Cannabis Use in Teenagers

The Importance of Preventing Cannabis Use in Teenagers

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Opioid Response Network

F.A.C.E. COALITION
Family Assistance & Community Empowerment Coalition

Working with communities.

- The SAMHSA-funded *Opioid Response Network (ORN)* assists states, organizations and individuals by providing the resources and technical assistance they need locally to address the opioid crisis and stimulant use.
- Technical assistance is available to support the evidence-based prevention, treatment and recovery of opioid use disorders and stimulant use disorders.

Funding for this initiative was made possible (in part) by grant no. 1H79TI083343 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Working with communities.

- The *Opioid Response Network (ORN)* provides local, experienced consultants in prevention, treatment and recovery to communities and organizations to help address this opioid crisis and stimulant use.
- *ORN* accepts requests for education and training.
- Each state/territory has a designated team, led by a regional Technology Transfer Specialist (TTS), who is an expert in implementing evidence-based practices.

Contact the Opioid Response Network

- To ask questions or submit a request for technical assistance:
  - Visit www.OpioidResponseNetwork.org
  - Email orn@aaap.org
  - Call 401-270-5900

Objectives

- Review the prevalence of adolescent use of cannabis
- Explore risk factors for adolescent cannabis use
- Discuss diagnosis of adolescent substance use
- Explore potential developmental, cognitive, psychiatric, and health consequences of cannabis use
- Review potential treatments for cannabis use
- Learn how to help prevent harmful substance use

ASAM Definition of Addiction

"a *treatable*, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's *life experiences*. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences"

- ASAM, Quality Care: Definition of Addiction. https://www.asam.org/quality-care/definition-of-addiction

Setting some ”ground rules”

INSTEAD OF…	TRY PERSON-FIRST LANGUAGE
Drug Abuse	Substance use disorder, addiction
Abuser, addict, junkie, alcoholic	Person with a substance use disorder
Clean	Abstinent, not using Negative test
Dirty	Actively using Positive test
Addicted baby	Baby with Neonatal Abstinence (or Opioid Withdrawal) Syndrome
Medication-Assisted Treatment	Medication or treatment for (substance) use disorder


Epidemiologic Trends


Source:
Medium

Question

Are teens using more or less marijuana now, than 30 – 40 years ago?

A. More
B. Less

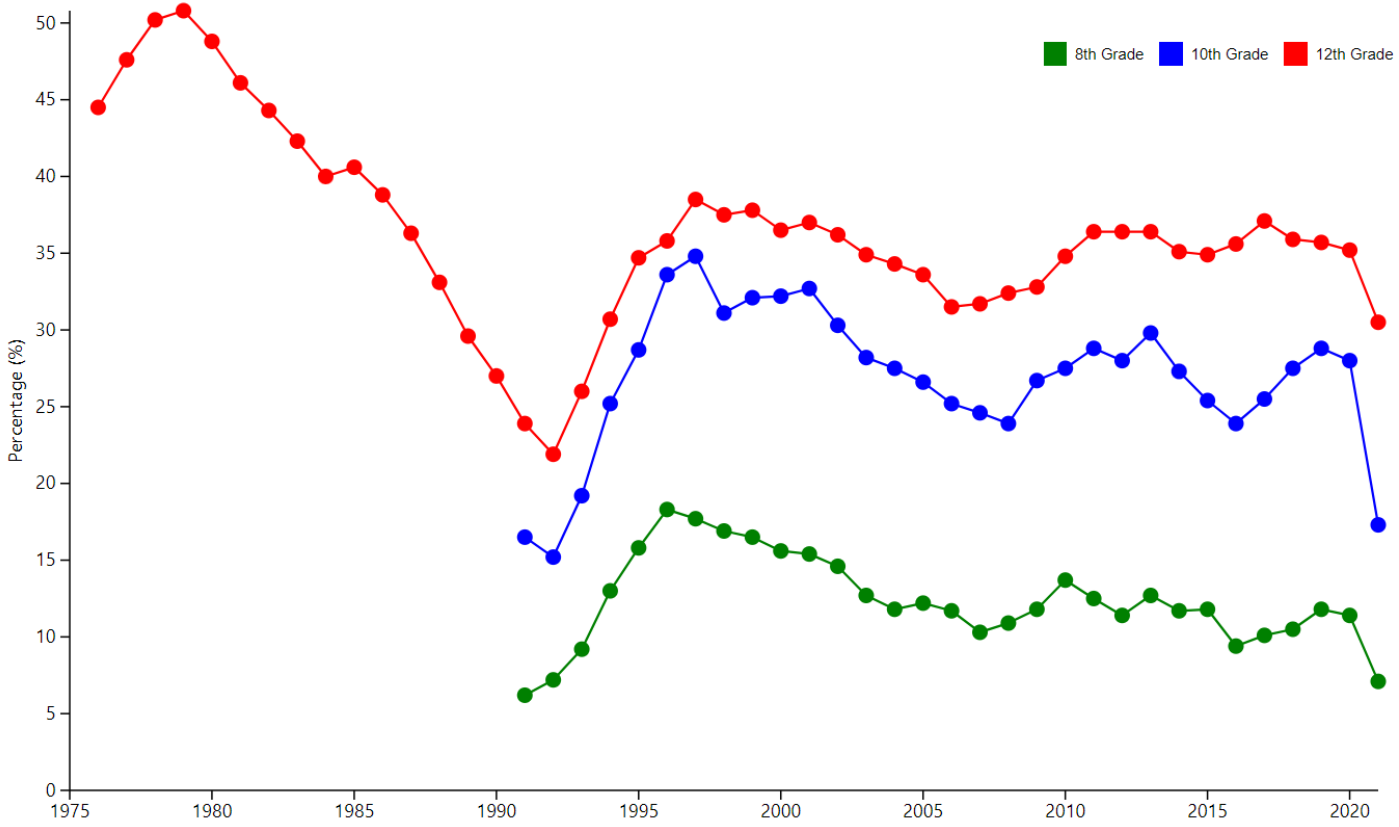
Are teens using more or less marijuana now, than 30 – 40 years ago?

A. More

B. Less

C. Actually about the same

Marijuana: Trends in Prevalence of 12 Month Use in 8th, 10th, and 12th Grade

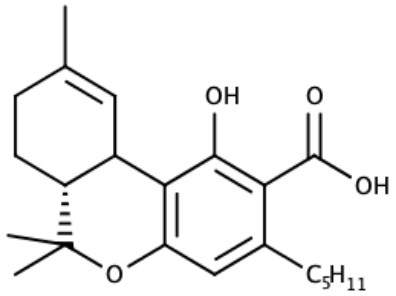


Source: Marijuana (monitoringthefuture.org)

Cannabinoids

Tetrahydrocannabinol (THC)

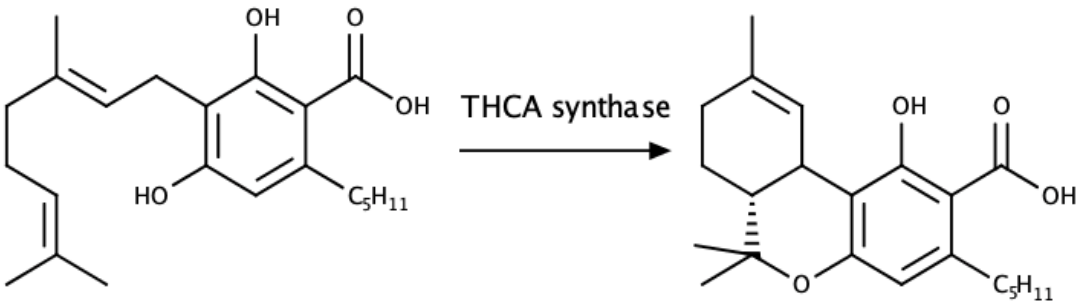
Biochemical Pathway



THCA

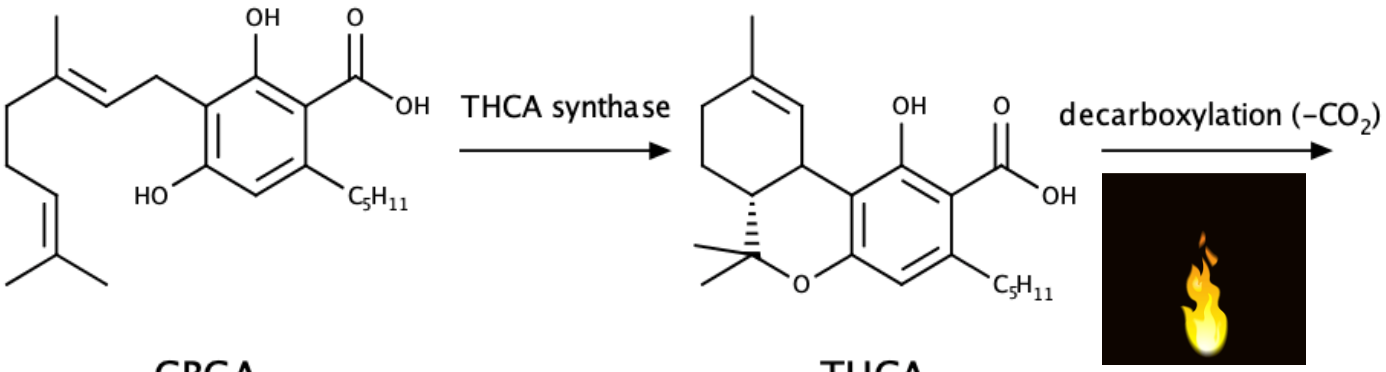
Tetrahydrocannabinolic acid

Biochemical Pathway



CBGA	THCA
Cannabigerolic acid	Tetrahydrocannabinolic acid

Biochemical Pathway



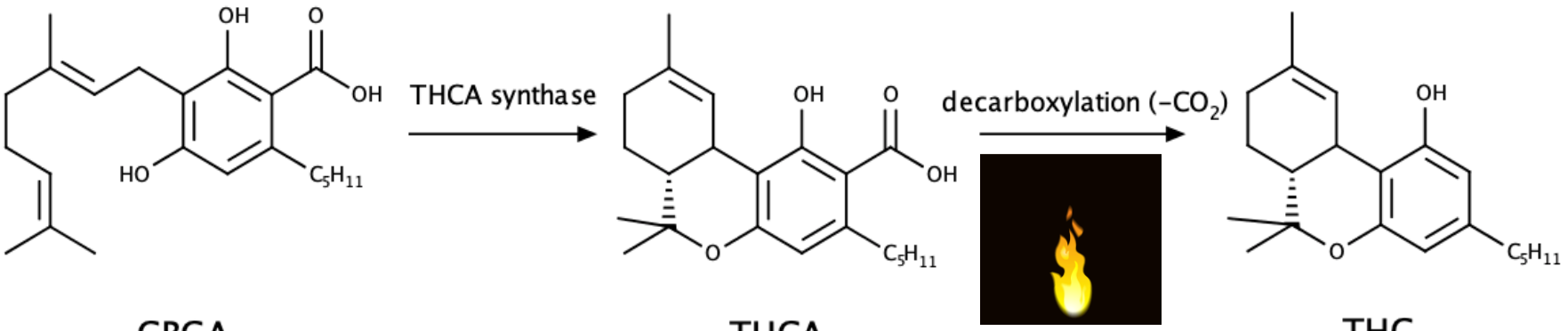
CBGA

Cannabigerolic acid

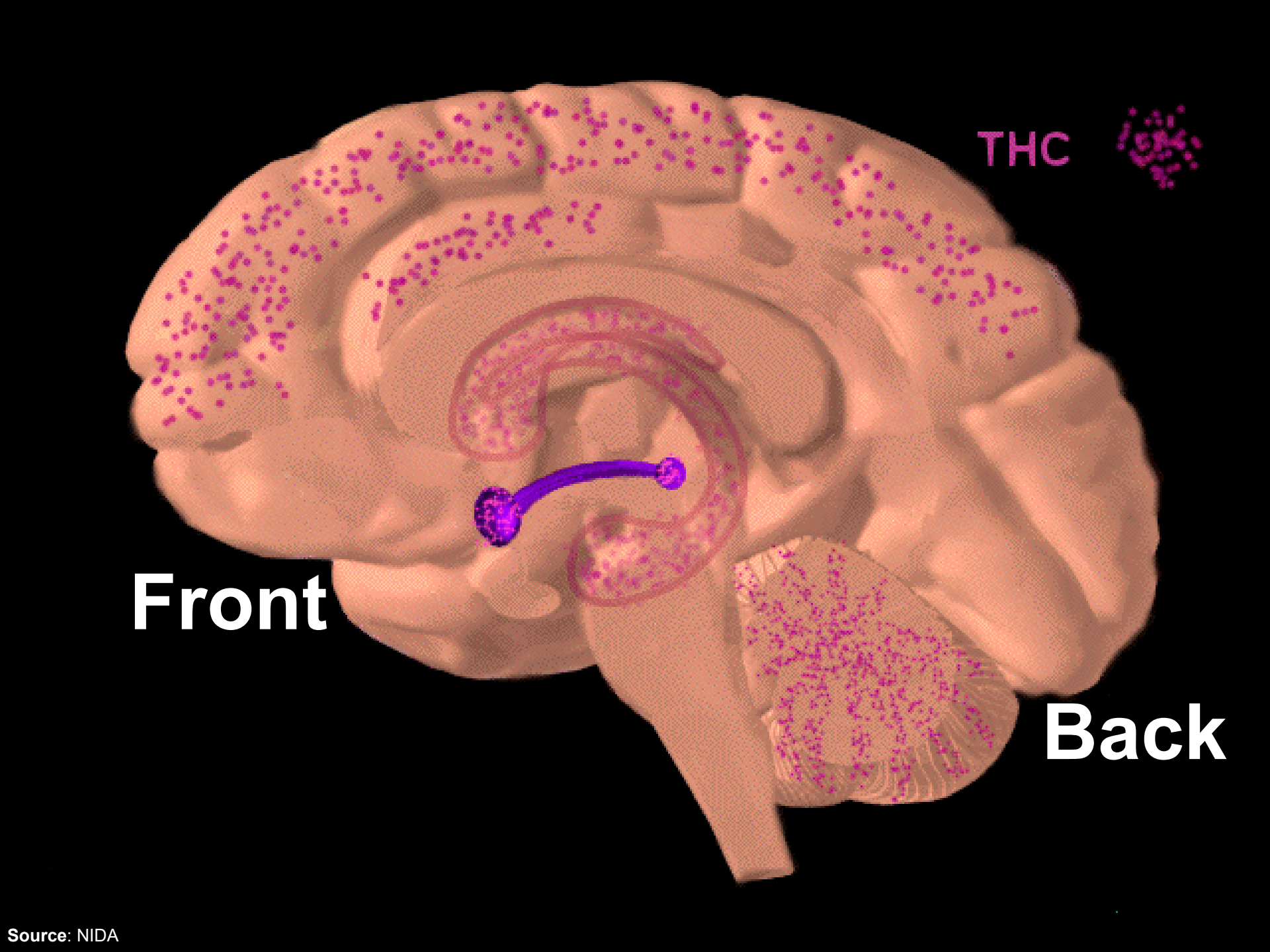
THCA

Tetrahydrocannabinolic acid

Biochemical Pathway

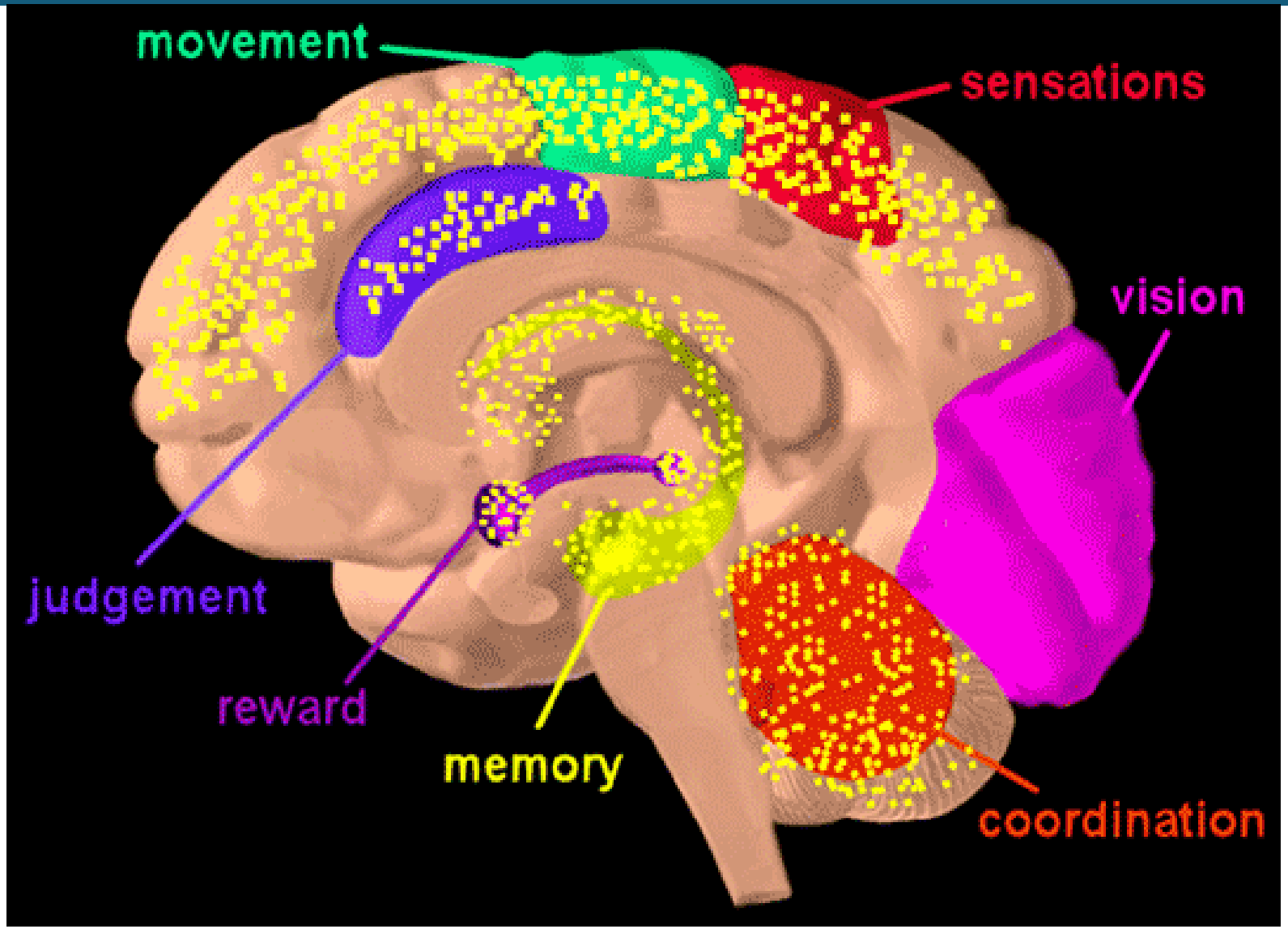


CBGA	THCA	THC
Cannabigerolic acid	Tetrahydrocannabinolic acid	Tetrahydrocannabinol



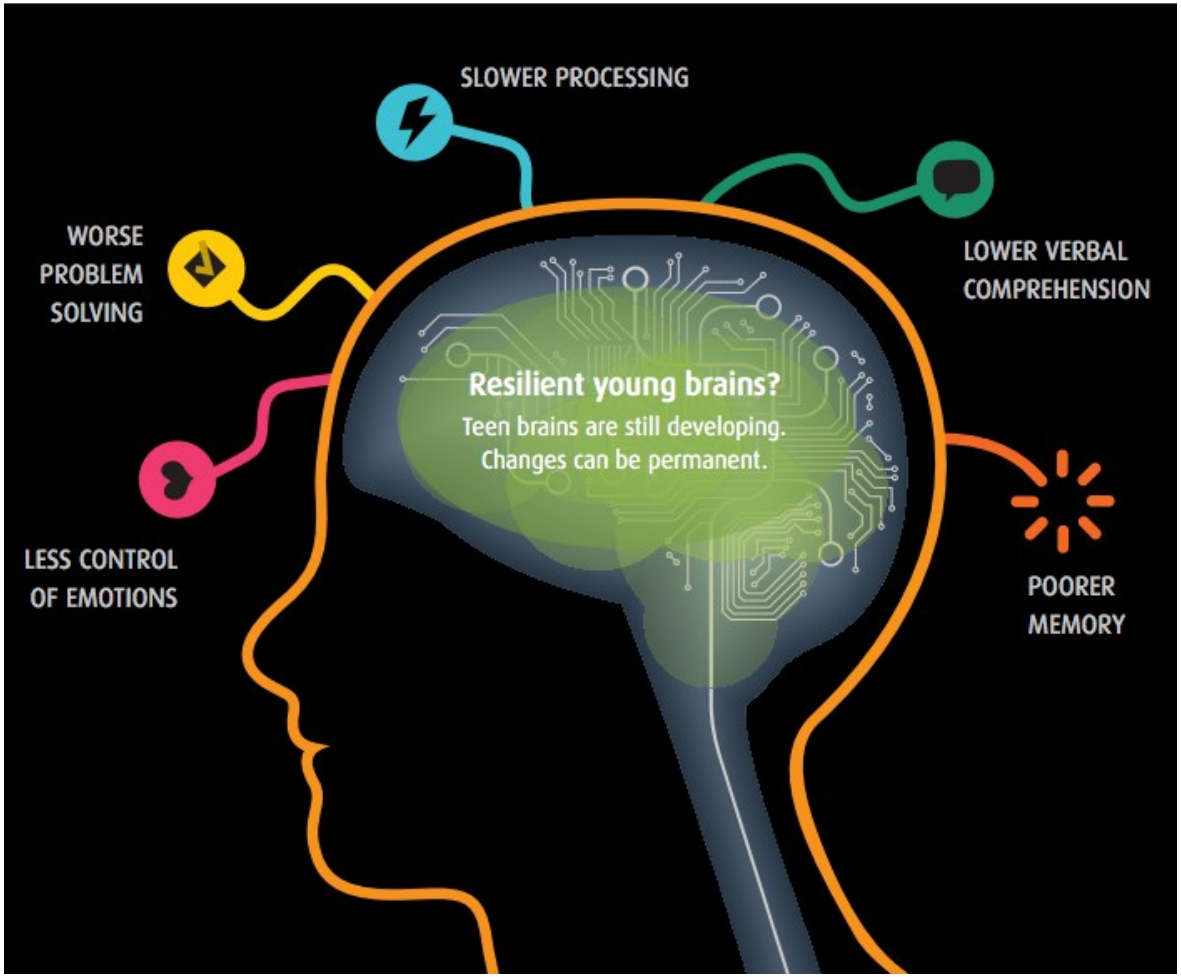
Source: NIDA

Marijuana affects on the brain



NIDA, “marijuana (Marijuana) DrugFacts”, 2019. https://nida.nih.gov/publications/drugfacts/marijuana-marijuana

