, the consumption of cannabis in the general population is rising. Data from preclinical models demonstrate that cannabinoid receptors are expressed in high density in areas involved in cognition and behavior, particularly during periods of active neurodevelopment and maturation. In addition, growing evidence highlights the role of endogenous cannabinoid pathways in the regulation of neurotransmitter release, synaptic plasticity, and neurodevelopment. In animal models, exogenous cannabinoids disrupt these important processes and lead to cognitive and behavioral abnormalities. These data correlate with the higher risk of cognitive impairment reported in some observational studies done in humans. It is unclear whether the effect of cannabis on cognition reverts after abstinence. However, this evidence, along with the increased risk of stroke reported in marijuana users, raises concerns about its potential long-term effects on cognitive function. This scientific statement reviews the safety of cannabis use from the perspective of brain health, describes mechanistically how cannabis may cause cognitive dysfunction, and advocates for a more informed health care worker and consumer about the potential for cannabis to adversely affect the brain.

Key Words: AHA Scientific Statements ■ brain ■ cannabis ■ cognition ■ marijuana ■ stroke

Author: Testai FD et al

PMID:35142225

Marijuana

Effects & Potency

- **Windows of vulnerability**
  - Subsequent neuroinflammatory response was associated with memory impairment during adulthood (in animal (Rat) model).

- Similar to the literature linking marijuana use with cardiovascular outcomes, evidence that marijuana consumption increases the prevalence of specific cerebrovascular risk factors and disease is **limited** by a preponderance of observational studies, cross-sectional studies, case reports, and case series prone to potential publication and other biases.

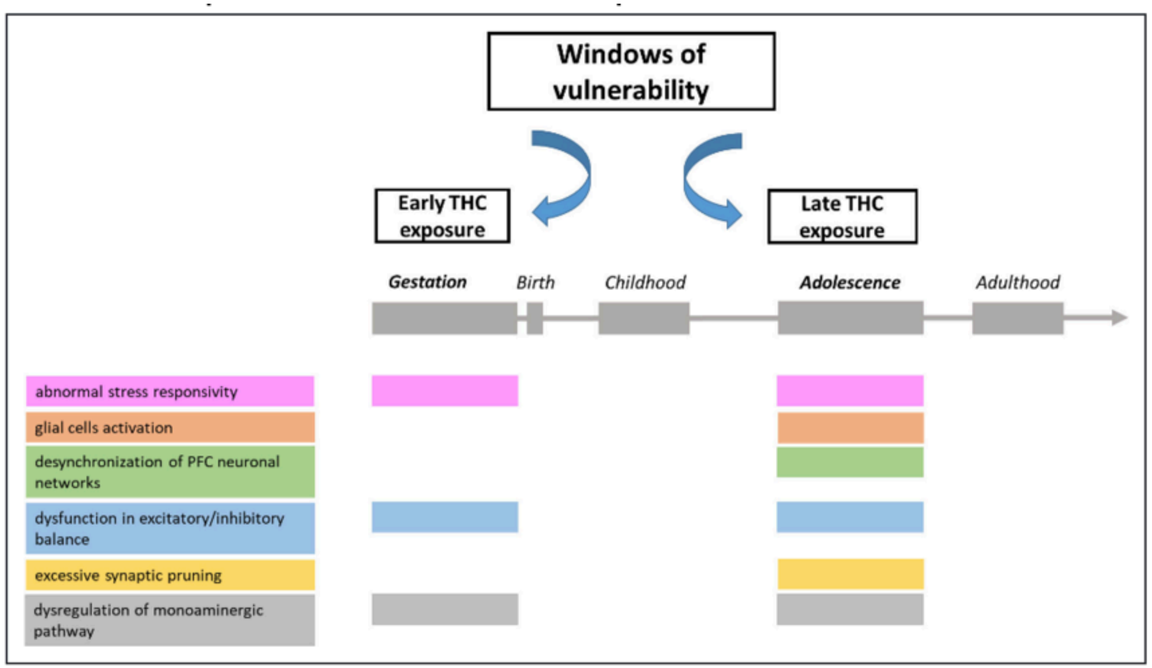


Figure. Effect of Δ^9-tetrahydrocannabinol (THC) on different neurobiological processes. The effect of THC on the brain constitutes a continuum throughout the lifetime of an individual. However, 2 windows of brain vulnerability have been identified in preclinical models. The colored boxes represent the different processes that have been demonstrated to be affected on exposure to THC during these sensitive developmental periods. PFC indicates prefrontal cortex.

