The Science of Cannabis and Clinical Observations in Adolescents

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Cannabis Education forum
for Legislators and Local Policy Makers
June 16th, 2021

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Objectives

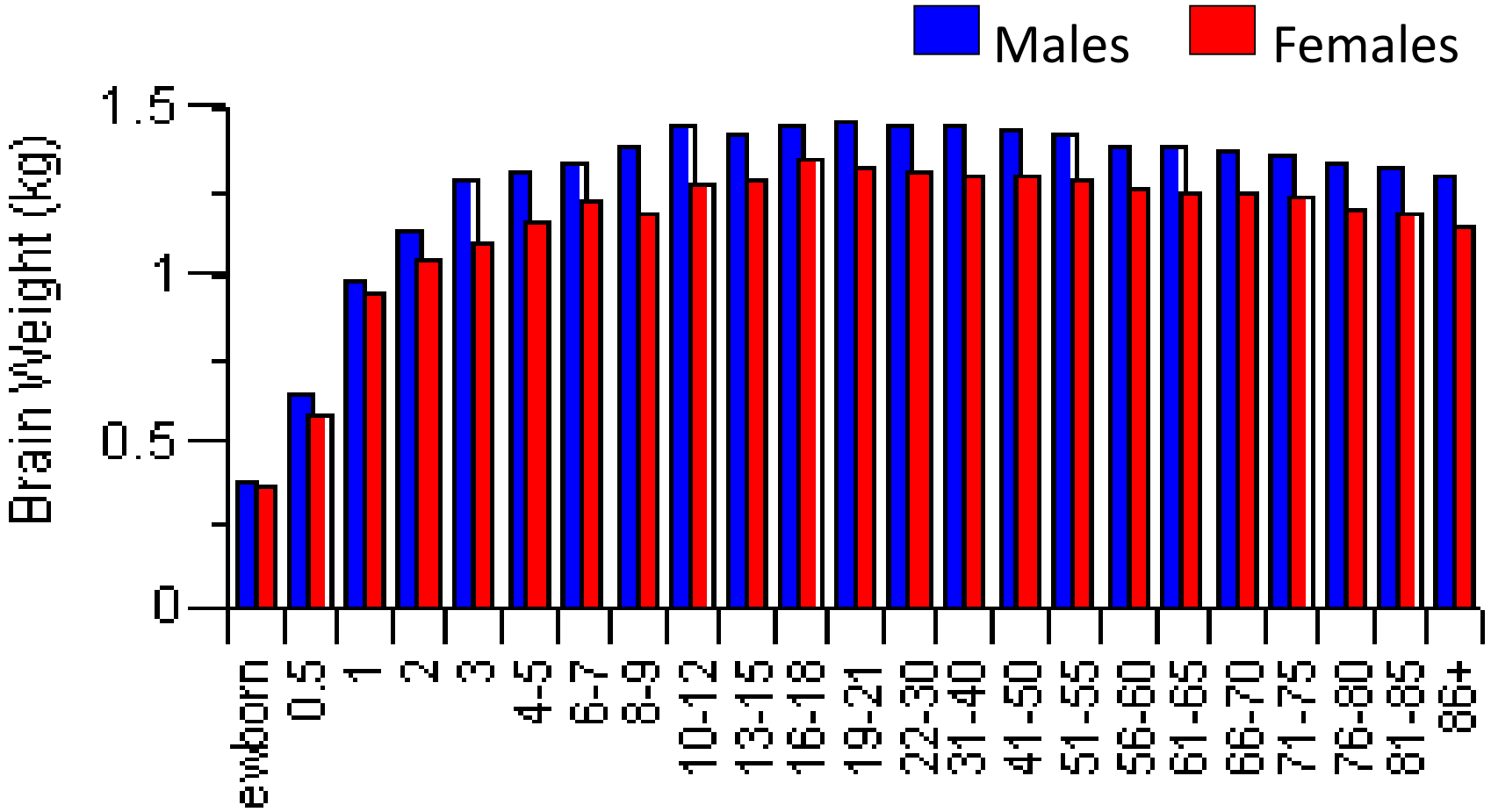
- Discuss the science of cannabis (marijuana)
  - Understanding the adolescent brain
  - Role of our endocannabinoid system
  - Impact of cannabis on the developing brain

- Clinical observations in Massachusetts
  - Cannabis related products used by youth
  - Risk and comorbidities associated with cannabis use
  - Two case representations of Cannabis-Induced Psychosis

Brain Growth in Childhood

- Throughout childhood the brain undergoes rapid growth…
  - Increase in number of neurons
  - Increase in the number of connections between neurons (blossoming)
  - This increase in brain size is complete by age 10-12