Long-term risks of marijuana use



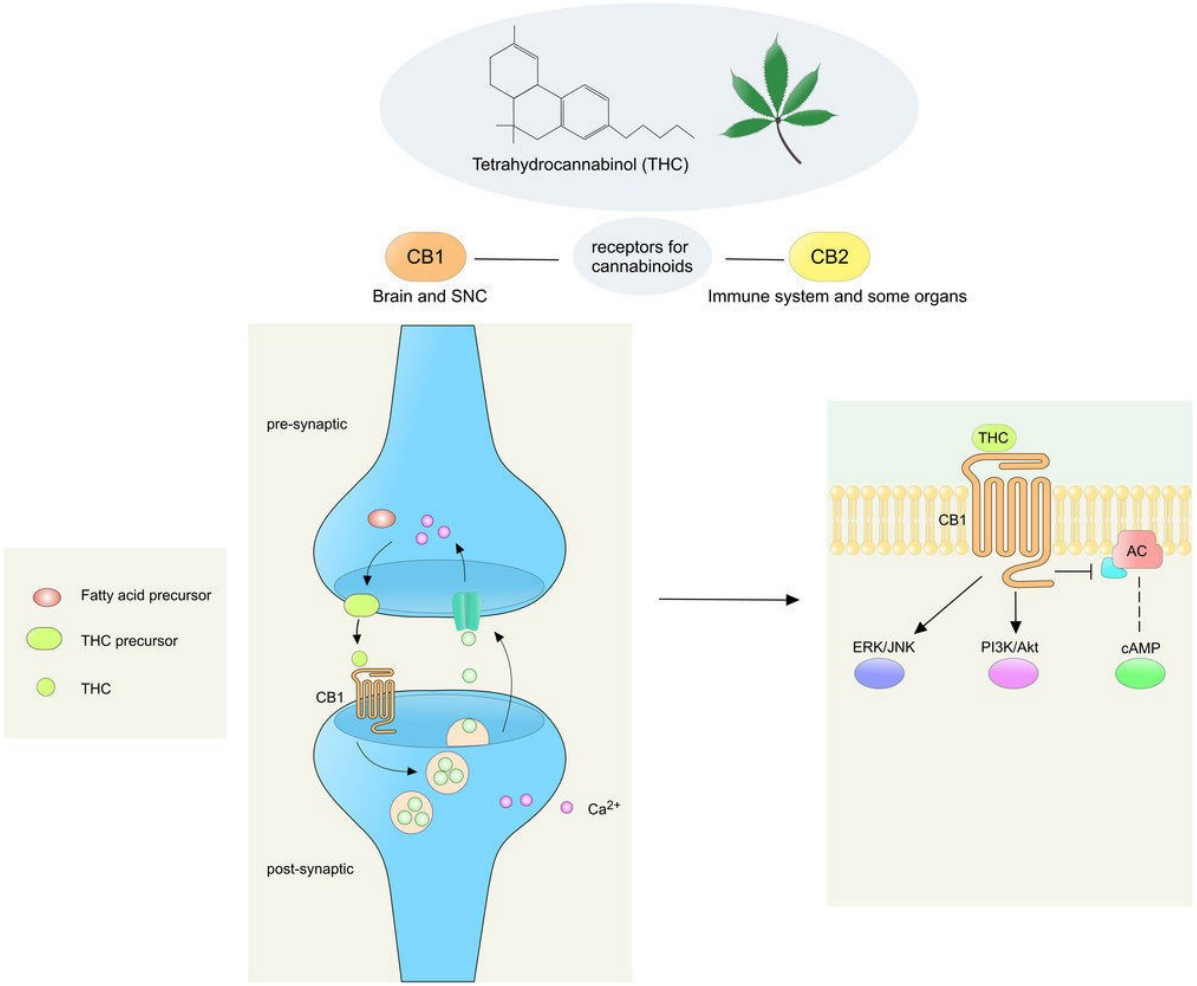
West Baltimore Drug Free Community Coalition; https://getsmartdfc.com/

- Cognitive & executive function impairment[1,2]
- Changes to the brain[3]
- Decreased IQ[4]
- Diminished school achievement
- Addiction
- Increased risk of psychosis disorders
- Depression, suicidality

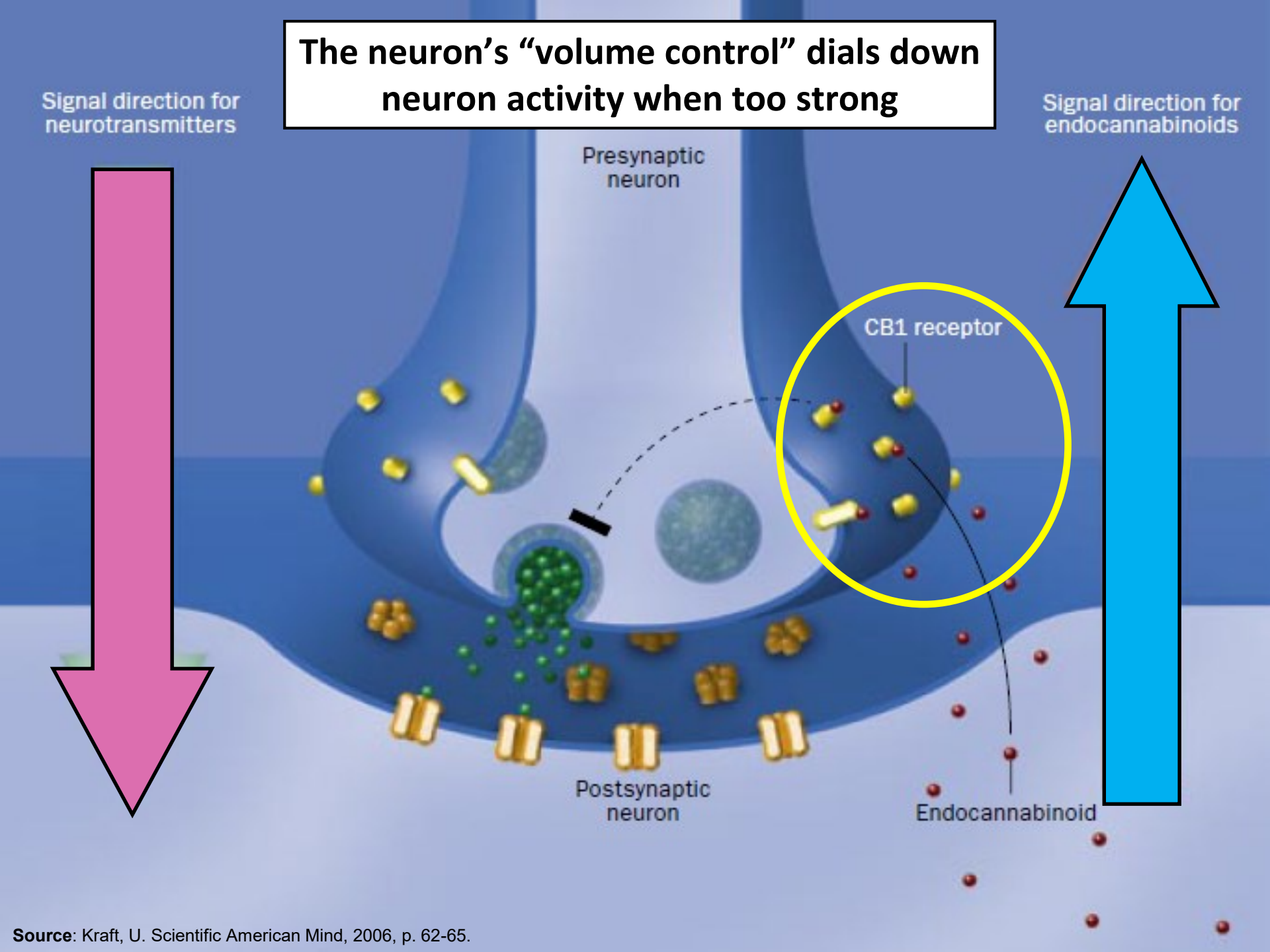
Volkow et al., *N Engl J Med,* 2014.

1. Batella et al., *PloS One,* 2013. 2. Filbey et al., *Proc Natl Acad Sci USA,* 2014. 3. Pagliaccio et al., *JAMA Psychiatry* 2015. 4. Meier et al., *Am J of Psychiatry*, 2022.

Endocannabinoid System



The neuron's "volume control" dials down neuron activity when too strong



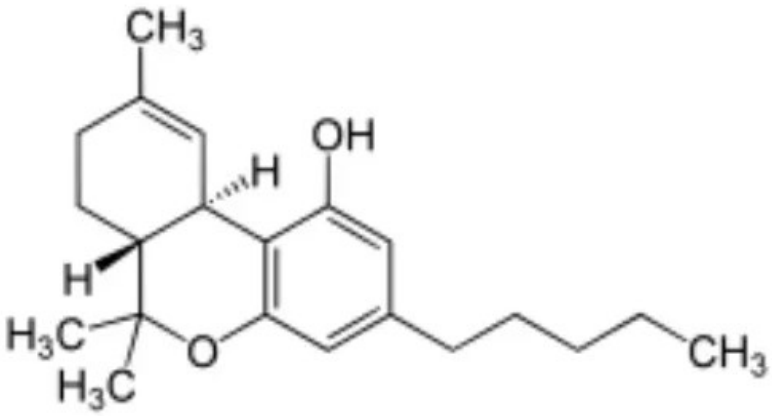
Source: Kraft, U. Scientific American Mind, 2006, p. 62-65.

Endogenous
Endocannabinoids

2-arachidonylglycerol

Anandamide

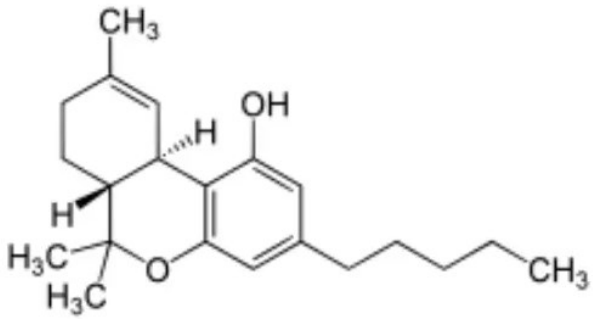
Phytocannabinoid



THC

Endocannabinoids +
Phytocannabinoid

[redacted]



2-arachidonylglycerol

Anandamide

THC

Lock & Key

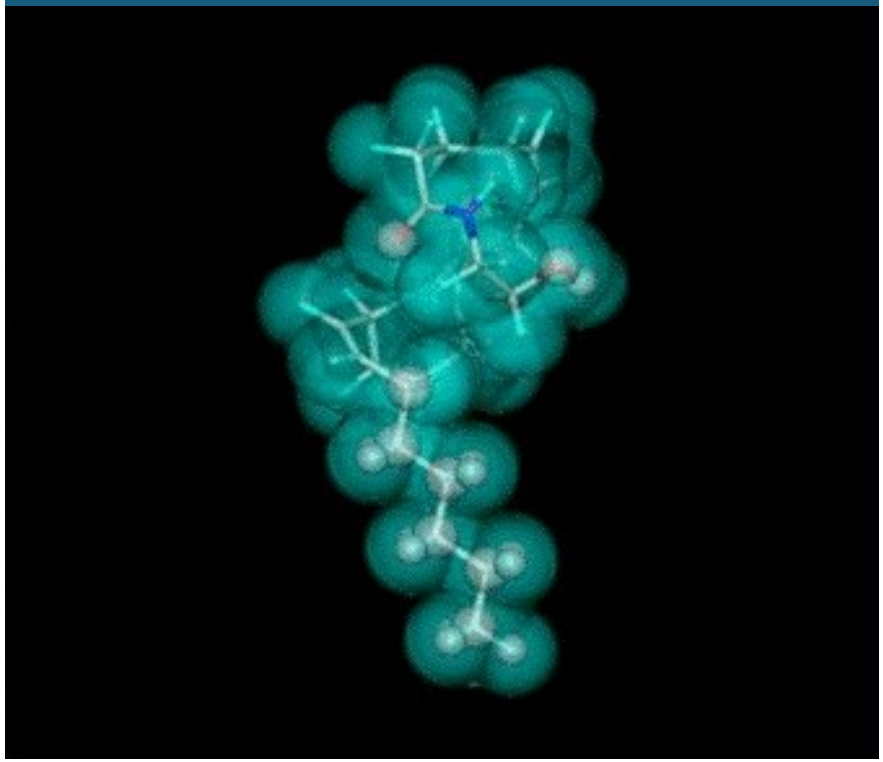
Cannabinoid

- Endocannabinoids
  - AEA, 2-AG, etc.
- Phytocannabinoids
  - THC, CBD, etc.
- Synthetics
  - Nabilone, (-)CP55940, WIN 55,212-2, etc.

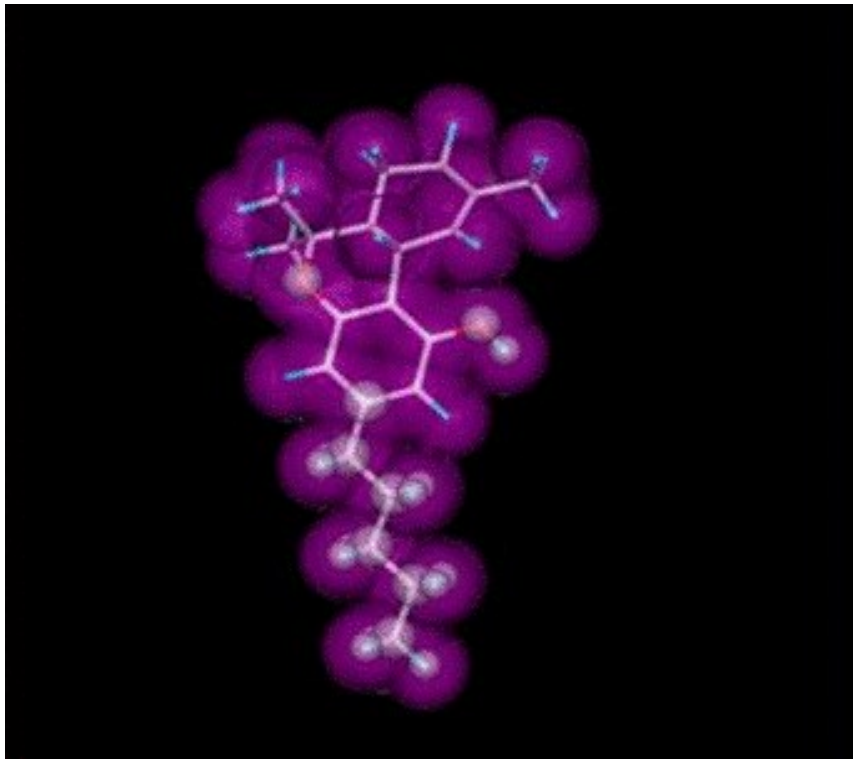
Cannabinoid Receptor

- CB1, CB2
- Non-cannabinoid receptors
  - GPR55, GPR18, GPR119, TRPV1, etc.

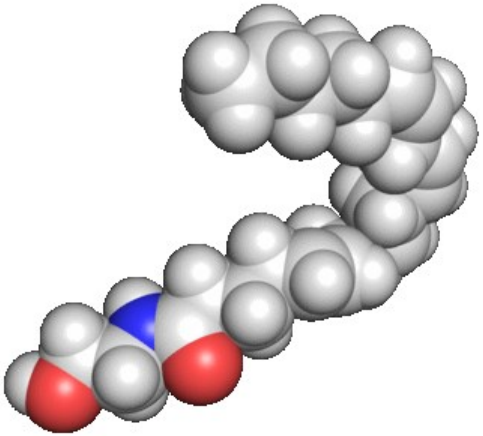
Anandamide



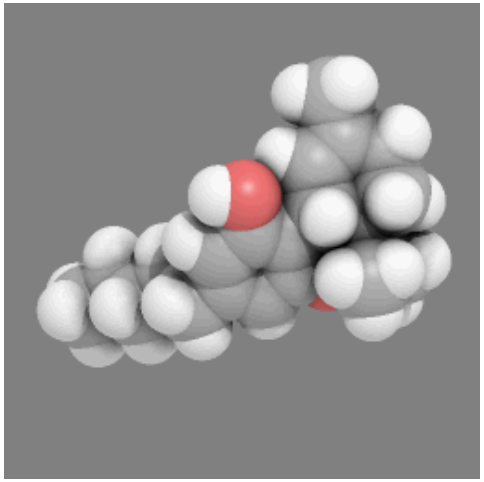
THC



Keys Look alike



Anandamide



THC

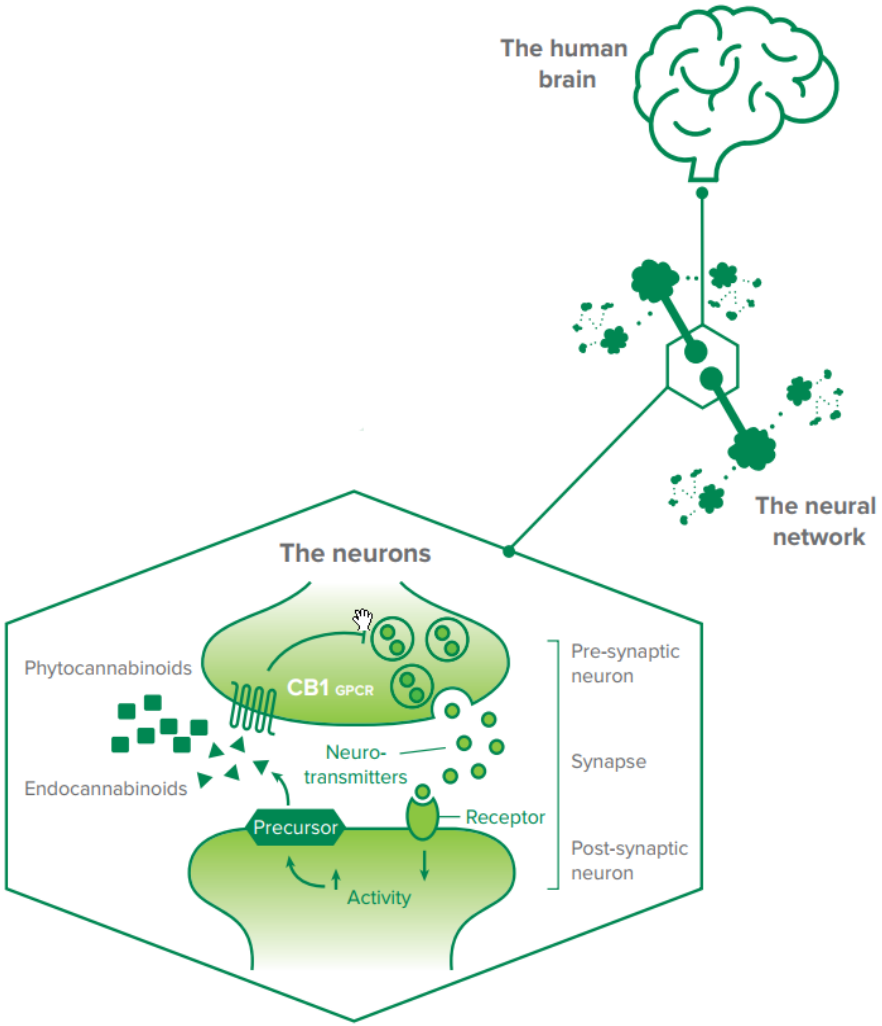
Receptor binding in brain tissue

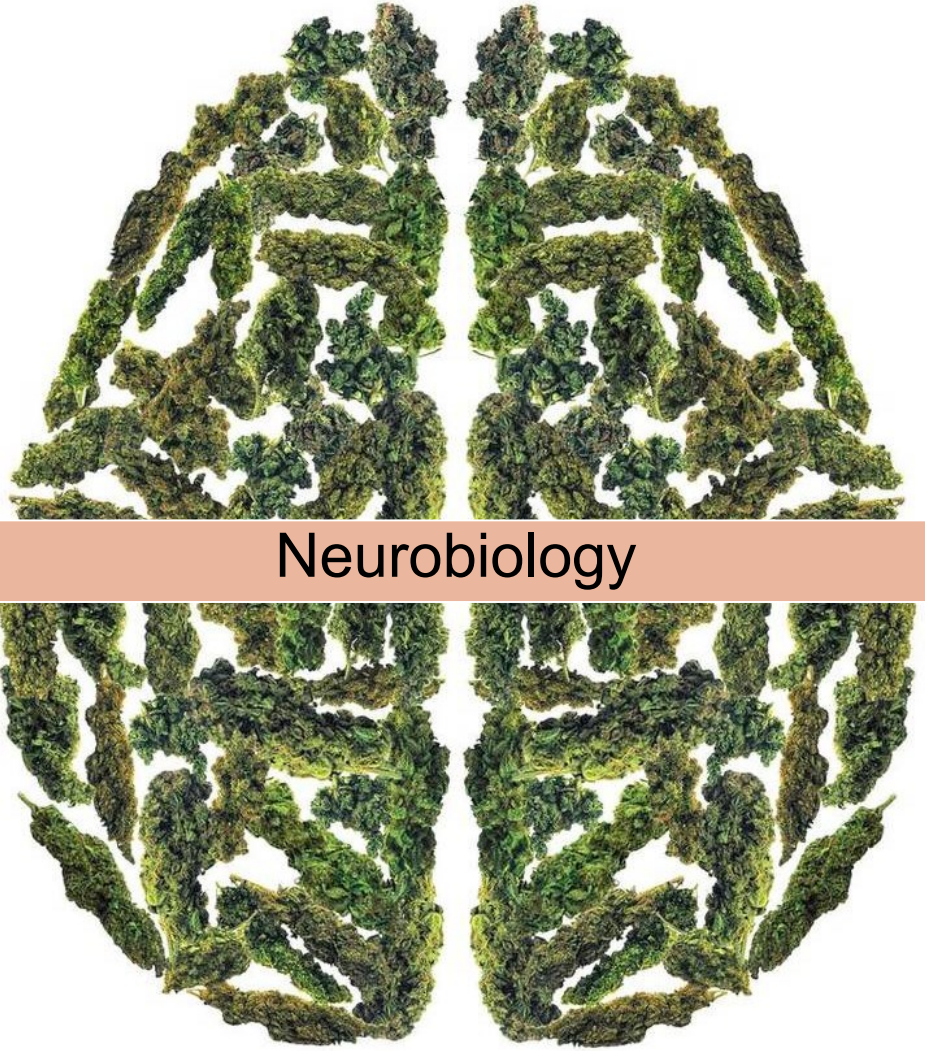
Compound	Potency relative to THC
(-)-Delta9-THC	1
Anandamide	.47*

*The affinity of anandamide for cannabinoid receptors ranges from about one-fourth to one-half that of THC. The differences depend on the cells or tissue that are tested and on the experimental conditions, such as the binding assay used.