Author: Testai FD et al

PMID:35142225

Risk of stroke in young users

Population study

- Cases of first-ever ischemic stroke (age 15-49) in Baltimore-Washington
- 751 cases matched to 813 controls
- Analyze relationship between marijuana-usr and risk of ischemic stroke
- Yielded non-significant trend towards increased risk (OR 1.9) of stroke among frequent users (>= 1 wk).

CLINICAL AND POPULATION SCIENCES

Marijuana Use and the Risk of Early Ischemic Stroke

The Stroke Prevention in Young Adults Study

Tara Dutta, MD; Kathleen A. Ryan, MPH; Oluwatosin Thompson, MD; Haley Lopez, BS; Natalie Fecteau, MPH; Mary J. Sparks, RN, BSN; Seemant Chaturvedi, MD; Carolyn Cronin, MD, PhD; Prachi Mehndiratta, MD; Joel R. Nunez Gonzalez, MD; Michael Phipps, MD, MPH; Marcella Wozniak, MD, PhD; Patrick F. McArdle, PhD; Steven J. Kittner, MD, MPH; John W. Cole, MD, MS

BACKGROUND AND PURPOSE: Few studies have examined the dose-response and temporal relationships between marijuana use and ischemic stroke while controlling for important confounders, including the amount of tobacco smoking. The purpose of our study was to address these knowledge gaps.

METHODS: A population-based case-control study with 1090 cases and 1152 controls was used to investigate the relationship of marijuana use and early-onset ischemic stroke. Cases were first-ever ischemic stroke between the ages of 15 and 49 identified from 59 hospitals in the Baltimore-Washington region. Controls obtained by random digit dialing from the same geographic region were frequency-matched to cases by age, sex, region of residence and, except for the initial study phase, race. After excluding subjects with cocaine and other vasoactive substance use, the final study sample consisted of 751 cases and 813 controls. All participants underwent standardized interviews to characterize stroke risk factors and marijuana use. Unconditional logistic regression analysis was used to assess the relationships between marijuana use and risk of ischemic stroke, adjusting for age, sex, race, study phase, the amount of current tobacco smoking, current alcohol use, hypertension, and diabetes.

RESULTS: After adjusting for other risk factors, including the amount of current tobacco smoking, marijuana use was not associated with ischemic stroke, regardless of the timing of use in relationship to the stroke, including ever use, use within 30 days, and use within 24 hours. There was a nonsignificant trend towards increased stroke risk among those who smoked marijuana at least once a week (odds ratio, 1.9 [95% CI, 0.8–4.9]).

CONCLUSIONS: These analyses do not demonstrate an association between marijuana use and an increased risk of early-onset ischemic stroke, although statistical power was limited for assessing the association among very heavy users.

Key Words: cannabis ■ ischemic stroke ■ population ■ risk factors ■ tobacco smoking

Author: Dutta T et al

PMID: 34266309

de los Ríos F et al. Trends in Substance Abuse Preceding Stroke Among Young Adults A Population-Based Study Stroke. 2012;43:3179-3183

Stroke patients aged 18 to 54 years
Greater Cincinnati and Northern Kentucky Study region
1993 to 1994, 1999, and 2005.

