PTTC Prevention Technology Transfer Center Network

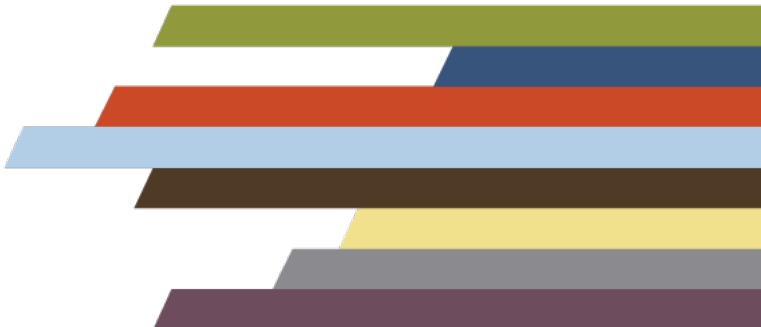
Funded by Substance Abuse and Mental Health Services Administration

Cannabis and the Adolescent Brain

Key Information for Prevention Practitioners to Share with Key Stakeholders and Communities

SAMHSA

Substance Abuse and Mental Health Services Administration



Acknowledgements

This slide deck was created in collaboration with the Prevention Technology Transfer Center Network Marijuana Risk Working Group, comprised of the following PTTC's:

- New England PTTC HHS Region 1
- Great Lakes PTTC HHS Region 5
- Pacific Southwest PTTC HHS Region 9
- Northwest PTTC HHS Region 10
- National American Indian and Alaska Native PTTC
- National Hispanic and Latino PTTC
- PTTC Network Coordinating Office

- The Prevention Technology Transfer Center Network is funded by the Substance Abuse and Mental Health Services Administration.

Purpose

Improve implementation and delivery of effective substance abuse prevention interventions

Provide training and technical assistance services to the substance abuse prevention field

- Tailored to meet the needs of recipients and the prevention field
- Based in prevention science and use evidence-based and promising practices
- Leverage the expertise and resources available through the alliances formed within and across the HHS regions and the PTTC Network.

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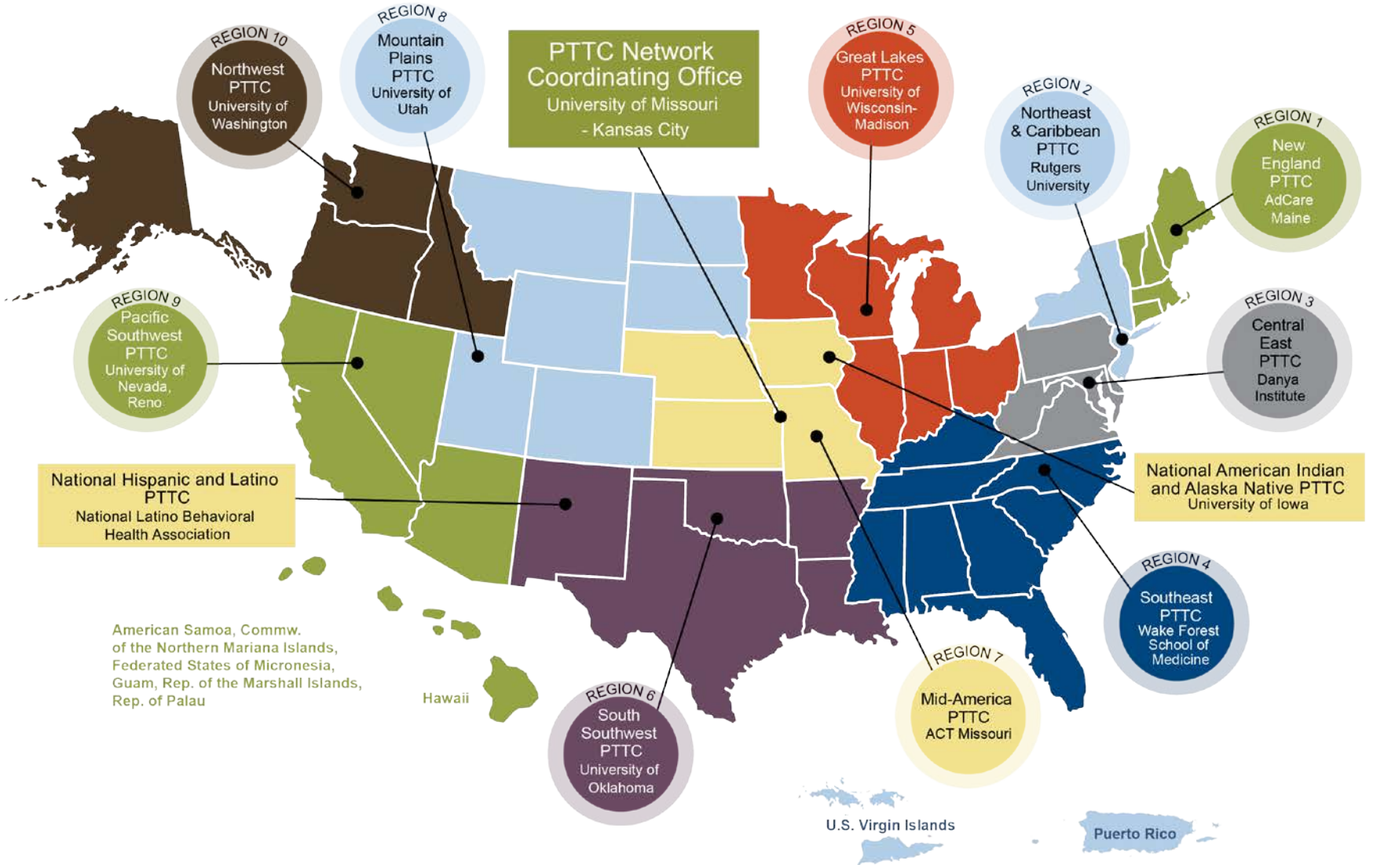
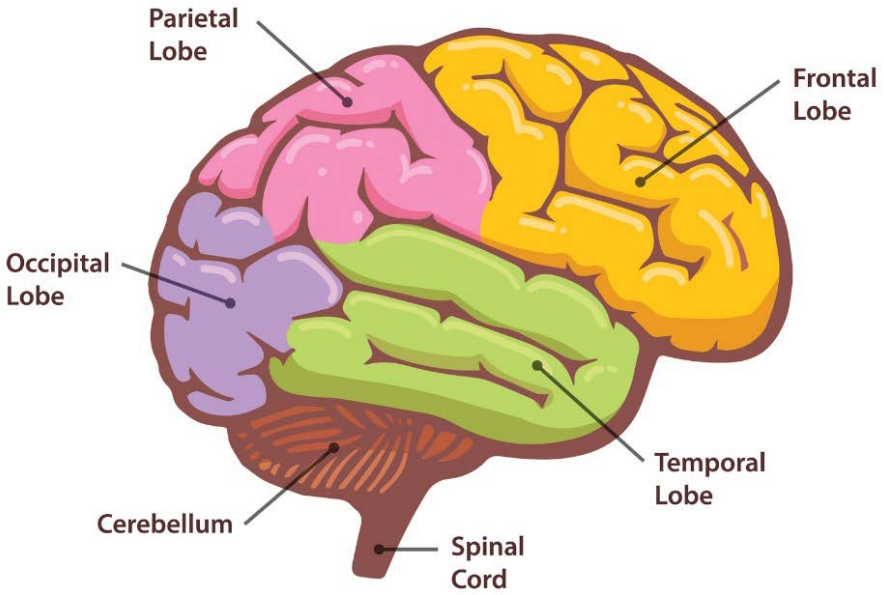
PTTC Network