Source: Joy J, Watson SJ, Benson JJ, eds. Cannabinoids and animal physiology. In: *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: Division of Neuroscience and Behavioral Health - Institute of Medicine. National Academies Press; 1999:288

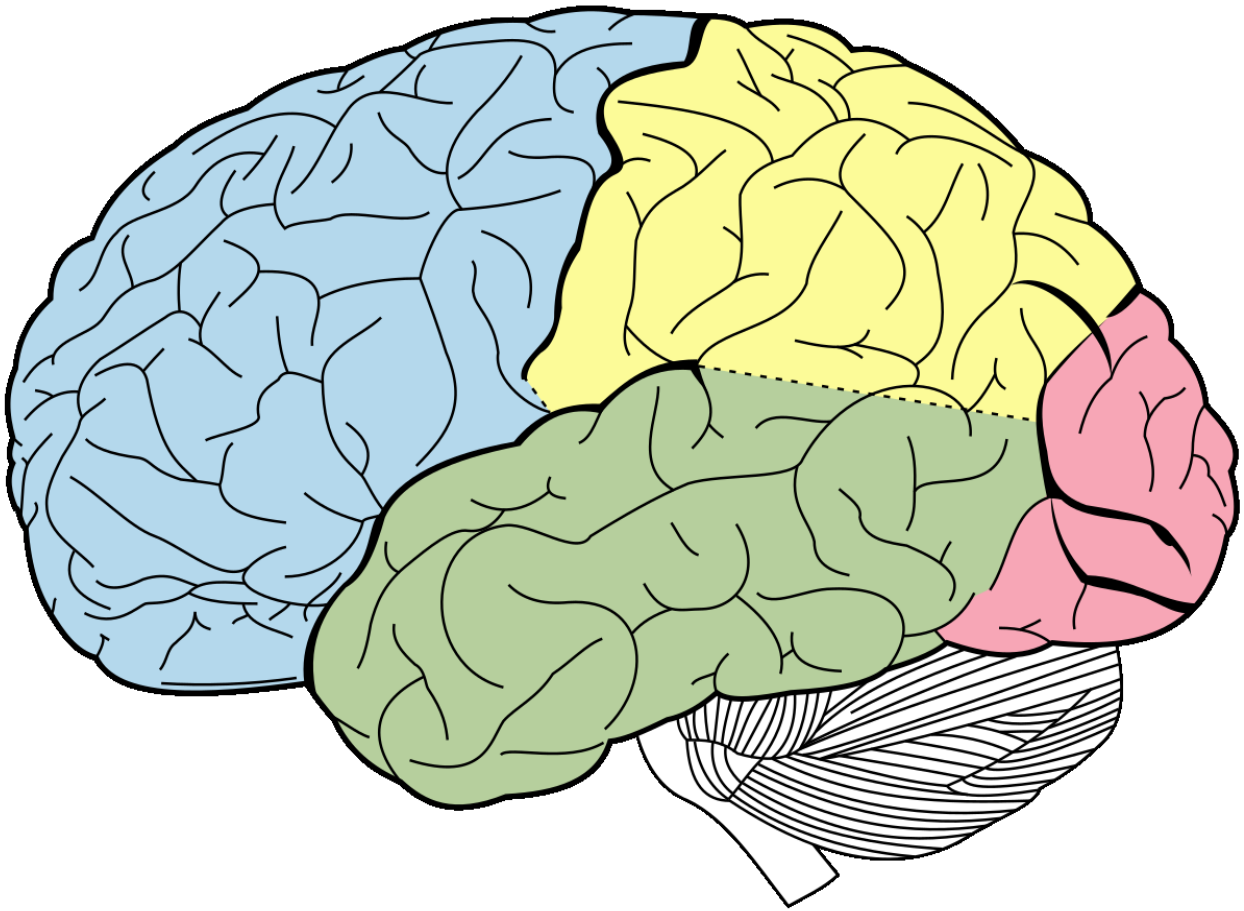
Keys Look alike



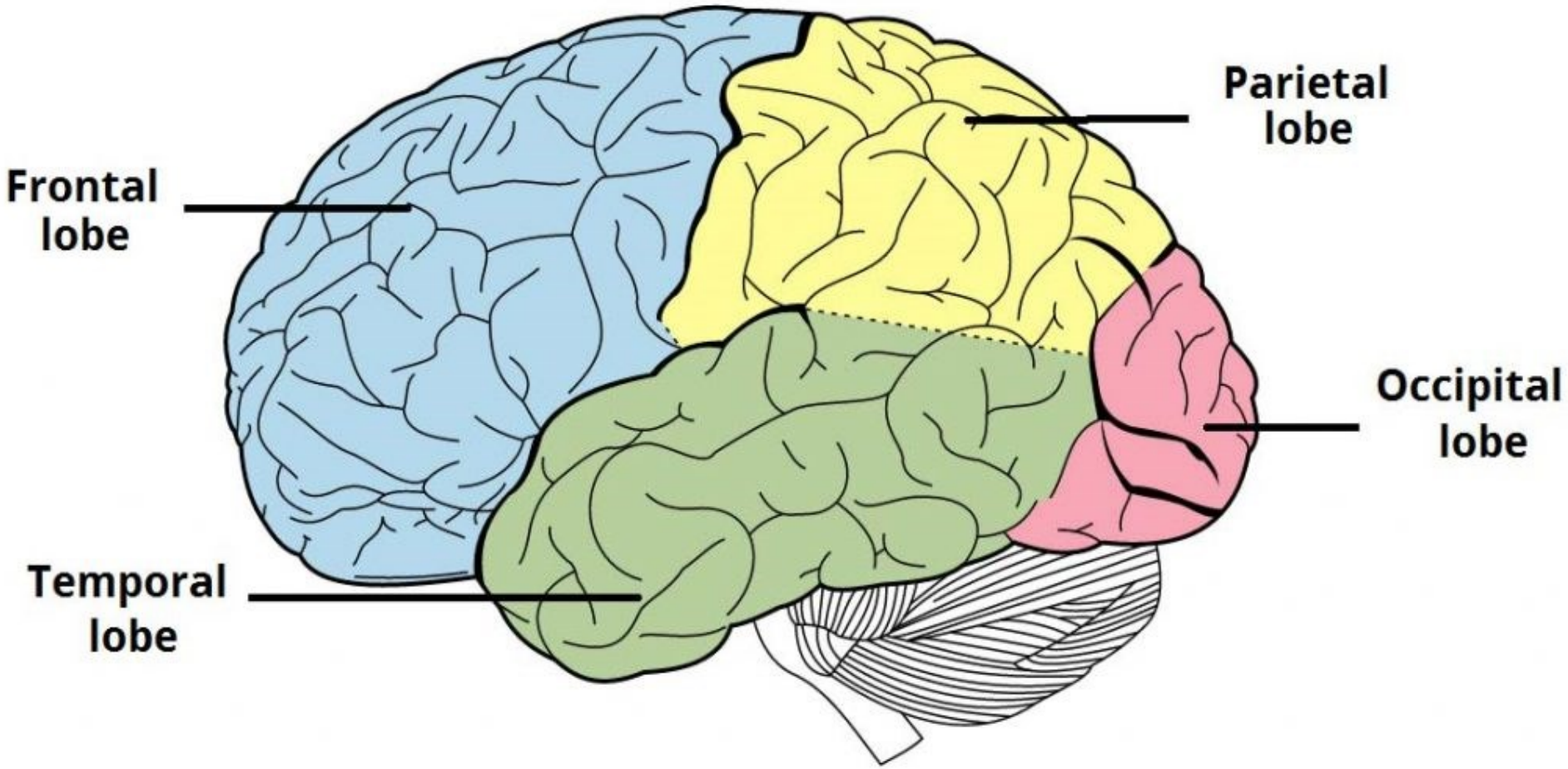


Neurobiology

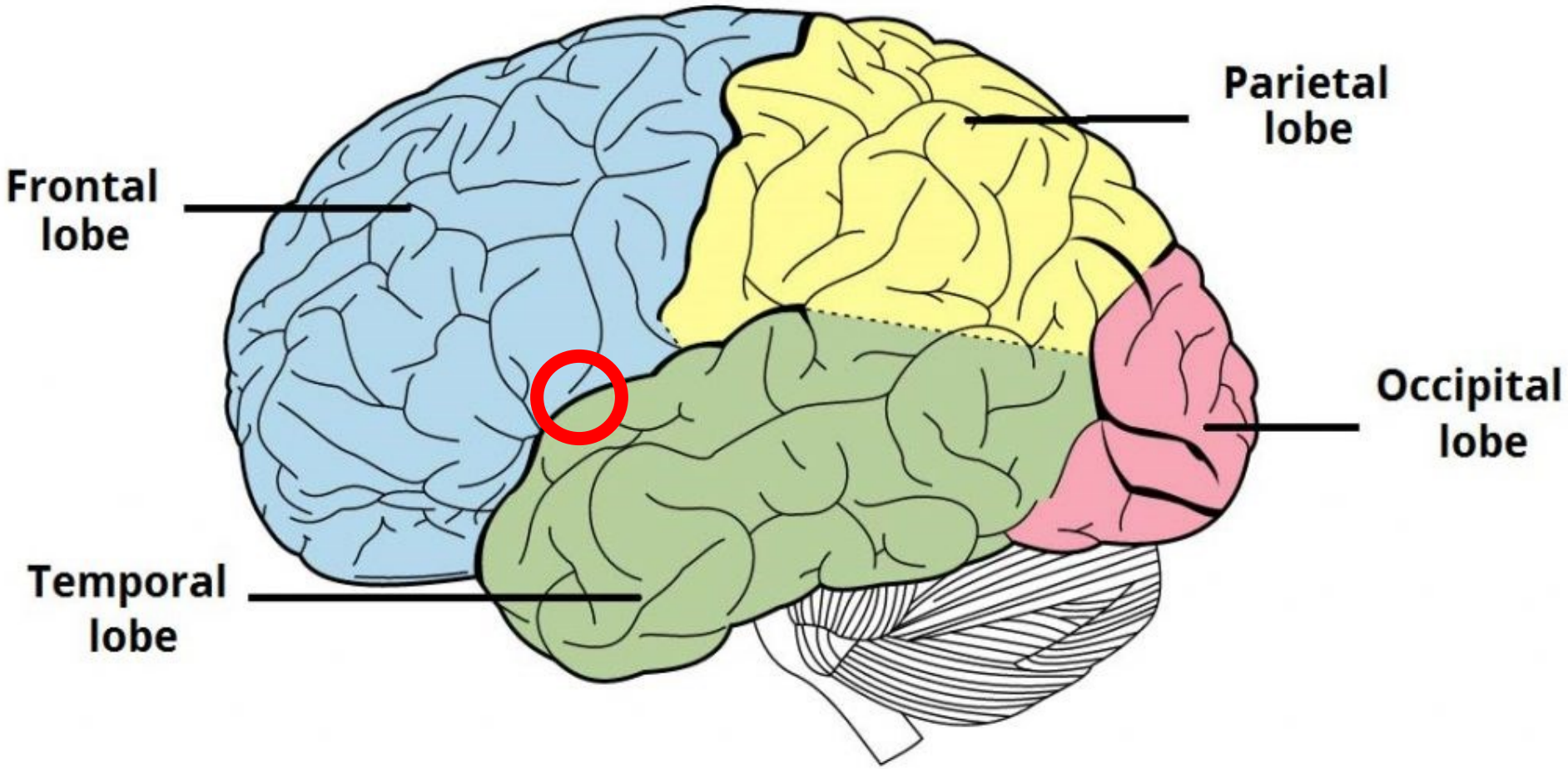
Brain



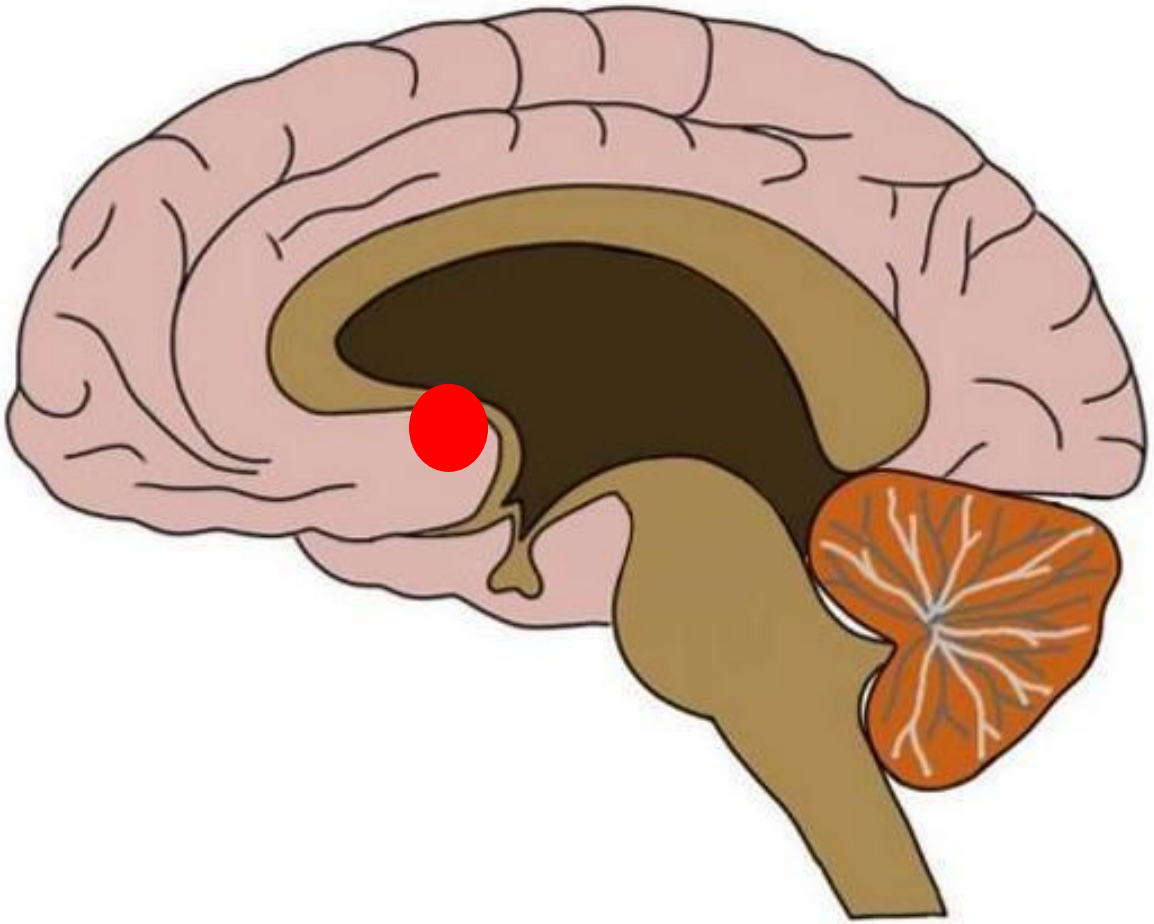
Brain – Labeled



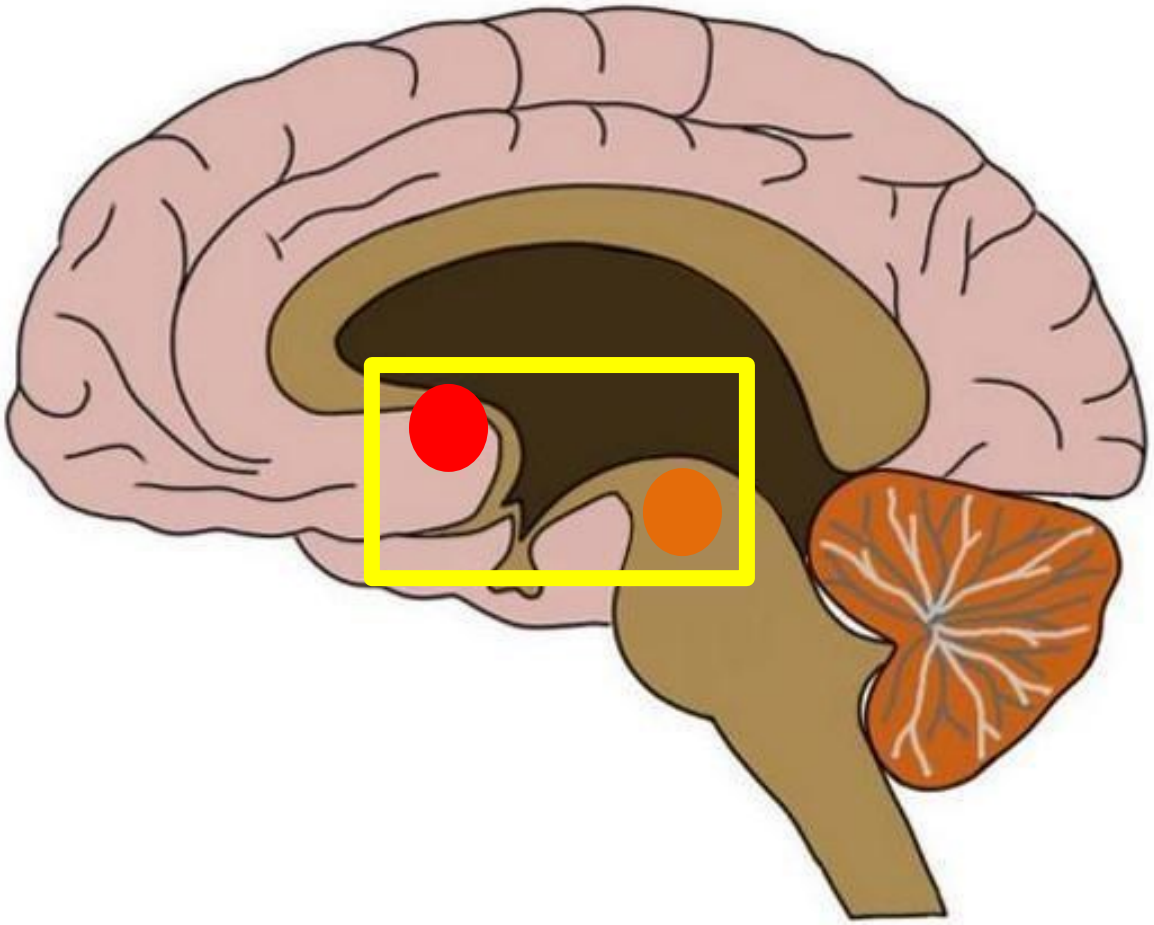
Brain – Lobes Labeled



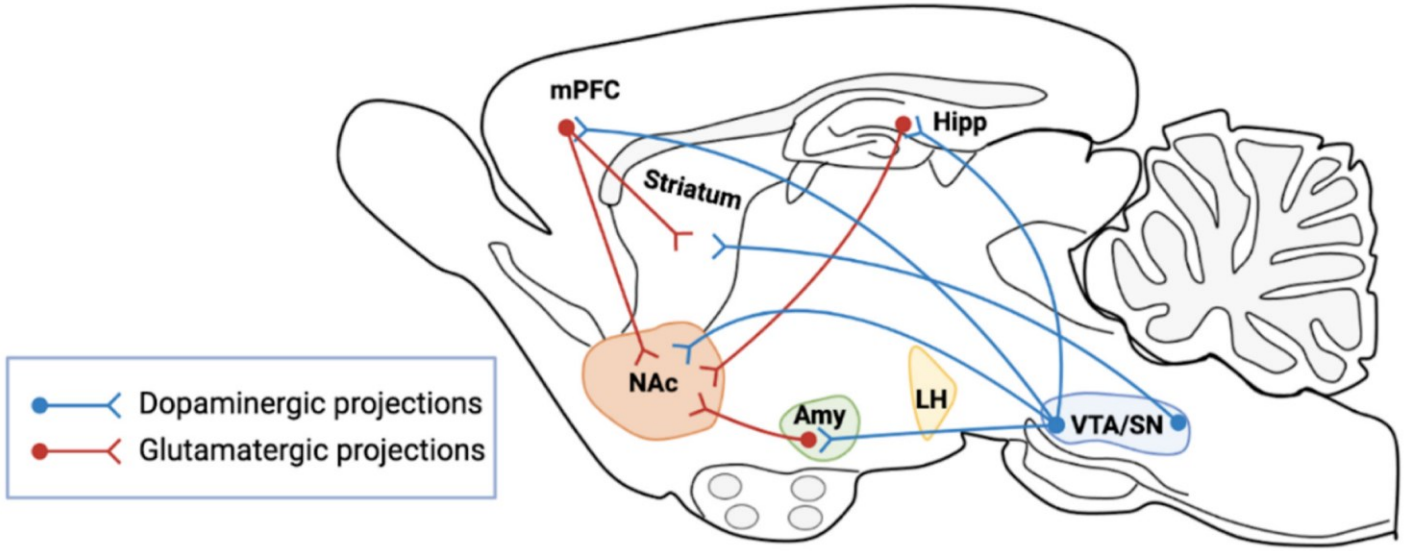
Brain – NAcc



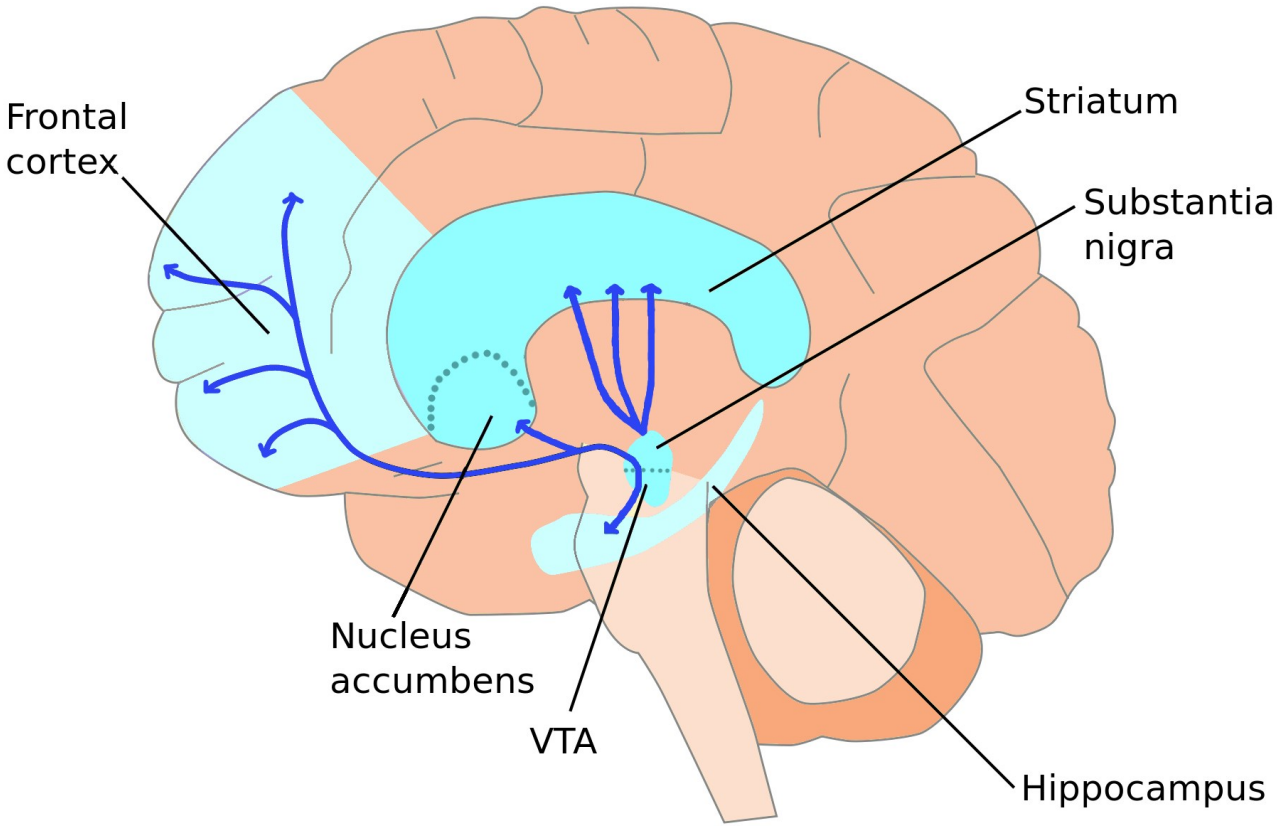
Brain – NAcc + VTA



Reward Pathway – Zoom In



Reward Pathway – Zoom Out



Activation of the reward pathway by addictive drugs

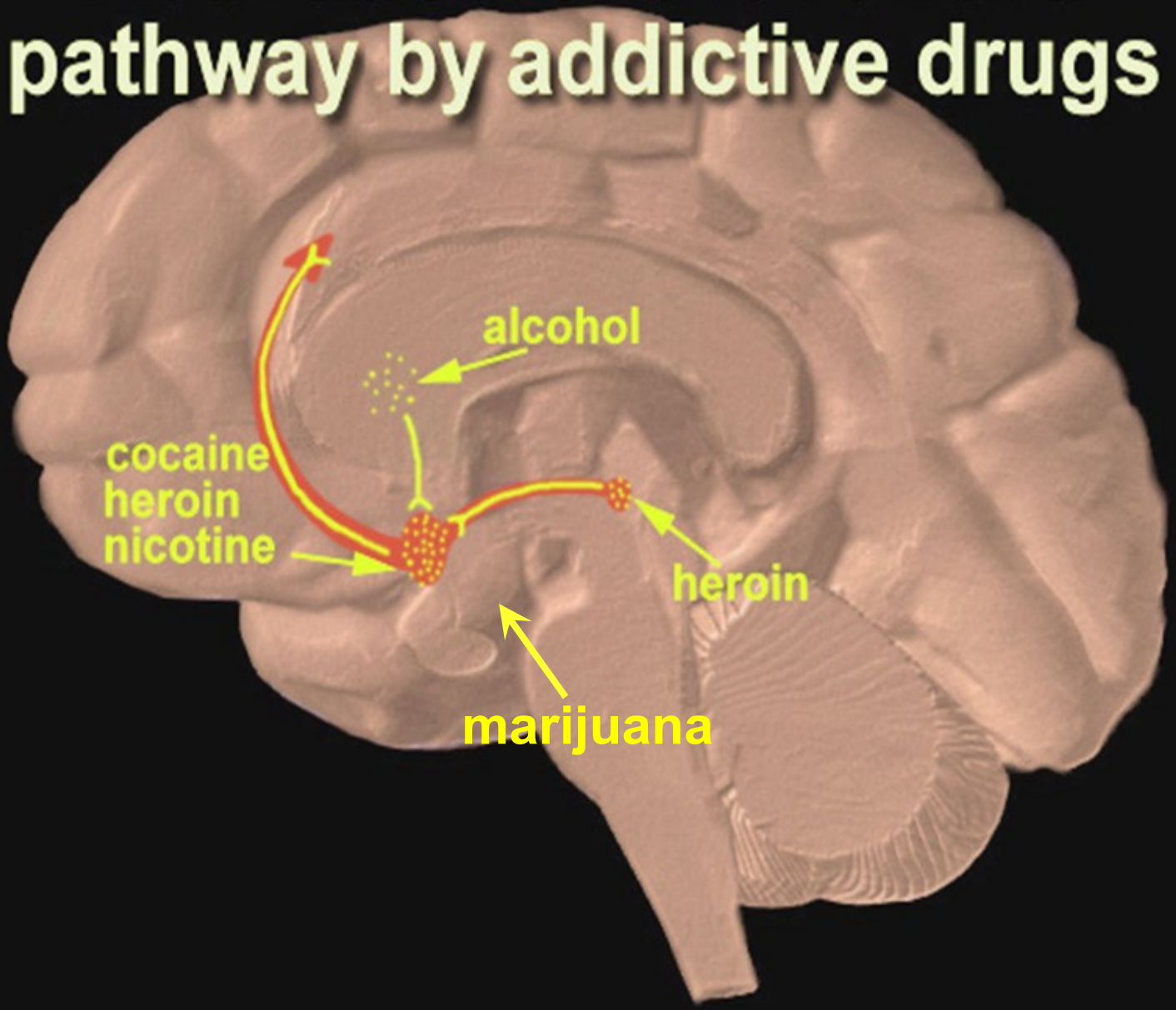


Image retrieved on February 17, 2015, from http://www.drugabuse.gov/publications/teaching-packets/neurobiology-drug-addiction/section-iv-action-cocaine/7-summary-addictive-drugs-activate-reward

