MOLECULAR ADVENTURES IN THE BRAIN WITH ALCOHOL AND CANNABIS

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Elizabethtown College

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"Although 20.8 million people (7.8 percent of the population) met the diagnostic criteria for a substance use disorder in 2015, only 2.2 million individuals (10.4 percent) received any type of treatment."

2016 Surgeon General Report, "Facing Addiction in America"

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- Factors affecting addiction
- Getting to know your brain
- Fundamentals of neurotransmission
- Dopamine hypothesis
- Action of cannabinoids
- Promiscuity of alcohol on the brain

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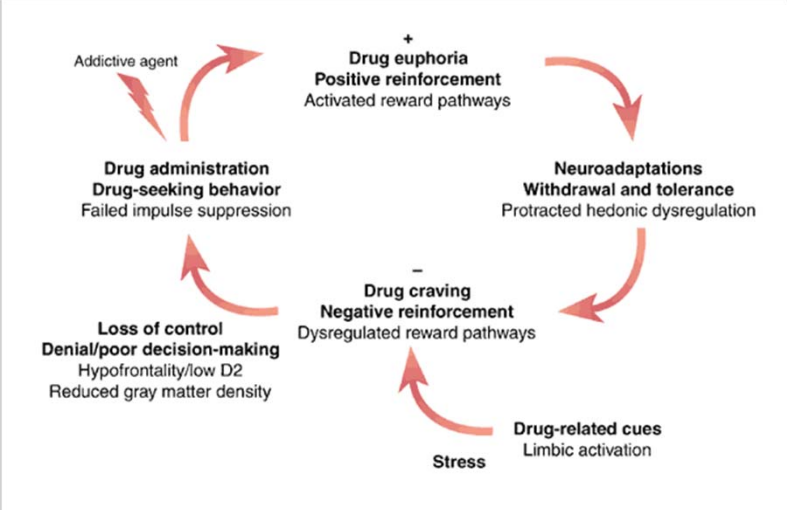
The Addiction Cycle



HTTP://WWW.NATURE.COM/NEURO/JOURNAL/V8/N11/FIG_TAB/NN1105-1431_F1.HTML

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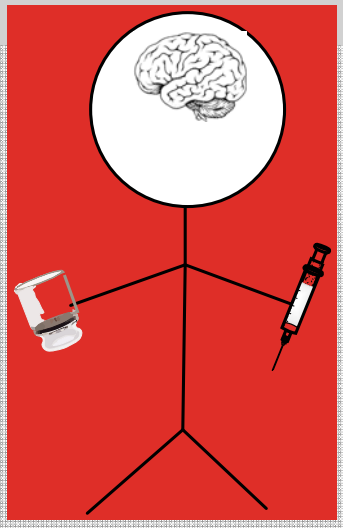
Why?



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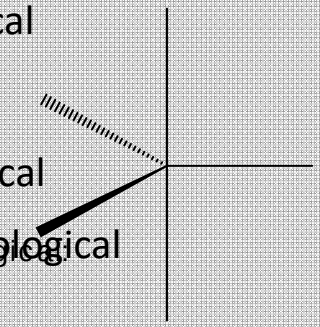
VARIOUS FACTORS INFLUENCING ADDICTION

- Psychological
- Sociological
- Genetic
- Biochemical
- Pharmacological



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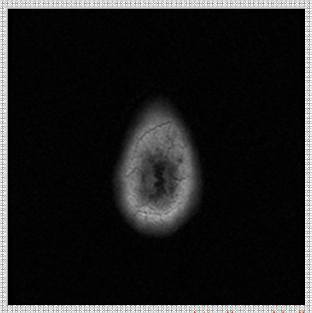
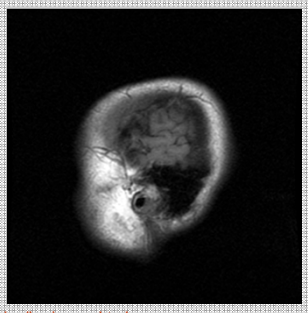
WHAT'S GOING ON HERE:





http://compbio.llnl.gov/barsky/brains/brain_cor.html

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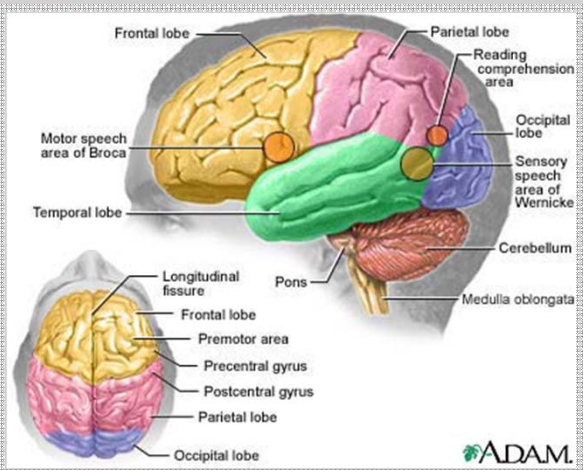
RELEVANT FACTS ABOUT THE HUMAN BRAIN



https://medlineplus.gov/ency/images/ency/fullsize/1074.jpg

- 80 ???
- 0.1- 25 microns
- Small ruler
- TGV
- Neurons are "social"