Table 1. Patient Characteristics Across Study Periods

	Patients		
	1993–1994 N=297	1999 N=376	2005 N=501
Race			
White	189 (69%)	239 (66%)	321 (63%)
Black	103 (30%)	134(34%)	176 (37%)
Other	5 (1.4%)	3 (0.7%)	4 (0.7%)
*Substance abuse†			
Present	138 (45%)	206 (52%)	286 (62%)
Alcohol or drugs within 24 h of stroke*	5 (1.4%)	25 (6.3%)	72 (12.8%)
Stroke type			
Ischemic	219 (78%)	260 (71%)	374 (69%)
Hemorrhagic	78 (22%)	114 (29%)	121 (22%)
Unknown	0 (0%)	2 (0.5%)	6 (9.2%)

Table 3. Substance Use by Age in Stroke Patients Across Study Periods

	Current Smoker			Illicit Drug Abuse		
Age	1993–1994	1999	2005	1993–1994	1999	2005
18–35 y	15 (38%)	17 (44%)	17 (36%)	5 (12%)	6 (15%)	13 (28%)
35–44 y	26 (41%)	45 (48%)	66 (55%)	2 (3%)	15 (16%)	24 (20%)*
45–54 y	88 (43%)	125 (47%)	162 (53%)	6 (2%)	18 (7%)	59 (19%)†

George MG et al. **Trends in Stroke Hospitalizations and Associated Risk Factors among Children and Young Adults, 1995–2008.** Ann Neurol 2011;70:713–721

Nationwide Inpatient Sample of the Healthcare Cost and Utilization Project.

Identified by ICD-9-CM code

TABLE 2: Prevalence of Acute Ischemic Stroke Hospitalization by Age and Gender

Age/Gender	Acute Ischemic Stroke				Relative Change[a]	*p* for Trends[b]
	1995–1996		2007–2008			
	Weighted No.	Rates/10,000 Hospitalizations (SE)	Weighted No.	Rates/10,000 Hospitalizations (SE)		
Age 5–14 years	441	3.2 (0.4)	527	4.2 (0.6)	31.3%	0.005
Male	231	3.1 (0.5)	316	4.7 (0.8)	51.6%	0.01
Female	210	3.4 (0.5)	197	3.5 (0.6)	2.9%	0.08
Age 15–34 years	6,776	5.0 (0.2)	9,237	6.5 (0.2)	30.0%	<0.0001
Male	3,027	10.3 (0.5)	4,339	15.0 (0.6)	45.6%	<0.0001
Female	3,749	3.5 (0.2)	4,889	4.3 (0.2)	22.9%	<0.0001
Age 35–44 years	19,110	28.2 (0.6)	27,210	38.6 (0.9)	36.9%	<0.0001
Male	9,693	35.7 (1.0)	13,809	53.7 (1.5)	50.4%	<0.0001
Female	9,418	23.3 (0.7)	13,396	30.0 (0.9)	28.8%	<0.0001

TABLE 4: Prevalence (%) of Risk Factors among Patients Hospitalized with Ischemic Stroke by Age and Gender