Brain Development

Neuron growth in brain development

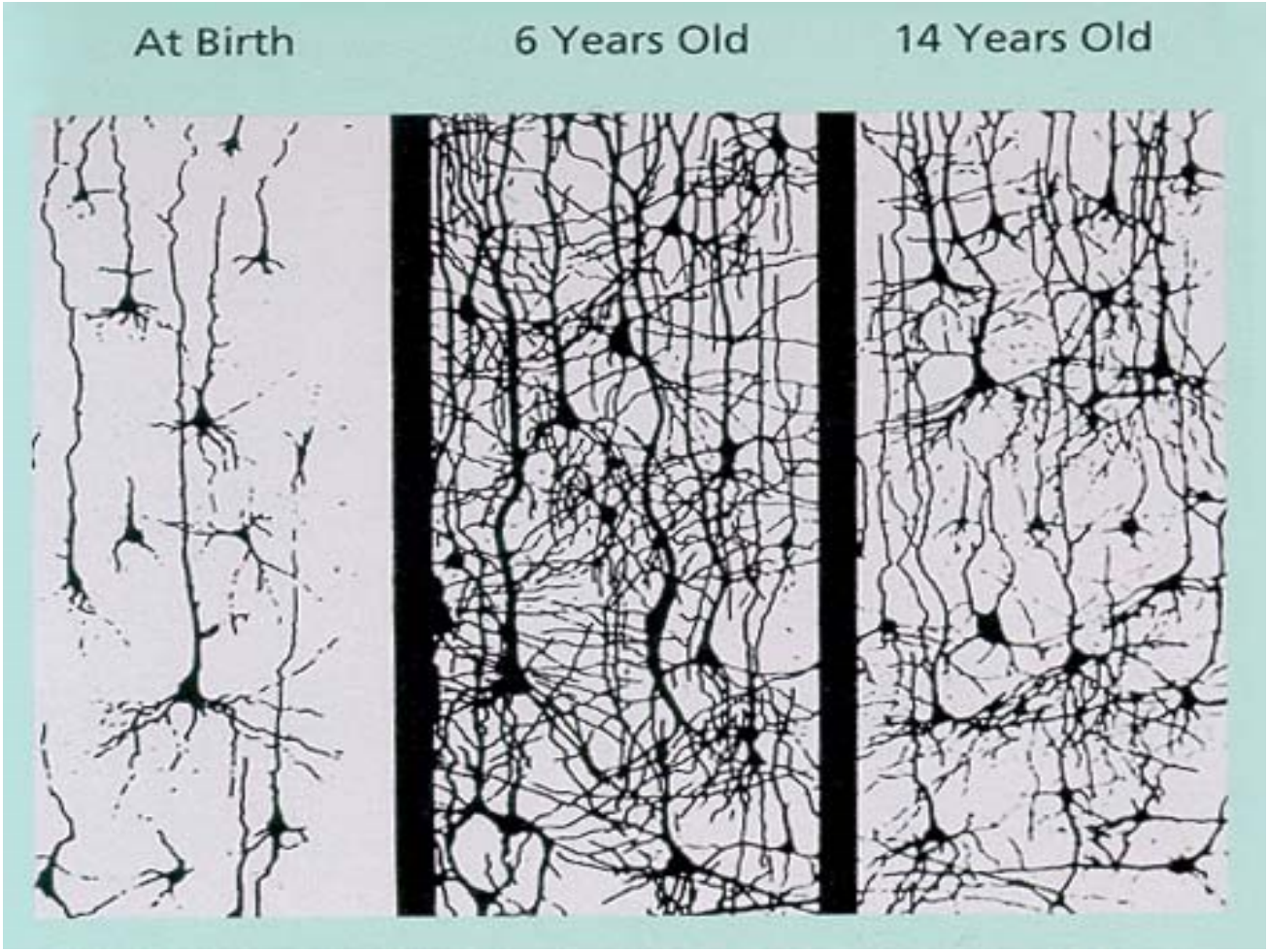
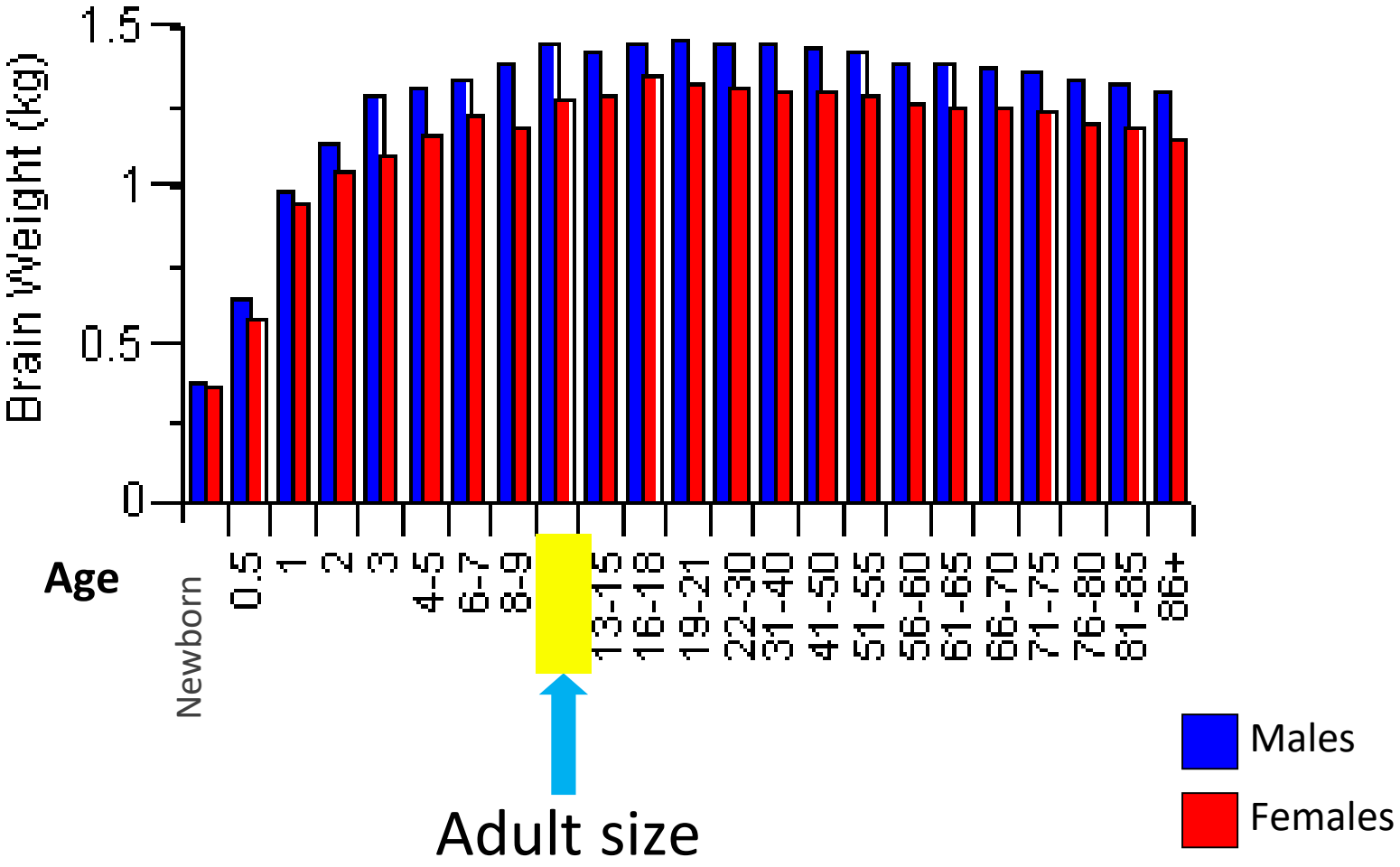


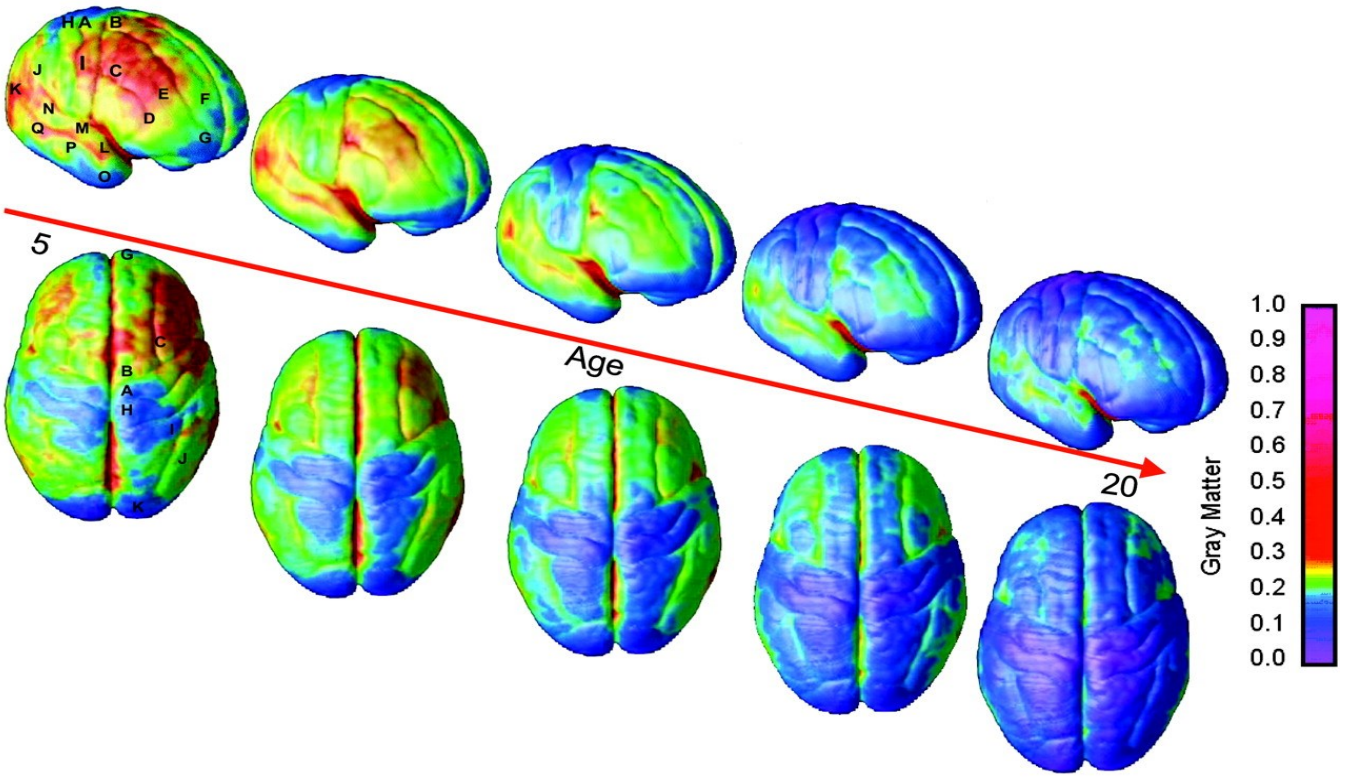
Image retrieved from: http://etec.ctlt.ubc.ca/510wiki/Brain-based_Learning

Brain weight by age

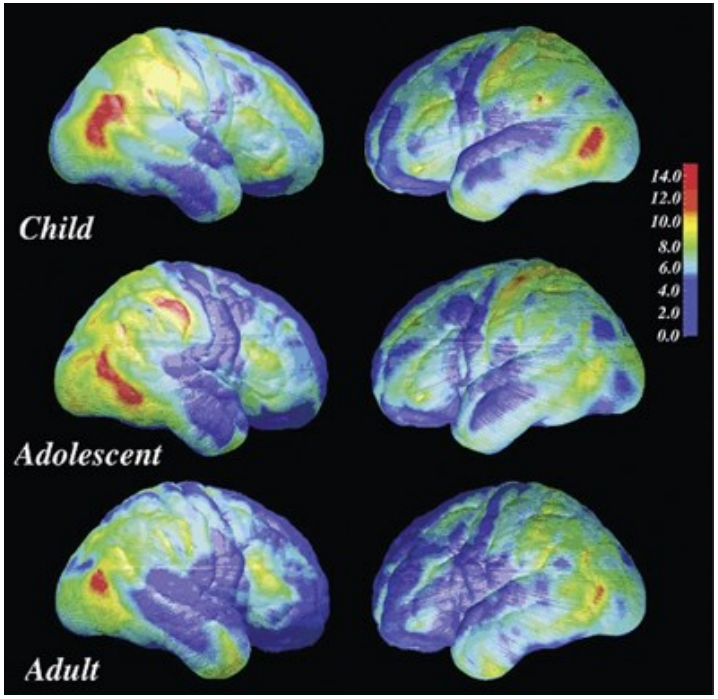


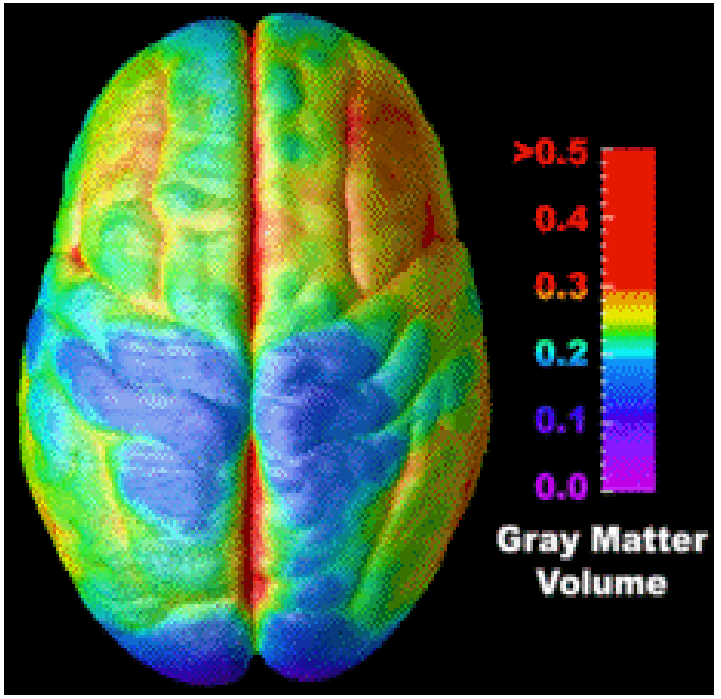
Source: Dekaban, A.S. and Sadowsky, D. (1978). *Annals of Neurology*, 4:345-356.

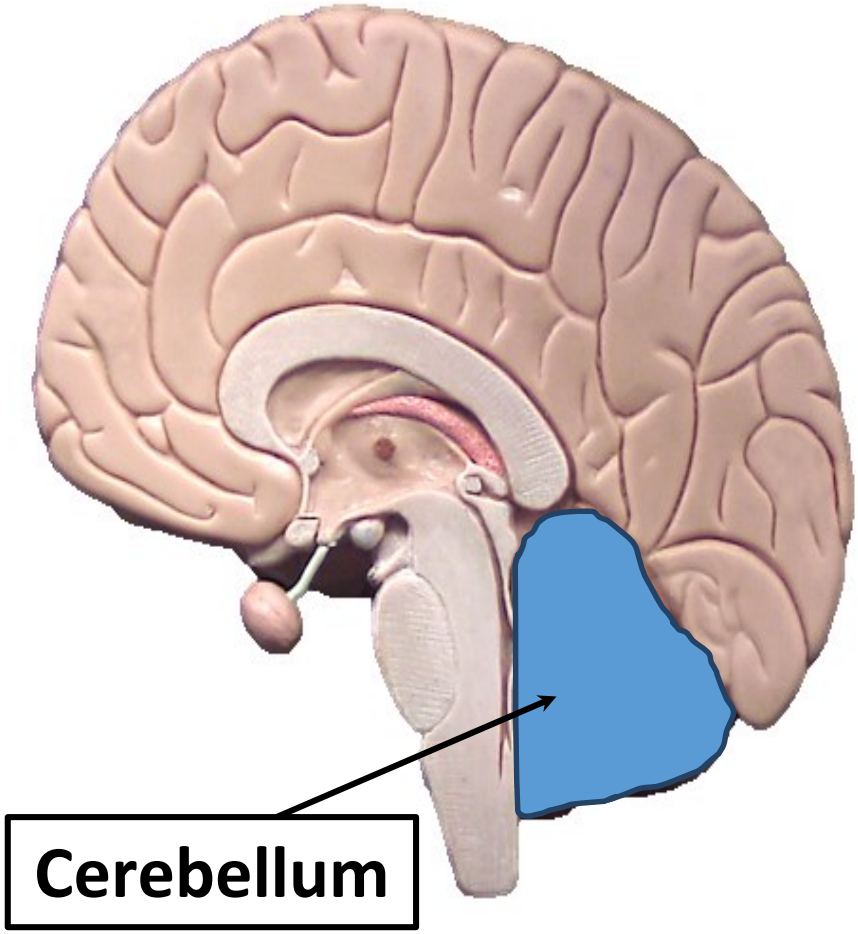
Brain Maturation

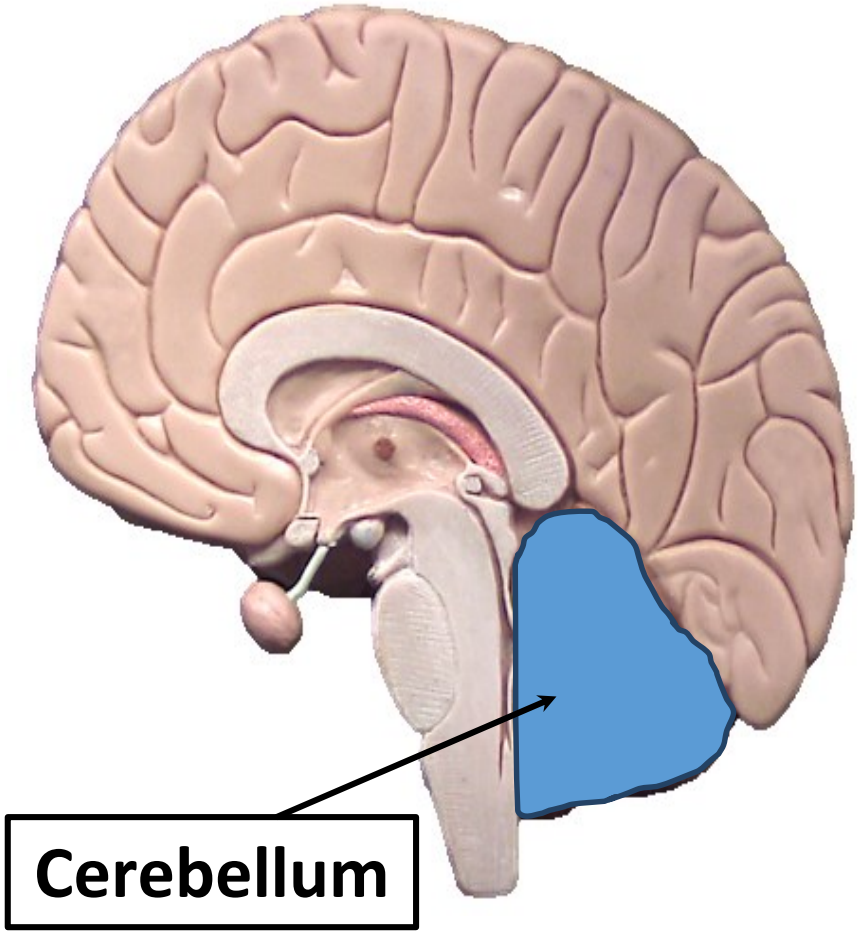


Brain Maturation – Time Lapse






Cerebellum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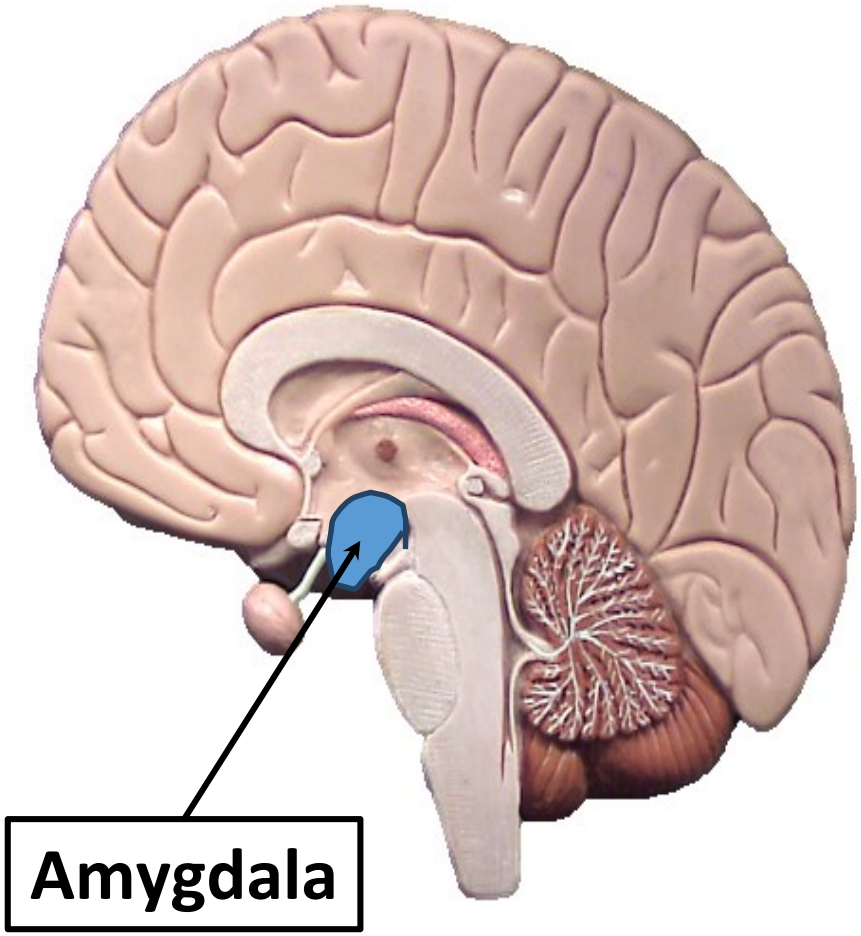
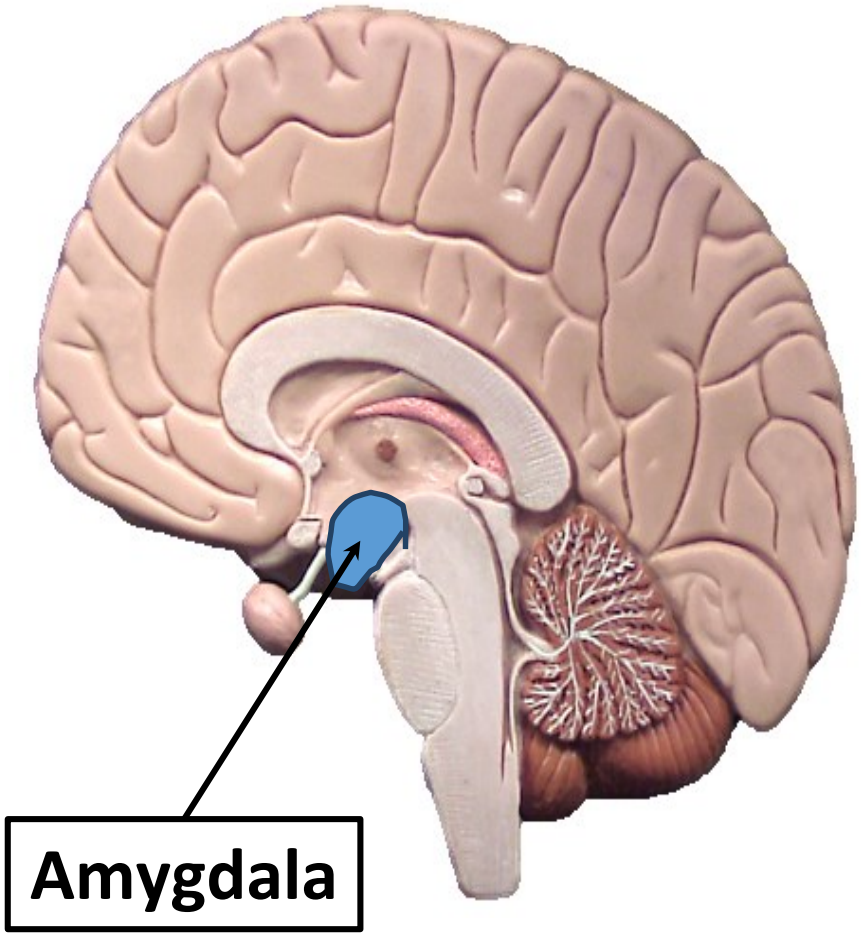