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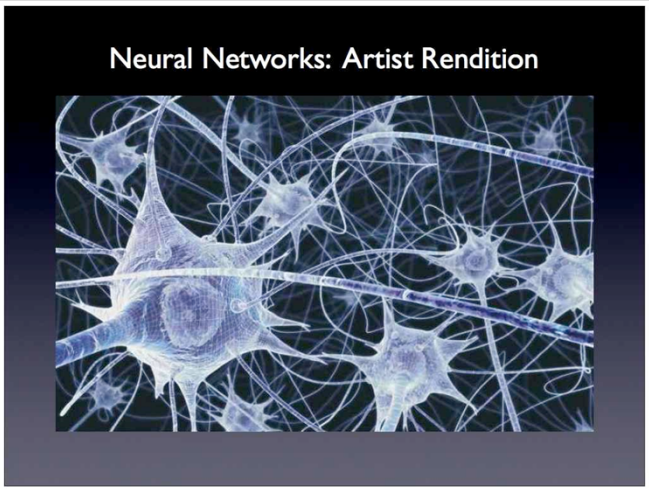
SIMPLE CONVERSATIONS?



http://cs.brown.edu/people/tld/note/blog/13/04/19/

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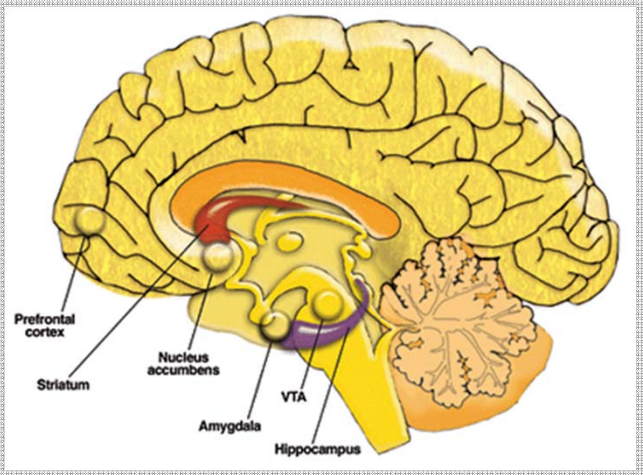
BRAIN REGIONS OF THE PLEASURE-REWARD CENTER



http://pubs.niaaa.nih.gov/publications/arh314/310-339.htm

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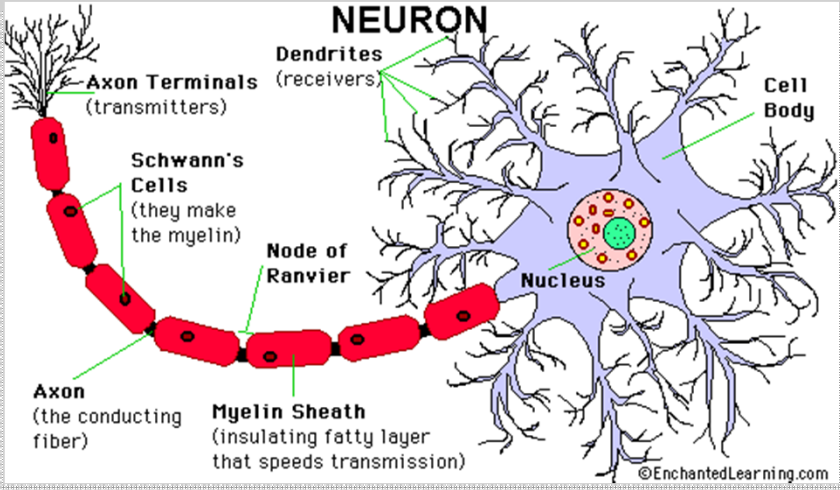
THE NEURON



https://www.enchantedlearning.com/subjects/anatomy/brain/Neuron.shtml

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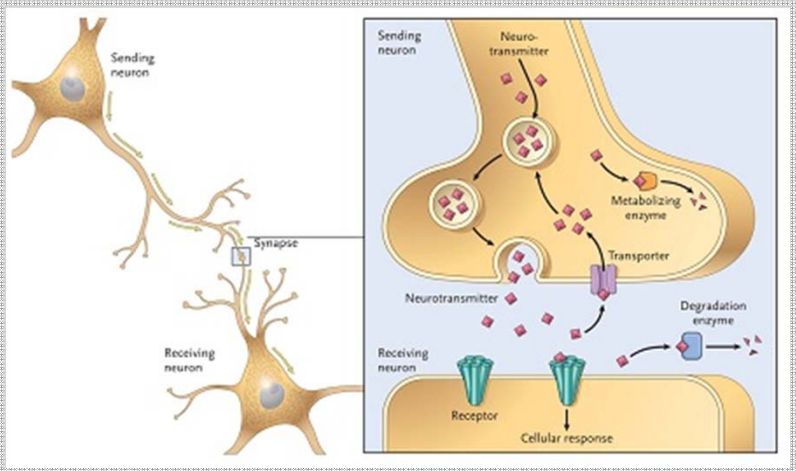
NEUROTRANSMITTERS, NEURORECEPTORS, AND NEURAL COMMUNICATION



https://lifesciences.umaryland.edu/neuroscience/Research-Focus-Groups/Synapses--Circuits/

