

# Midwest Institute for Addiction

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Inpatient & Outpatient Programs

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[www.MidwestAddiction.org](http://www.MidwestAddiction.org)

# ASAM Addiction Defined (Aug 2011)

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A stress-induced (HPA axis), genetically-mediated (polymorphisms, epigenetic mechanism) primary, chronic and relapsing brain disease of reward (nucleus accumbens), memory (hippocampus & amygdala), motivation and related circuitry (ACC, basal forebrain) that alters motivational hierarchies such that addictive behaviors supplant healthy, self-care behavior.



# Genetic Predisposition

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Studies have found:

- Correlations in brain structure and addiction (Ersche, K. et al, 2012)
- Correlations in brain function and addiction (Everitt, B. et al, 2008)
- Gene predisposition
  - Example: polymorphism at VAL-158-MET gene for catechol-O-methyltransferase influences impulsive decision making
  - Individuals homozygous for more active 158-VAL allele have an increased tendency to choose immediate over delayed rewards

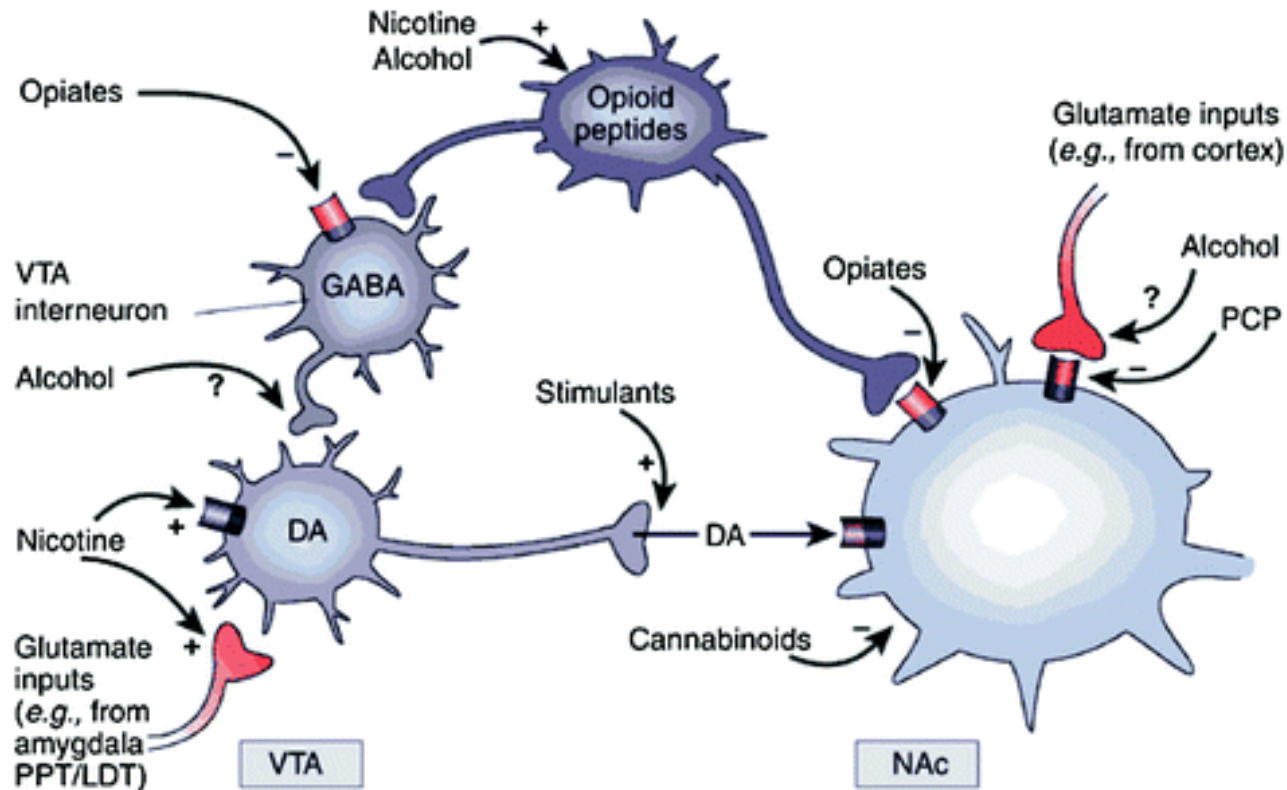


# Physiological Responses

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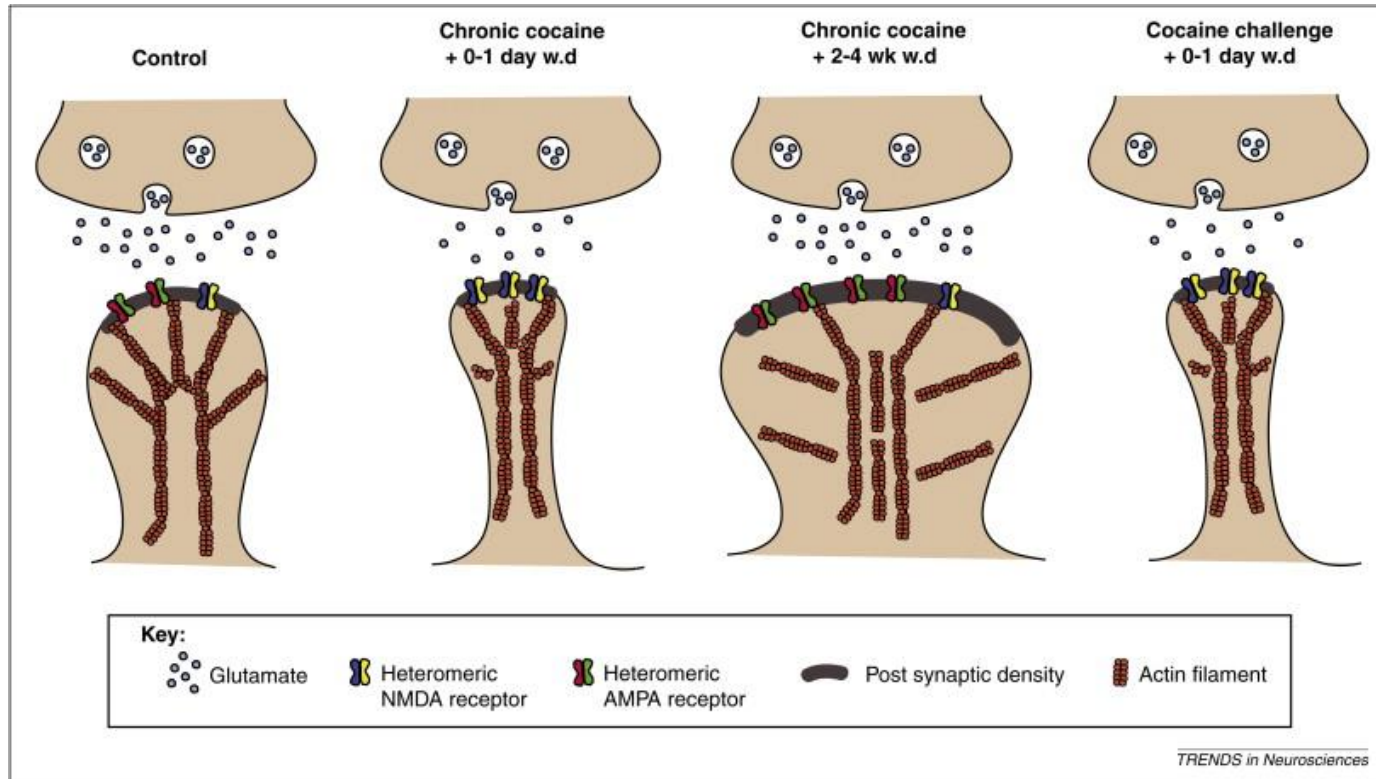