Amygdala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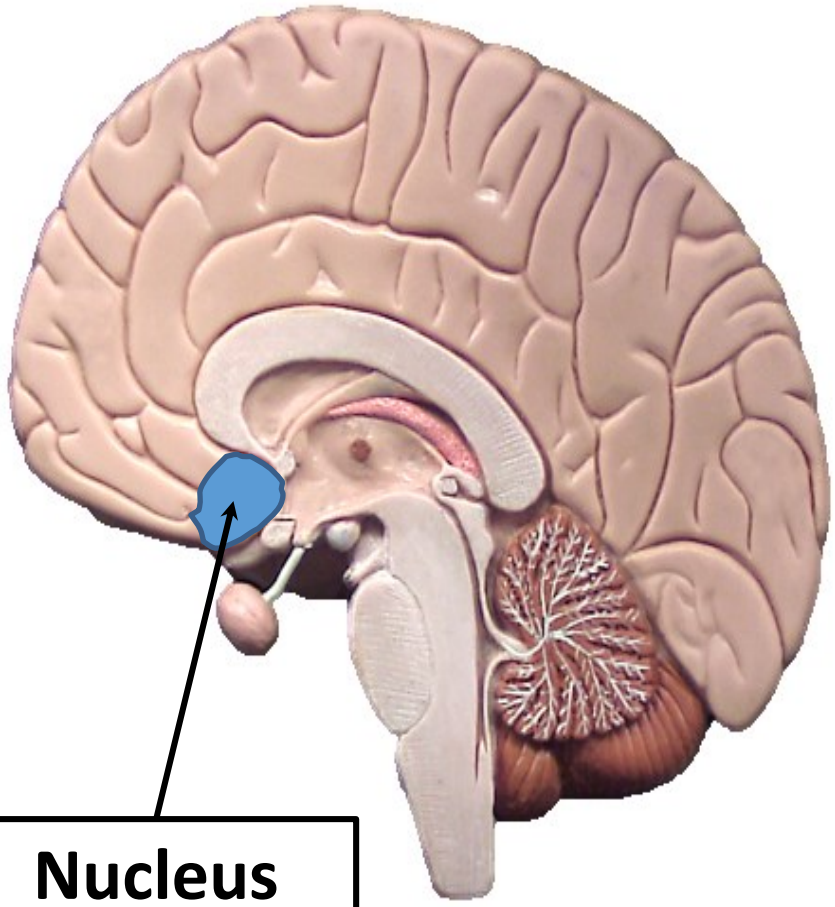
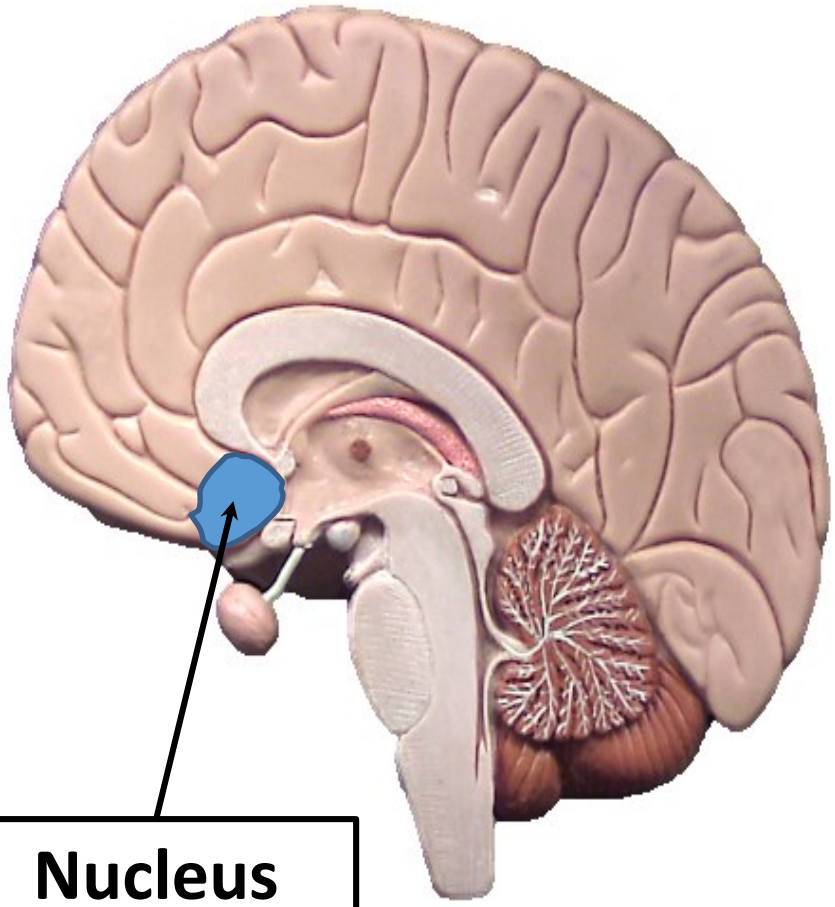
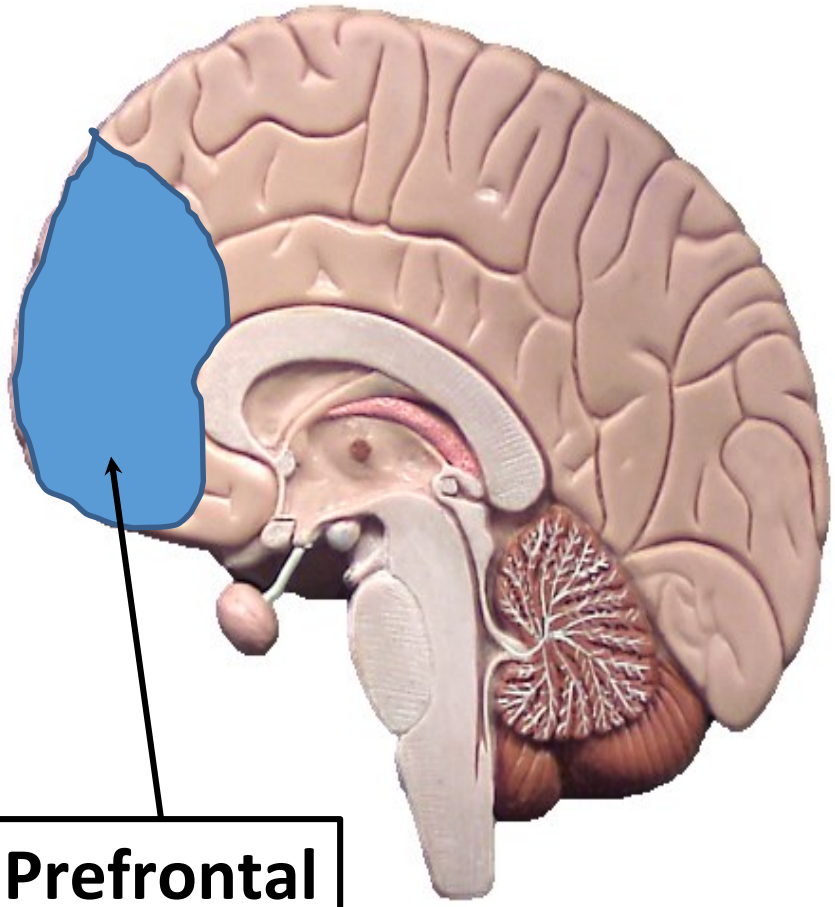
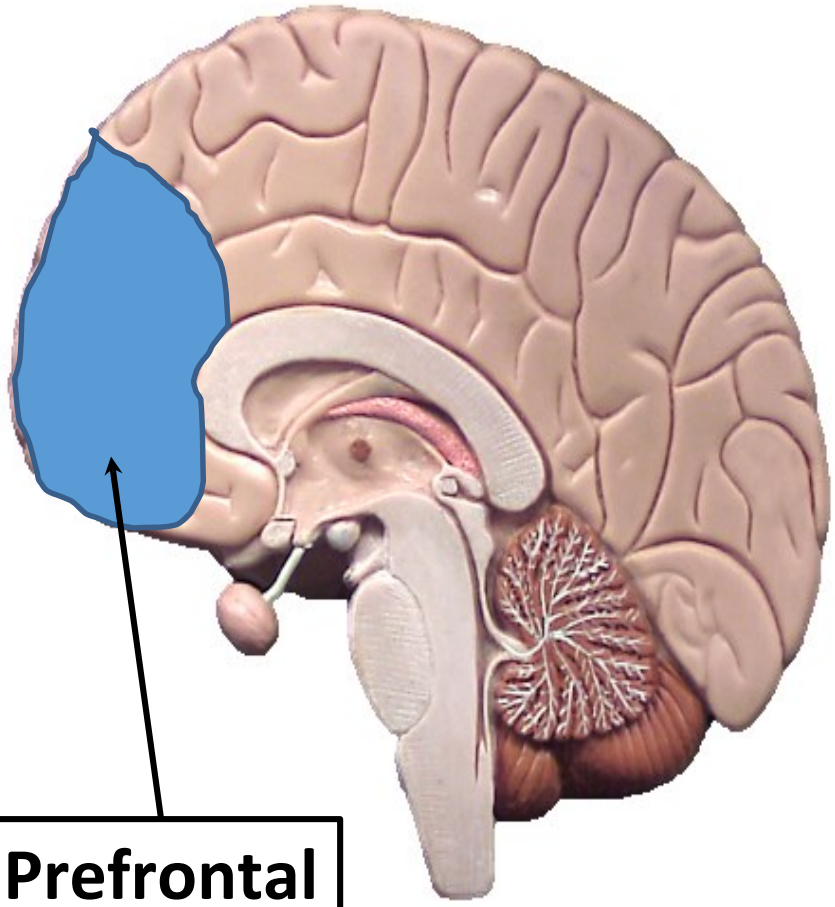


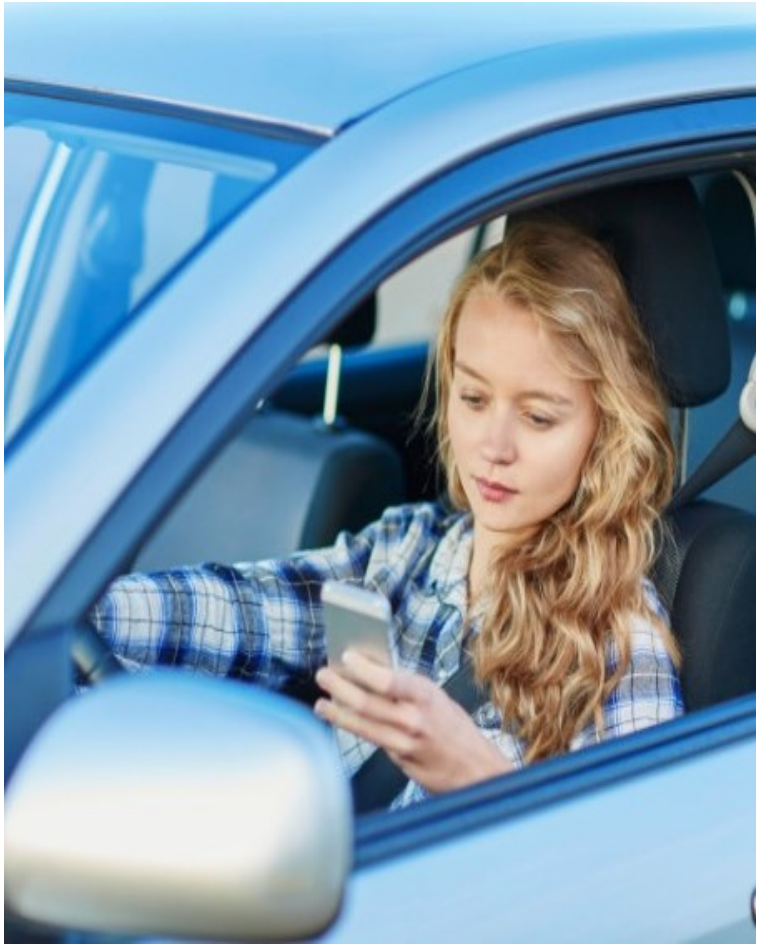
Nucleus accumbens

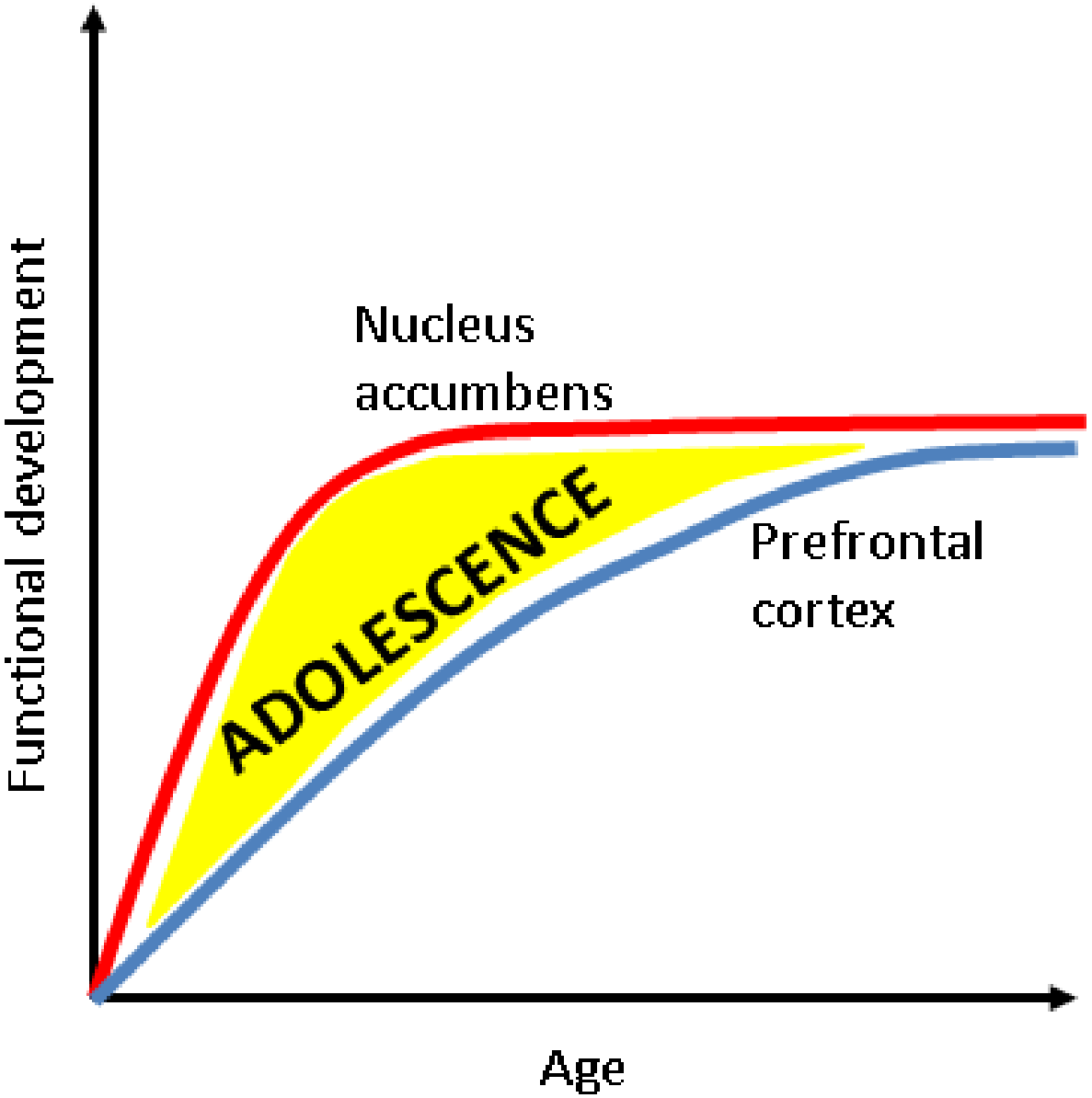


Nucleus accumbens


Prefrontal cortex


Prefrontal cortex

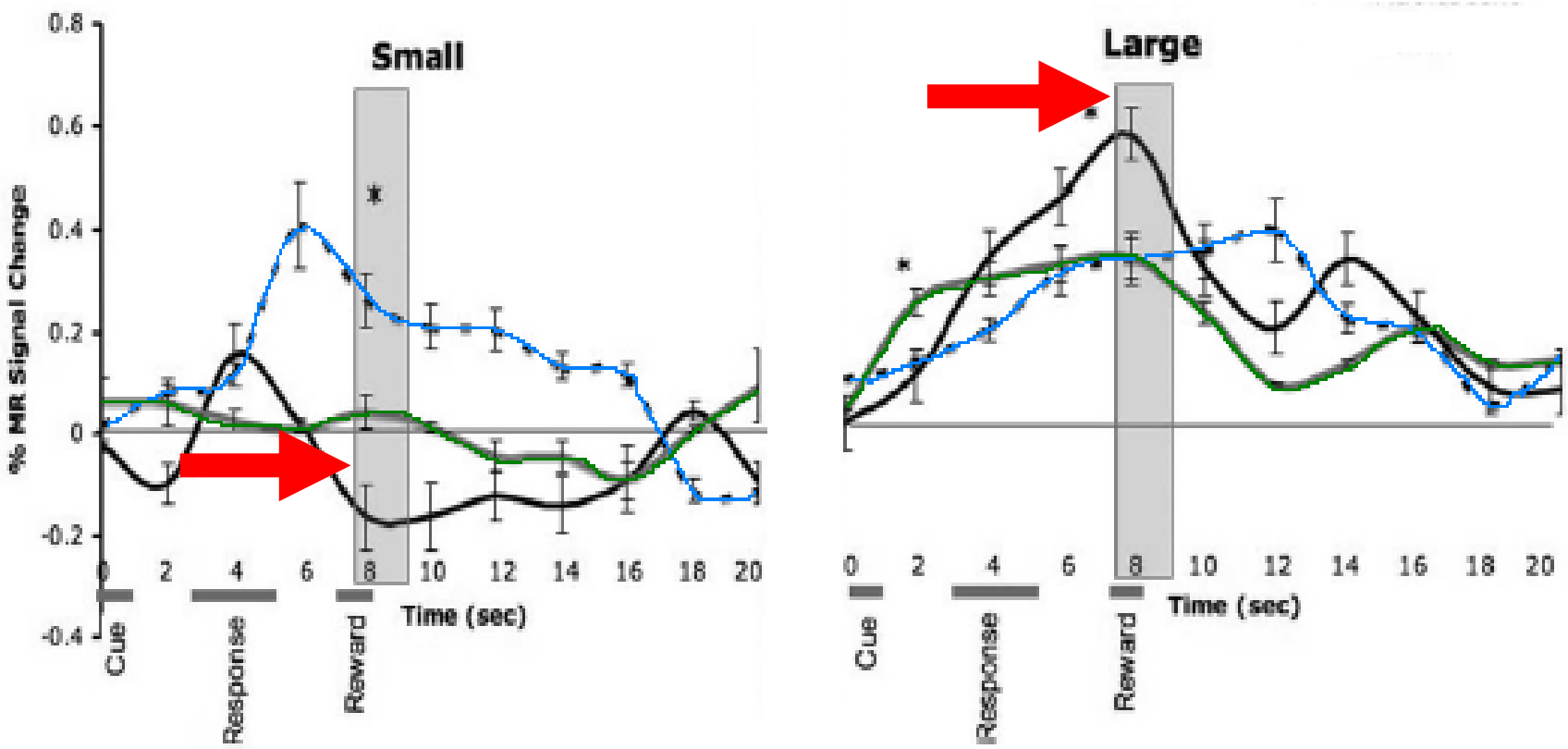




Source: Casey BJ, et al., Development Reviews. 2008; 28: 62-77.

Changes in the Nucleus Accumbens with Small and Large Rewards

Teens Like Big Rewards



Children, ages 7-11

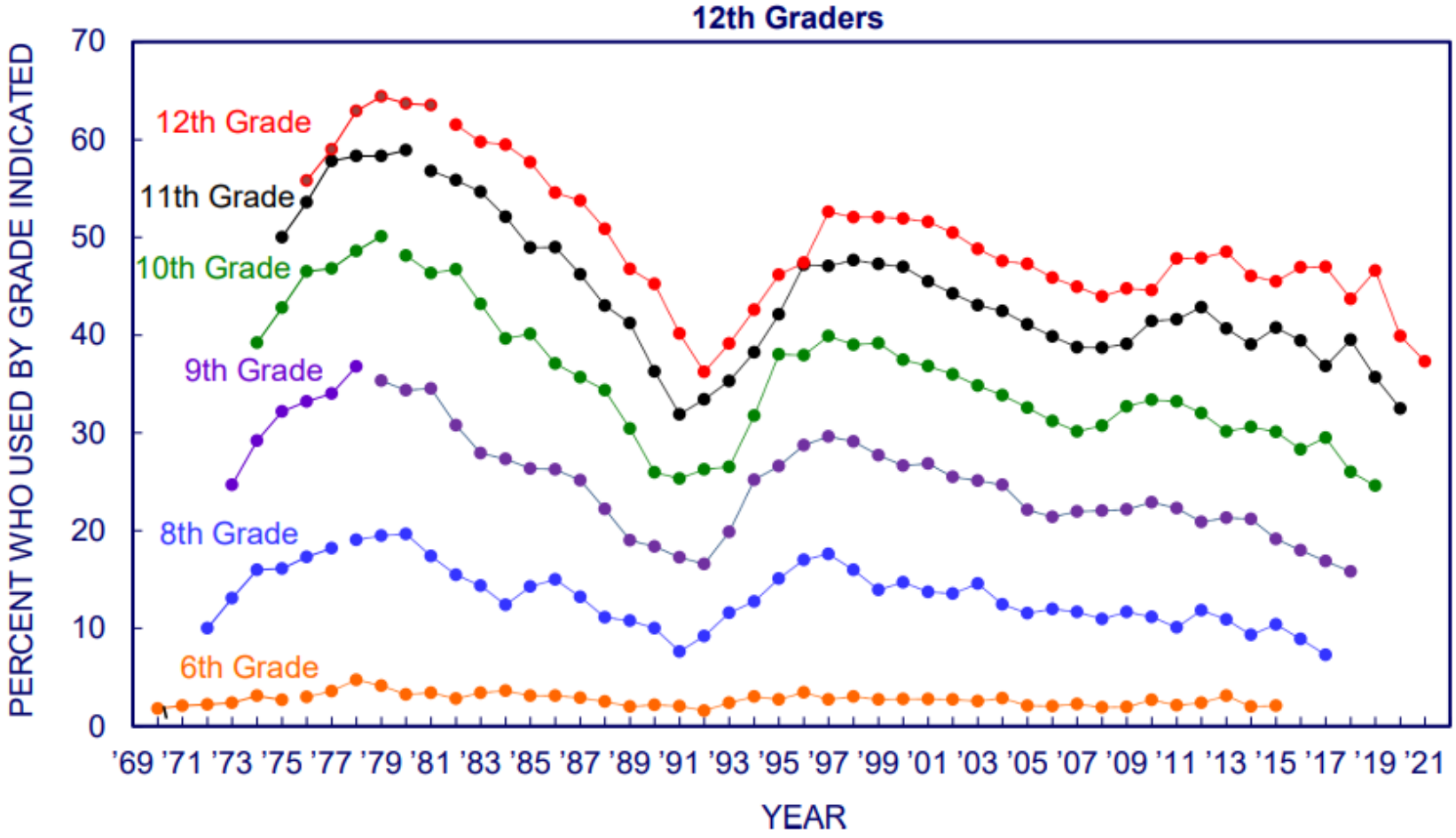
Teens, ages 13-17

Adults, ages 23-29

Adolescents are **developmentally primed** to use drugs

Most drug use starts in adolescence

Grade of Substance Use Initiation Reported by 12th Graders



Source. The Monitoring the Future study, the University of Michigan.