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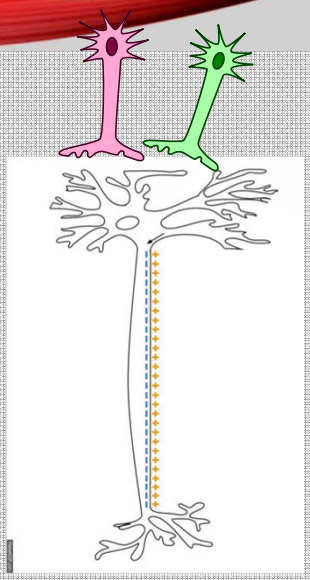
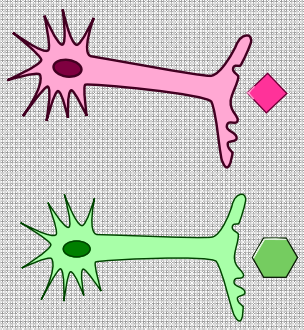
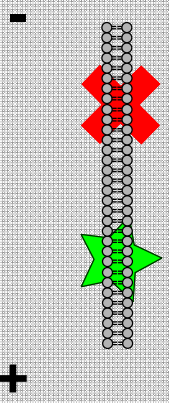
EXCITATORY VERSUS INHIBITORY NEURONS/NEUROTRANSMITTERS







https://commons.wikimedia.org/wiki/File:Action_Potential.gif

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ENDOGENOUS SYSTEM AND PSYCHOTROPICS

- Dopaminergic (Ex & Inh)
- Anandamidergic (mod)
- Opioidergic (Inh.)
- Serotonergic (Ex & Inhib)
- (Acetyl)cholinergic (Ex.)
- Glutamatergic (Ex.)
- GABAergic (Inh.)
- Adenosinergic (Inh.)

- Cocaine
- Cannabis
- Heroin (ag.)
- LSD
- Nicotine (ag.)
- PCP (an.)
- Alcohol (ag.)
- Caffeine (an.)

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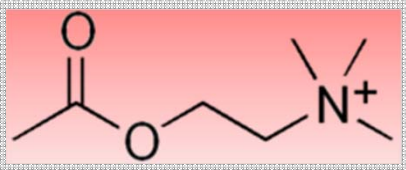
ENDOGENOUS VS EXOGENOUS



Acetylcholine

Nicotine

Imposters, molecular distant relatives, or just willing and able?

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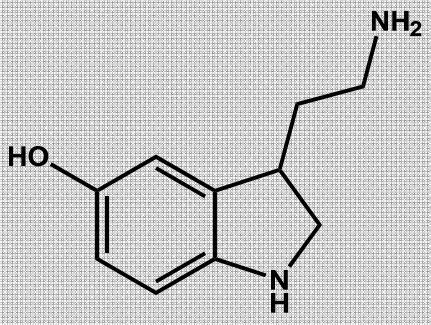
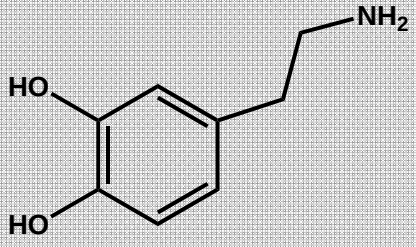
BEHAVIOR AND PLEASURE

- Serotonin



- Dopamine



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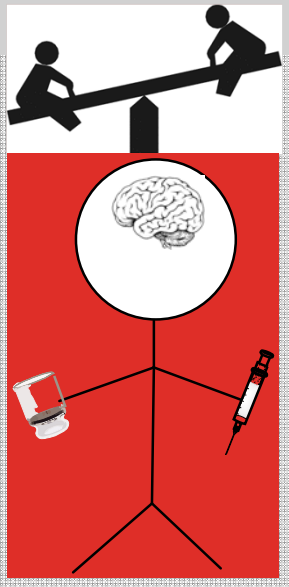
HOMEOSTASIS



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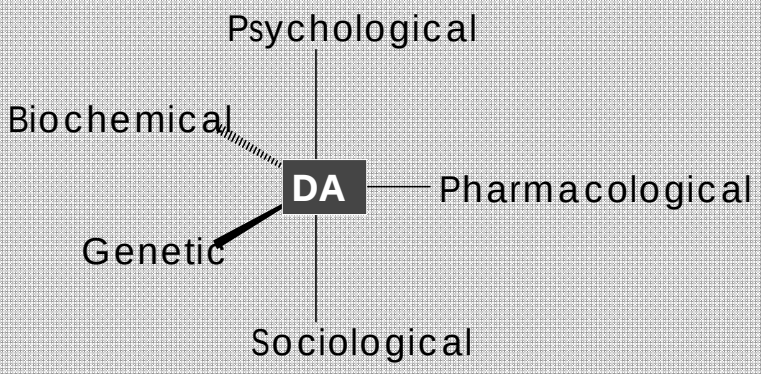
Dopamine Hypothesis: Connecting the Dots