Brain Weight by Age



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

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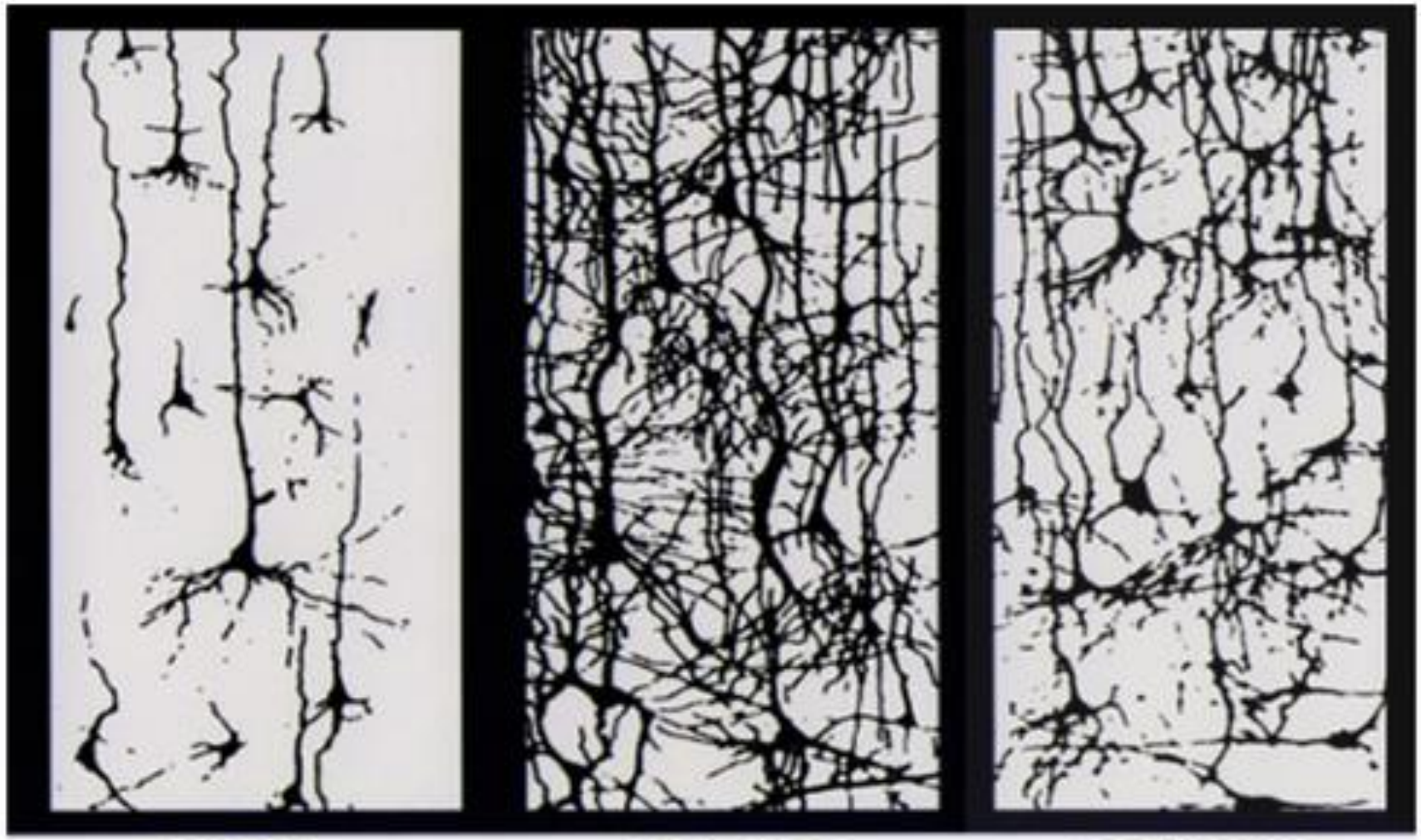
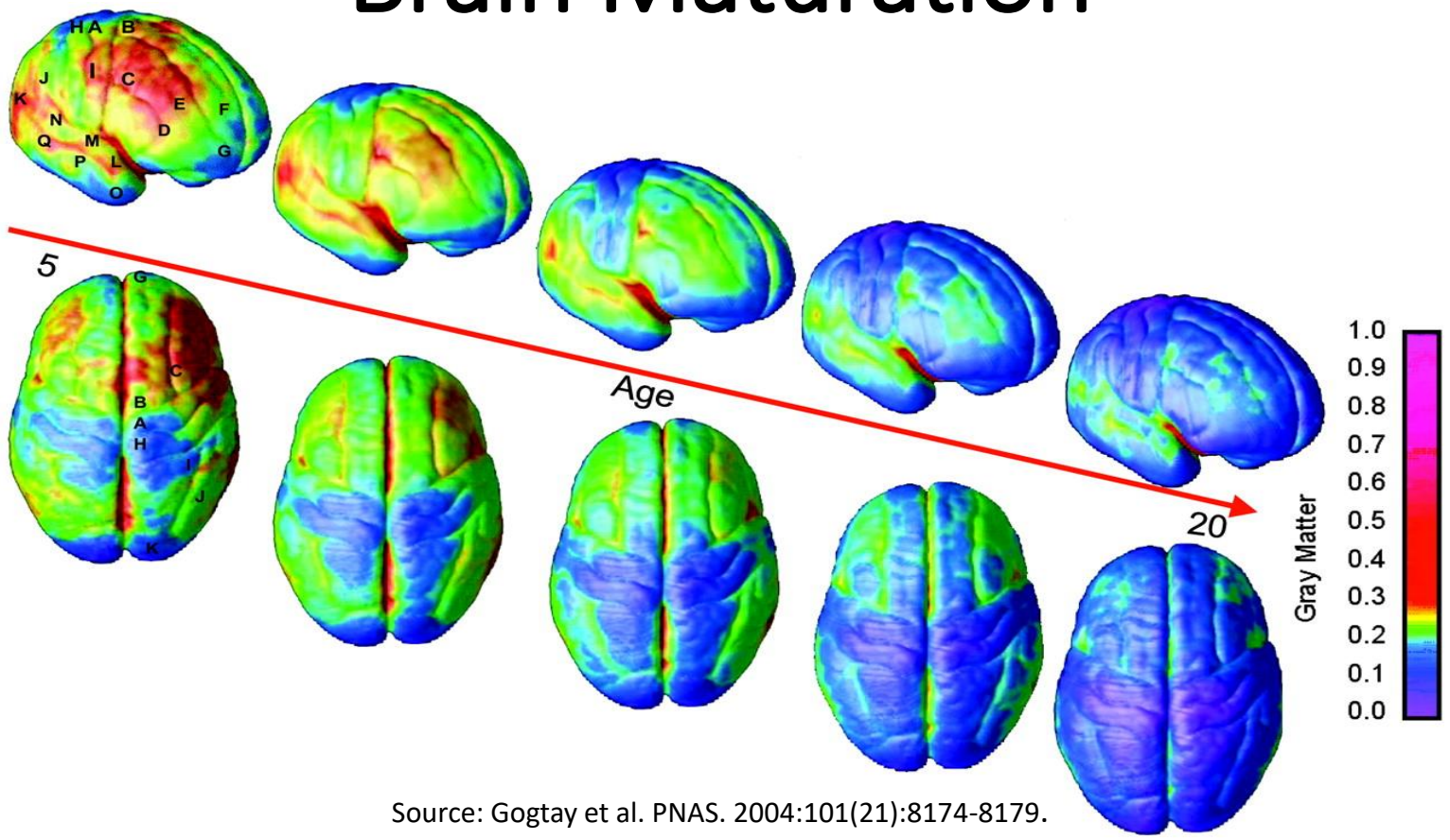
Experience Shapes Brain Architecture by Over-Production of Connections Followed by Pruning