Adolescents are **developmentally vulnerable** to develop substance use disorders

Risk Factors

Associated Risk Factors

Familial

Biologic

Parent(s)

Peer Group

Community / Cultural

Psychiatric Conditions

Biologic – Genetic Roots

A large-scale genome-wide association study meta-analysis of cannabis use disorder

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DNA Analyzed

21,000 people with CUD

360,000 people without CUD

Findings

CUD associated with ***FOXP2* gene on Ch7**

CUD associated with ***CHRNA2* gene on Ch8**

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Age of Initiation

Research Letter

March 29, 2021

Prevalence of Substance Use Disorders by Time Since First Substance Use Among Young People in the US

Nora D. Volkow, MD[1]; Beth Han, MD, PhD, MPH[1]; Emily B. Einstein, PhD[1]; et al

» Author Affiliations | Article Information

JAMA Pediatr. 2021;175(6):640-643. doi:10.1001/jamapediatrics.2020.6981

Table. Prevalence of Specific Substance Use Disorders Among Individuals With Lifetime Substance Use Aged 12 to 25 Years by Time Since First Substance Use[a]

	Weighted % (95% CI)					
		Time since initiation, mo				
Measure	Total	≤12	>12-≤24	>24-≤36	>36	*P* value
Lifetime cannabis use, age 12-17 y						
No.	10 800	3500	3300	2000	2100	NA
12-mo Cannabis use disorder						
Unadjusted	15.1 (14.3-16.0)	8.5 (6.2-7.4)	14.0 (12.5-15.5)	18.7 (16.6-20.9)	25.1 (22.8-27.6)	<.001
Adjusted	NA	10.7 (9.3-12.3)[b]	14.6 (13.2-16.2)[b]	16.8 (15.0-18.8)[b]	20.1 (18.0-22.3)[b]	<.001
Lifetime cannabis use, age 18-25 y						
No.	35 100	2100	3300	3800	26 000	NA
12-mo Cannabis use disorder						
Unadjusted	10.2 (9.8-10.7)	4.8 (3.8-6.1)	7.8 (6.7-9.0)	9.4 (8.2-10.7)	11.1 (10.6-11.7)	<.001
Adjusted	NA	6.4 (5.2-7.9)	8.5 (7.4-9.8)	9.1 (8.0-10.4)	10.9 (10.3-11.4)	<.001

Abbreviation: NA, not applicable.

[a] Data from 2015 to 2018 National Surveys on Drug Use and Health (NSDUH). Prevalence controlled for age, sex, race/ethnicity, family income, age at first tobacco use (excluded from nicotine dependence analysis), age at first alcohol use (excluded from alcohol use disorder analysis), nicotine dependence (excluded from nicotine dependence analysis), major depressive episode, alcohol use disorder (excluded from alcohol use disorder analysis), cannabis use disorder (excluded from cannabis use disorder analysis), cocaine use or disorder (excluded from cocaine use disorder analysis), hallucinogen use or disorder, prescription tranquilizer/sedative use disorder, prescription stimulant use disorder, and prescription opioid or heroin use disorder (heroin use disorder analysis: entered prescription opioid use disorder).

[b] Adjusted estimate for adolescents was significantly different from adjusted estimate for young adults within the same period ($P < .05$).

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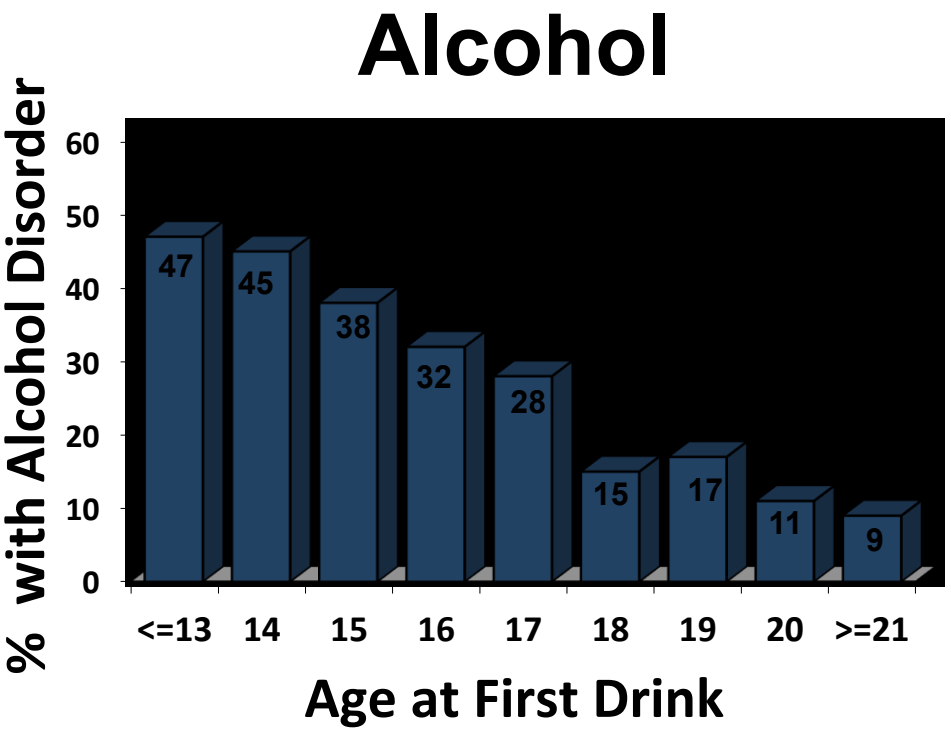
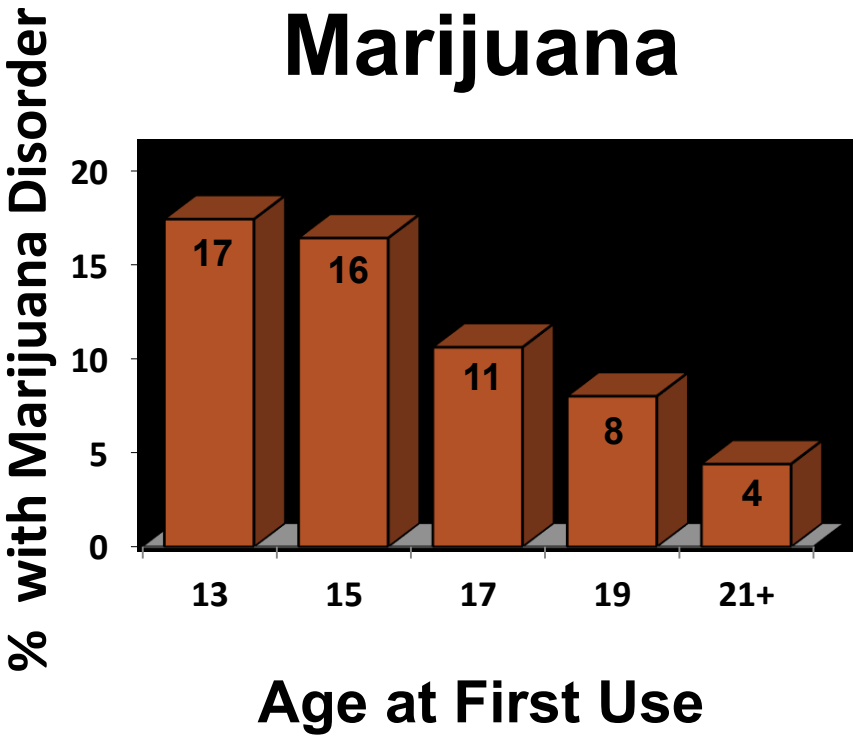
Age at first use and later risk

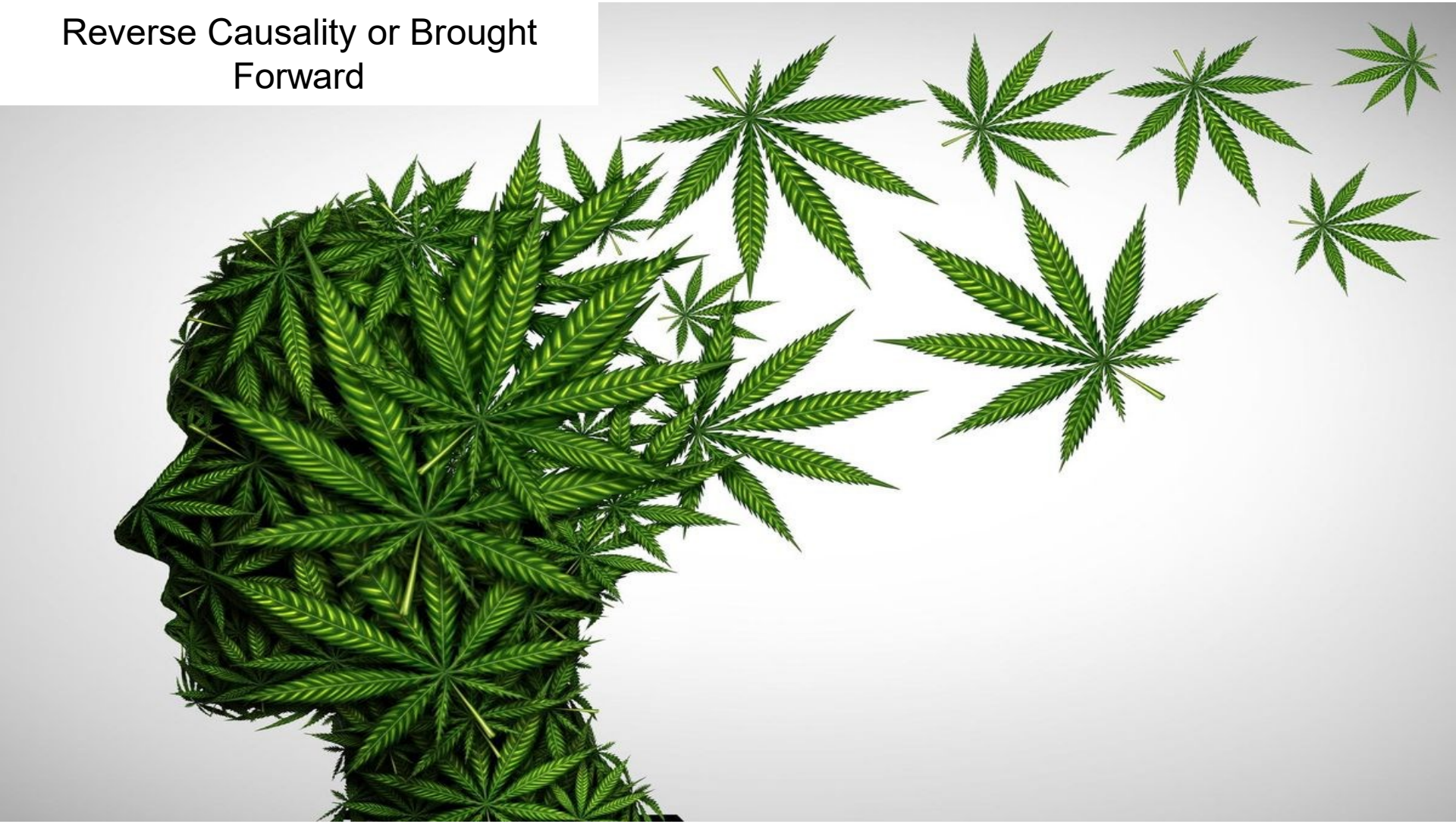




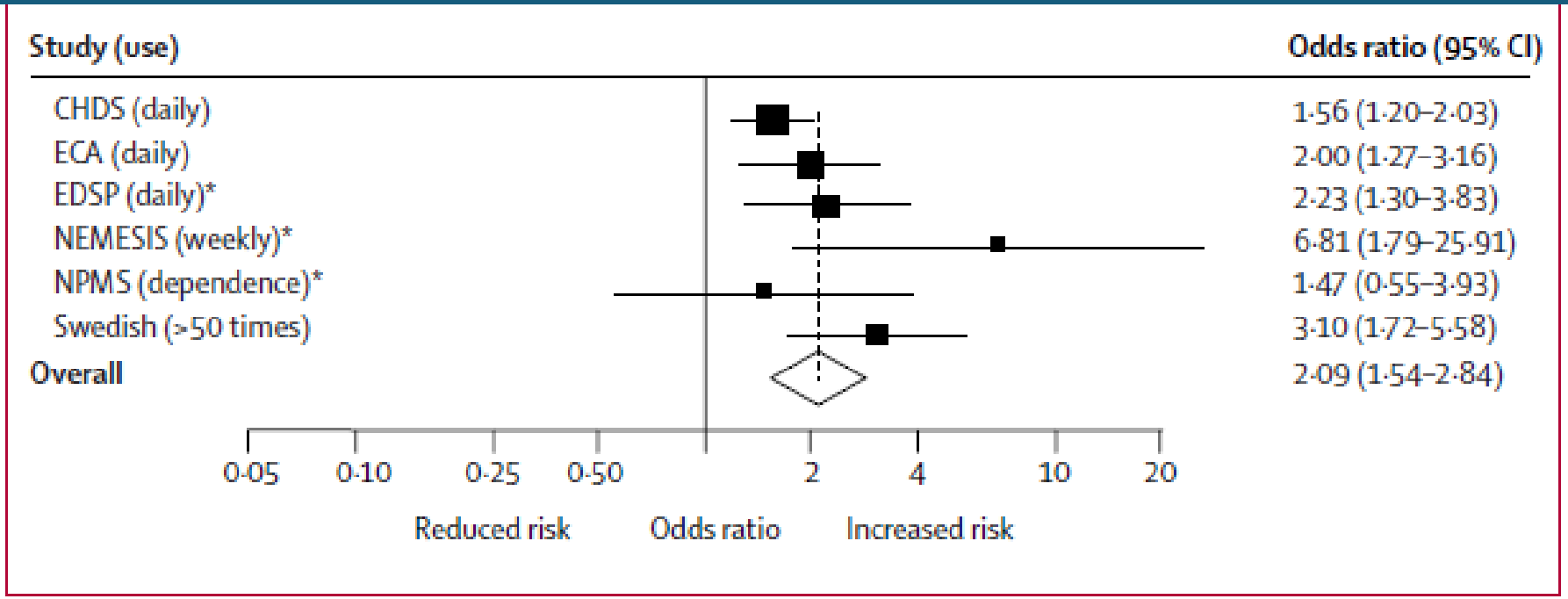
Source: Hingson RW, Heeren T, Winter MR. Age at drinking onset and alcohol dependence. *Arch Pediatr Adolesc Med.* 2006;160:739-746.

Cannabis Use Disorder & Other Mental Health Conditions

Reverse Causality or Brought Forward



Marijuana use and psychotic disorders



A meta-analysis of 6 studies found an increased risk of psychotic outcome among those who used cannabis most frequently compared with non-users (Adjusted Odds Ratio: 2.09, 95% CI: 1.54-2.84).

Source: Moore et al. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet* 370(9584):319–28.

Association between cannabis use and schizoaffective disorder

	# Exposure	# Cases	HR Crude	HR adjusted*
Never used cannabis	39, 978	47	1	1
Ever used cannabis	5,109	12	2.1 (1.1-3.8)	0.8 (0.2-2.9)
>50 times	855	7	7.5 (3.4-16.7)	**7.4 (1.0-54.3)**

*Adjustments for: prior personality disorders at conscription, IQ, disturbed behavior in childhood, social adjustment, risky use of alcohol, smoking, early adulthood socioeconomic position, use of other drugs, brought up in a city. The category "Ever used cannabis" includes all individuals who reported cannabis use, including those who reported ">50 times".

Sources: Griffith-Lendering, Addiction, 108(4), 733-740. Manrique-Garcia, BMC Psychiatry, 12, 112.

Odds Ratio MH & CUD

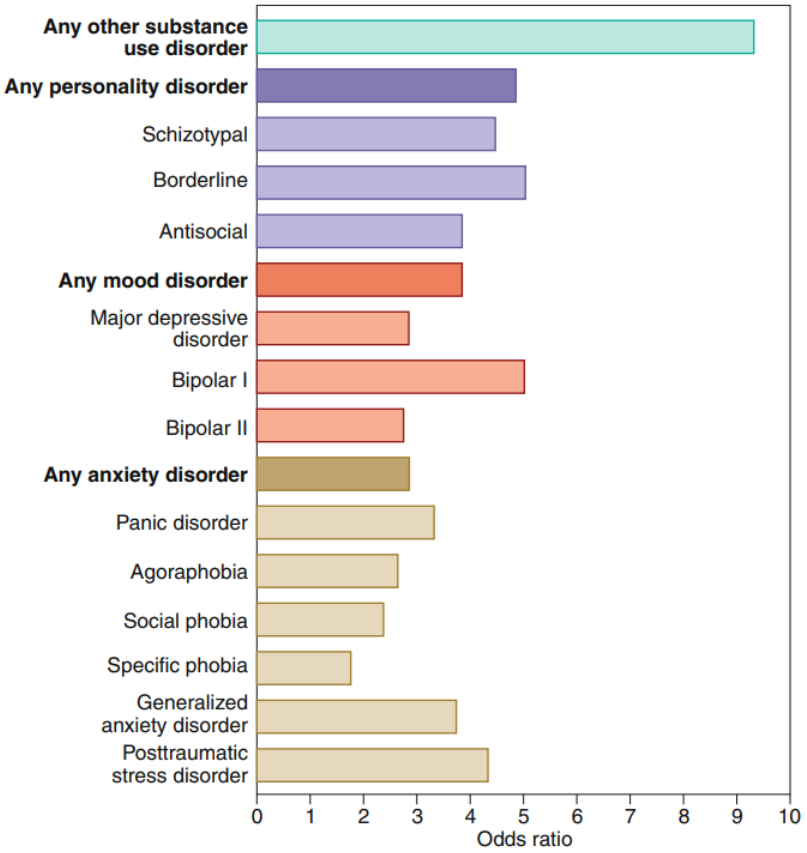


Fig. 1 | Odds ratios of psychiatric conditions associated with CUD. Data based on the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study[6]. Illustrator: Debbie Maizels/Springer Nature.

Difficult to tease out

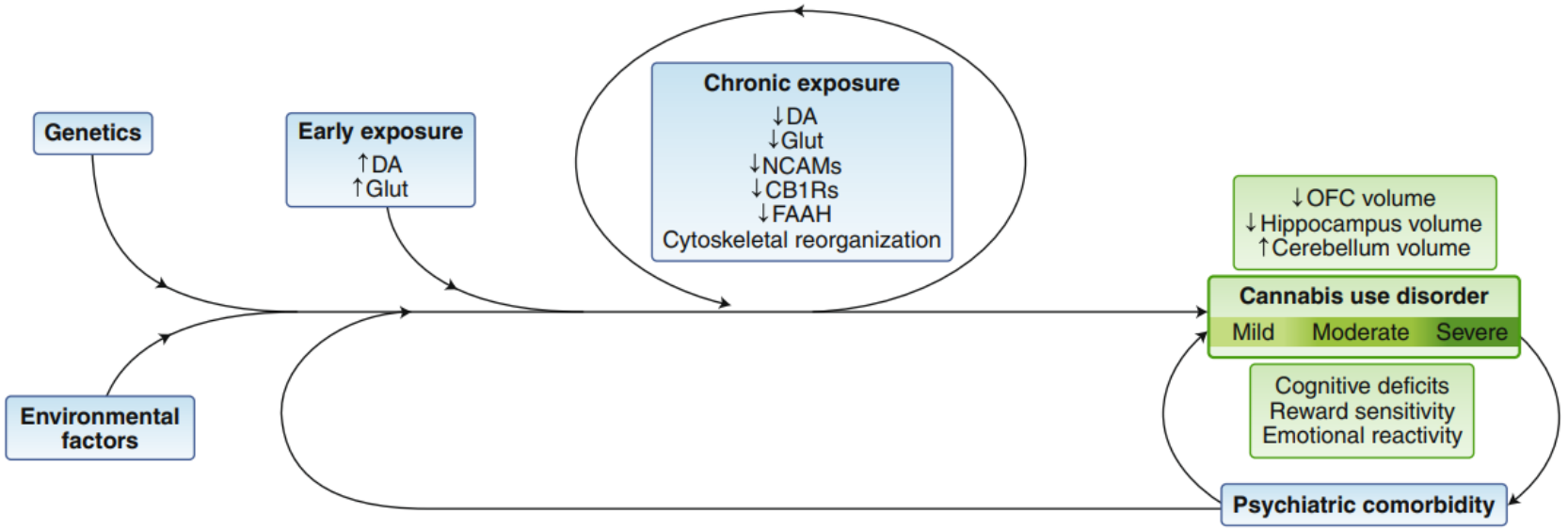


Fig. 6 | Factors contributing to CUD. Schematic summary of multiple factors that contribute to the neurobiological patterns documented in relation to cannabis use and eventual CUD, where the more pronounced neurobiological alterations are associated with greater severity of the disorder and behavioral consequences. FAAH, fatty acid amide hydrolase; Glut, glutamate; Vol, volume. Illustrator: Debbie Maizels/Springer Nature.

Cannabis Use Disorder – Criteria

The 5 C's of Addiction

1. Cravings
2. Compulsive use
3. Control has been lost
4. Continue use despite harms
5. Chronic maladaptive behaviors

DSM – 5, SUD
Criteria

"A problematic pattern of substance use leading to clinically significant impairment…manifested by at least 2 of the following, occurring within a 12 month period…"

DSM – 5, SUD
Criteria

Impaired Control

1. Use protracted
2. Failed attempts to quit
3. Time use/recover
4. Cravings

Social Impairment

5. Role obligation failure
6. Interpersonal problems
7. Sacrificing activities

Risk Use

8. Use in hazardous situations
9. Continued use despite exacerbation of problems

Neuro/Physiologic Adaptation

10. Tolerance
11. Withdrawal

DSM – 5, SUD Criteria

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1. Use protracted
2. Failed attempts to quit
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Social Impairment

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9. Continued use despite exacerbation of problems

Neuro/Physiologic Adaptation

10. Tolerance
11. Withdrawal

Symptoms	Severity
2 – 3	Mild
4 – 5	Moderate
≥ 6	Severe

Cannabis

Symptoms reported by adolescents who use cannabis:

- Hallucinations (27%)
- Paranoia/Anxiety (33.6%)
- Any psychotic symptom (42.9%)

Levy S, Weitzman, ER. Acute mental health symptoms in adolescent marijuana users. *JAMA Pediatrics*. 2018 Dec 17;doi 10.1001/jamapediatrics.2018

Marijuana Intoxication

Marijuana Intoxication

Munchies

Autonomic hyperactivity BP↑

Racing heart "♡"

Injection (conjunctival scleral)