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USER VARIABLES CRITICAL TO THE DRUG & ADDICTIONS EXPERIENCE:

- **Psyche**
  - Psychological makeup
  - Individual's expectations
- **Setting**
  - Social environment and
  - Physical setting
- **Drug variables**
  - Chemical structure
  - Dose (i.e., amount)
  - Frequency
  - Time since last dose
- **Individual's biochemistry**
  - Expression of genes
  - Activity of proteins

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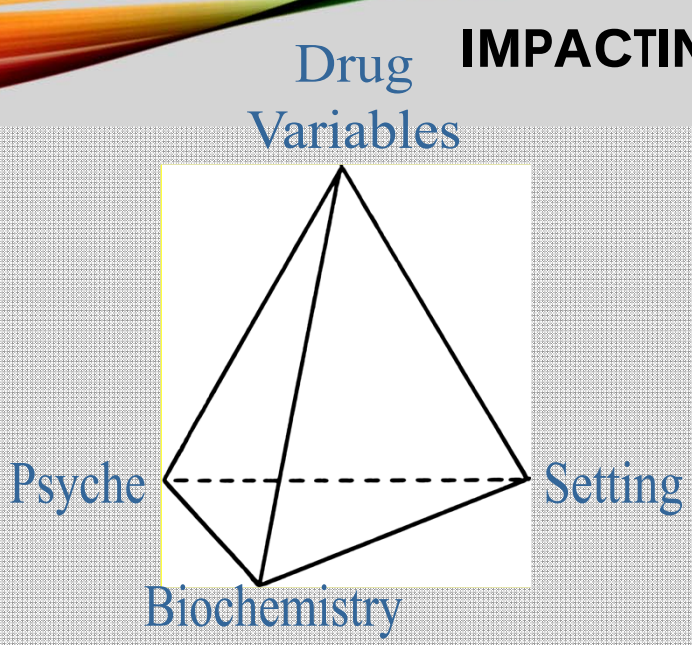
IMPACTING THE USER



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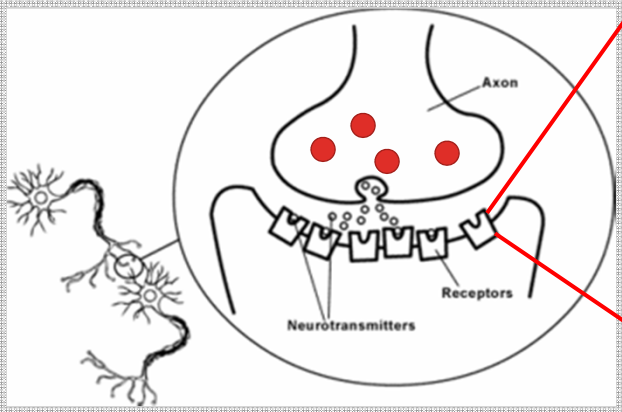
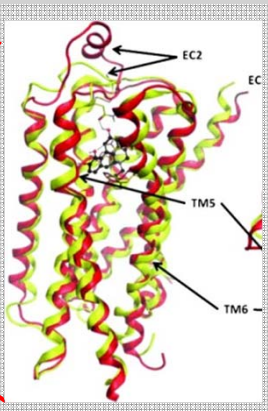
NEUROMOLECULAR IMPACT





Proteins and Enzymes

https://www.drugabuse.gov/publications/brain-power/grades-4-5/neurotransmission-module-3/background

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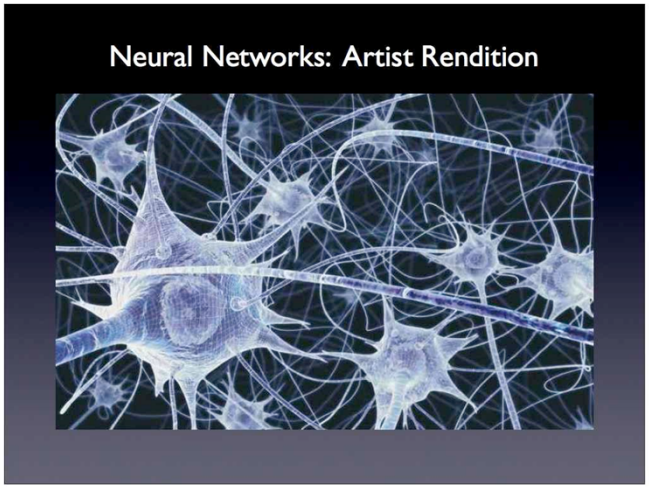
REMEMBER THOSE MULTIPLE CONVERSATIONS?