# The Disease Model



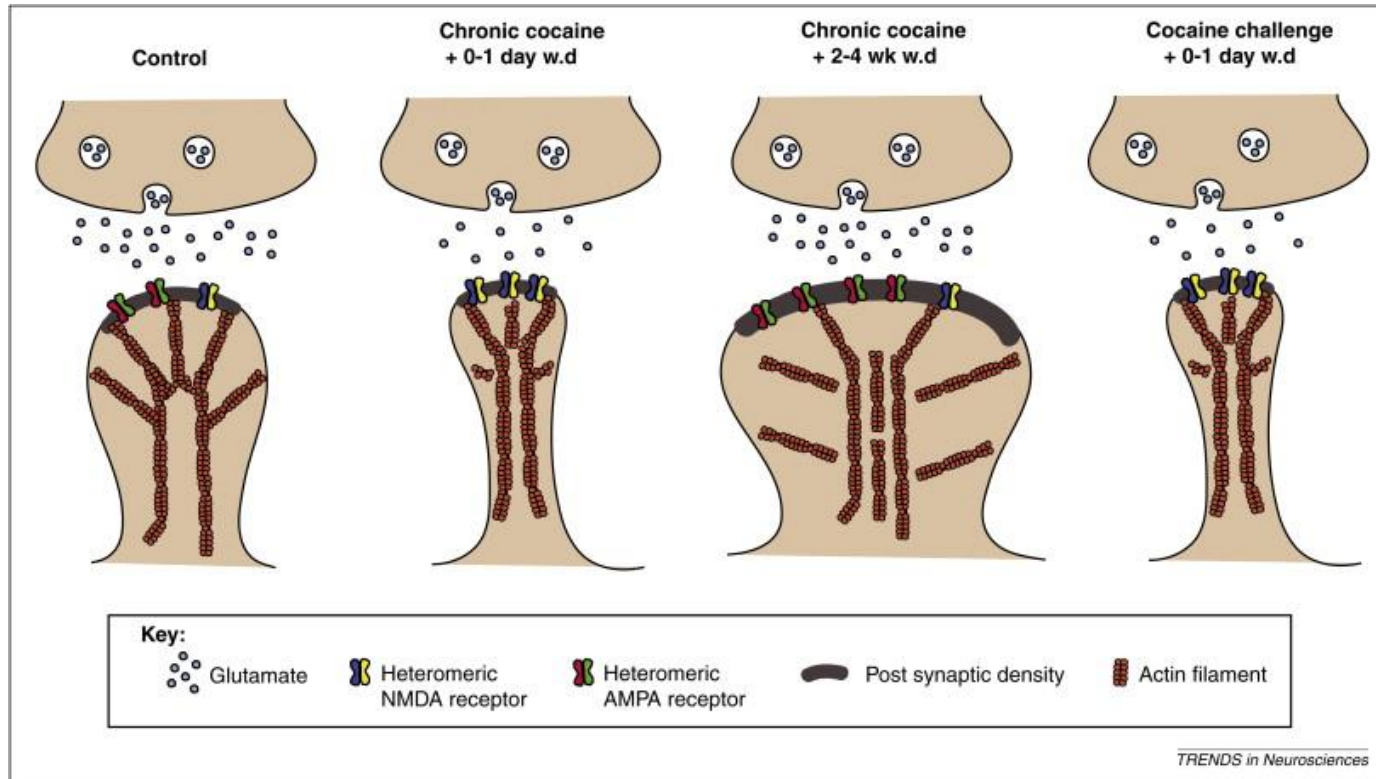
While the mechanisms of various chemicals of abuse differ, their role in the disease concept are very interconnected.

# The Disease Model



Glutamate is generally acknowledged to be the most important transmitter for normal brain function. Nearly all excitatory neurons in the central nervous system are glutamatergic, and it is estimated that over half of all brain synapses release this agent.

# The Disease Model



As the image above shows, increases in post-synaptic neuron receptor site density occur with prolonged chemical abuse.

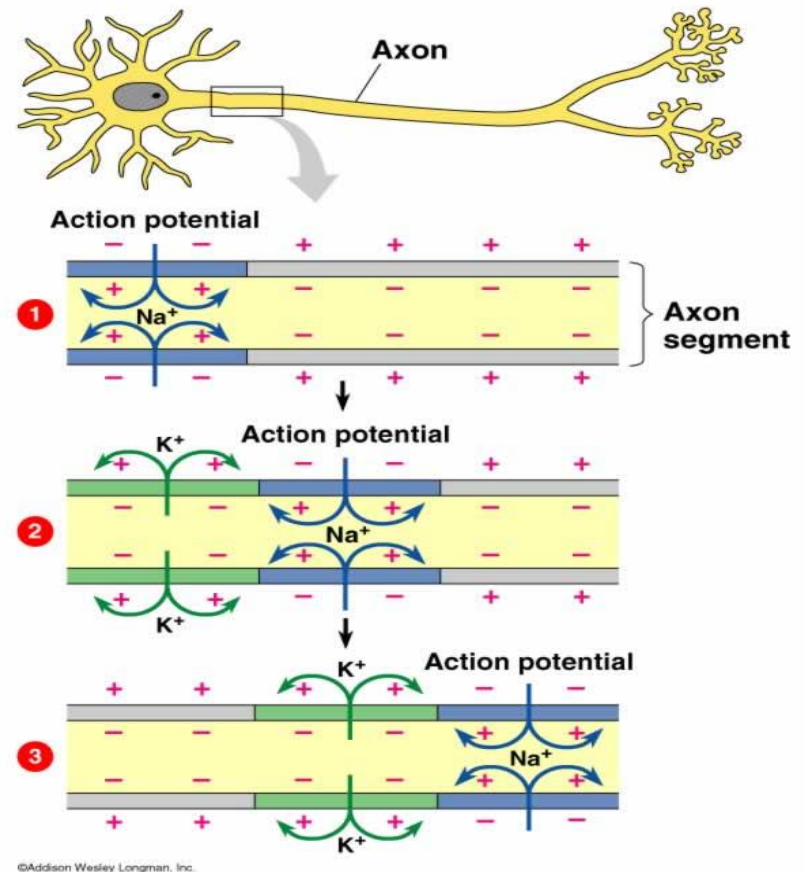
What happens then when the chemicals are no longer introduced to the system?



# Withdrawal

Physical Dependency: *substance dependence in which there is evidence of tolerance, withdrawal, or both*

1. Action potential occur in “all-or-none” fashion
  1. Sodium (Na) influx and Potassium (K) efflux
  2. Initiated by neurotransmitters from the presynaptic neuron binding to and changing permeability of the membrane of the postsynaptic neuron
2. Allow communication throughout the CNS
3. Effects of chemical abuse
  1. Excess amounts of Neurotransmitters
    1. Agonists
    2. Increase production or release
    3. Inhibited re-uptake
  2. Increase in postsynaptic neuron receptor site density
  3. Deviated function





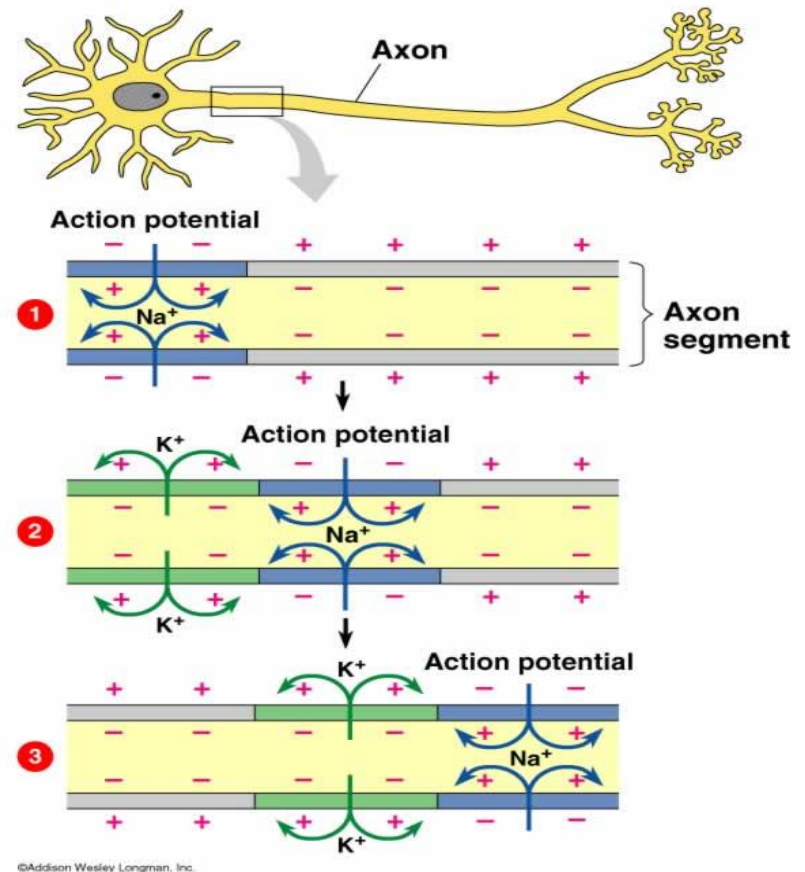
# Withdrawal

*Drugs and alcohol affect mood by altering brain chemistry, specifically the production of neurotransmitters.*

Neurotransmitters are chemicals in the central nervous system that enable nerve impulses to travel through the central nervous system and regulate thought processes, behavior, and emotion.

Drugs that temporarily elevate neurotransmitter levels are called stimulants. Drugs that decrease neurotransmitter levels and depress the central nervous system are called depressants; they include opiates and sedative-hypnotic drugs such as alcohol and barbiturates. (There are exceptions: Benzodiazepine elevates the level of an inhibitory neurotransmitter, GABA, therefore it serves as a tranquilizer.)

When drug or alcohol consumption becomes chronic, the body adjusts to the constant presence of the substance by changing its normal production of neurotransmitters. If drug and alcohol use suddenly stops, the body and central nervous system react to the absence of the substance with an array of symptoms known collectively as withdrawal syndrome.