Judgement impaired

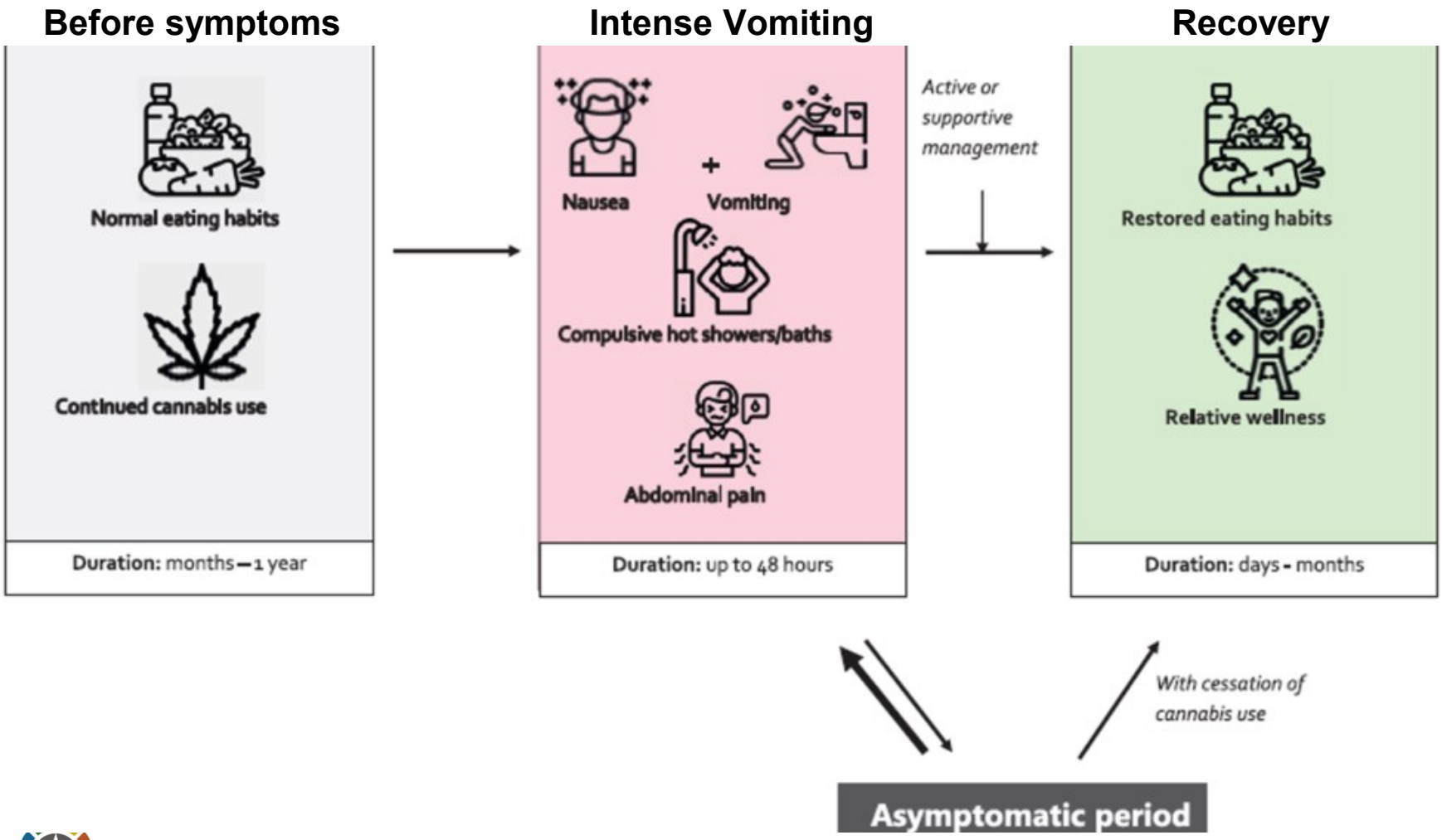
eUphoria

Anxiety

Nystagmus

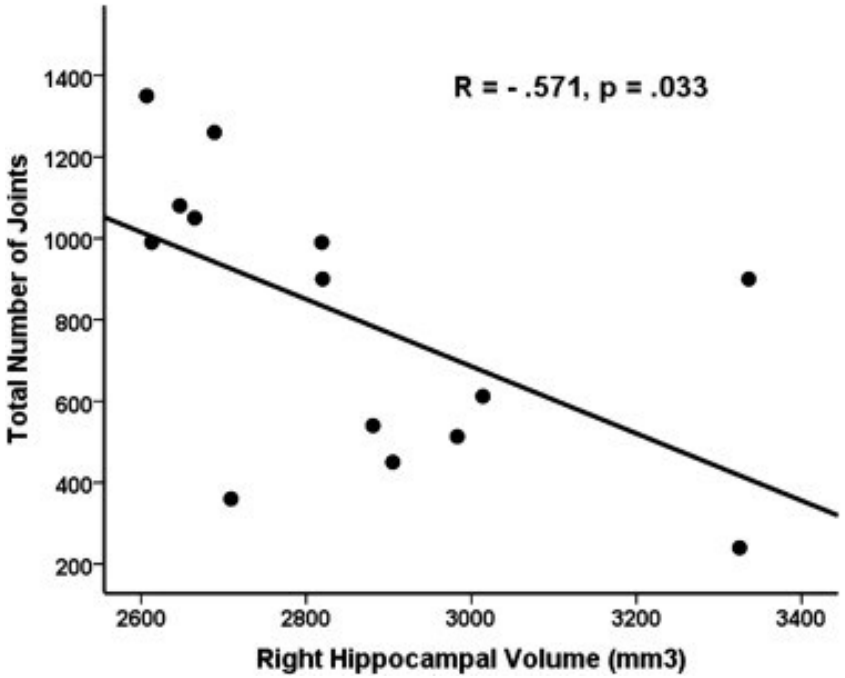
Ataxia

Cannabis Hyperemesis Syndrome



Zhu et al., Diagnosis and acute management of adolescent cannabinoid hyperemesis syndrome: a systematic review. *J of Adol Health,* 2021.

The effect of cannabis on hippocampus size



Source: Ashtari et al. (2011) Medial temporal structures and memory functions in adolescents with heavy cannabis use. J Psychiatr Res. 2011 Aug;45(8):1055-66. doi: 10.1016/j.jpsychires.2011.01.004.

Chronic Exposure = Reward Altered

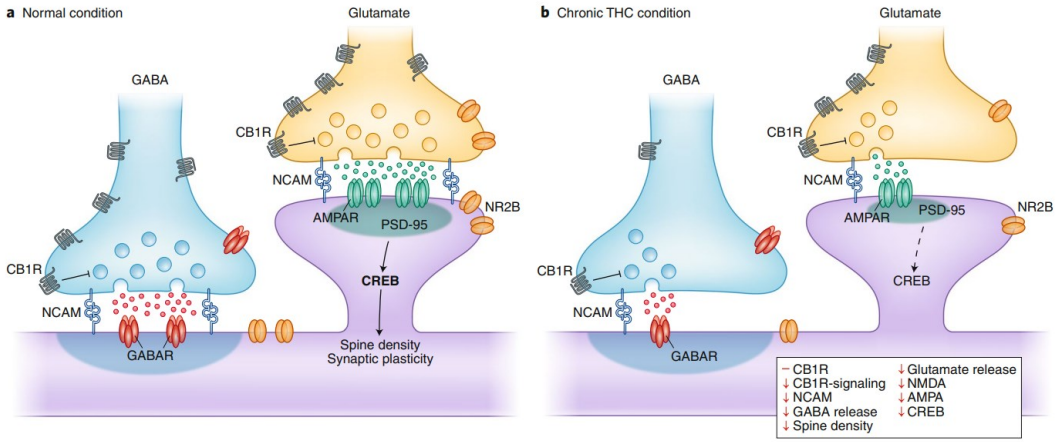


Fig. 5 | Synaptic perturbations based on animal models associated with chronic THC exposure (right) as compared to control condition (left) in glutamate and GABA synapses in the cortex. THC is known to have a greater effect on the interneuronal GABA microcircuit, most likely due to the greater (~20-fold) number of CB1R on cortical GABAergic interneuron axon terminals compared to glutamatergic terminals[150]. AMDAR, AMDA receptor; GABAR, GABA receptor; NCAM, neural cell adhesion molecule; NMDAR, NMDA receptor. Illustrator: Debbie Maizels/Springer Nature.

Research

JAMA Psychiatry | Original Investigation

Association of Marijuana Use With Blunted Nucleus Accumbens Response to Reward Anticipation

Meghan E. Martz, MS; Elisa M. Trucco, PhD; Lora M. Cope, PhD; Jillian E. Hardee, PhD; Jennifer M. Jester, PhD; Robert A. Zucker, PhD; Mary M. Heitzeg, PhD

IMPORTANCE Marijuana use may alter ventral striatal response to reward, which might heighten susceptibility to substance use disorder. Longitudinal research is needed to determine the effects of marijuana use on neural function involved in reward response.

OBJECTIVE To determine whether marijuana use among young adults prospectively affects nucleus accumbens (NAcc) activation during reward anticipation.

DESIGN, SETTING, AND PARTICIPANTS One hundred eight young adults were recruited from the Michigan Longitudinal Study, an ongoing study of youth at high risk for substance use disorder and a contrast sample of control families. Participants underwent 3 consecutive functional magnetic resonance imaging scans at approximate ages of 20 (time 1), 22 (time 2), and 24 (time 3) years. Self-report data on marijuana and other drug use occasions were collected annually since age 11 years.

MAIN OUTCOMES AND MEASURES Cross-lagged models were used to test the association of marijuana use with neural response in the NAcc to reward anticipation during a monetary incentive delay task controlling for sex, age, other substance use, and family history of substance use disorder.

RESULTS Of 108 participants, 39 (36.1%) were female and mean (SD) age at baseline was 20.1 (1.4) years. Greater marijuana use was associated with later blunted activation in the NAcc during reward anticipation (time 1 to time 2: $\beta = -0.26$, $P = .04$; time 2 to time 3: $\beta = -0.25$, $P = .01$). When the cross-lagged model was tested with the inclusion of previous and concurrent cigarette use, the effect of marijuana use from time 2 to time 3 remained significant ($\beta = -0.29$; $P = .005$) and the effect of cigarette use was nonsignificant.

CONCLUSIONS AND RELEVANCE The findings of this study indicate that marijuana use is associated with decreased neural response in the NAcc during the anticipation of nondrug rewards. Over time, marijuana use may alter anticipatory reward processing in the NAcc, which may increase the risk for continued drug use and later addiction.

JAMA Psychiatry. 2016;73(8):838-844. doi:10.1001/jamapsychiatry.2016.1161
Published online July 6, 2016.

Editorial page 773
Supplemental content at jamapsychiatry.com

Author Affiliations: Addiction Research Center, Department of Psychiatry, University of Michigan, Ann Arbor (Martz, Trucco, Cope, Hardee, Jester, Zucker, Heitzeg); Department of Psychology, University of Michigan, Ann Arbor (Martz, Zucker); Center for Children and Families, Department of Psychology, Florida International University, Miami (Trucco).

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Boston Children's Hospital
Until every child is well
HARVARD MEDICAL SCHOOL

Persistent cannabis users show neuropsychological decline from childhood to midlife

Madeline H. Meier[a,b,1], Avshalom Caspi[a,b,c,d,e], Antony Ambler[e,f], HonaLee Harrington[b,c,d], Renate Houts[b,c,d], Richard S. E. Keefe[d], Kay McDonald[f], Aimee Ward[f], Richie Poulton[f], and Terrie E. Moffitt[a,b,c,d,e]

[a]Duke Transdisciplinary Prevention Research Center, Center for Child and Family Policy, [b]Department of Psychology and Neuroscience, and [c]Institute for Genome Sciences and Policy, Duke University, Durham, NC 27708; [d]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC 27710; [e]Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; and [f]Dunedin Multidisciplinary Health and Development Research Unit, Department of Preventive and Social Medicine, School of Medicine, University of Otago, Dunedin 9054, New Zealand

Source: Meier et al. Proceedings of the National Academy of Sciences. 2012. Available at: www.pnas.org/cgi/doi/10.1073/pnas.1206820109

The Dunedin Study

N = 1,037

13 yrs (Pre-initiation) **18 yrs** **21 yrs** **32 yrs** **38 yrs**

1 **2** **3** **4** **5**

Assessment ages

Source: Meier et al. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. *P Nat Acad Sci* 109(40):E2657–E2664.

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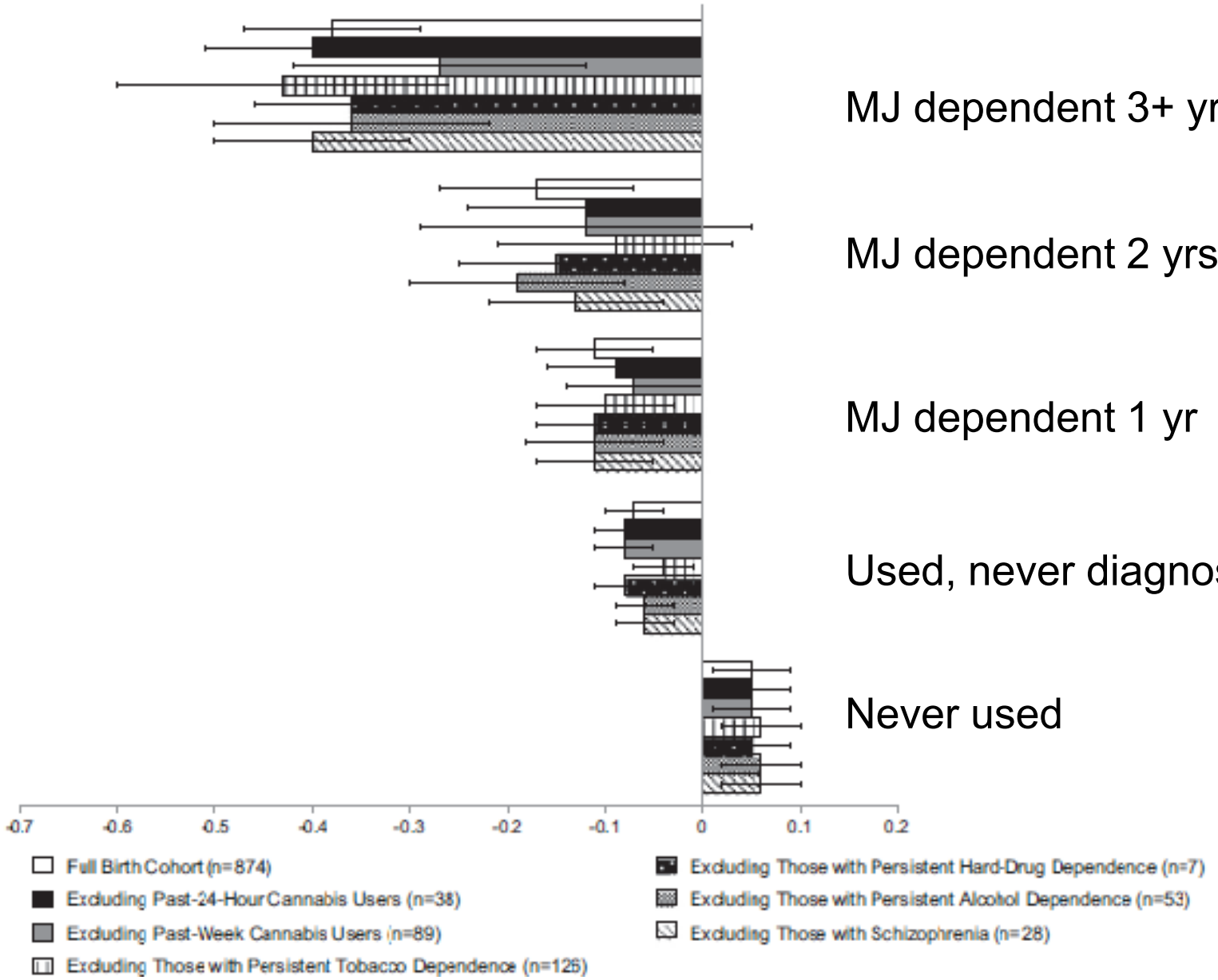

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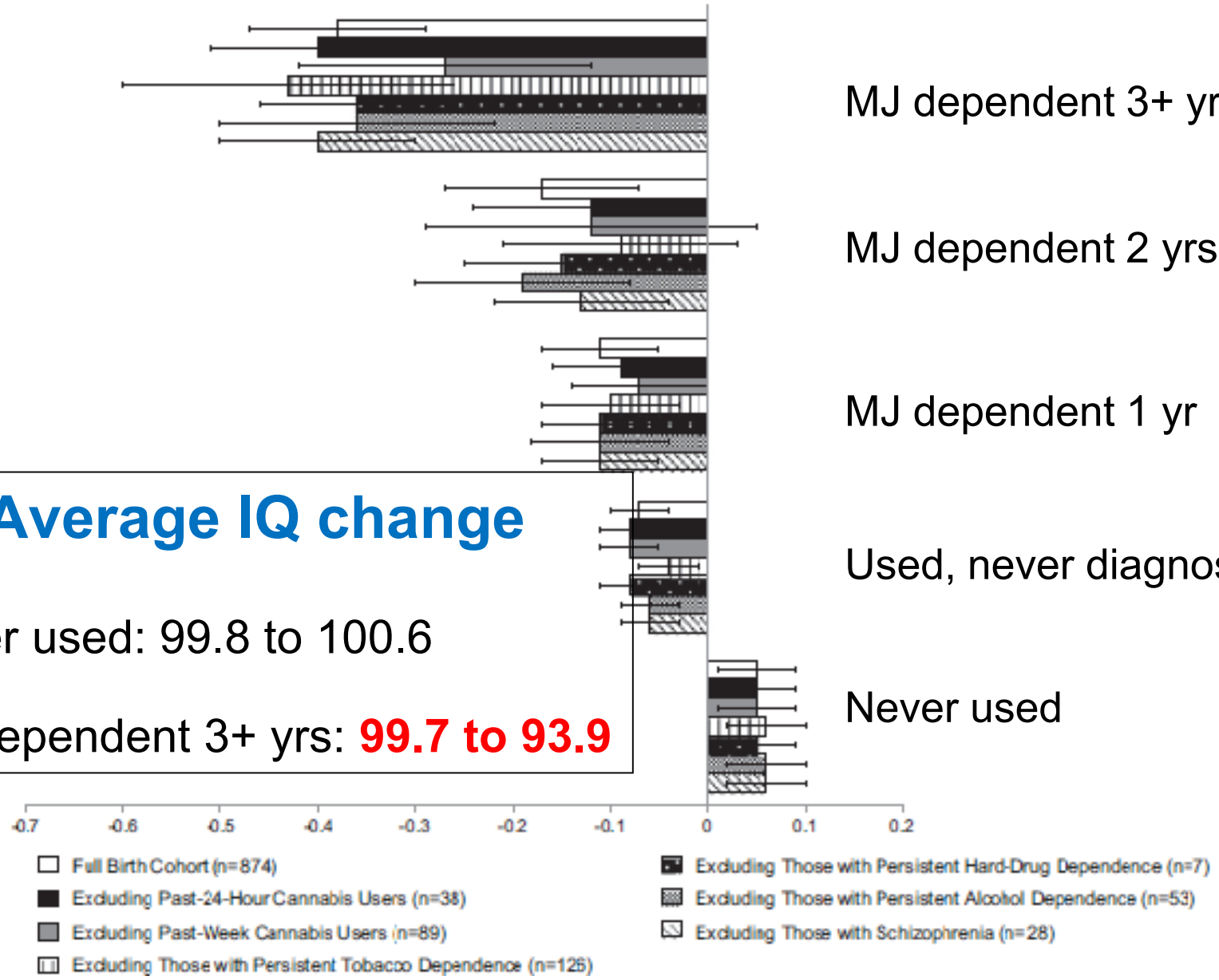


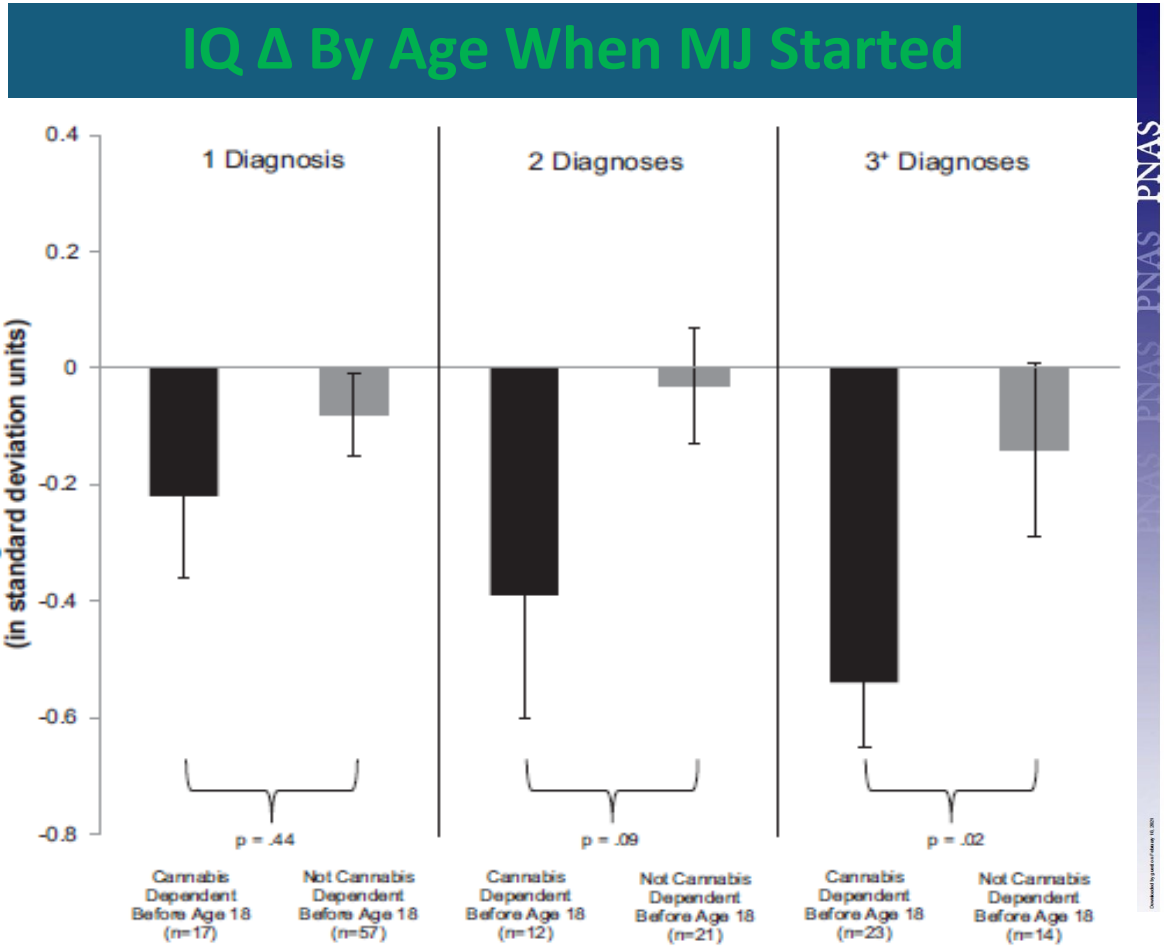
Average IQ change

Never used: 99.8 to 100.6

MJ dependent 3+ yrs: **99.7 to 93.9**

Source: Meier et al. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. *P Nat Acad Sci* 109(40):E2657–E2664.

Chronic Exposure = IQ Changes



Persistent cannabis users show neuropsychological decline from childhood to midlife

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Edited by Michael I. Posner, University of Oregon, Eugene, OR, and approved July 30, 2012 (received for review April 23, 2012)

Recent reports show that fewer adolescents believe that regular cannabis use is harmful to health. Concomitantly, adolescents are initiating cannabis use at younger ages, and more adolescents are using cannabis on a daily basis. The purpose of the present study was to test the association between persistent cannabis use and neuropsychological decline and determine whether decline is concentrated among adolescent-onset cannabis users. Participants were members of the Dunedin Study, a prospective study of a birth cohort of 1,037 individuals followed from birth (1972/1973) to age 38 y. Cannabis use was ascertained in interviews at ages 18, 21, 26, 32, and 38 y. Neuropsychological testing was conducted at age 13 y, before initiation of cannabis use, and again at age 38 y, after a pattern of persistent cannabis use had developed. Persistent cannabis use was associated with neuropsychological decline broadly across domains of functioning, even after controlling for years of education. Informants also reported noticing more cognitive problems for persistent cannabis users. Impairment was concentrated among adolescent-onset cannabis users, with more persistent use associated with greater decline. Further, cessation of cannabis use did not fully restore neuropsychological functioning among adolescent-onset cannabis users. Findings are suggestive of a neurotoxic effect of cannabis on the adolescent brain and highlight the importance of prevention and policy efforts targeting adolescents.

marijuana | longitudinal | cognition

Cannabis, the most widely used illicit drug in the world, is increasingly being recognized for both its toxic and its therapeutic properties (1). Research on the harmful and beneficial effects of cannabis use is important because it can inform decisions regarding the medicinal use and legalization of cannabis, and the results of these decisions will have major public-health consequences. As debate surrounding these issues continues in the United States and abroad, new findings concerning the harmful effects of cannabis on neuropsychological functioning are emerging.

Accumulating evidence suggests that long-term, heavy cannabis use may cause enduring neuropsychological impairment—impairment that persists beyond the period of acute intoxication (2). Studies of long-term, heavy cannabis users fairly consistently show that these individuals perform worse on neuropsychological tests (2–5), and some (6–8) but not all (9) studies suggest that impairment may remain even after extended periods of abstinence. The magnitude and persistence of impairment may depend on factors such as the quantity, frequency, duration, and age-of-onset of cannabis use (2), as more severe and enduring impairment is evident among individuals with more frequent and prolonged heavy use and a younger age-of-onset (3, 6, 8, 10–16).

The extant evidence base draws on case–control studies of recruited cannabis users and comparison subjects. These studies screen participants for potential confounding factors, such as alcohol and drug dependence, and compare them on neuropsychological test performance after a period of abstinence from cannabis. There are two commonly cited potential limitations of this approach. One is the absence of data on initial, precannabis-use neuropsychological functioning. It is possible that differences in test performance between cannabis users and controls are attributable to premorbid rather than cannabis-induced deficits (17–20). A second limitation is reliance on retrospectively reported quantity, frequency, duration, and age-of-onset of cannabis use, often inquired about years after initiation of heavy use.