http://cs.brown.edu/people/tld/note/blog/13/04/19/

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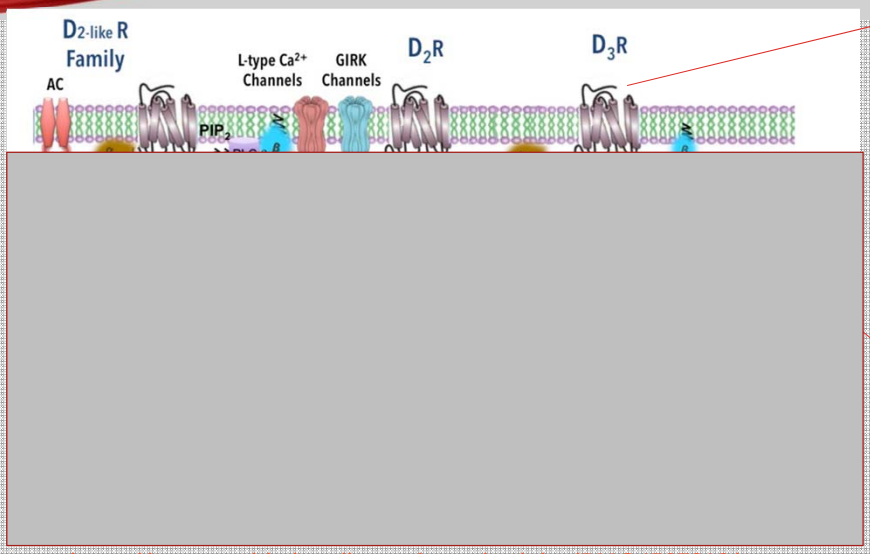
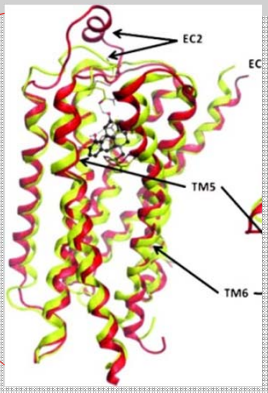
MOLECULAR CHOREOGRAPHY





https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4567218/

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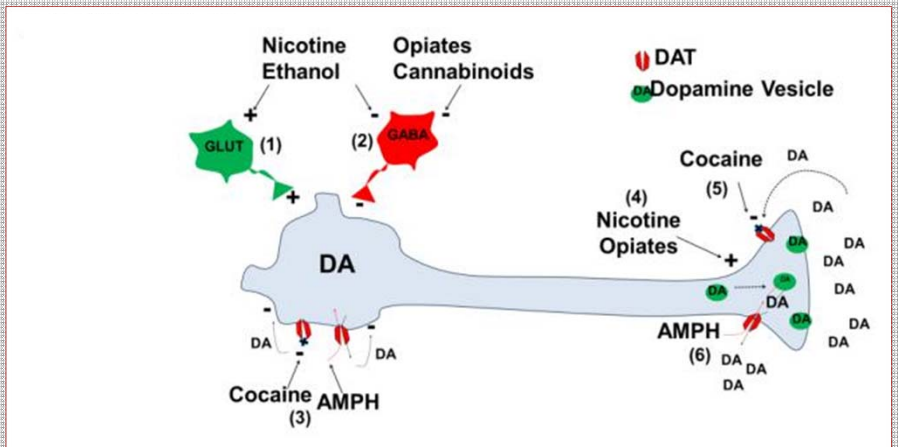
SYNAPTIC [DOPAMINE] FROM THE VTA



http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4064368/

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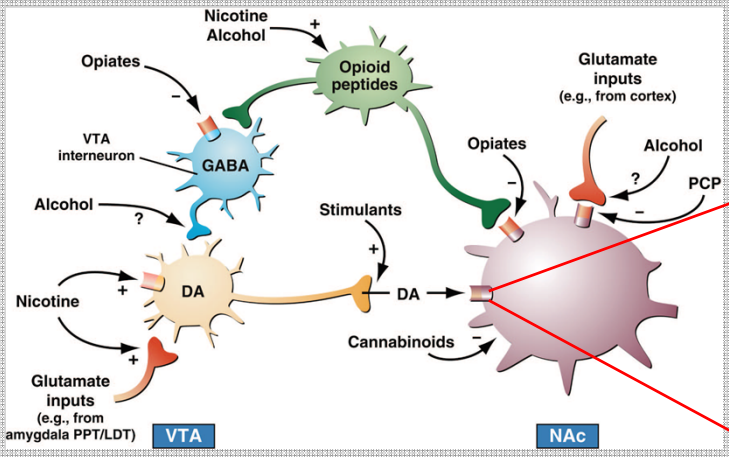
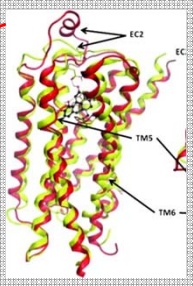
DOPAMINE HYPOTHESIS