BIRTH 6 YEARS 14 YEARS

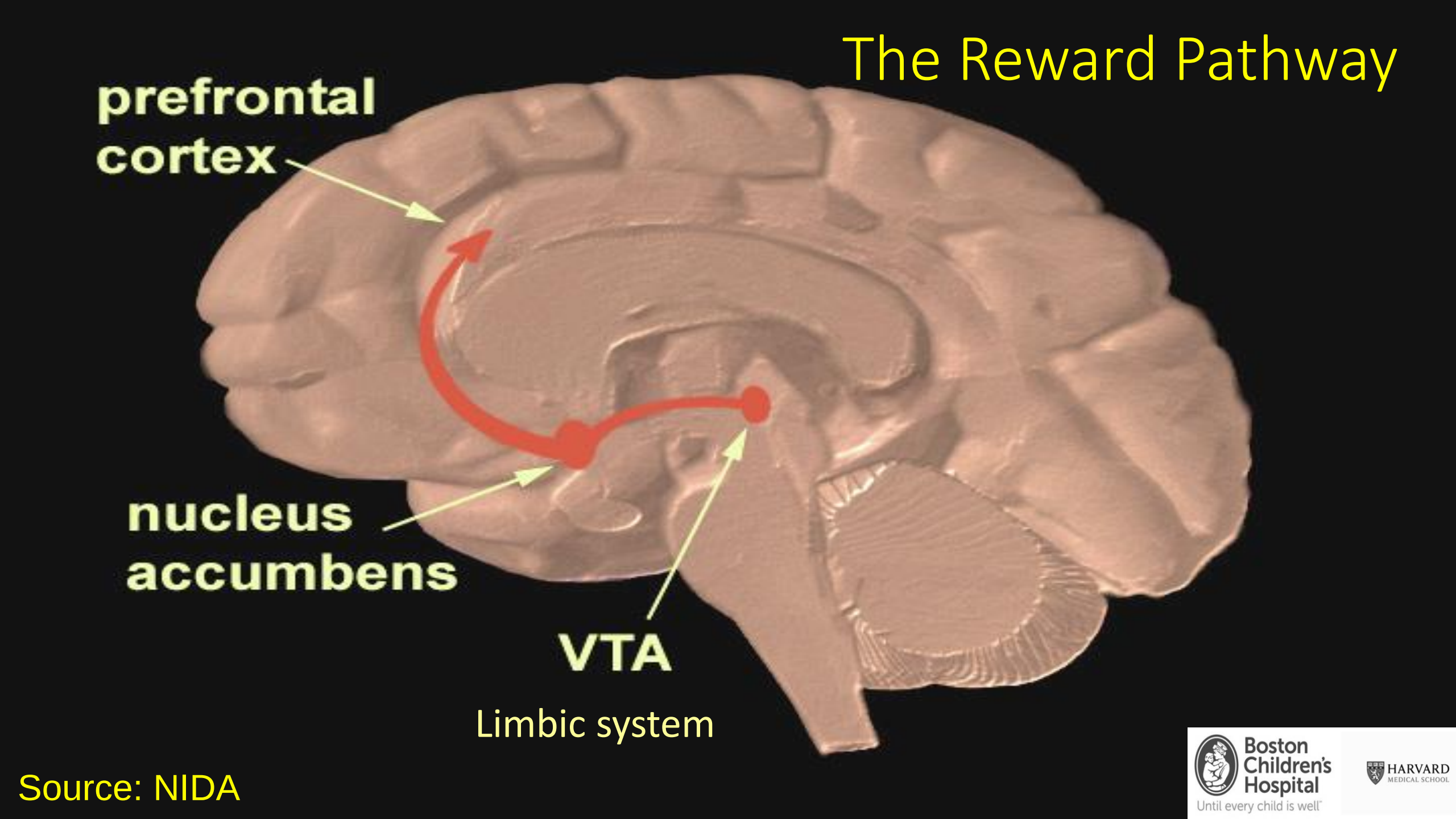
Brain Maturation



Source: Gogtay et al. PNAS. 2004:101(21):8174-8179.

Note that the brain matures from back to front, with the prefrontal cortex, which responsible for executive functioning, the last area to develop.