Health Conditions	Male						Female					
	Age 15–34 Years			Age 35–44 Years			Age 15–34 Years			Age 35–44 Years		
	1995–1996	2007–2008	*p* for Trends[a]	1995–1996	2007–2008	*p* for Trends[a]	1995–1996	2007–2008	*p* for Trends[a]	1995–1996	2007–2008	*p* for Trends[a]
Hypertension	25.3 (1.9)[b]	37.2 (1.7)[b]	<0.001	47.9 (1.2)[b]	63.0 (1.0)[b]	<0.001	19.2 (1.5)[b]	32.2 (1.6)[b]	<0.001	47.5 (1.4)[b]	56.0 (1.1)[b]	<0.001
Diabetes	10.6 (1.4)[b]	16.8 (1.4)[b]	0.002	19.8 (0.9)[b]	29.0 (0.9)[b]	<0.001	7.4 (1.1)	17.1 (1.3)[b]	<0.001	21.4 (1.1)[b]	25.9 (0.9)[b]	<0.001
Obesity	3.3 (0.7)	9.1 (1.0)	<0.001	4.4 (0.5)	10.5 (0.6)[b]	<0.001	5.6 (1.0)	13.7 (1.2)[b]	<0.001	9.8 (0.8)	14.6 (0.7)[b]	<0.001
Lipid disorders	3.3 (0.7)	21.6 (1.5)[b]	<0.001	9.9 (0.7)	41.3 (1.0)[b]	<0.001	3.9 (0.9)	16.0 (1.3)[b]	<0.001	7.9 (0.7)	31.0 (0.9)[b]	<0.001
Ischemic heart disease	3.8 (0.8)	4.7 (0.7)	0.15	9.5 (0.7)	11.0 (0.6)[b]	0.32	[c]	2.9 (0.5)	[c]	6.5 (0.7)	7.0 (0.5)	0.23
Congenital heart disease	4.4 (0.8)	13.2 (1.3)[b]	<0.001	1.9 (0.3)	7.3 (0.6)	<0.001	5.8 (1.0)	13.6 (1.4)[b]	<0.001	1.6 (0.3)	8.0 (0.6)	<0.001
Valvular heart disease	8.4 (1.2)	8.1 (0.9)	0.69	8.4 (0.7)	6.7 (0.5)	0.02	12.2 (1.3)[b]	9.0 (0.9)	0.03	10.7 (0.8)[b]	7.4 (0.5)	<0.001
Arrhythmia	5.8 (0.9)	11.2 (1.0)[b]	<0.001	7.5 (0.6)	8.6 (0.5)	<0.001	5.8 (0.9)	8.4 (0.9)	0.0001	5.2 (0.5)	7.3 (0.5)	0.002
Cardiomyopathy	5.4 (0.9)	7.1 (0.9)	0.048	3.8 (0.4)	5.9 (0.5)	<0.001	2.7 (0.6)	3.1 (0.6)	0.37	2.6 (0.5)	3.3 (0.3)	0.07
Patent foramen ovale	2.4 (0.6)	11.8 (1.3)[b]	<0.001	1.4 (0.3)	6.5 (0.5)	<0.001	3.1 (0.7)	11.0 (1.2)[b]	<0.001	1.4 (0.3)	7.4 (0.6)	<0.001
Coagulation defects	2.2 (0.7)	8.0 (1.0)	<0.001	2.4 (0.4)	4.1 (0.4)	<0.001	4.2 (0.8)	11.7 (1.1)[b]	<0.001	2.2 (0.3)	8.0 (0.5)	<0.001
Alcohol abuse	3.1 (0.7)	9.5 (1.1)	<0.001	4.1 (0.5)	9.6 (0.6)	<0.001	[c]	1.8 (0.4)	[c]	1.5 (0.3)	3.4 (0.3)	<0.001
Tobacco use	8.6 (1.3)	32.0 (1.6)[b]	<0.001	12.7 (0.9)[b]	38.4 (1.1)[b]	<0.001	9.5 (1.2)	26.3 (1.5)[b]	<0.001	9.9 (0.8)	32.4 (1.0)[b]	<0.001
Drug abuse (other than alcohol)	12.3 (1.4)[b]	13.2 (1.3)[b]	0.01	7.8 (0.7)	11.8 (0.7)[b]	<0.001	8.0 (1.2)	5.6 (0.8)	0.09	4.9 (0.6)	7.8 (0.5)	<0.001
Migraine	2.4 (0.6)	4.7 (0.7)	0.001	1.7 (0.3)	3.4 (0.3)	<0.001	9.8 (1.1)	12.7 (1.0)	0.046	6.0 (0.6)	9.0 (0.6)	<0.001
Meningitis, encephalitis, or sepsis	1.9 (0.6)	3.3 (0.6)	0.015	1.5 (0.3)	2.0 (0.3)	0.74	1.9 (0.5)	2.0 (0.5)	0.98	1.4 (0.3)	2.4 (0.3)	0.02
Lupus	[c]	[c]	[c]	[c]	0.4 (0.1)	[c]	6.2 (0.9)	4.6 (0.7)	0.10	3.8 (0.5)	2.6 (0.3)	0.07
HIV	5.8 (1.0)	2.4 (0.6)	<0.001	2.9 (0.4)	2.4 (0.3)	0.39	1.9 (0.5)	1.7 (0.5)	0.59	1.6 (0.3)	2.0 (0.3)	0.24
Other malignancy	2.1 (0.6)	1.7 (0.4)	0.53	2.1 (0.4)	2.2 (0.3)	0.40	1.3 (0.4)	2.3 (0.5)	0.35	3.2 (0.4)	4.3 (0.4)	0.31