http://www.nature.com/neuro/journal/v8/n11/fig_tab/nn1578_F1.html

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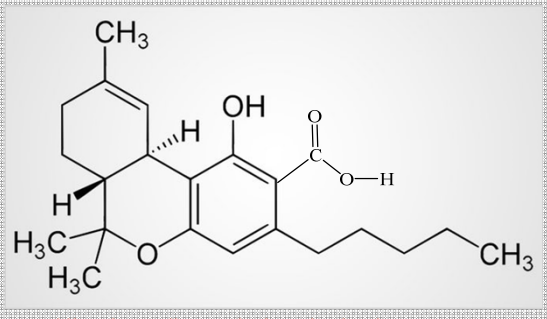
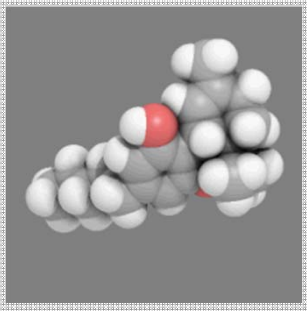
THC: TETRAHYDROCANNABINOL

$C_{21}H_{30}O_2$

(6aR,10aR)-6,6,9-Trimethyl-3-pentyl-6a,7,8,10a-tetrahydro-6H-benzo[c]chromen-1-ol



https://herb.co/learn/what-is-thc/



https://en.wikipedia.org/wiki/Space-filling_model

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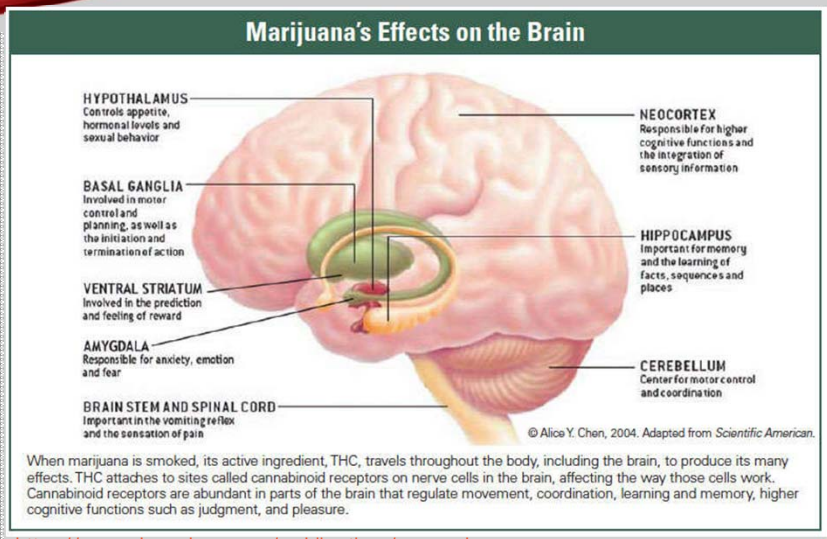
THC AND THE BRAIN



https://www.drugabuse.gov/publications/research-reports/marijuana/how-does-marijuana-produce-its-effects

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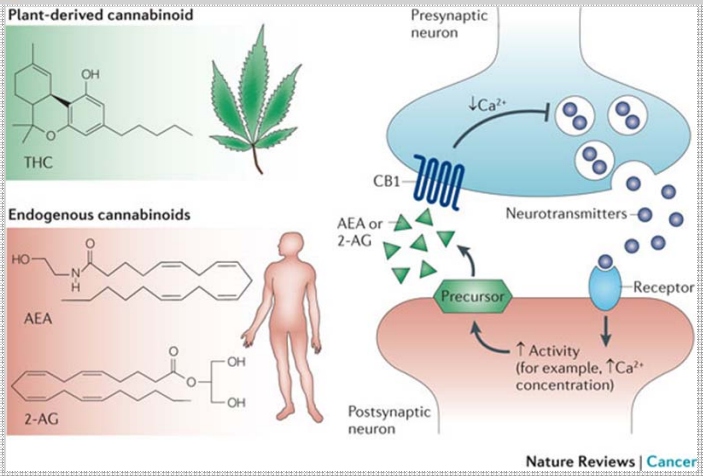
CANNABIS



http://www.nature.com/nrc/journal/v12/n6/fig_tab/nrc3247_F1.html

Arachidonoylglycerol (2-AG)

arachidonoylethanolamine (AEA); AKA anandamide

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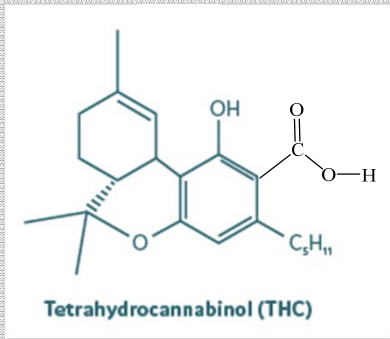
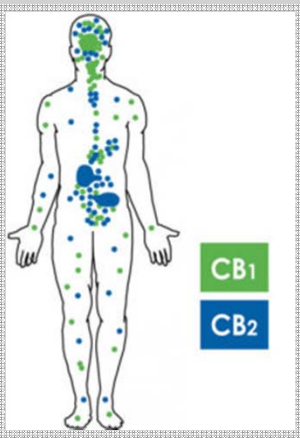
THC: CBD $C_{21}H_{30}O_2$