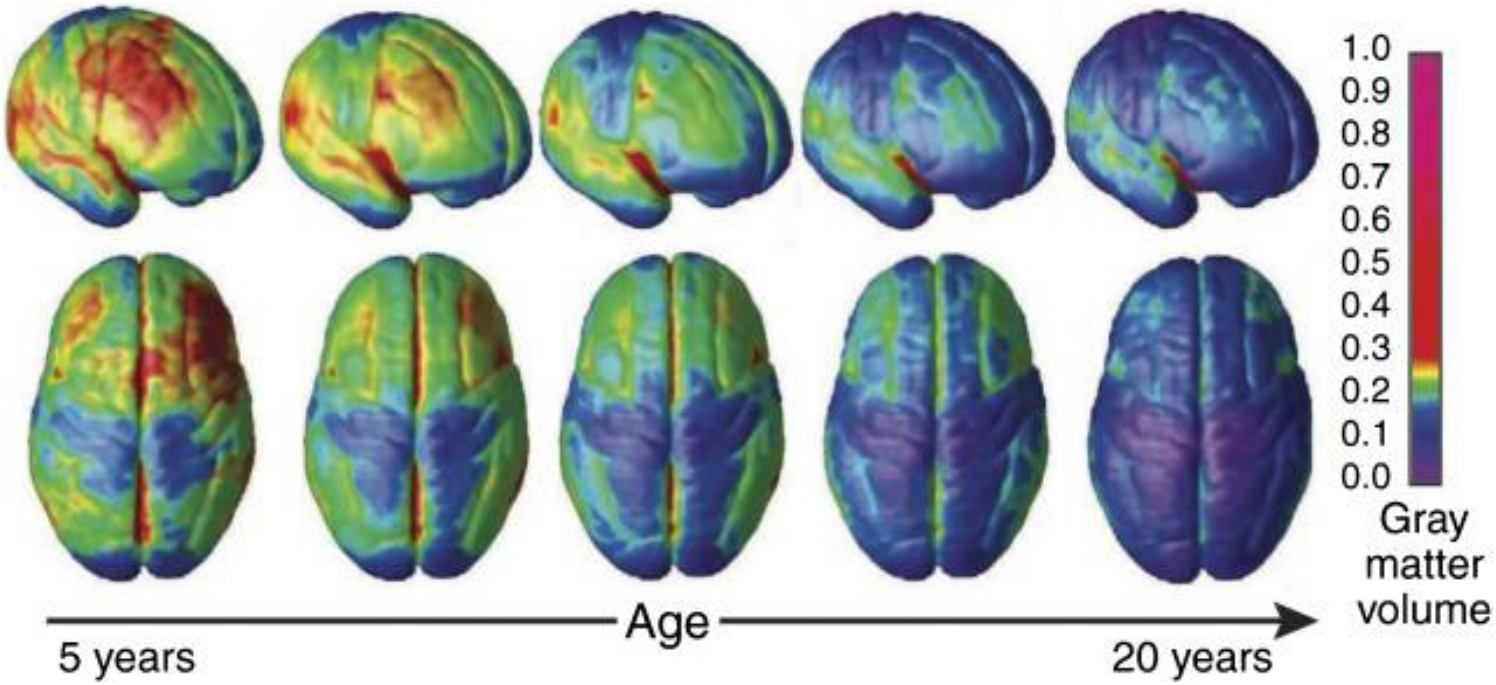
Adolescent Development

Parts of the Human Brain and their Functions

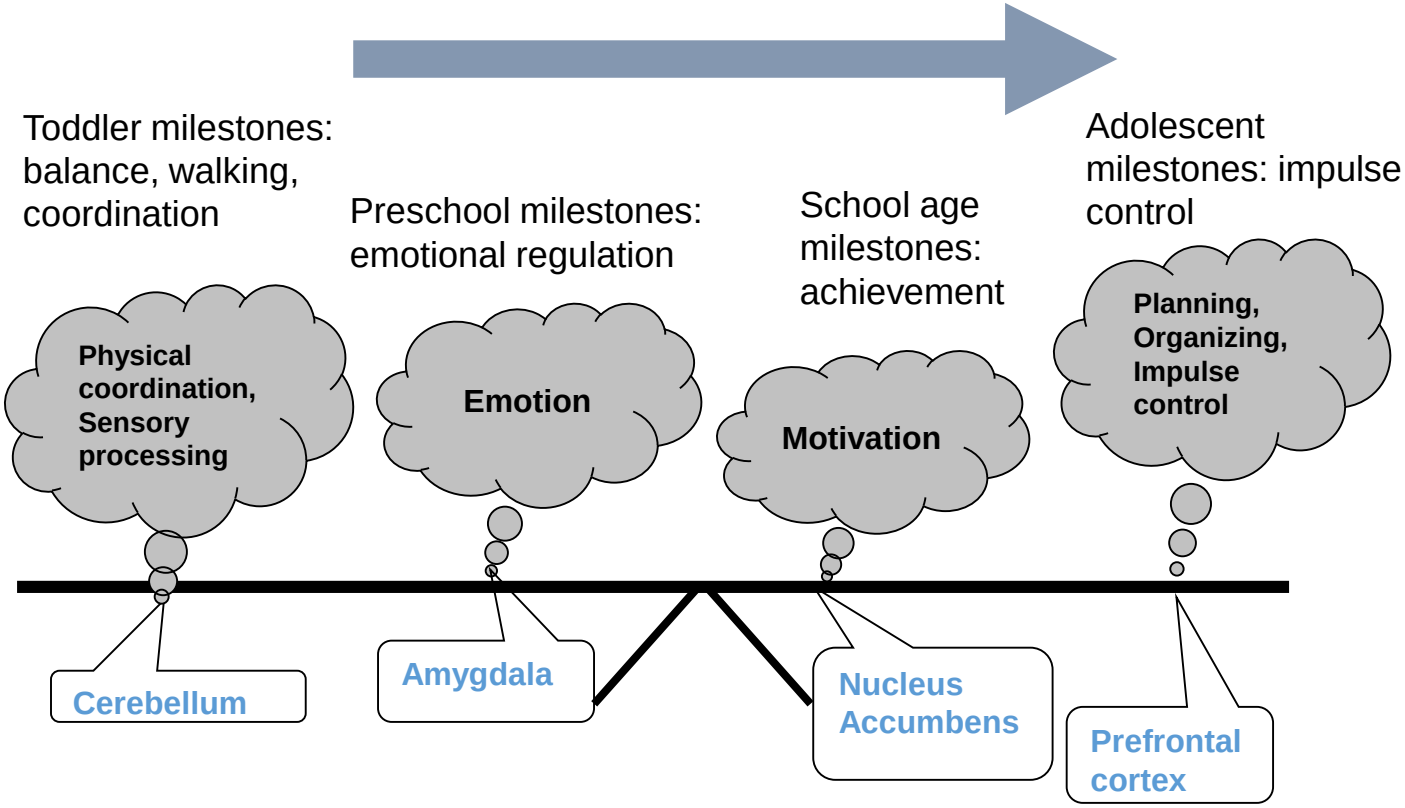


Click here to show NIDA video
