

Pleasure Unwoven:
A Personal Journey about Addiction

companion handouts to the DVD

Adapted from the lecture “Is Addiction Really a Disease?” by Kevin
McCauley
and produced by the Institute for Addiction Study, Salt Lake City, UT

Any good theory of addiction has to explain ...

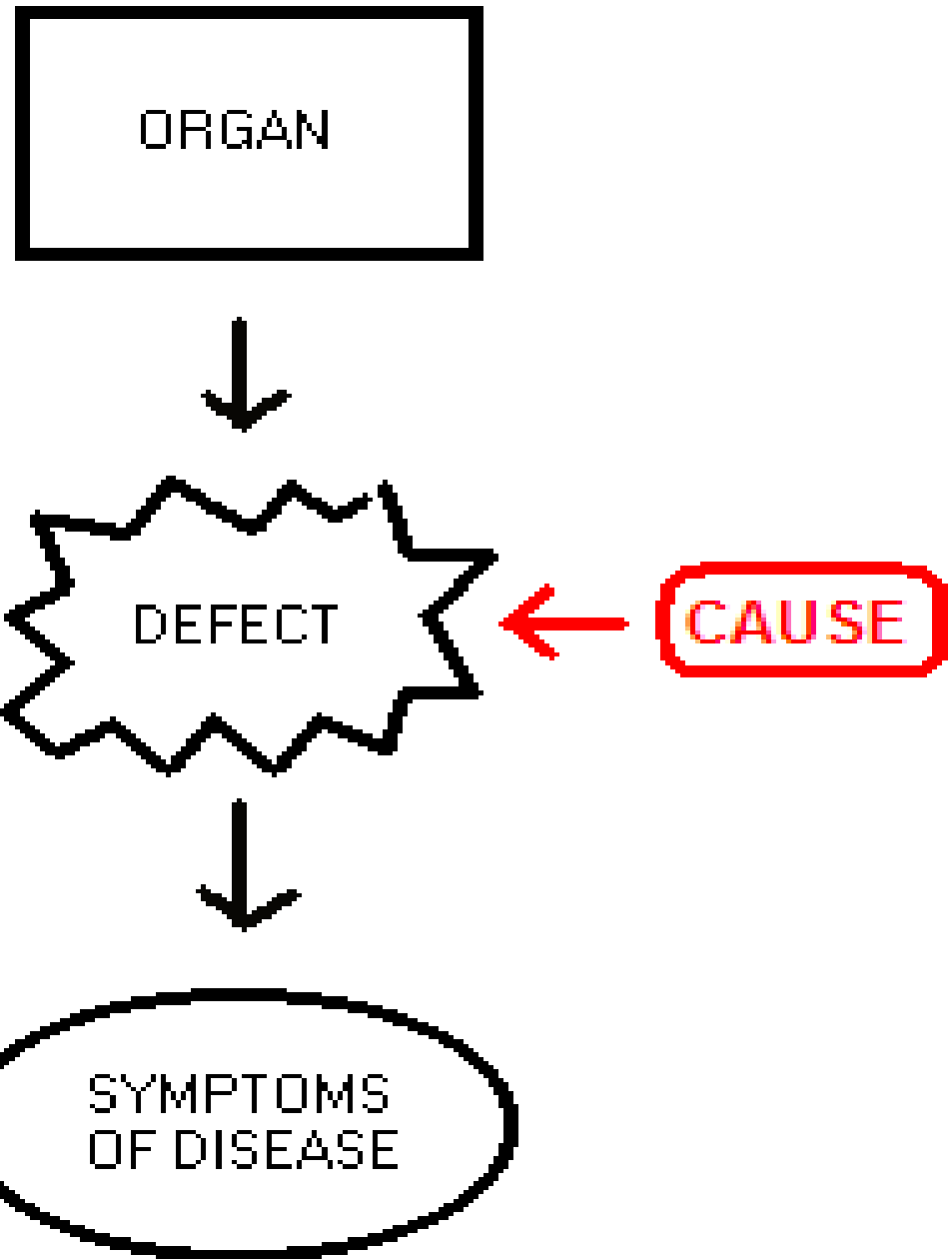
- Genetic vulnerability
- Why some and not others?
- Loss of Control
- Persistent Use Despite Negative Consequences
- Drug of Choice
- Relapse
- Cross-Addictions
- Special utility of social/spiritual solutions
- Unpredictability of rewards/punishments in stopping addiction
- Why some are “instantly addicted”
- Why some drink/use socially for long periods & only later develop problems
- Sudden “cures”
- Self “cures”
- Personality changes
- Problematic history of pharmacological treatments
- Psychiatric co-morbidity
- Emotional “longing”

“Choice” vs.