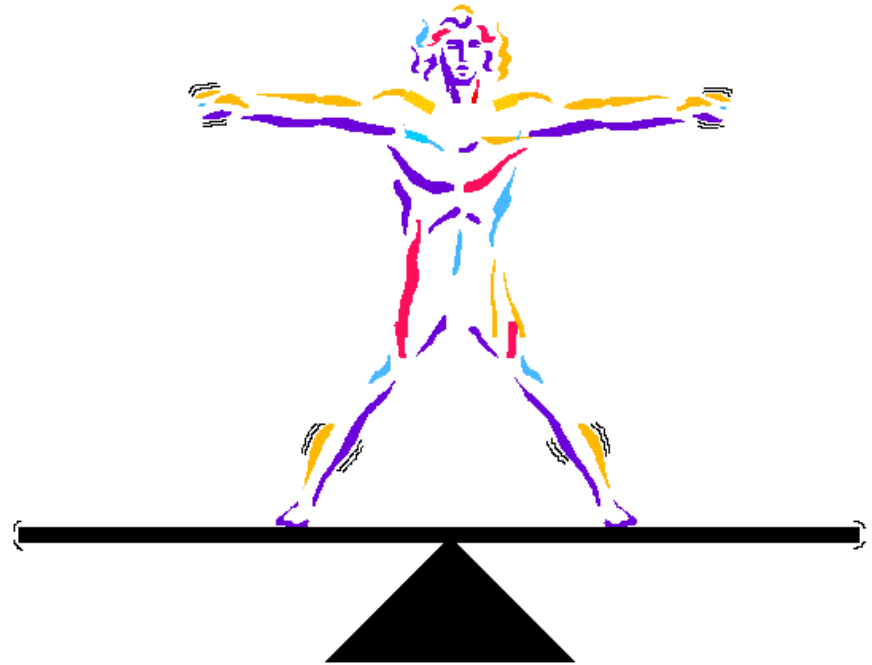


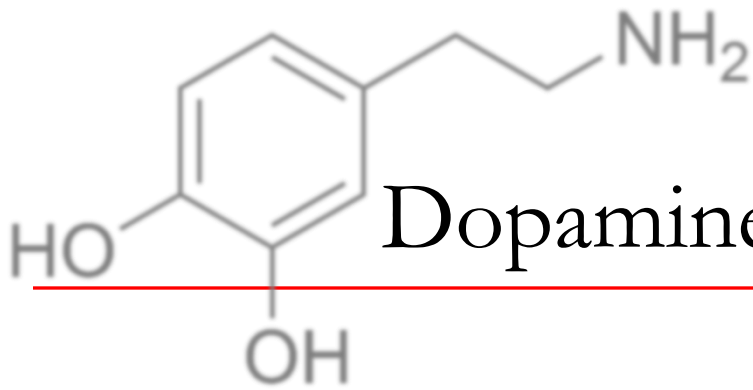
# Deviations in Homeostasis

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There are also deviations in the body's systems and functions that in themselves can pose stress to the individual; and in turn drug and/or alcohol use.

- Hormonal
- Dopamine and Norepinephrine
- Et cetera



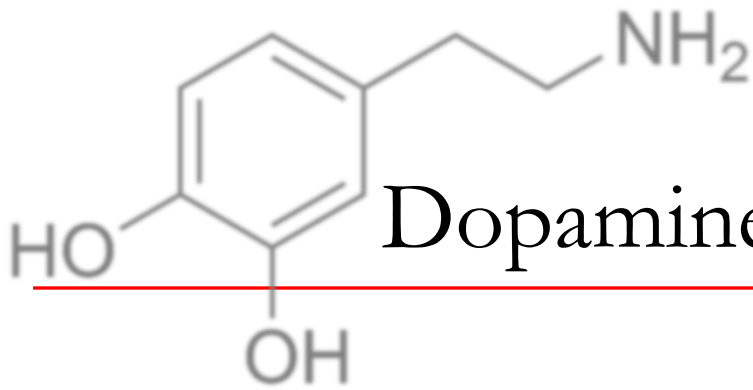


# Dopamine's Role in Addiction

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All drugs of abuse and potential compulsive behaviors release dopamine (DA)

- **DA is the first chemical in the cascade of chemicals that generate rewarding experience**
- **DA is the chemical of survival importance**
- **DA is more about “wanting” than “liking”**
- **DA is more about expectation than consummation**



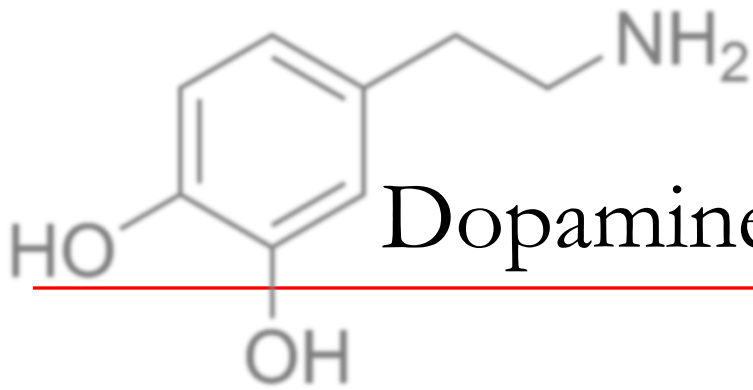
# Dopamine's Role in Addiction

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## Incentive-Sensitization (Robinson & Berridge)

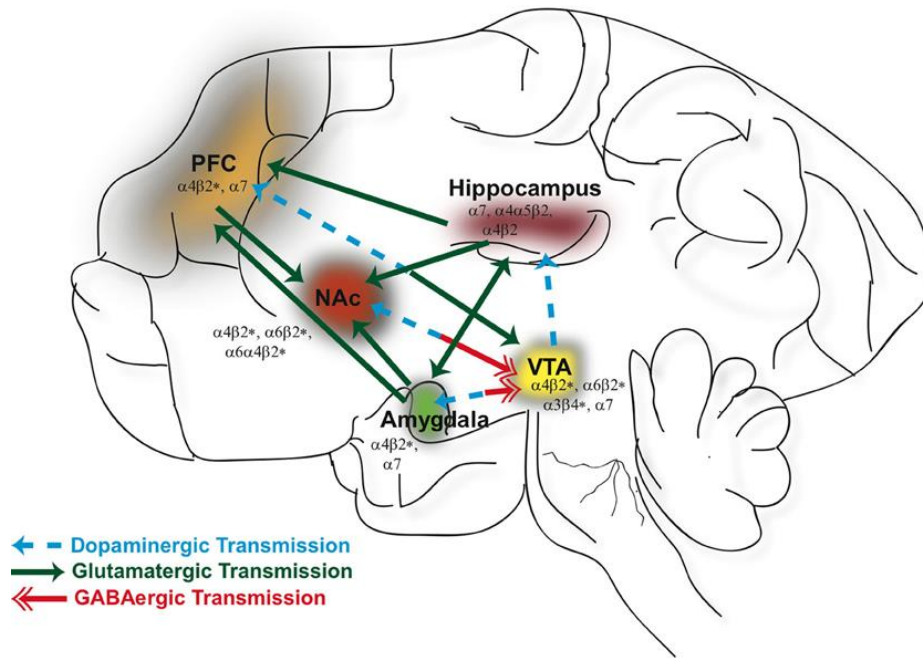
- Distinguished between a “Liking” and “Wanting” Role (it is more about wanting)
- Created mice with increased synaptic DA
- Observed increased intake of reinforcing substances in these mice and greater thwarting of obstacles to get them
- Did not observe greater liking of these substances in mice





# Dopamine's Role in Addiction

## Dopamine and Nucleus Accumbens



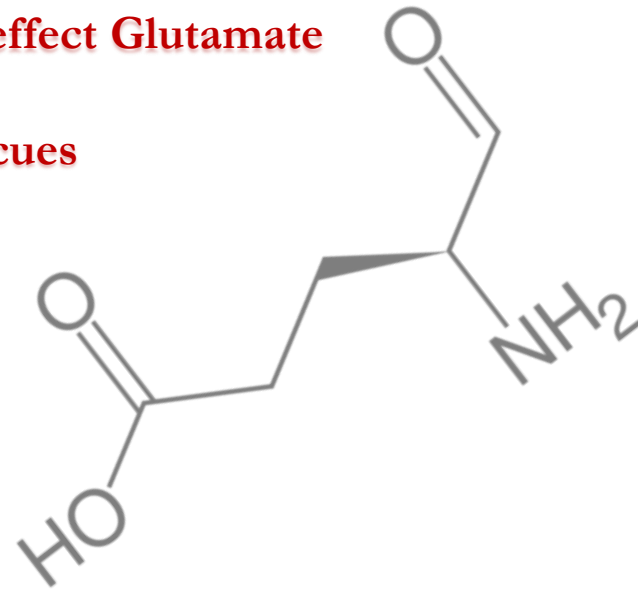
- Do more than encode receipt of reward
  - Expectancy of reward
  - Delay of reward
  - Errors in reward prediction
  - Motivation for drug seeking
  - Contribute to synaptic neuroplasticity that underlies the acquisition of addictive behaviors