The Human Brain: Major Structures and Functions

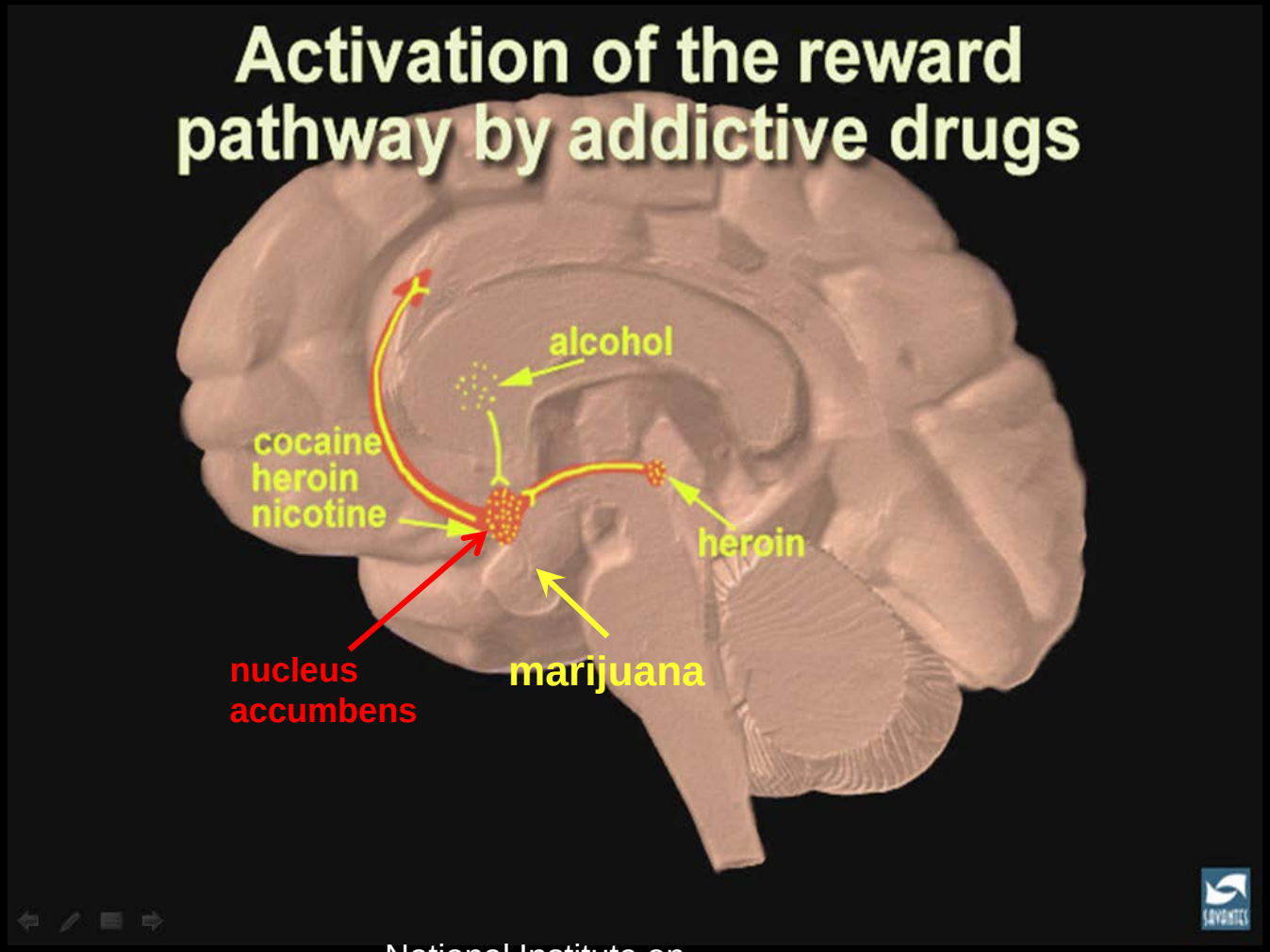
Changes in Brain Structure



Changes in Brain Function

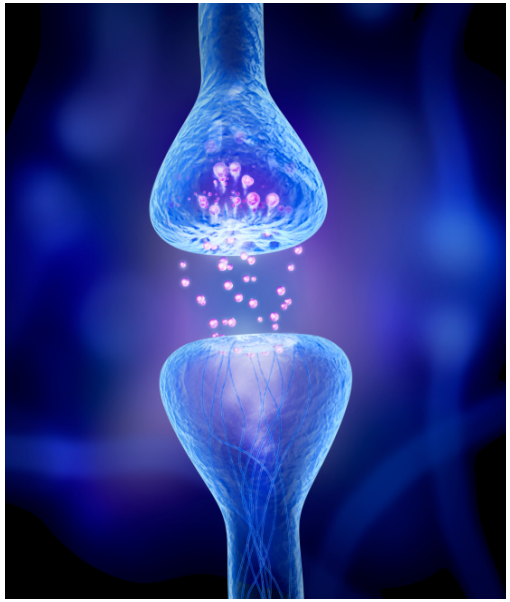