[a] *p* value was obtained by using a linear regression model to assess the linear trends across the 7 time periods.
[b] Indicates prevalence ≥10%.
[c] Not reportable based on the estimates with a relative standard error >0.30.
HIV = human immunodeficiency virus.

de los Ríos F et al. Trends in Substance Abuse Preceding Stroke Among Young Adults A Population-Based Study Stroke. 2012;43:3179-3183

Marijuana

Summary

Table 2. Key Summary Points

Section	Notes
Actions of Cannabis in Animal Models	THC disrupts endocannabinoid signaling pathways and affects synaptic plasticity. In the short term, this affects the strength of interneuronal connections; in the long term, it leads to changes in the functioning of neuronal networks. Exposure to THC during adolescence can lead to structural, molecular, and functional alterations of brain circuits, particularly in areas involved in cognition and behavior.
Effect of Prenatal Exposure to Cannabinoid Agonist	In preclinical models, THC disrupts the normal signaling of the endocannabinoid system during development and throughout ontogenesis and results in abnormal neurotransmission. Prenatal THC affects neuroanatomic areas associated with cognition and emotional regulation, including the PFC, limbic system, and ventral tegmentum of the midbrain.
Effects of Marijuana Use on Human Cognition	Acute intoxication with marijuana affects memory, behavior, and impulsivity. The long-term effect of cannabis on cognition may be domain specific. Neuroimaging studies have shown structural changes in cannabis users; however, the results are inconsistent. Functional changes may be observed in areas of the brain involved in cognition among cannabis users. Early exposure to cannabis may have a negative effect on cognitive function.
Effects of Marijuana Use on Cerebrovascular Risk and Disease	Several studies have described an association between cannabis use and increased risk of stroke. Data from population survey studies indicate that the pattern (heavy vs less) and frequency (>10 d/mo) of cannabis use may increase the risk of stroke. Cigarette smoking is common in cannabis users and may be an important modifier or confounder of the relationship between cannabis use and stroke risk. Given the potential role of cannabis as a vasoactive substance and its potential role in cardiac pathology and atherosclerosis development, cannabis use also may increase stroke risk via reversible cerebral vasoconstriction syndromes or may indirectly increase stroke risk. It is possible that differences among some study findings may be attributable to the years in which population cohorts were studied or recruited because most population cohorts were assembled before 2012. Over the past decade, strains of cannabis have been evolving, resulting in plants with high THC concentrations and some preparations that may have synthetic cannabinoids such as Spice, which may influence the association of cannabis use with stroke.
Education and Future Directions	The cumulative evidence collected in clinical and preclinical studies suggests that the consumption of marijuana can have a detrimental effect on brain health. The exact ramifications, however, have not been precisely established. Emerging evidence questions the widely accepted belief that marijuana is innocuous and suggests that cannabis, particularly THC, negatively affects brain health through direct and indirect mechanisms. Health care professionals and consumers should receive education on the potential beneficial and harmful effects associated with the use of marijuana, including the increased risk of stroke and cognitive decline.

CBD indicates cannabidiol; PFC, prefrontal cortex; and THC, Δ^9-tetrahydrocannabinol.