# L-Glutamate's Role in Addiction

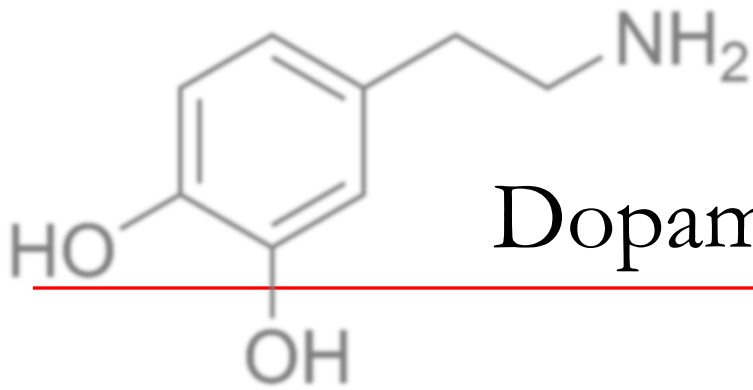
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The most abundant neurochemical in the brain

- Critical in memory formation and consolidation
- All drugs of abuse and many addicting behaviors effect Glutamate which preserves drug memories and creates drug cues
- Glutamate is the neurochemical of “motivation”
  - It initiates drug seeking







# Dopamine & Glutamate

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DA

Salience

“this is important”

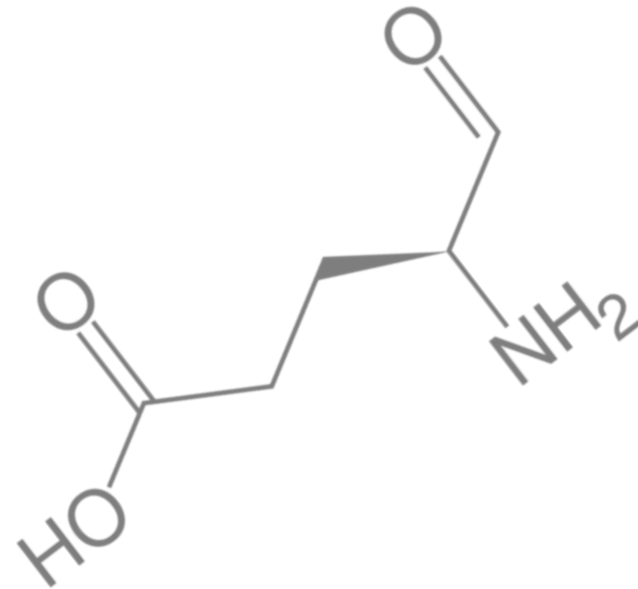
“I really want this”

Glu

Memories & Seeking

“OK, I’ll remember”

“Fine, I” go and get it”



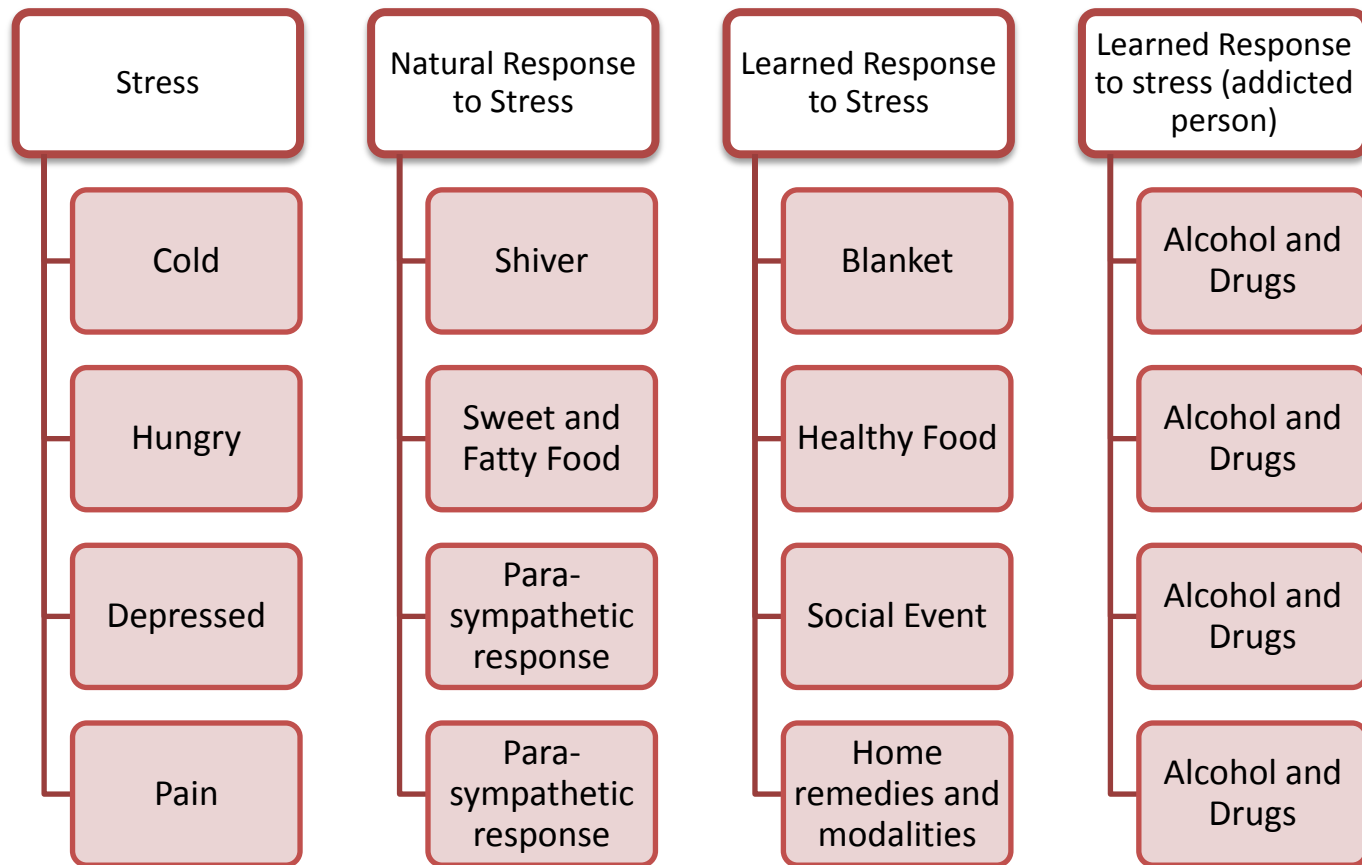
# Psycho-Social Responses

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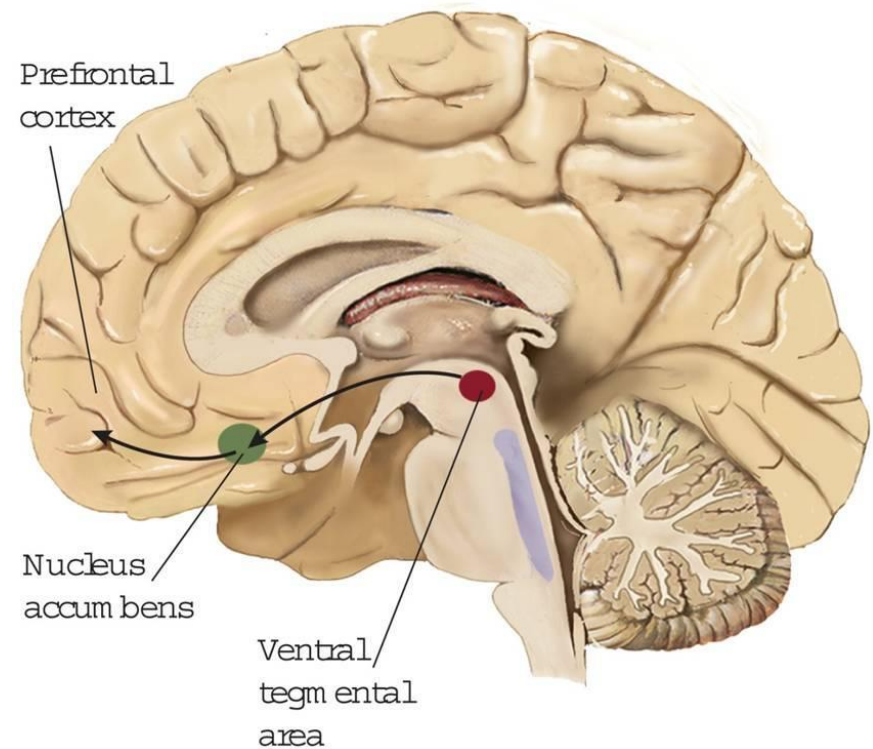
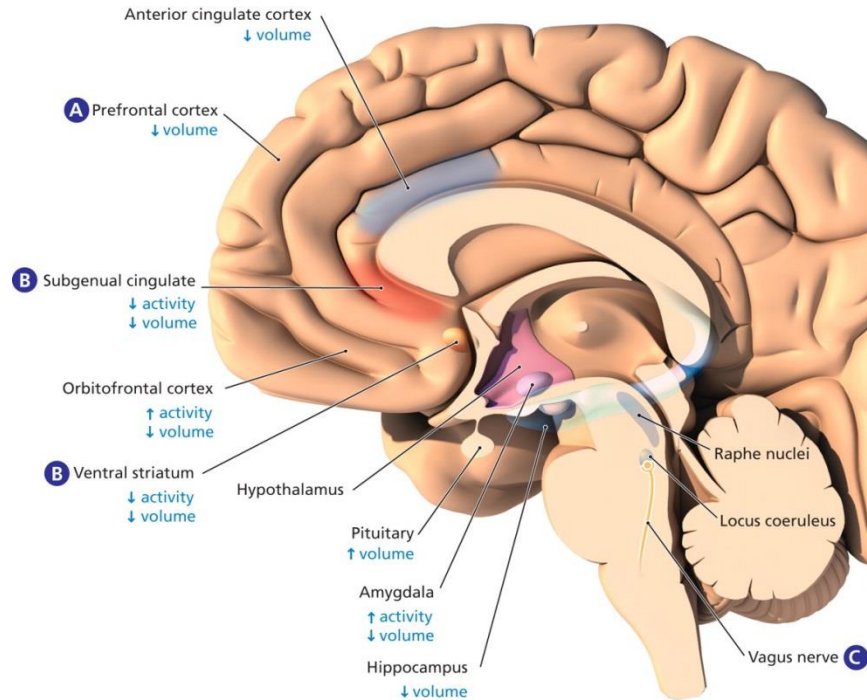