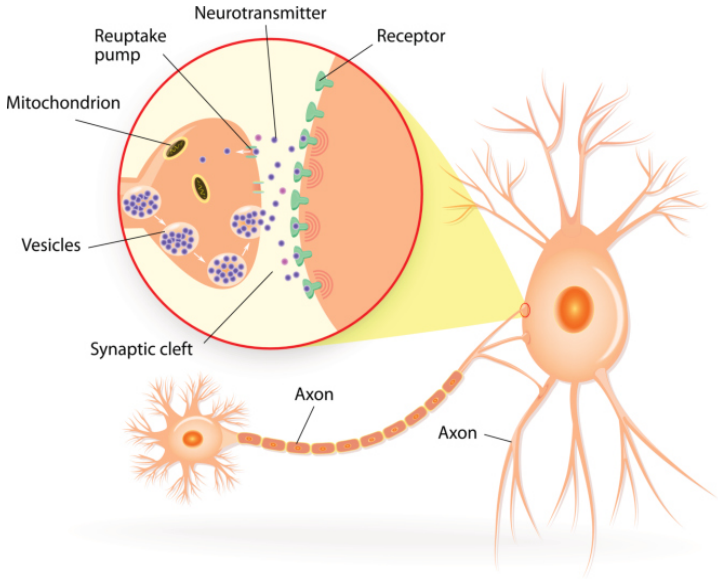
Slide adapted from Ken Winters, PhD.



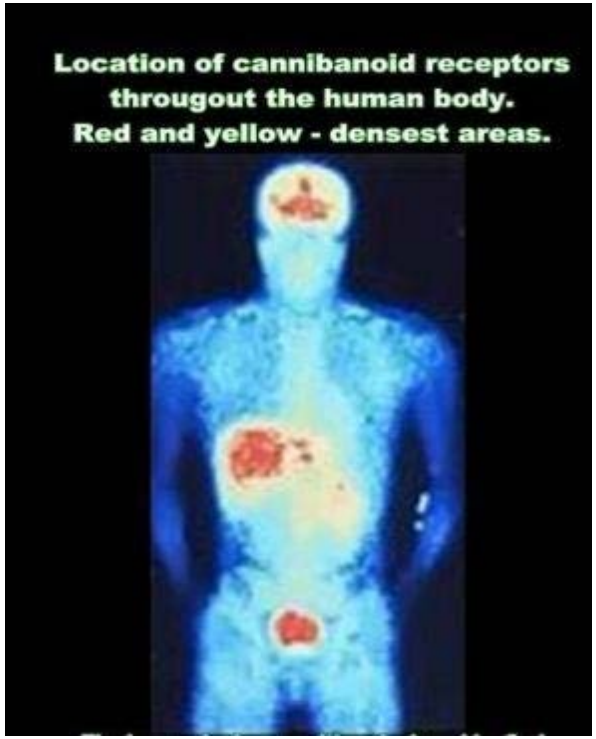
National Institute on Drug Abuse (2007)