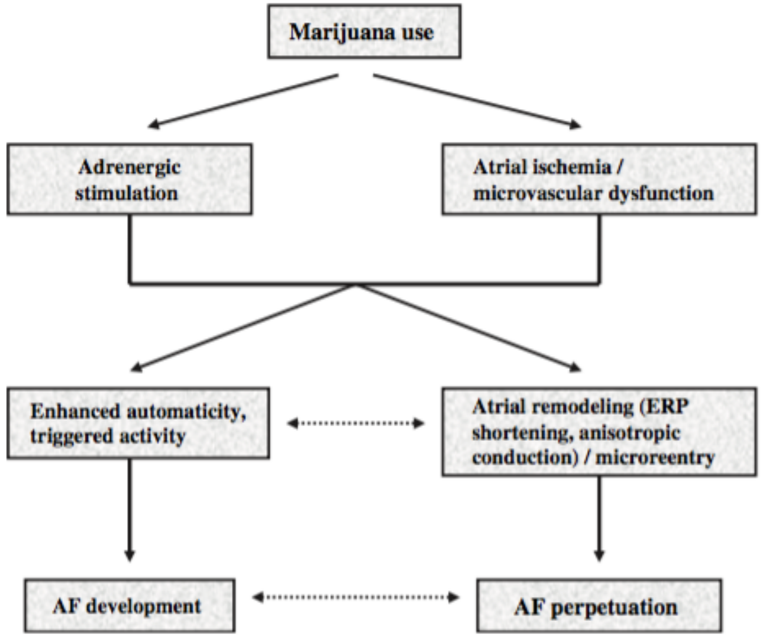
Author: Testai FD et al

PMID: 35142225

Marijuana

Nationwide Inpatient sample study using codes for marijuana use showed 17% relative risk, and concomitant tobacco use increased this to 31%. Another study using the Nationwide Inpatient Sample observed higher risk with odds ratio of 1.24. Another study using EHR showed (2015- 2017) found no association.

Proposed pathogenesis of marijuana-induced atrial fibrillation.



Marijuana

Reversible Vasoconstriction Syndrome

JVIN Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

Marijuana induced Reversible Cerebral Vasoconstriction Syndrome

Nnamdi Uhegwu, MD[1*], Asif Bashir, MD[1*], Mohammed Hussain, MD[1*], Haitham Dababneh, MD[1*], Sara Misthal, BA[1], and Aaron Cohen-Gadol, MD[2]

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Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a transient multifocal arterial vasoconstriction and dilatation. The term was proposed by a panel of experts[1] as a unifying term for a variety of a syndromes characterized by cerebral vasospasms and resultant clinical manifestations of cerebral ischemia. These syndromes include Call–Fleming syndrome, drug-induced cerebral angiopathy, benign angiopathy of the CNS, postpartum cerebral angiopathy, and migrainous vasospasm. Drug abuse, especially cannabis, is an important etiologic factor for RCVS. It is one of the most widely used recreational substances in the world, considered by many consumers as a relatively safe drug with few significant side-effects.[2] Cannabis contains 9-tetrahydrocannabinol (THC), which is rapidly absorbed when smoked, reaching a peak plasma concentration at 10–30 min, and is lipid soluble with a large volume of distribution.[3] Cannabinoids bind to cannabinoid receptors, CB1 in the central nervous system and CB2 in the immune system.

On admission, the patient was started on aspirin and received physical therapy. He showed marked improvement with mild residual dysarthria. The patient continued to improve and was discharged on Hospital Day 4 with a National Institutes of Health Stroke Scale of 0. A repeat CT angiography at discharge showed patent cerebral vasculature with improved flow in the bilateral higher convexities (Figure 3).