# Psycho-Social Responses

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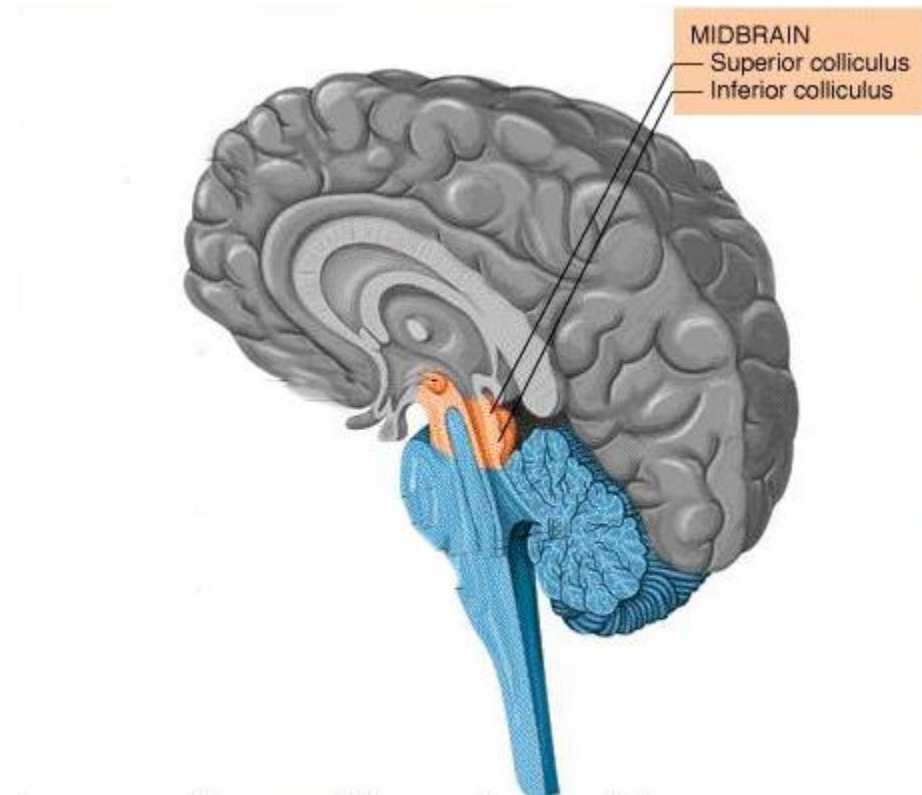
# Brain Function and Addiction



# Midbrain

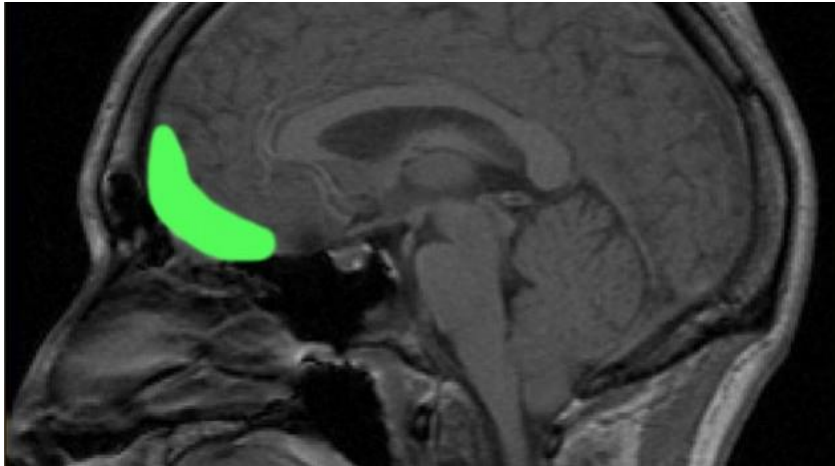
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- Associated with sensory functions, motor functions, sleep/wake cycle, arousal, temperature regulation, etc.
- Survival of self and species
- Subconscious part of the brain



# Orbitofrontal Cortex

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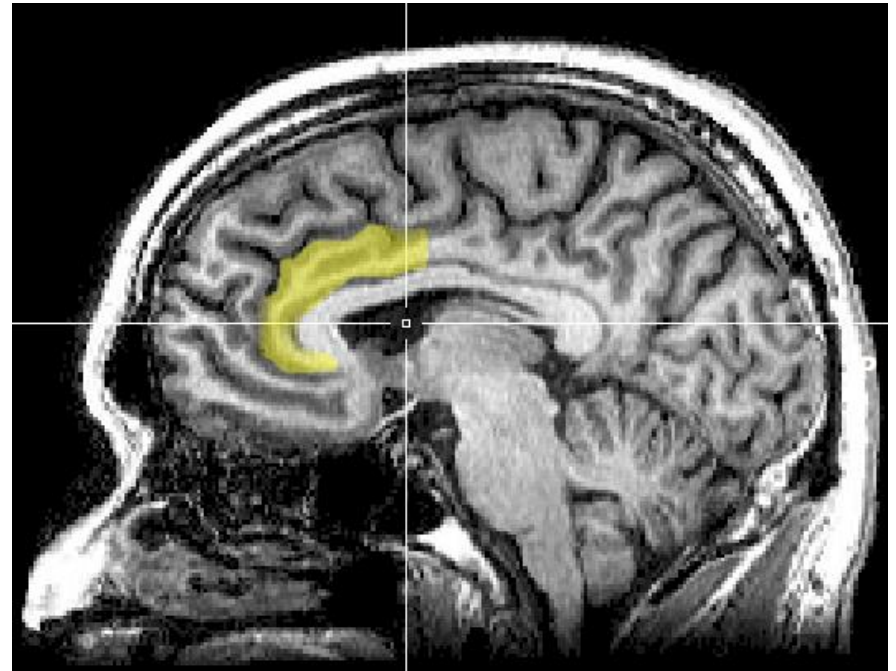
- Decision Making
  - Guided by reward
- Assigns value to environmental stimuli to motivate or inhibit choices and actions
- The “I” of the “Chalk Talk” I over E



# Anterior Cingulate Cortex (ACC)

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- Works with OFC: For reward based decision making
- Generates actions based on historical rewards/punishments
- Social Cues
- Associated with many functions which are correlated with conscious experience



# Prefrontal Cortex (PFC)

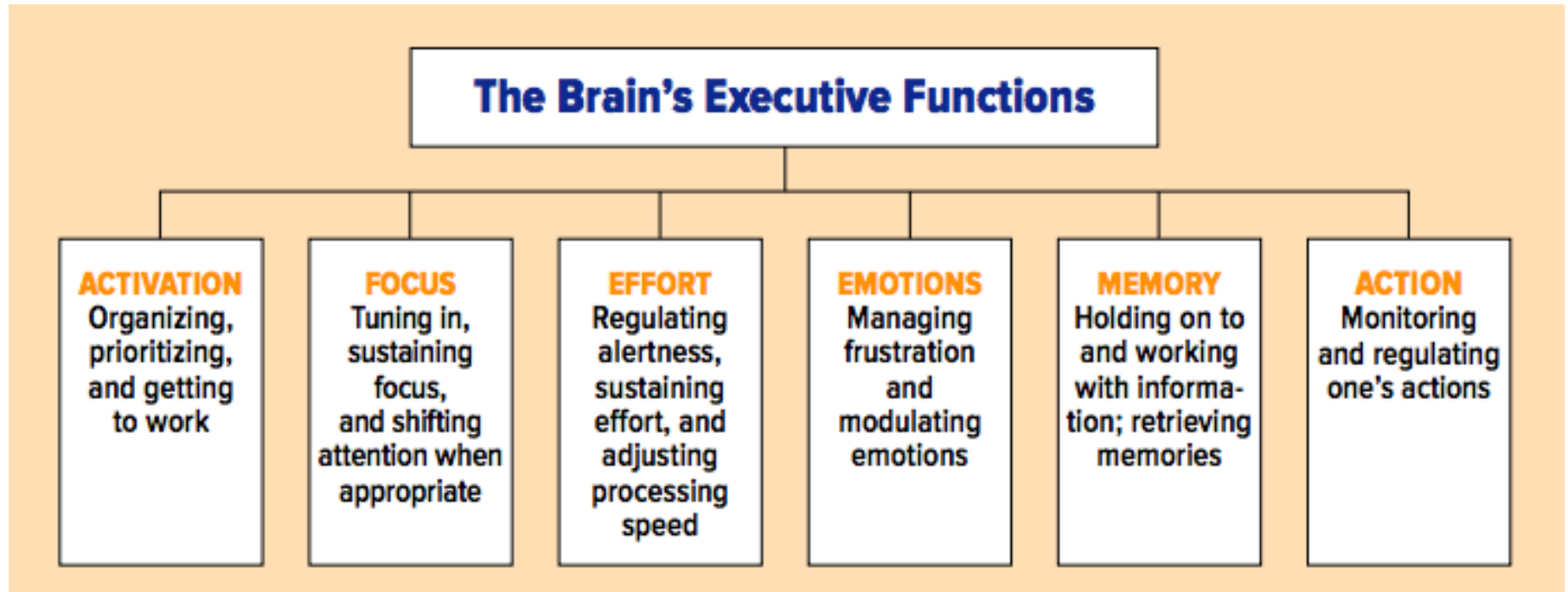
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- Behavior Regulation
- Reflective Decision-making
- Inhibition of socially inappropriate actions
- Emotional and sensory integration
- Planning complex behaviors