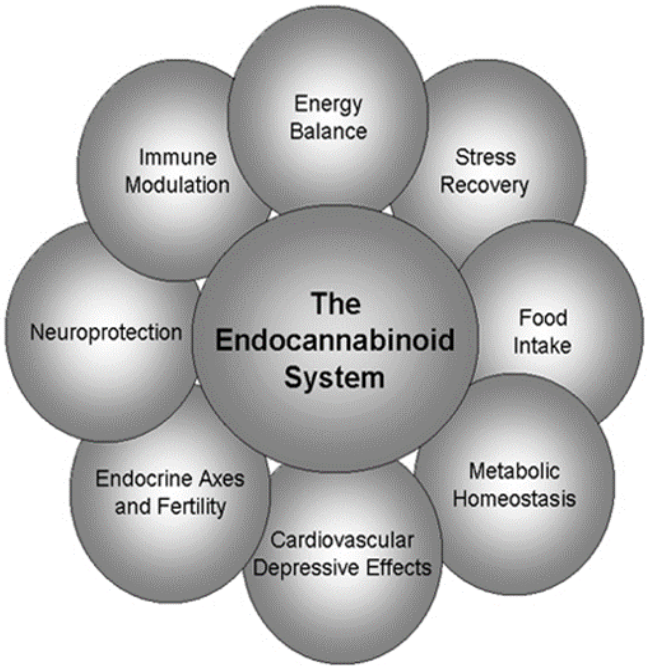
Addiction and the Brain



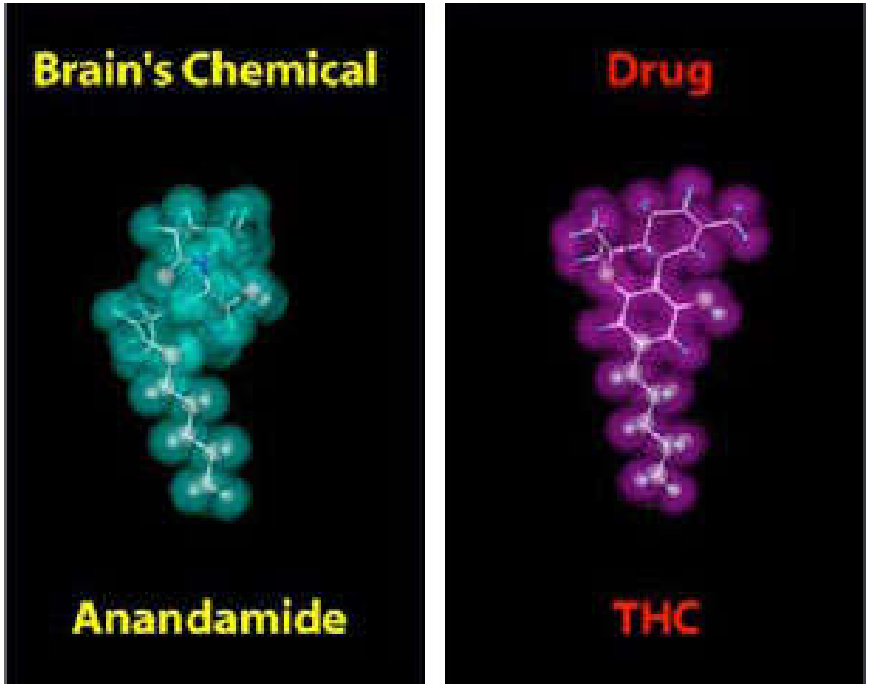


Made in the Brain: Endogenous Endocannabinoids





Endocannabinoids and THC

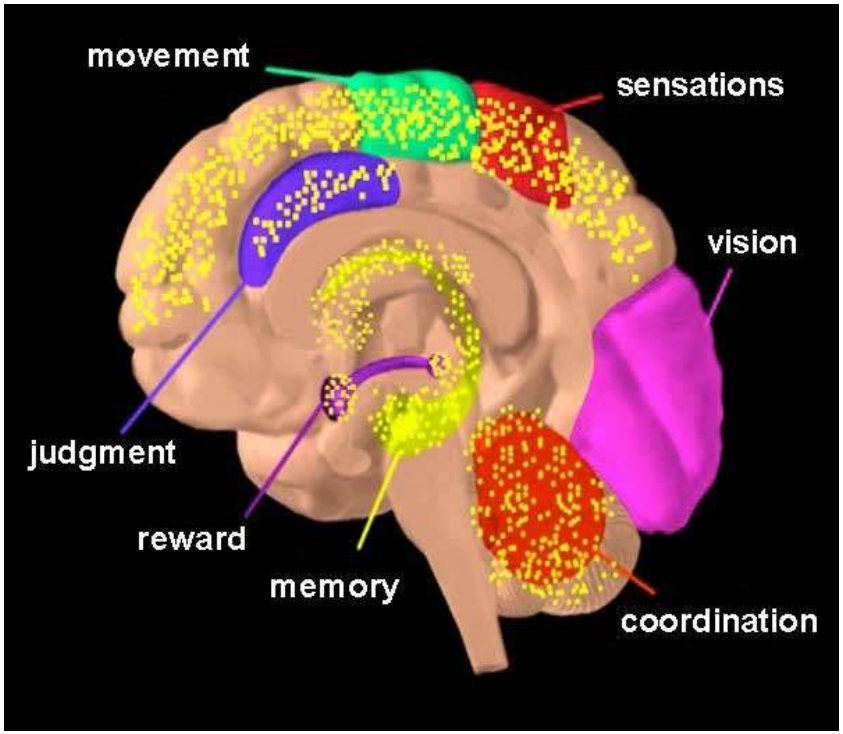


Brain Cannabinoid Receptor Sites

- Nucleus Accumbens
- Hippocampus
- Amygdala
- Hypothalamus
- Medulla
- Cerebellum

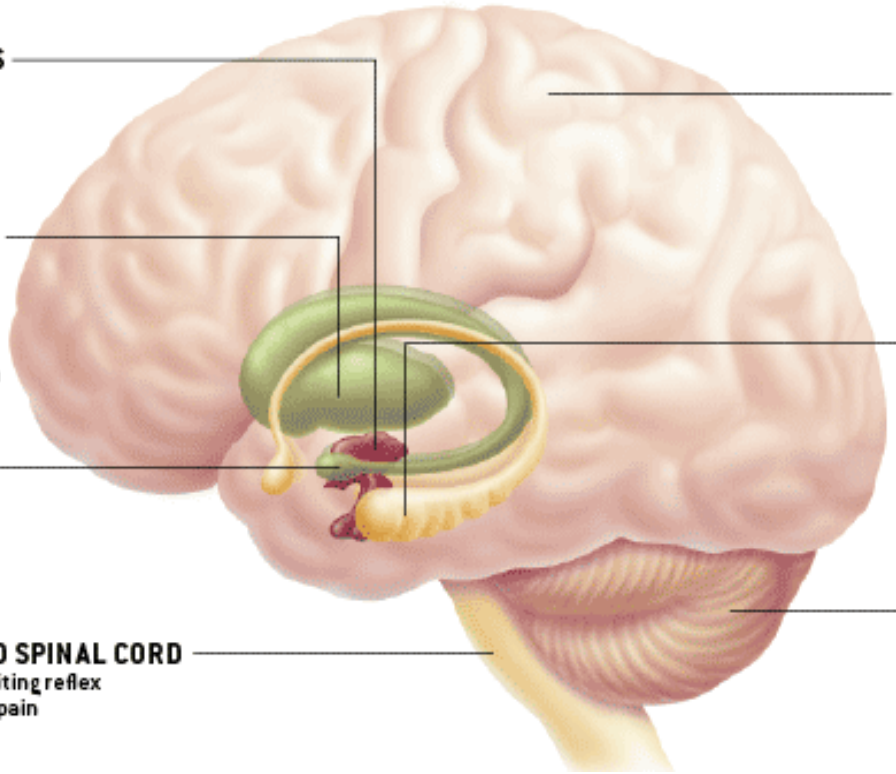
(Zhang, H., et al., 2014; Ait-Daoud Tiouririne, N. (n.d.).

Click here to watch the NIDA video: The Reward Circuit: How the Brain Responds to Marijuana



WHERE MARIJUANA ACTS

The drug *Cannabis sativa* binds to the brain's own cannabinoid receptors in many different areas, including those highlighted below. This widespread influence accounts for the diverse effects the drug—and its relatives made by the brain—can have and offers exciting opportunities for devising medications that can specifically target certain sites to control, say, appetite or pain.