The Reward Pathway



Limbic system

Source: NIDA

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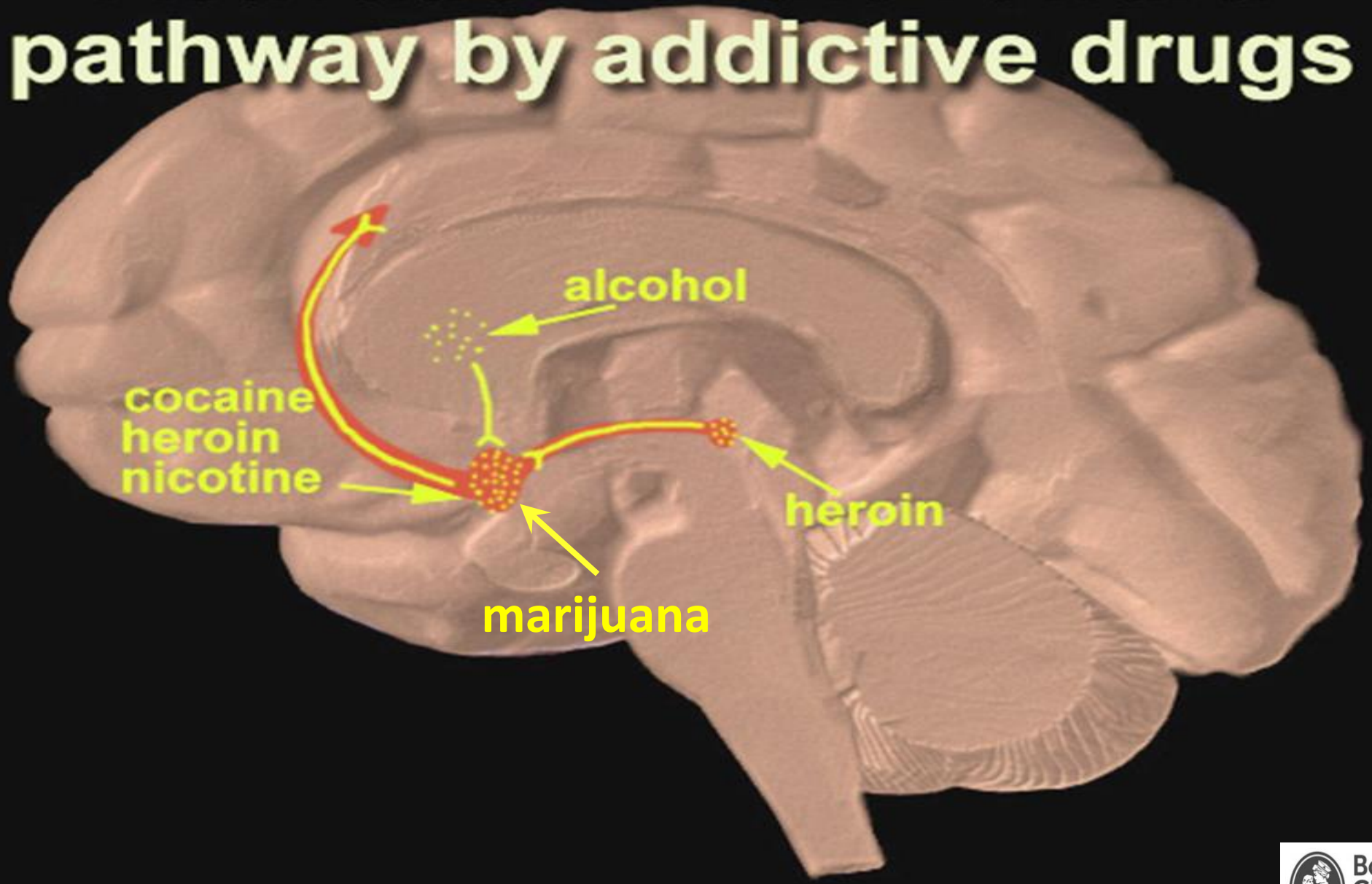
Activation of the reward pathway by addictive drugs