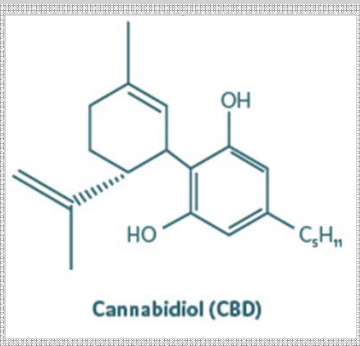


Tetrahydrocannabinol (THC)

CB1 agonist



https://www.farmapdx.com/the-ecs-at-a-glance/



Cannabidiol (CBD)

CB1 negative modulator

Inhibits FAAH

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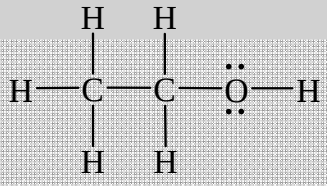
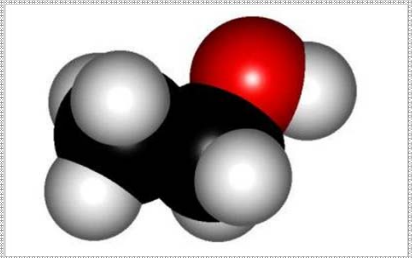
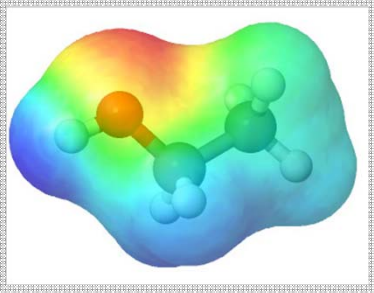
ETHANOL

C_2H_5OH





http://www.chim.lu/ch0335.php



http://asd.molfield.org/php/view_details.php?id=120

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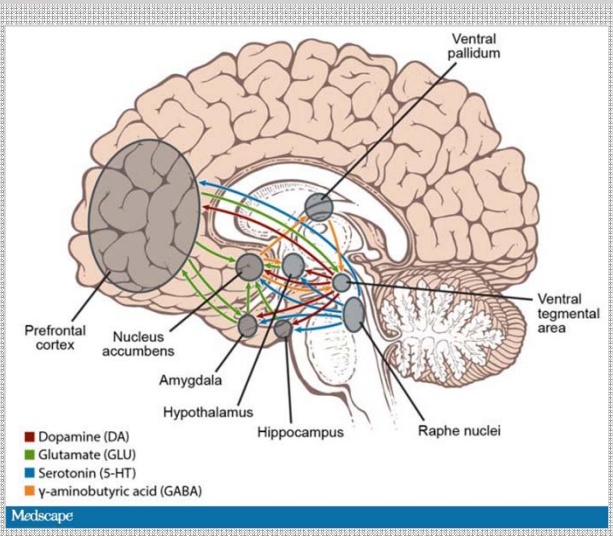
EFFECTS OF ETHANOL ON THE BRAIN



https://www.medscape.org/viewarticle/838083_3

REWARD

- Increased glutamate
- Decreased GABA
- Increased dopamine

CORROLARY DAMAGE

- Memory
- Coordination
- Learning

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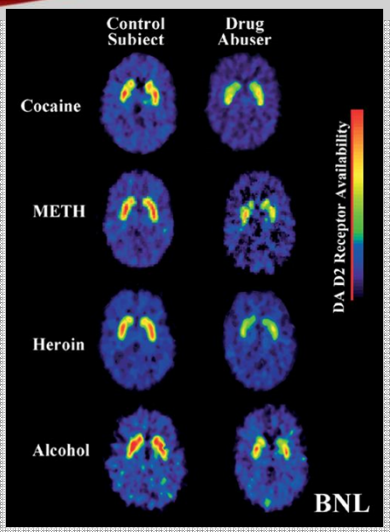
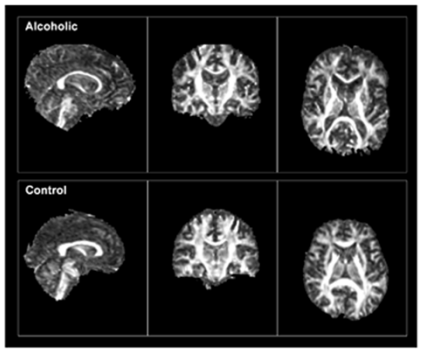
INSIGHT THROUGH IMAGING STUDIES



https://www.nature.com/articles/4001507?proof=true#f4



https://pubs.niaaa.nih.gov/publications/arh314/362-376.htm

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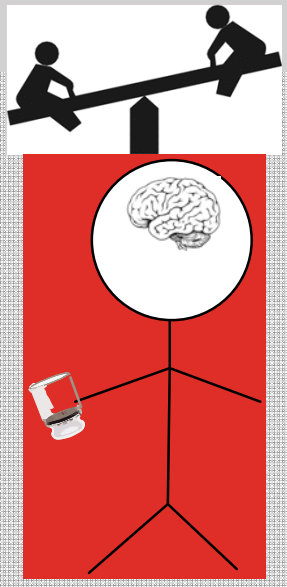
Withdrawal