# Executive Functioning

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# Executive Functioning

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Failure of Executive Functioning....

- Premature, risky, poorly planned actions
- Urgency
- Sensation seeking
- Emotions inappropriate to situation
- Deficits in attention, lack of perseverance
- Insensitive to consequences

Sound like someone you know?...



# Impulse Control

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A person's inability to delay gratification

Condition associated with deficits in impulse control include:

- Adolescence
- Alcohol use disorders
- Substance abuse
- ADHD
- Conduct/anti-social personality disorder
- depression

# James Olds, PhD (1922-1976)

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- Discovery of the reward system in the midbrain
- Mice self-administered electric currents to the VTA
- Preferred stimulation to other survival rewards such as food



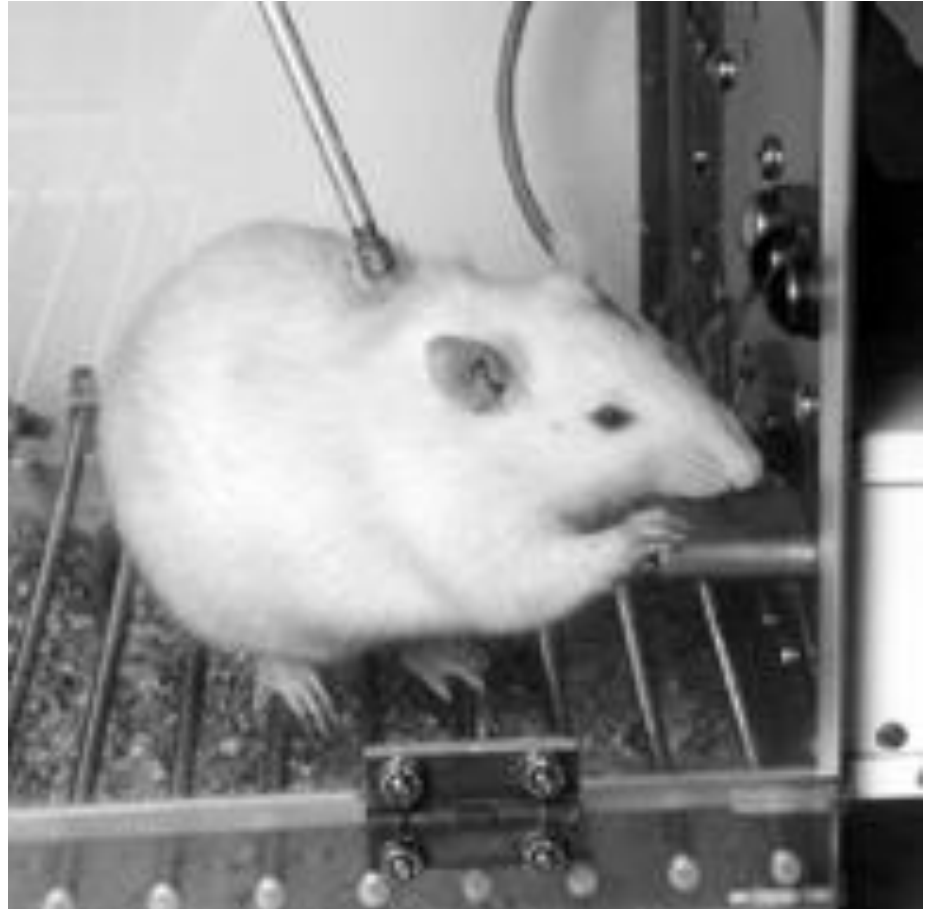
# Olds and Milner Experiment

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Rats self-administered electric stimulation to the septal areas of the brain

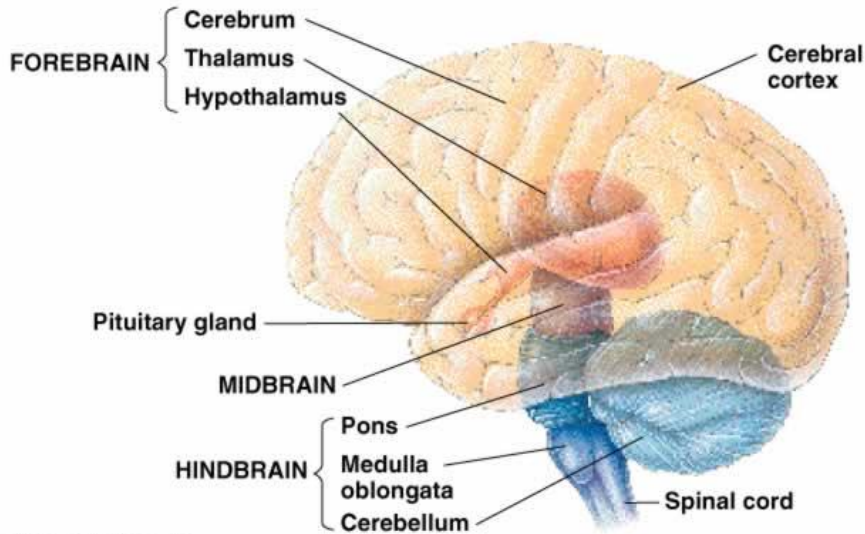
Hyper-prioritization

1. DRUG (new priority)
2. Eat
3. Self preservation
4. Sex



# Olds and Milner (Midbrain)

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Mice preferred self-administration of drugs of abuse, such as Cocaine, only to the reward centers of the brain

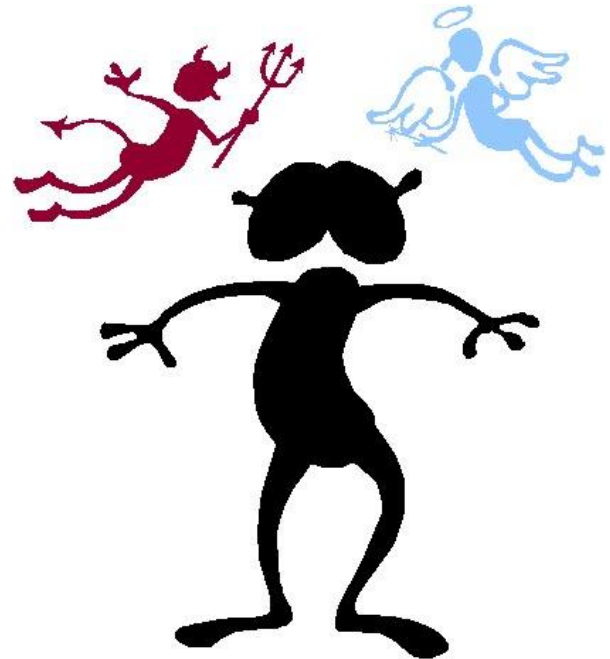
- Without regard for all other survival behaviors
- To the point of DEATH