Discussion

Cardiovascular side effects of marijuana have been documented, including tachycardia, hypertension, postural hypotension, and increased levels of carboxyhemoglogin.[4] There have been several reports of stroke following cannabis use.[5] Since 1987, fewer than 25 cases of ischemic stroke associated with cannabis smoking have been published.[6–8] Postulated mechanisms for such stroke include cerebral vasospasm,[9–11] vasculitis, and postural hypotension with impairment in cerebral autoregulation of the brain blood flow.[8, 12]

Author: Uhegwu N et al

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[CASE REPORT]

Marijuana-related Reversible Cerebral Vasoconstriction Syndrome

Takahisa Mikami[1,2], Reiichiro Obata[1], Daniel I. Steinberg[1], Maryna Skliut[3] and Irene Boniece[3]

Abstract:

The legalization of recreational marijuana in some countries has been accompanied by an increased number of case reports of serious cardiovascular and cerebrovascular complications. However, there have been few studies describing the detailed clinical course of reversible cerebral vasospasm syndrome (RCVS) associated with marijuana use. We herein report a unique case of recurrent bi-fronto-parietal subcortical (watershed) infarction in the setting of chronic daily marijuana use for several years, with evidence of bilateral anterior cerebral artery vasoconstriction. The quick resolution of symptoms with treatment and the normalization of cerebral vasoconstriction on follow-up imaging lend high certainty to the diagnosis of RCVS.

Key words: RCVS, cannabinoid, marijuana

(Intern Med 60: 795-798, 2021)
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UPSTATE UNIVERSITY HOSPITAL

Author: Mikami T et al

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Reversible Vasoconstriction Syndrome

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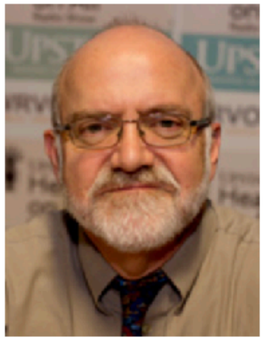
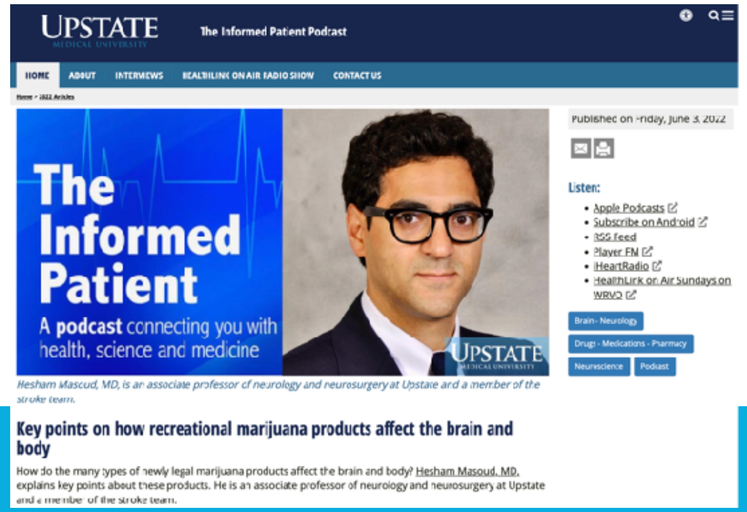
Radio for informed Patient Counseling on Marijuana

Production Team

The host is Amber Smith, a veteran medical journalist who covered Upstate Medical University during her tenure at Syracuse's daily newspaper, The Post-Standard. Early in her career she worked as a volunteer paramedic. Later, she earned a master's degree in health services management and policy. She taught newswriting and reporting at Syracuse University's Newhouse School. She also edits Upstate's consumer health magazines, Upstate Health and Cancer Care. Reach her at smithamb@upstate.edu.

Producer Jim Howe draws on decades of experience in newspaper reporting and editing as he organizes "The Informed Patient" interviews and programming for "HealthLink on Air." He has a master's degree in journalism from Syracuse University, and he previously worked in a number of editing roles at the Syracuse Post-Standard. At Upstate, he writes about a variety of topics for the quarterly magazines, Upstate Health and Cancer Care. Reach him at howeja@upstate.edu.





For patient info on Marijuana and Brain Health

https://www.upstate.edu/informed/2022/052322-masoud-podcast.php

UPSTATE UNIVERSITY HOSPITAL

Thanks.