HYPOTHALAMUS
Controls appetite, hormonal levels and sexual behavior

BASAL GANGLIA
Involved in motor control and planning, as well as the initiation and termination of action

AMYGDALA
Responsible for anxiety, emotion and fear

BRAIN STEM AND SPINAL CORD
Important in the vomiting reflex and the sensation of pain

NEOCORTEX
Responsible for higher cognitive functions and the integration of sensory information

HIPPOCAMPUS
Important for memory and the learning of facts, sequences and places

CEREBELLUM
Center for motor control and coordination

ALICE CHEN

Cannabis and the Adolescent Brain

- Regular cannabis use early in life can result in impairments such as:

- Poor academic performance

- Deficits in attention, information processing, and memory

(Batalla, A,et.al., 2013;
Bossong, M., et.al., 2012)

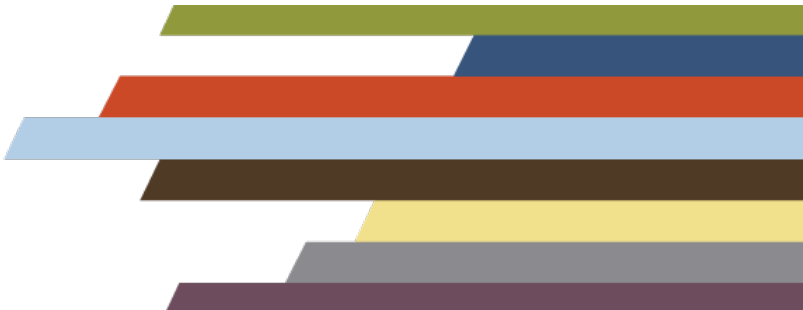
Brain Differences in Adolescent who Use Cannabis: Structural

- Structural differences are apparent in brain images of adolescents who have used cannabis compared to those who have not. These differences include:
  - Size (both increases and decreases)
  - Connectivity
  - Quality of various brain structures
- The earlier that individuals started regular use, the more impaired the nerve connections were in the brain. Those who began using cannabis at a later age did not experience the same negative effects (Schacht,J., et.al., 2013).

Brain Differences in Adolescent who Use Cannabis: Functional

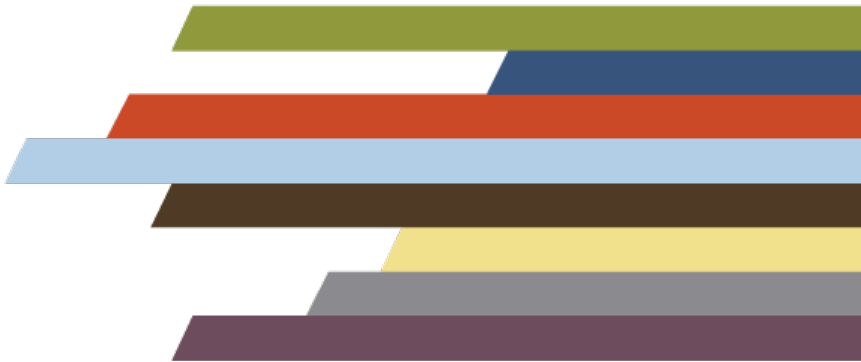
- Functional differences are also found in brain images of adolescents who use cannabis compared to those who don’t use, particularly greater activity while completing tasks:
  - This increased activity indicates the brain was working harder to perform a task
  - These differences were observed in brain regions critical for executive functioning (e.g., planning and decision making, establishing and completing goals) (Smith, A., et.al., 2010; Smith, A., et.al., 2011; Hatchard, T., et.al.,2014).

Pharmocokinetics



Pharmacokinetics

- Pharmacokinetics is a term that encompasses:
  - how we take in a substances,
  - where the substance is stored in our bodies,
  - how we metabolize or break down the substance, and
  - how we get rid of the substance.
- Varies by route of administration



Routes of absorption – Oral (Edibles, Tinctures, & Beverages)

- Onset of effect delayed: 60-120 min
- Effects may last 4-8 hours
  - Maximum levels of THC in blood may take 2-5 hours
- Bioavailability(low): 6% - 7%

(Koob, G., and Le Moal, M. ,2006; Francis, M., 2016; Gaston, T., and Friedman, D., 2017).

Routes of Absorption - Trans-Mucosal: Sublingual, Intranasal & Ophthalmic

- Onset in 5-30 minutes
- Effects may lasts 2-4 hours
- Bioavailability: ~6% - 46%
- Avoids first-pass metabolism
- Sativex: Sublingual for MS

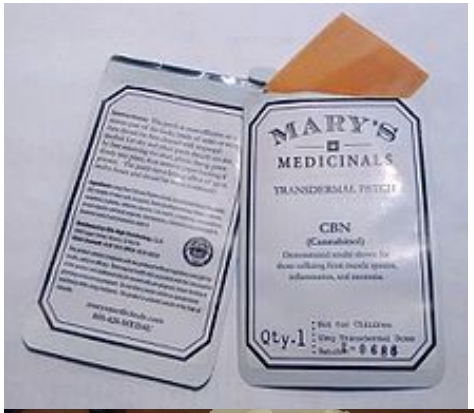
(Koob, G., and Le Moal, M., 2006; Francis, M., 2016)

Routes of Absorption – Transdermal

- Onset in approximately 30 minutes
- Effects may last 48 hours
- Bioavailability: Not available
- Avoids first-pass metabolism

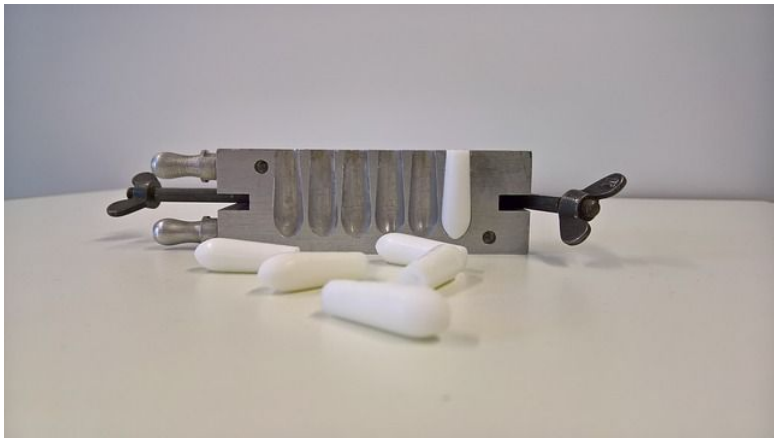
- Transdermal patches
  - 10mg – CBD, CBN, THC, CBD/THC
  - 20mg – THC Indica, THC Sativa

(Koob, G., and Le Moal, M., 2006; Francis, M., 2016; Schachter, S., 2016)



Routes of Absorption – Rectal

- Onset for rectal is faster than oral
- Effects peak within 2-8 hours
- Bioavailability: 13.5%
- Avoids first-pass metabolism
- Marinol Suppositories for Spasticity



(Koob, G., Le Moal, M., 2006; Gaston, T., and Friedman, D., 2017; Englund, A., Stone, J., and Morrison, P., 2012)

Routes of Absorption – Intravenous

- Onset in < 5 minutes.
- Bioavailability: 100%
- Avoids first-pass metabolism
- Intravenous resulted in acute paranoia, Schizophrenia-like symptoms, cognitive deficits (Koob, G., and Le Moal, M., 2006; Gaston, T., and Friedman, D., 2017; Englund, A., Stone, J., and Morrison, P., 2012).