# Mice as Addicts...

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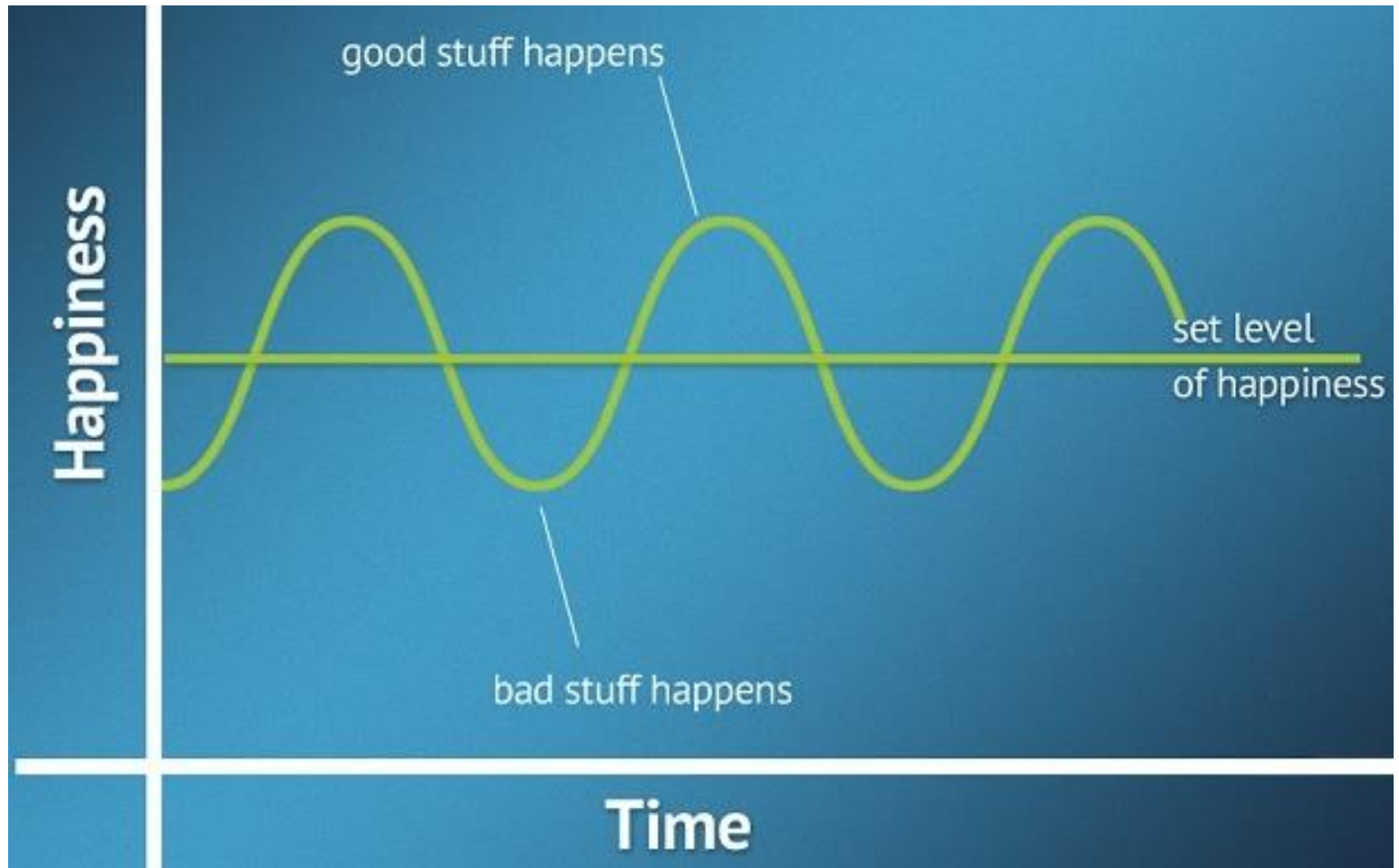
As Dr. Kevin T. McCauley would say....

- Mice do not weigh moral decisions
- Mice do not consult a “mouse God”
- Mice are not sociopaths
- Mice do not have bad parents
- Mice do not belong to gangs

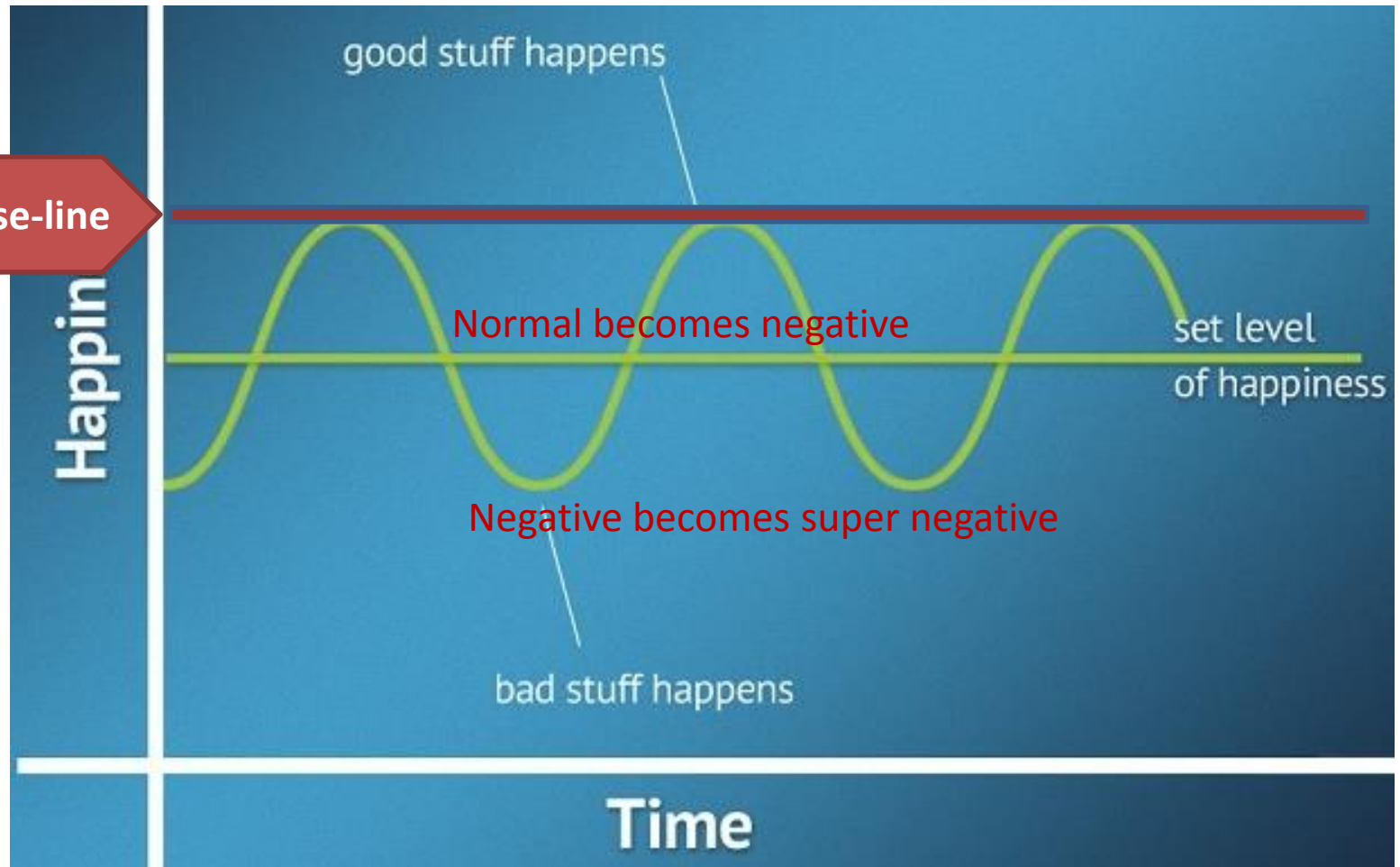


# Hedonic Set Point

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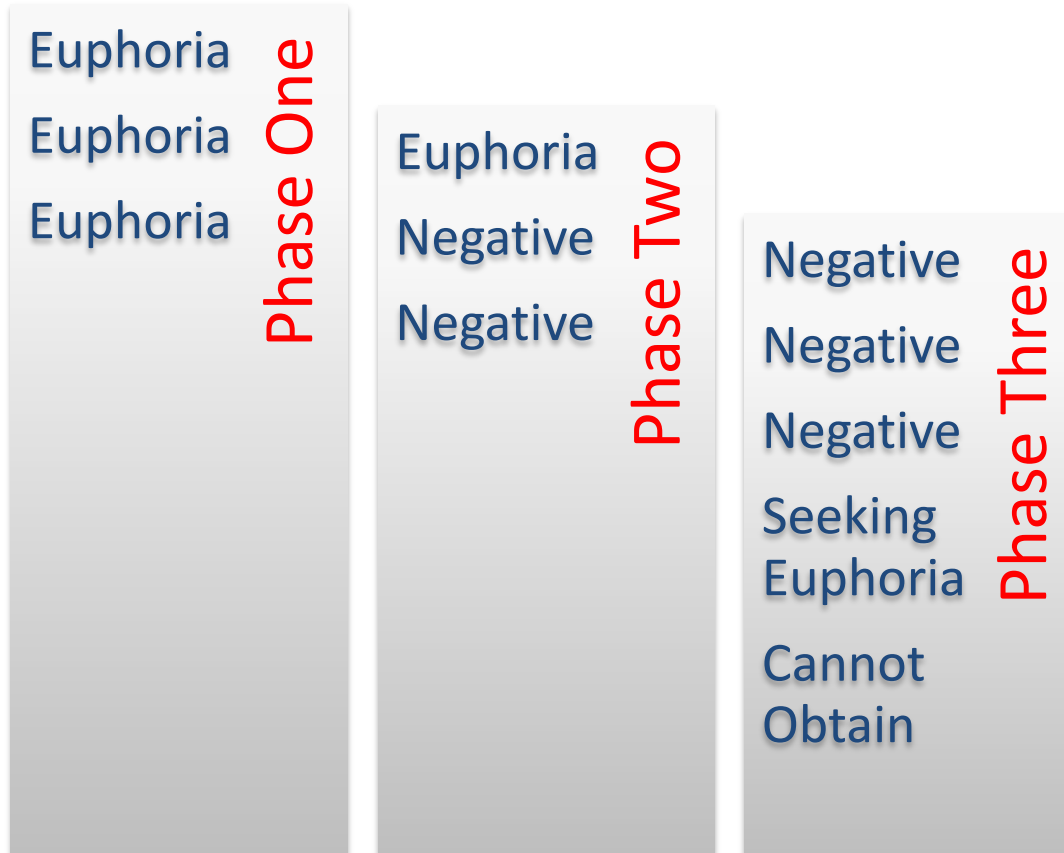