A prospective, longitudinal investigation of the association between cannabis use and neuropsychological impairment could redress these limitations and strengthen the existing evidence base by assessing neuropsychological functioning in a sample of youngsters before the onset of cannabis use, obtaining prospective data on cannabis use as the sample is followed over a number of years, and readministering neuropsychological tests after some members of the sample have developed a pattern of long-term cannabis use. To our knowledge, only one prospective, longitudinal study of the effects of cannabis on neuropsychological functioning has been conducted (21), and, in this study, the sample was small and the average duration of regular cannabis use was only 2 y.

In the present study, we investigated the association between persistent cannabis use—prospectively assessed over 20 y—and neuropsychological functioning in a birth cohort of 1,037 individuals. Study members underwent neuropsychological testing in 1985 and 1986 before the onset of cannabis use and again in 2010–2012, after some had developed a persistent pattern of cannabis use. We tested six hypotheses. First, we tested the "cognitive decline" hypothesis that persistent cannabis users evidence greater decline in test performance from childhood to adulthood than nonusers. By examining within-person change in neuropsychological functioning, any effect of premorbid deficits on later (postcannabis-initiation) test performance was nullified. Second, we tested the "specificity" hypothesis to address whether impairment is confined to specific neuropsychological domains or whether it is more global. To test this hypothesis, we administered multiple tests for each of five specific domains, as different tests may be differentially sensitive to cannabis-associated neuropsychological impairment. In conducting our analyses, we tested alternative explanations for the association between per-

Author contributions: M.H.M., A.C., and T.E.M. designed research; M.H.M., A.C., A.A., H.H., R.H., R.S.E.K., K.M., A.W., R.P., and T.E.M. performed research; M.H.M., A.C., R.H., and T.E.M. analyzed data; and M.H.M., A.C., and T.E.M. wrote the paper.

The authors declare no conflict of interest.

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See Commentary on page 15970.

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See Author Summary on page 15980 (volume 109, number 40).

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Cannabis & Driving

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Full length article

Recreational cannabis use impairs driving performance in the absence of acute intoxication

M. Kathryn Dahlgren[a,b,c], Kelly A. Sagar[a,b,c], Rosemary T. Smith[a,b], Ashley M. Lambros[a,b], Madeline K. Kuppe[a,b], Staci A. Gruber[a,b,c,*]

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ARTICLE INFO

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ABSTRACT

Background: Across the nation, growing numbers of individuals are exploring the use of cannabis for medical or recreational purposes, and the proportion of cannabis-positive drivers involved in fatal crashes increased from 8 percent in 2013 to 17 percent in 2014, raising concerns about the impact of cannabis use on driving. Previous studies have demonstrated that cannabis use is associated with impaired driving performance, but thus far, research has primarily focused on the effects of *acute* intoxication.

Methods: The current study assessed the potential impact of cannabis use on driving performance using a customized driving simulator in *non-intoxicated*, heavy, recreational cannabis users and healthy controls (HCs) without a history of cannabis use.

Results: Overall, cannabis users demonstrated impaired driving relative to HC participants with increased accidents, speed, and lateral movement, and reduced rule-following. Interestingly, however, when cannabis users were divided into groups based on age of onset of regular cannabis use, significant driving impairment was detected and completely localized to those with early onset (onset before age 16) relative to the late onset group (onset ≥16 years old). Further, covariate analyses suggest that impulsivity had a significant impact on performance differences.

Conclusions: Chronic, heavy, recreational cannabis use was associated with worse driving performance in non-intoxicated drivers, and earlier onset of use was associated with greater impairment. These results may be related to other factors associated with early exposure such as increased impulsivity.

Introduction

To date, several countries, including Canada and Uruguay have pletely legalized cannabis, while in the United States, recreational nabis use is legal for adults in 11 US states and Washington DC; an litional 33 states have fully legalized medical cannabis programs tional Conference of State Legislatures NCSL, 2019). In the US, ional surveys indicate that approximately 123.9 million people aged or older have tried cannabis at least once, and 27.7 million report t month use (Substance Abuse and Mental Health Services ministration SAMHSA, 2019). In addition, a recent Canadian survey icated that approximately 4.4 million Canadians aged 15 or older orted using cannabis at least once in the past year (Canadian tobacco, Alcohol and Drugs Survey CTADS, 2019). Further, the most recent US National Roadside Survey, which collected data from 2013 to 2014, reported that cannabis is the second most commonly detected substance (second only to alcohol) in randomized, voluntary assessments of drivers; 12.6 % of weekend, night-time drivers aged 16 or older tested positive for cannabis, representing a 48 % increase from the last national survey performed in 2007 (Berning et al., 2015). Additional data from the US National Survey of Drug Use and Health collected between 2002 and 2014 indicates that 3.2 % of individuals aged 16–25 reported driving while intoxicated with cannabis (Azofeifa et al., 2015). Similarly, the Canadian Road Safety Monitor survey, which has gathered information on drugged driving since 2002, indicated that approximately 2.9 % of Canadians reporting driving within two hours of using cannabis (Robertson et al., 2017).

Significant evidence suggests that acute cannabis intoxication, the result of exposure to Δ-9 tetrahydrocannabinol (THC), the primary psychoactive constituent of the plant, is associated with impaired

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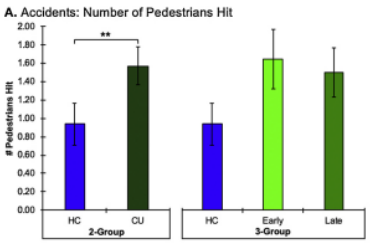

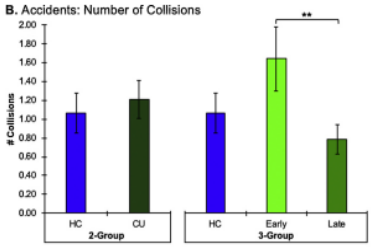

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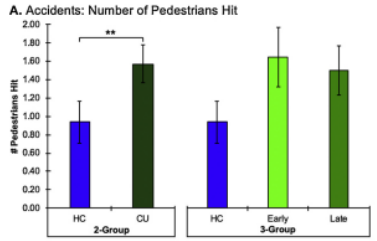

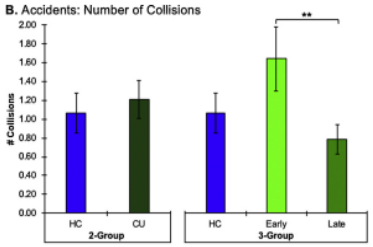

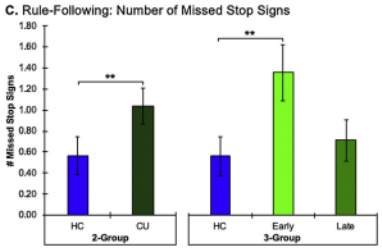

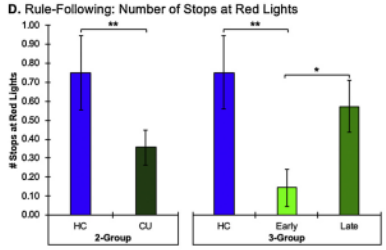

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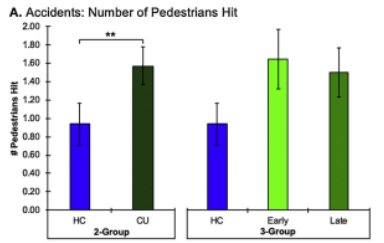
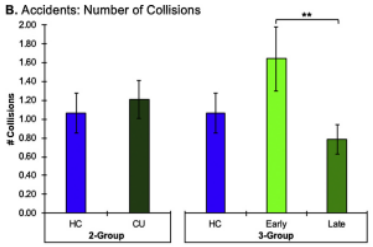
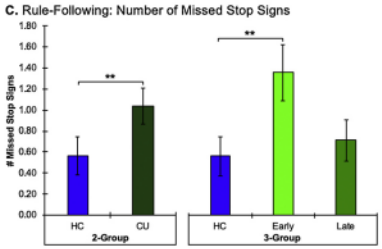
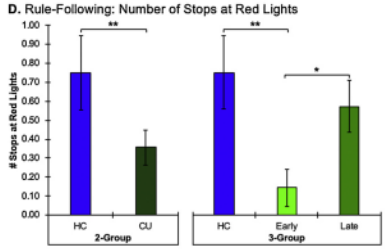
HARVARD MEDICAL SCHOOL

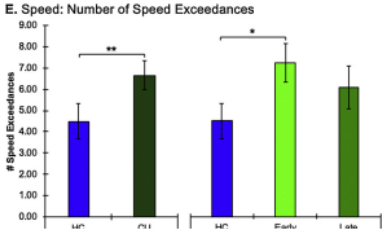
Cannabis & Driving

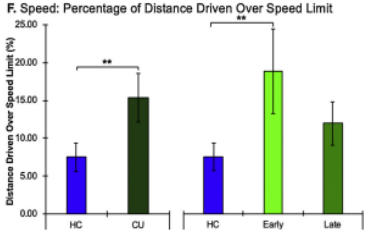












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Full length article

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[c] Department of Psychiatry, Harvard Medical School, Boston, MA, USA

ARTICLE INFO

Keywords:
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Driving
Safety
Age of onset
Executive function
Impulsivity

ABSTRACT

Background: Across the nation, growing numbers of individuals are exploring the use of cannabis for medical or recreational purposes, and the proportion of cannabis-positive drivers involved in fatal crashes increased from 8 percent in 2013 to 17 percent in 2014, raising concerns about the impact of cannabis use on driving. Previous studies have demonstrated that cannabis use is associated with impaired driving performance, but thus far, research has primarily focused on the effects of *acute* intoxication.

Methods: The current study assessed the potential impact of cannabis use on driving performance using a customized driving simulator in *non-intoxicated*, heavy, recreational cannabis users and healthy controls (HCs) without a history of cannabis use.

Results: Overall, cannabis users demonstrated impaired driving relative to HC participants with increased accidents, speed, and lateral movement, and reduced rule-following. Interestingly, however, when cannabis users were divided into groups based on age of onset of regular cannabis use, significant driving impairment was detected and completely localized to those with early onset (onset before age 16) relative to the late onset group (onset ≥16 years old). Further, covariate analyses suggest that impulsivity had a significant impact on performance differences.

Conclusions: Chronic, heavy, recreational cannabis use was associated with worse driving performance in non-intoxicated drivers, and earlier onset of use was associated with greater impairment. These results may be related to other factors associated with early exposure such as increased impulsivity.

1. Introduction

To date, several countries, including Canada and Uruguay have completely legalized cannabis, while in the United States, recreational cannabis use is legal for adults in 11 US states and Washington DC; an additional 33 states have fully legalized medical cannabis programs (National Conference of State Legislatures NCSL, 2019). In the US, national surveys indicate that approximately 123.9 million people aged 12 or older have tried cannabis at least once, and 27.7 million report past month use (Substance Abuse and Mental Health Services Administration SAMHSA, 2019). In addition, a recent Canadian survey indicated that approximately 4.4 million Canadians aged 15 or older reported using cannabis at least once in the past year (Canadian Tobacco, Alcohol and Drugs Survey CTADS, 2019). Further, the most recent US National Roadside Survey, which collected data from 2013 to 2014, reported that cannabis is the second most commonly detected substance (second only to alcohol) in randomized, voluntary assessments of drivers; 12.6 % of weekend, night-time drivers aged 16 or older tested positive for cannabis, representing a 48 % increase from the last national survey performed in 2007 (Berning et al., 2015). Additional data from the US National Survey of Drug Use and Health collected between 2002 and 2014 indicates that 3.2 % of individuals aged 16–25 reported driving while intoxicated with cannabis (Azofeifa et al., 2015). Similarly, the Canadian Road Safety Monitor survey, which has gathered information on drugged driving since 2002, indicated that approximately 2.9 % of Canadians reporting driving within two hours of using cannabis (Robertson et al., 2017).

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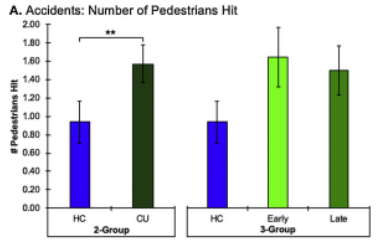

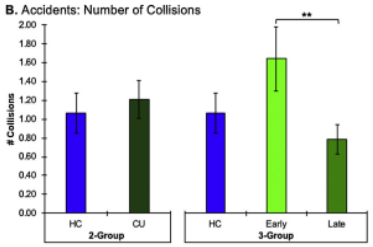

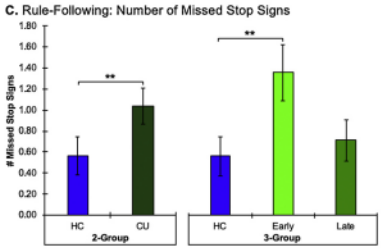

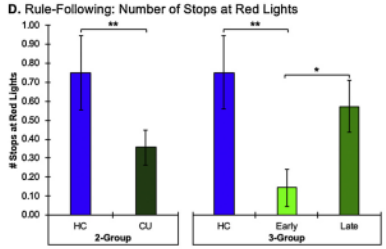

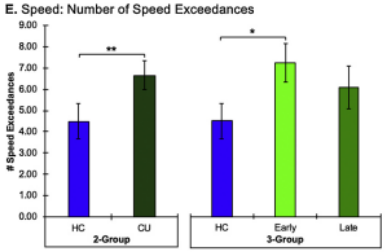

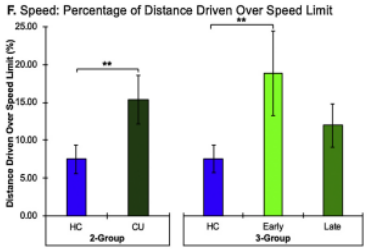

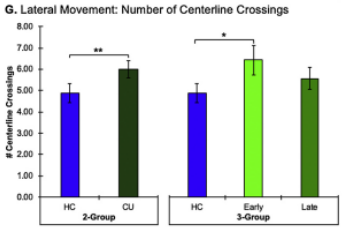

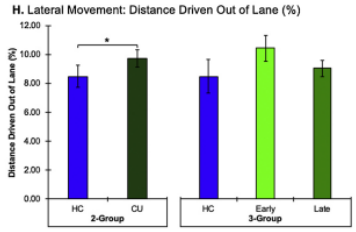

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Consequences of marijuana use

Behavioral effects

- Paranoia
- Psychosis, hallucinations
- Irritability
- Impaired short-term memory
- Poor attention/judgment
- Poor coordination/balance
- Distorted spatial perception
- Altered awareness of the passage of time

Physiologic effects

- Rapid heart rate
- High blood pressure
- Dry mouth and throat
- Eye redness & watering

Slide content courtesy of Dr. Mimi Schizer & Volkow et al., *N Engl J Med,* 2014.

CANNABIDIOL (CBD)

CANNABIDIOL (CBD)

IS CBD SAFE?

CBD INTERACTIONS WITH MEDICATION AND SUPPLEMENTS

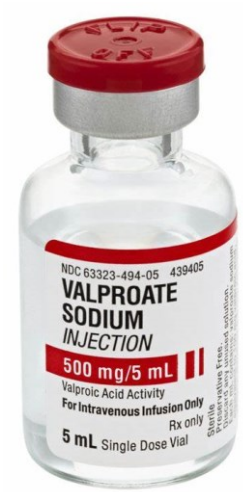
- SEDATION AND DROWSINESS WITH:

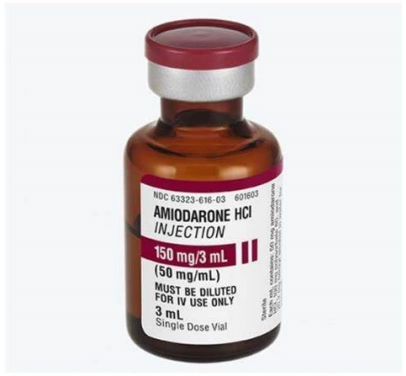
MEDICATIONS

HERBAL SUPPLEMENTS

Kocis, P. T., & Vrana, K. E. (2020). Delta-9-Tetrahydrocannabinol and Cannabidiol Drug-Drug Interactions. *Medical Cannabis and Cannabinoids*, *3*(1), 61–73. https://doi.org/10.1159/000507998

CBD CAUSES ALTERATIONS IN BLOOD CONCENTRATION OF DRUGS:





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Cannabis Edibles such as Delta-8

- Anxiety
- Dizziness
- Confusion
- Loss of consciousness
- Hallucinations
- Vomiting
- Tremor

[5 Things to Know about Delta-8 Tetrahydrocannabinol – Delta-8 THC | FDA]

FDA WARNINGS

- 1. Delta-8 THC products have not been evaluated or approved by the FDA for safe use and may be marketed in ways that put the public health at risk.
- 2. The FDA has received adverse event reports involving delta-8 THC-containing products.
- 3. Delta-8 THC has psychoactive and intoxicating effects.
- 4. Delta-8 THC products often involve use of potentially harmful chemicals to create the concentrations of delta-8 THC claimed in the marketplace.
- 5. Delta-8 THC products should be kept out of the reach of children and pets.

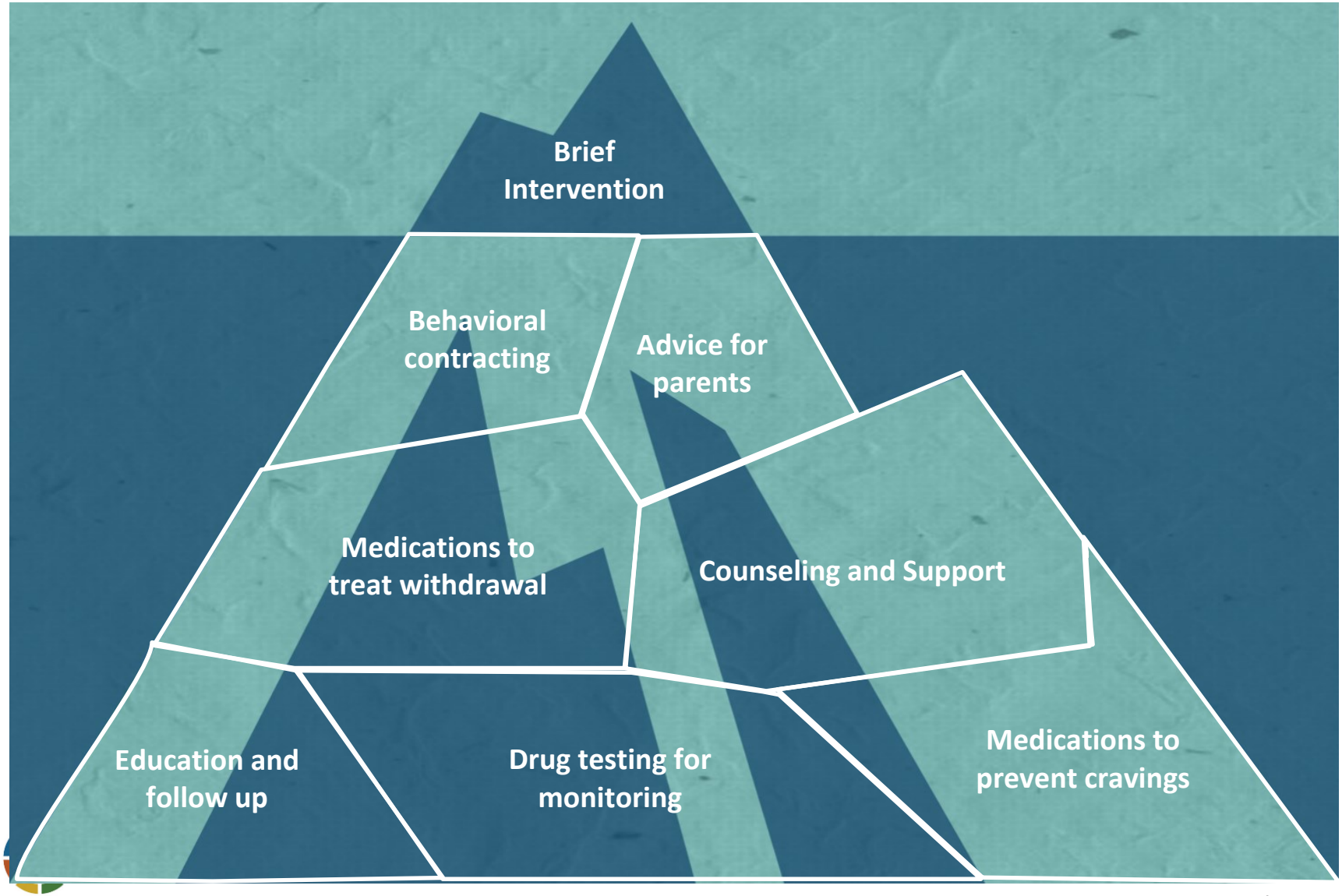
How to report complaints and cases of accidental exposure or adverse events:

- If you think you are having a serious side effect that is an immediate danger to your health, call 9-1-1 or go to your local emergency room. Health care professionals and patients are encouraged to report complaints and cases of accidental exposure and adverse events to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:
- Call an FDA Consumer Complaint Coordinator if you wish to speak directly to a person about your problem.
- Complete an electronic Voluntary MedWatch form online or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the form, or submit by fax to 1-800-FDA-0178.
- Complete a paper Voluntary MedWatch form and mail it to the FDA.
- To report adverse events in animals to the FDA's Center for Veterinary Medicine, please download and submit Form FDA 1932a found at: www.fda.gov/ReportAnimalAE.

Summary

- Adolescent development primes teens for substance use.
- All psychoactive substance use triggers dopamine release. Without the protection of the frontal cortices, adolescents are at greater risk for neurological changes associated with addiction.
- Substances each have unique impacts on certain areas of the brain leading to the unique clinical picture resulting from long term use.

Treating adolescent substance use



Slide courtesy of Sharon Levy, MD

Substance use treatment

Medications	Behavioral Interventions
Alcohol use: naltrexone (18+), acamprosate Marijuana use: n-acetylcysteine (off-label) Nicotine use: nicotine replacement, varenicline (17+), bupropion Opioid use: buprenorphine/naloxone (16+), methadone, naltrexone	Cognitive Behavioral Therapy Motivational Enhancement Therapy Dialectical Behavioral Therapy Contingency Management

Substance use treatment

Family Support	Community Support
Advice & support for parents Working with family to establish goals & expectations Family-based therapies: - Community Reinforcement & Family Training - Multidimensional Family Therapy - Functional Family Therapy - Brief Strategic Family Therapy - Multisystemic Therapy	Groups: NA, AA, SMART Recovery, Young People in Recovery Peer mentors Addiction medicine specialists

How can we prevent substance use & related problems?

Promote protective factors

1. Engagement in school, hobbies, extracurriculars
2. Academic achievement
3. Family bonding
4. Parental monitoring

https://youth.gov/youth-topics/substance-abuse

Address substance use early

What if I'm worried about a friend?

1. TRUST YOUR INSTINCTS.

If you think your friend has a problem, you're probably right, says Jamison Monroe, founder of California's Newport Academy teen treatment centers.

2. DON'T IGNORE THE SIGNS.

Changes in behavior and mood could signal that someone has a problem. A pal may start acting distant, secretive, or angry. You may also notice health and hygiene issues, including a messy appearance, extreme tiredness, frequent illness, weight loss or gain, and nosebleeds.

3. ENCOURAGE THEM TO GET HELP.

They can visit the Partnership for Drug-Free Kids at www.drugfree.org/heroin for a guide to resources and treatment centers in your state.

4. TALK TO A TRUSTED ADULT.

Whether you go to a parent, counselor, or a coach, a grown-up may be able to better intervene. "Yes, your friend is going to be angry with you in the short term, but ultimately they're going to thank you," says Monroe.

5. KNOW WHEN TO WALK AWAY.

You're not responsible for anyone else's recovery. If a friend's drug use negatively affects your life, it may be time to end the relationship.

https://choices.scholastic.com/issues/2017-18/040118/a-prescription-for-addiction.html

Resources

- NIDA for Teens: https://teens.drugabuse.gov/
- Partnership to End Addiction: drugfree.org
- Frontiers for Young Minds: “What is Vaping?”
- http://www.staytruetoyou.org/
- https://truthinitiative.org/
- https://teen.smokefree.gov/

- Young People in Recovery: youngpeopleinrecovery.org
- SMART Recovery Young Adults: https://www.smartrecovery.org/young-adults/

Questions?

Thank you!

Adam Ramsey, MD
Adam.Ramsey@childrens.harvard.edu

ORN Survey

To better improve our services at the Opioid Response Network, we respectfully request you take this brief survey about our performance.

Thank you so much for your cooperation!

Please Use the QR Code or Click Here