Source: NIDA

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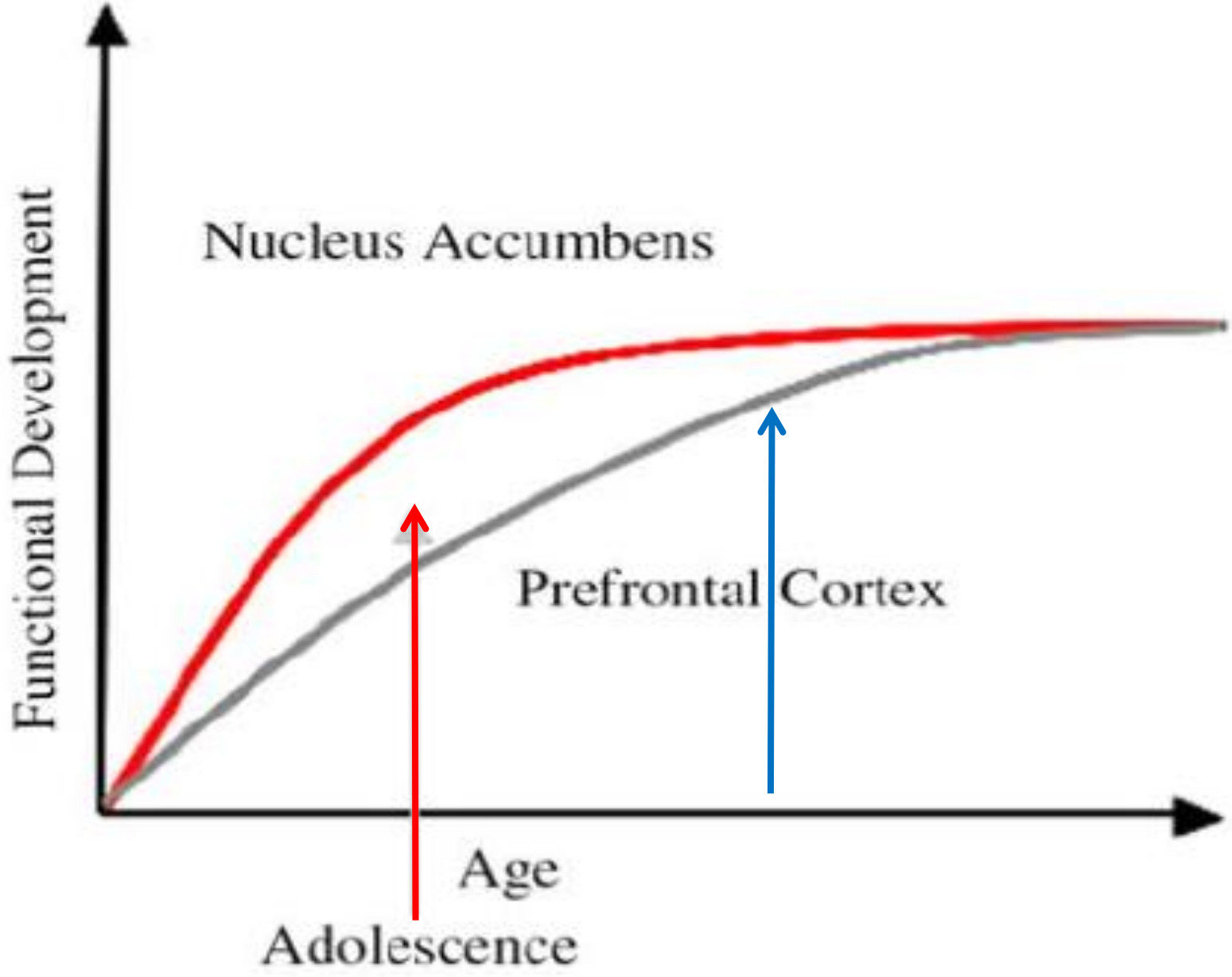
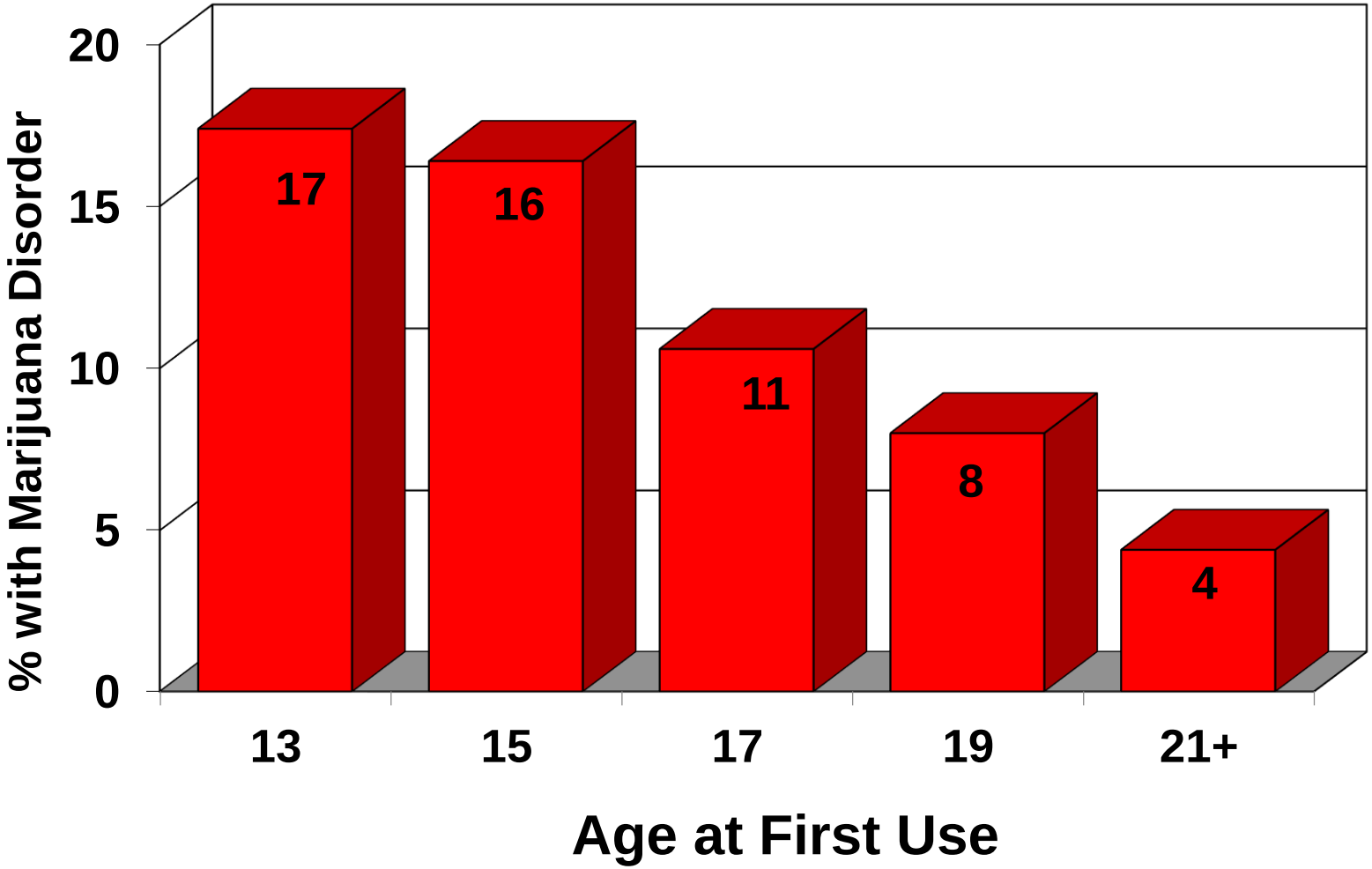


Age at First Use and Risk of Developing Cannabis Use Disorder



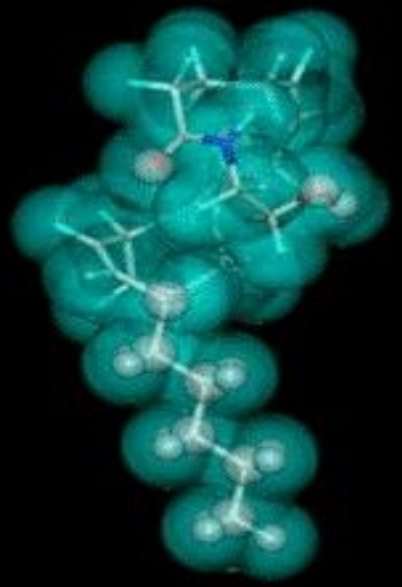
Source: Substance Abuse and Mental Health Services Administration. (2010). *Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of National Findings* (Office of Applied Studies, NSDUH Series H-38A, HHS Publication No. SMA 10-4586Findings). Rockville, MD.