# Hedonic Set Point



# Phases of Addiction

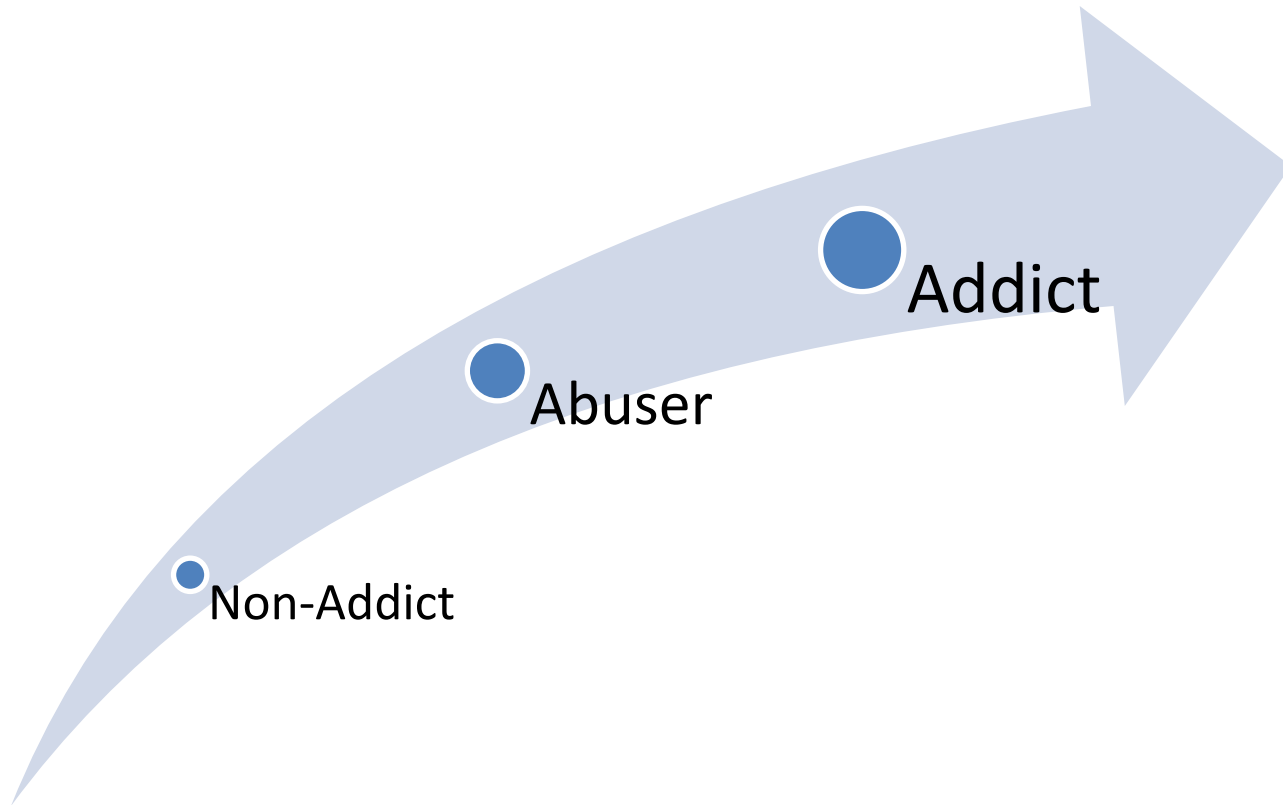
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At a point the line is crossed where Drug becomes more than a drug but is survival

# User Spectrum

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At a point the line is crossed where Drug becomes more than a drug but is survival

# DSM-IV Criteria for Substance Abuse

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- Inability to reduce usage
- More drug used than intended
- A lot of time spent using, recovering, and acquiring
- Tolerance
- Isolation from friends, family, and old activities
- Withdrawal
- Negative consequences



# Five Theories of Addiction

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1. Genetic Vulnerability (Schuckit et al)
2. Incentive-sensitization of reward (Robinson & Berridge)
3. Pathology of Learning and Memory (Hyman, Everitt & Robbins)
4. Stress and Allostasis (Koob & LeMoal)
5. Pathology of Motivation and Choice (Kalivas & Volkow)

No contradictions between the five theories

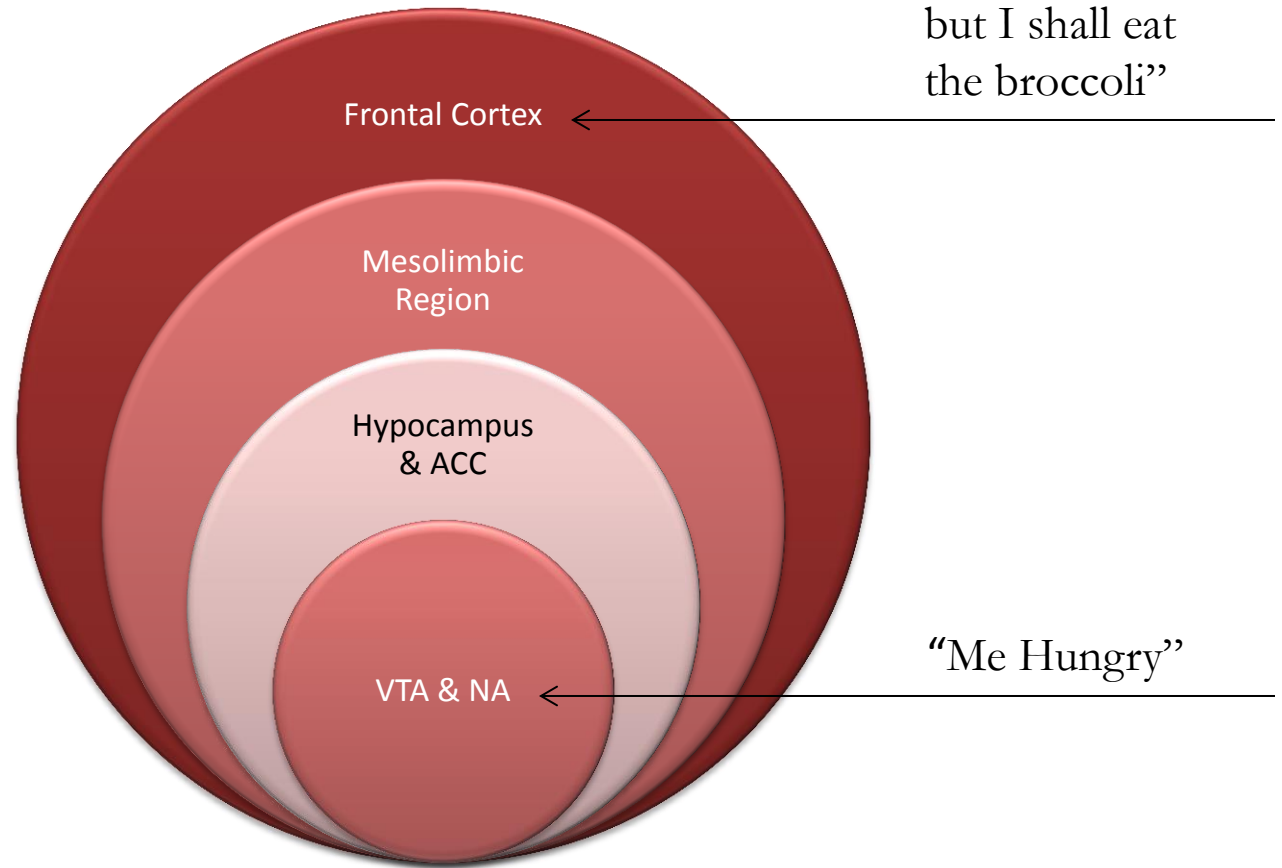
# A disorder of...

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1. Choice (Motivation)
2. Stress (Anti-reward system)
3. Memory (learning)
4. Reward (hedonic system)
5. Genes (vulnerability)

# Layers of thought

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# Resources

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McCauley, K. (2013) The Neuroscience of Addiction and Recovery. Educational Lecture. St. Louis, MO. August 23<sup>rd</sup>, 2013.

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