Routes of Absorption – Smoking/Inhalation

- Gravity Bongs, Vaping, & Dabbing
  - Butane Hash Oil
    - (BHO, 710, Butter, Wax, Honey Oil, Shatter)
- Onset: Peak plasma levels in 6-10 minutes
- Effect lasts 2-3 hours
- Bioavailability: 2-56%
- Releases >100 highly carcinogenic compounds and over 2000 compounds in total

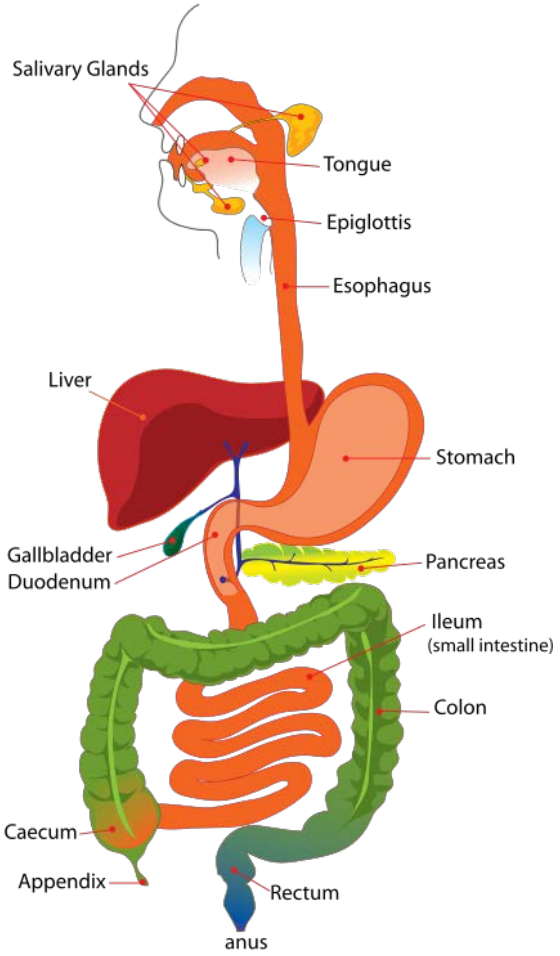
(Gaston, T., and Friedman, D., 2017;

Huestis, M., 2007)

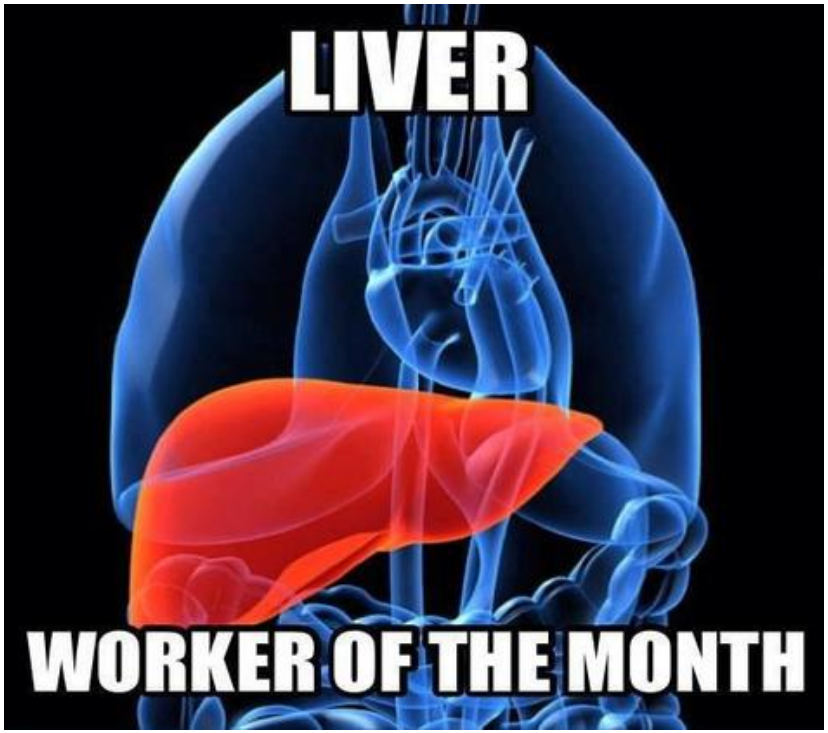
Distribution

- Lipophilic: Rapidly taken up by Heart, Liver, Brain and Lung
- Residual concentrations remain in the brain, after no longer in the blood
- THC rapidly crosses the placenta
- THC is found in breast milk

(Huestis, M., 2007)



Absorption Depends on the Route of Intake

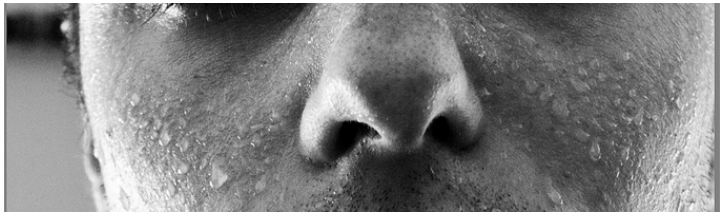


- Oral absorption - First pass Metabolism - Liver (CYP 450 & other enzymes) and Extra-Hepatic Tissues: Converts THC to >100 metabolites, some of which are psychoactive
- Mucosal, Rectal, Dermal, Inhalation, & Intravenous – Bypass the digestive system so the drug is absorbed directly into the system

(Gaston, T., and Friedman, D., 2017; Huestis, M., 2007)

Excretion and Elimination

- Feces (Primary)
- Urine (Secondary)
- Sweat
- Oral fluid (e.g., Saliva)
- Hair



(Gaston, T., and Friedman, D., 2017; Musshoff, F., and Madea, B., 2006; Kintz, P., Cirimele, V., and Ludes, B., 2000)

Quitting & Detecting Use

- THC half-life in plasma and urine: 20-60 hours
- Elimination half-life of metabolites: 5-6 days
- Chronic User: May still be detectable for > 1 month
- Cause: Slow release from lipid-storage
  - Binds to lipoproteins
  - The human organs that contain the most fat (and therefore store the most THC), are the brain and reproductive organs (ovaries or testicles).