Marijuana

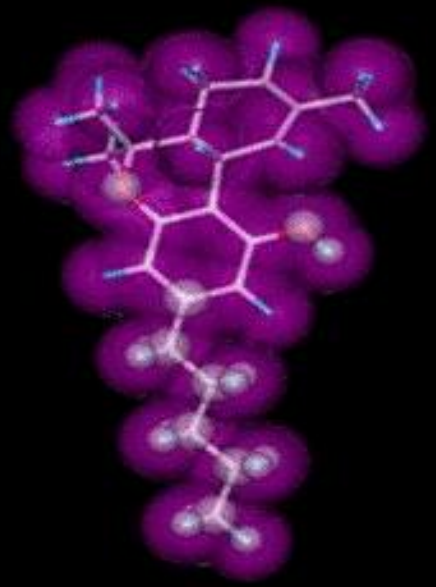
- Contains many chemicals called cannabinoids such as…
  - delta-9-tetrahydrocannabinol (THC)
  - delta-8-tetrahydrocannabinol
  - cannabidiol
  - cannabinol
  - cannabichromene
  - cannabigerol
  - Etc.

Source: Mechoulam R, Hanus L, The cannabinoid system from the point of view of a chemist. In *Marijuana and Madness.* ed. Castle, Murray. Cambridge University Press, 2004

Endo-cannabinoid
(Anandamide)

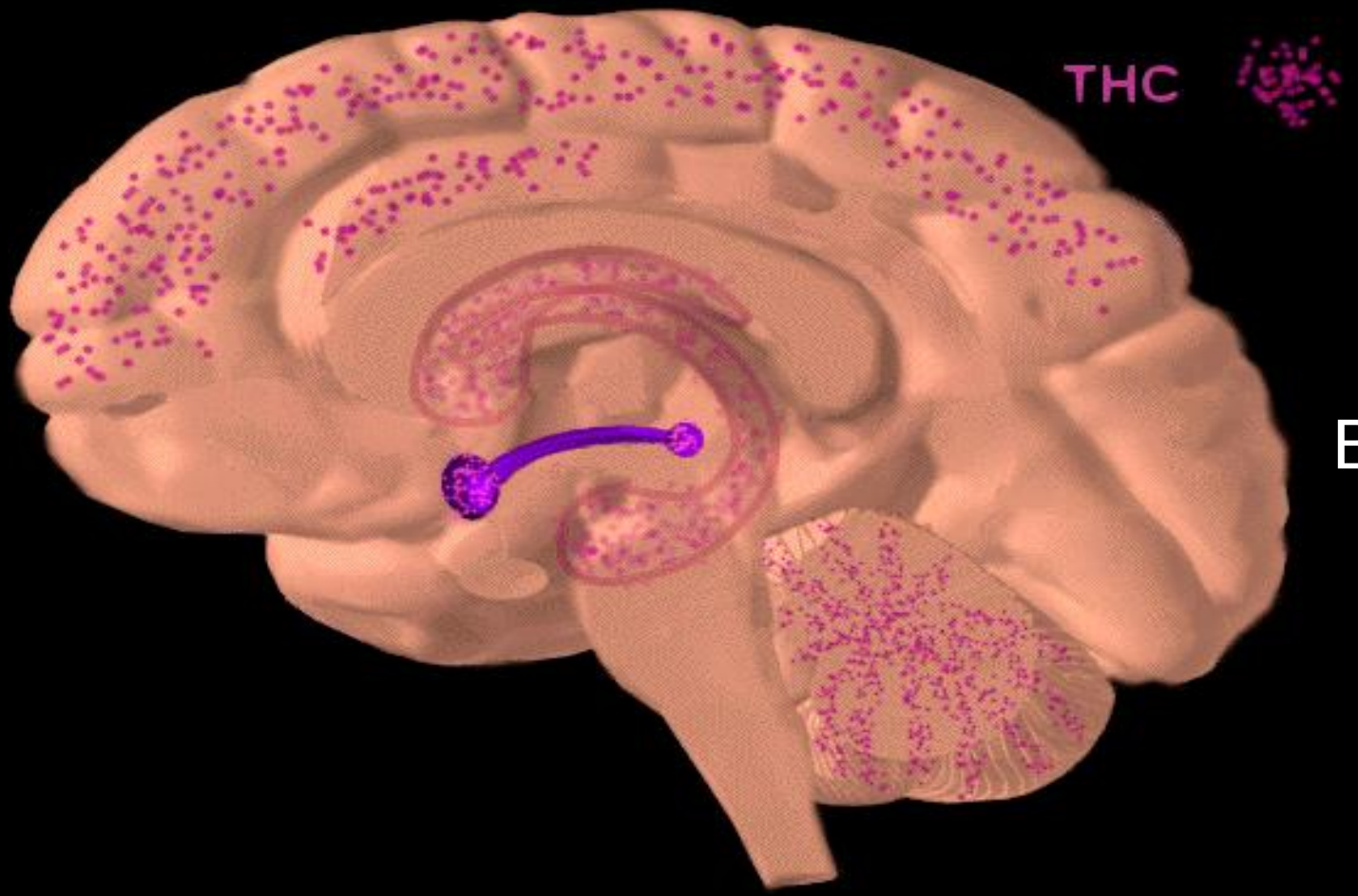


Marijuana
(**T**etra**H**ydro**C**annabinol)