- Motivation for continued drinking
- Physiological changes (e.g. nausea, headache, sweating)
- Behavioral changes (e.g., isolationism, lack of focus, aggravation)



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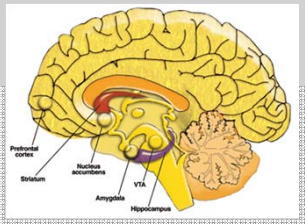
SUMMARY

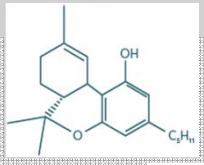
Psychological

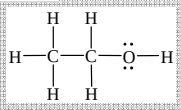
Biochemical — DA — Genetic

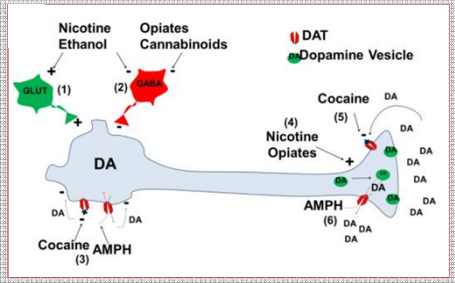
Sociological

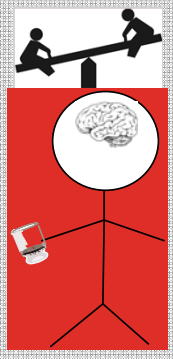
Pharmacological

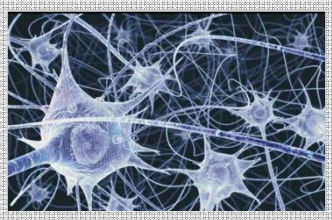












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- Amy Sechrist
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- Millersville University
- Elizabethtown College
- My FYS students

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QUESTIONS

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DSM-V: ABUSE, ADDICTION, OR MIS-USE?

1. Using in larger amounts or for longer than intended
2. Wanting to cut down or stop using, but not managing to
3. Spending a lot of time to get, use, or recover from use
4. Craving
5. Inability to manage commitments due to use
6. Continuing to use, even when it causes problems in relationships
7. Giving up important activities because of use
8. Continuing to use, even when it puts you in danger
9. Continuing to use, even when physical or psychological problems may be made worse by use
10. Increasing tolerance
11. Withdrawal symptoms

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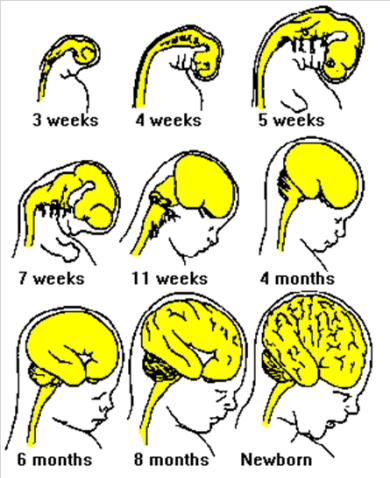
NEURAL PLASTICITY



- Neurons respond to internal and external stimuli.
- Synaptogenesis
- Up/down regulation of receptors
- Increased/decreased activity between various sets of neurons (recall 10-15K?)
- Functioning within brain is altered

https://faculty.washington.edu/chudler/dev.html

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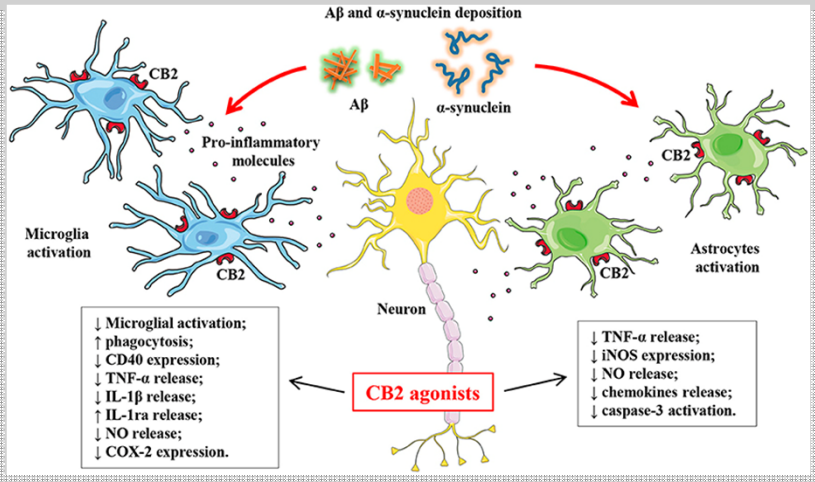
CB2 RECEPTOR



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