(Koob, G., and Le Moal, M., 2006; Lowe, R., Abraham, T., Darwin, W., Herning, R., Lud Cadet, J., and Huestis, M., 2009).

PTTC Resources

PTTC

Prevention Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

More prevention training and technical assistance resources, including more resources for marijuana prevention, available from SAMHSA's Prevention Technology Transfer Center Network

Visit: pttcnetwork.org to learn more.

References, I

Ait-Daoud Tiouririne, N. (n.d.). A review on medical marijuana. Virginia Summer Institute for Addiction Studies, Williamsburg, VA. Retrieved from http://www.vsias.org/wp-content/uploads/2015/07/VSIAS_July-14-2015_AitDaoud_Review-of-Medical-Marijuana.pptx

Batalla, A., Bhattacharyya, S., Yucel, M., Fusar-Poli, P., Crippa, J.A., Nogue, S., … Marin-Santos, R. (2013). Structural and functional imaging studies in chronic cannabis users: A systematic review of adolescent and adult findings. PLoS One, 8(2), e55821.

Bossong, M.G., Jansma, J.M., van Hell, H.H., Jager, G., Oudman, E., Sliasi, E., … Ramsey, N.F. (2012). Effects of delta 9-tetrahydrocannabinol on human working memory function. Biological Psychiatry, 71, 693–699.

Englund, A., Stone, J. M., & Morrison, P. D. (2012). Cannabis in the arm: What can we learn from intravenous cannabinoid studies? Current Pharmaceutical Design, 18(32), 4906-4914.

Francis, M. (2016). The different methods of cannabis ingestion. Crescolabs. Retrieved from http://www.crescolabs.com/cannabis-ingestion-methods/

Gaston, T. E., & Friedman, D. (2017). Pharmacology of cannabinoids in the treatment of epilepsy. Epilepsy & Behavior, 70, 313-318.

Hatchard, T., Fried, P.A., Hogan, M.J., Cameron, I., & Smith, A.M. (2014). Does regular cannabis use impact cognitive interference? An fMRI investigation in young adults using the Counting Stroop task. Journal of Addiction Research and Therapy, 5(4), 197–203.

Houck, J. M., Bryan, A. D., & Feldstein Ewing, S. W. (2013). Functional connectivity and cannabis use in high-risk adolescents. The American Journal of Drug and Alcohol Dependence, 39(6), 414–423.

Huestis, M. S. (2007). Human cannabinoid pharmacokinetics. Chemistry & Biodiversity, 4(8), 1770-1804. doi: 10.1002/cbdv.200790152

Inaba, D. & Cohen, W. E. (2012). Uppers, Downers, All Arounders: Physical and Mental Effects of Psychoactive Drugs. Langara College: Vancouver, B.C.

References, II

Kintz, P., Cirimele, V., & Ludes, B. (2000). Detection of cannabis in oral fluid (saliva) and forehead wipes (sweat) from impaired drivers. Journal of Analytical Toxicology, 24, 557-561.

Konrad, K., Firk, C., & Uhlhaas, P. J. (2013). Brain development during adolescence: neuroscientific insights into this developmental period. Deutsches Arzteblatt international, 110(25), 425–431. doi:10.3238/arztebl.2013.0425.

Koob, G. F. & Le Moal, M. (2006). Neurobiology of addiction (Chapter 7). Boston, MA: Elsevier Inc. ISBN-13: 978-0-12-419239-3.

Lowe, R. H., Abraham, T. T., Darwin, W. D., Herning, R., Lud Cadet, J., & Huestis, M. A. (2009). Extended urinary Δ9-Tetrahydrocannabinol excretion in chronic cannabis users precludes use as a biomarker of new drug exposure. Drug & Alcohol Dependence, 105(1-2), 24-32. doi: 10.1016/j.drugalcdep.2009.05.027.

Musshoff, F., & Madea, B. (2006). Review of biologic matrices (Urine, blood, hair) as indicators of recent or ongoing cannabis use. Therapeutic Drug Monitoring, 28(2), 155-163.

Orr, C., Morioka, R., Behan, B., Datwani, S., Doucet, M., Ivanovic, J., … Garavan, H. (2013). Altered resting-state connectivity in adolescent cannabis users. American Journal of Drug and Alcohol Abuse, 39(6), 372–381.

Schachter, S. (2016). Mary's medicinals review: Transdermal patch, CBD capsules & more. Retrieved from http://blog.getnugg.com/marys-medicinals-review-transdermal-patch/

Schacht, J.P., Hutchison, K.E., & Filbey, F.M. (2012). Associations between cannabinoid receptor-1 (CNR1) variation and hippocampus and amygdala volumes in heavy cannabis users. Neuropsychopharmacology, 37, 2368–2376.

Smith, A.M., Longo, C.A., Fried, P.A., Hogan, M.J., & Cameron, I. (2010). Effects of cannabis on visuospatial working memory: An fMRI study in young adults. Psychopharmacology, 210(3), 429–438.

References, III

Smith, A.M., Zunini, R.A., Anderson, C.D., Longo, C.A., Cameron, I., Hogan, M.J., & Fried, P.A. (2011). Impact of cannabis on response inhibition: An fMRI study in young adults. Journal of Behavioural and Brain Sciences, 1, 24–33.

The National Institute on Drug Abuse. The Neurobiology of Drug Addiction - 7: Summary: addictive drugs activate the reward system via increasing dopamine neurotransmission. 2007. https://www.drugabuse.gov/publications/teaching-packets/neurobiology-drug-addiction/section-iv-action-cocaine/7-summary-addictive-drugs-activate-reward

Zhang, H. Y., et al. (2014). Cannabinoid CB2 receptors modulate midbrain dopamine neuronal activity and dopamine-related behavior in mice. *Proceeding of the National Academy of Sciences, 111*(46), E5007-15. doi: 10.1073/pnas.1413210111.Epub 2014 Nov 3.

Additional NIDA Videos

- The Dopamine System
- https://youtu.be/yeAN26kJuTQ

- Teen Brain Development
- https://youtu.be/EpfnDijz2d8

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SAMHSA

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