Source: NIDA

Cannabinoid Binding Sites



Front

Back

Source: NIDA

Endocannabinoid System: Regulation

- Neuron "volume control": dials down neuron activity when too strong
- Regulates important neurotransmitters affecting pleasure, mood, pain, appetite, sleep, motivation, focus, memory, attention etc. (dopamine, serotonin, endorphins)
- Helps keep neuron activity in balance, not underactive or overactive

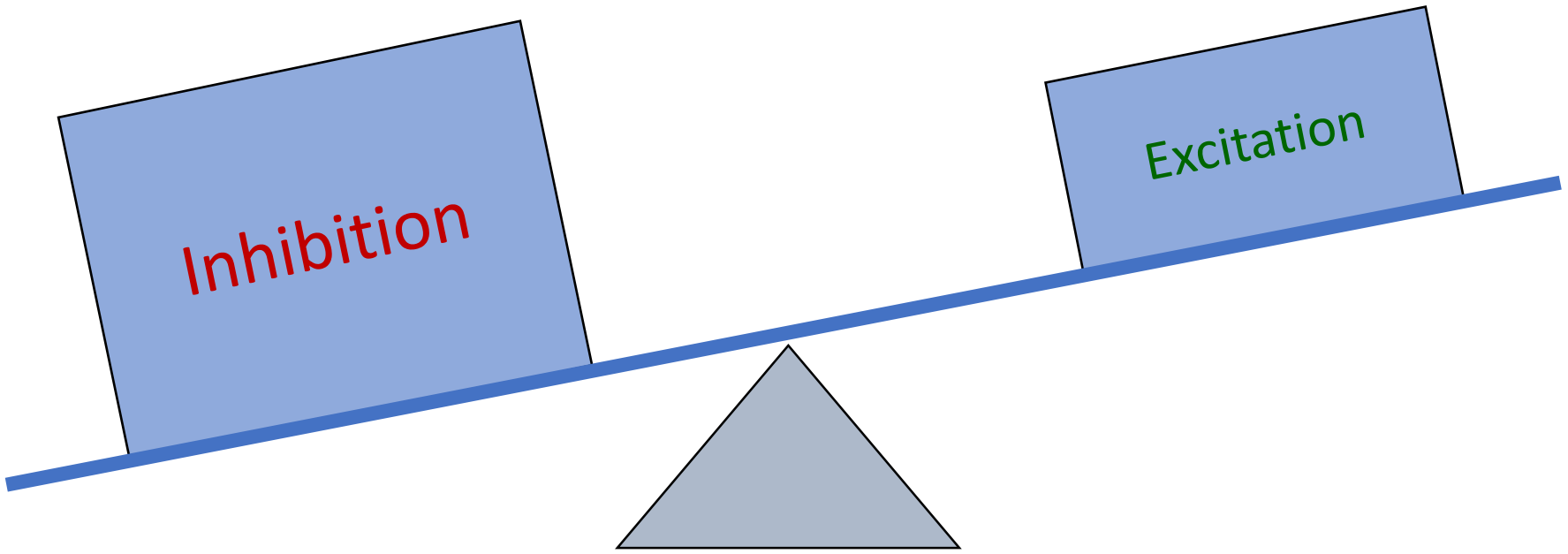
Endocannabinoid System: Growth

- Shapes brain development by…
  - guiding neurons to grow to the right places in the brain for correct function
  - controlling neuron activity, thereby shaping brain wiring
  - supporting myelin growth on neurons

THC vs. Anandamide

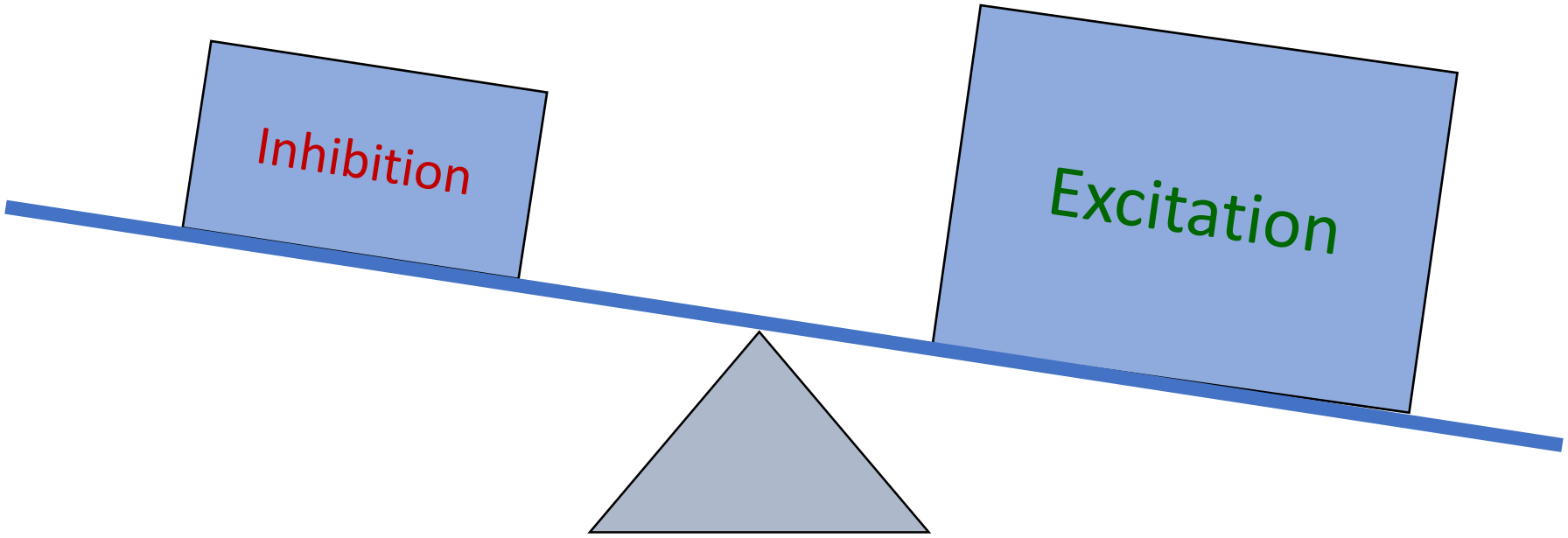
- Both dial down neuron activity to change neurotransmitter release
- THC has a **MUCH STRONGER, LONGER** effect than anandamide on brain cells
- THC **interferes** with anandamide function, so it can't do its job to protect and balance cell activity

Cannabis tilts the balance towards *inhibition*



Source: Valenzuela CF, Alcohol and neurotransmitter actions. Alcohol Health & Research World, 1997; 21(2), 144-148.

Chronic exposure causes brain to increase *excitation* to compensate



Source: Valenzuela CF, Alcohol and neurotransmitter actions. Alcohol Health & Research World, 1997; 21(2), 144-148.

Cannabis Withdrawal Symptoms

- Restlessness, anxiety
- Increased irritability, anger, aggression
- Insomnia, nightmares/strange dreams
- Decreased appetite
- Weight loss

Source: Budney et al. Arch Gen Psych 58(10):917-924, 2001.

Clinical Observations

MARIJUANA USE – MASSACHUSETTS HIGH SCHOOL STUDENTS [Click back to Table of Contents]

Percentage of Massachusetts High School Students who reported:		Ever using marijuana	Using marijuana, past 30 days	Using marijuana before age of 13	Ever using synthetic marijuana	Parental/Family disapproval of marijuana use
Overall (95% Confidence Interval)		**37.9 (33.9 - 41.9)**	**24.1 (21.3 - 26.9)**	**4.4 (3.4 - 5.5)**	**5.0 (4.4 - 5.6)**	**71.0 (68.5 – 73.4)**
Grade	**9th Grade**	19.4 (15.9 - 22.8)	11.9 (9.5 - 14.3)	4.7 (3.1 - 6.2)	4.0 (2.3 - 5.6)	73.4 (67.9 – 78.2)
	10th Grade	35.0 (30.9 - 39.1)	22.5 (18.4 - 26.6)	4.5 (2.6 - 6.4)	4.2 (2.9 - 5.4)	72.7 (69.4 – 75.8)
	11th Grade	45.2 (40.4 - 50.1)	29.6 (25.2 - 34.0)	4.0 (2.1 - 5.9)	6.2 (4.6 - 7.7)	71.5 (66.7 – 75.8)
	12th Grade	54.1 (47.1 - 61.0)	33.0 (27.1 - 38.9)	4.6 (2.7 - 6.6)	5.8 (3.4 - 8.1)	66.0 (61.0 – 70.6)
Gender	**Male**	37.5 (33.0 - 41.9)	24.9 (21.4 - 28.4)	6.0 (4.3 - 7.6)	5.7 (4.4 - 7.0)	69.5 (66.1 – 72.8)
	Female	38.4 (34.1 - 42.6)	23.2 (19.6 - 26.7)	2.8 (1.8 - 3.9)	4.2 (3.2 - 5.2)	72.6 (69.9 – 75.2)
Race/Ethnicity	**White, NH**	39.5 (34.6 - 44.4)	25.5 (22.1 - 28.9)	3.7 (2.4 - 5.0)	4.3 (3.5 - 5.0)	71.5 (68.7 – 74.2)
	Black, NH	33.1 (26.9 - 39.4)	21.6 (15.9 - 27.3)	6.6 (3.7 - 9.5)	5.6 (2.9 - 8.2)	68.8 (62.4 – 74.5)
	Hispanic	41.6 (35.2 - 48.0)	26.6 (21.4 - 31.7)	6.3 (3.6 - 9.0)	7.9 (4.8 - 11.1)	68.7 (62.2 – 74.5)
	Asian, NH	16.1 (7.2 - 25.1)	9.0 (4.2 - 13.9)	-	-	80.9 (73.2 – 86.7)
	Other/Multiracial, NH	39.4 (30.8 - 48.1)	23.3 (15.1 - 31.5)	10.0 (4.5 - 15.4)	4.3 (1.8 - 6.7)	65.3 (55.6 – 73.8)

Data source: Massachusetts Youth Risk Behavior Survey 2017.

Footnote: Statistically significant difference between percentages can be assessed if their 95% confidence intervals do not overlap. White, Black, Asian, and Multiracial categories refer to non-Hispanic (NH). Categories of American Indian or Alaskan Native and Native Hawaiian or Other Pacific Islander were not presented due to insufficient sample sizes for a majority of survey questions. Estimates and their 95% confidence intervals were suppressed (-) if the underlying sample size was <100 respondents and/or the relative standard error was >30%.

Products Used

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Patient Case #1

- 16yo Girl
- No past psychiatric history
- ER presentation: paranoia, disorganized thoughts, and responding to internal stimuli
- Toxicology screen: Only THC +
- Diagnosis: Cannabis Induced Psychosis
- Plan: admit to inpatient psychiatry unit (Hospitalized > 1 month)

Patient Case #2

- 15yo boy
- History of anxiety
- ER presentation: panic attack, racing thoughts unable to be controlled, and suicide attempt
- Toxicology screen: Only THC +
- Diagnosis: Cannabis Induced Mood Disorder
- Plan: admit to inpatient psychiatry unit (Hospitalized > 1 month)

Cannabis use in adolescents increases the risk of mental illness in adulthood

- Regular cannabis use during adolescence found to increase risk 2 to 5x of developing psychosis, schizophrenia, anxiety, depression, and suicidality in adulthood.

Gobbi G, Atkin T, Zytynski T, et al. Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review and Meta-analysis. *JAMA Psychiatry.* 2019;76(4):426–434. doi:10.1001/jamapsychiatry.2018.4500

Di Forti M, Quattrone D, Freeman TP, et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. The Lancet 2019;6(5);427-436

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