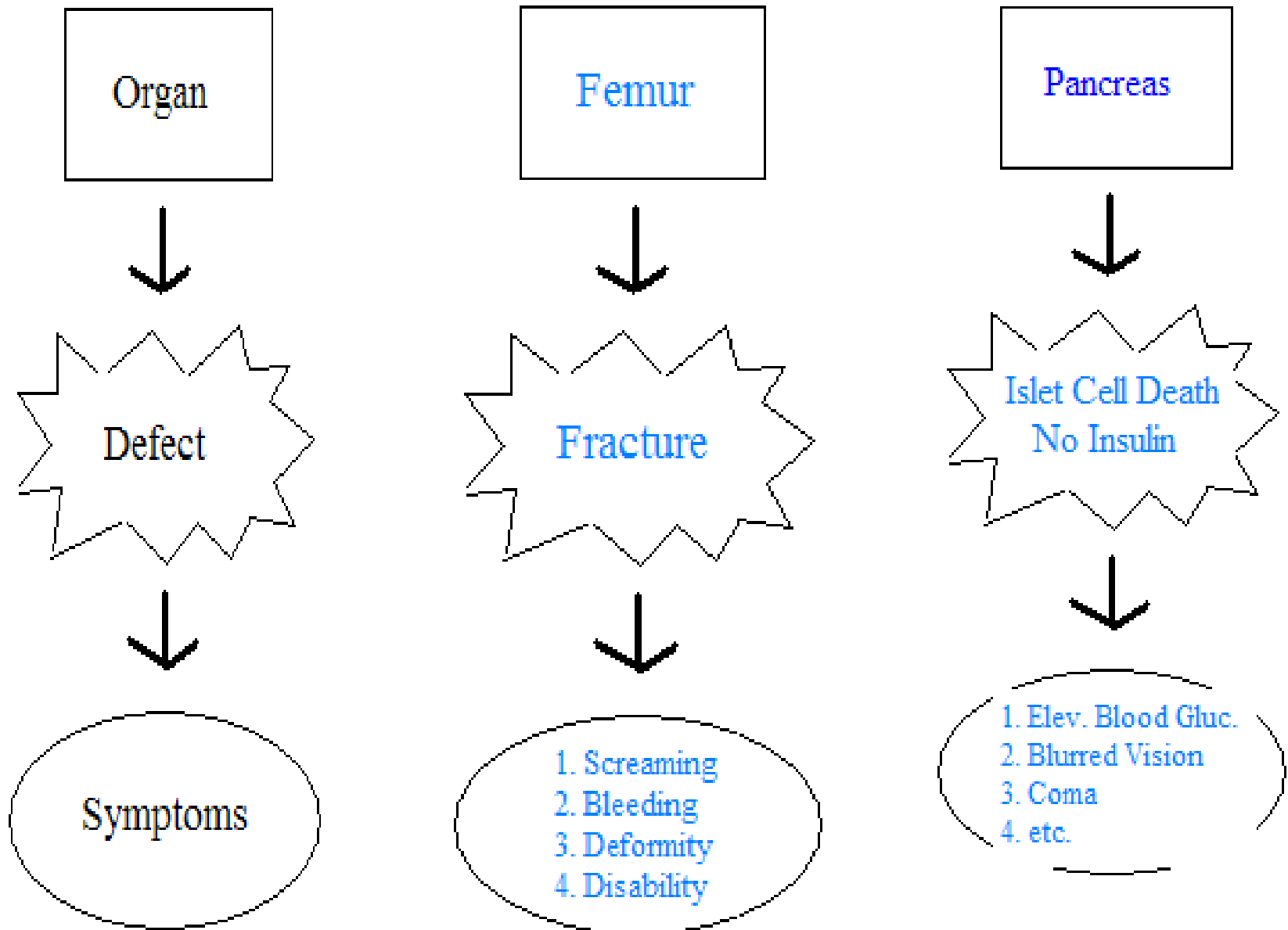
“Disease”

- Free Will exists
 - Responsibility
 - Can stop
 - Punishment and Coercion DO work
 - BEHAVIORS
- No Free Will
 - No Responsibility
 - Can't stop
 - Punishment and Coercion DON'T work
 - SYMPTOMS

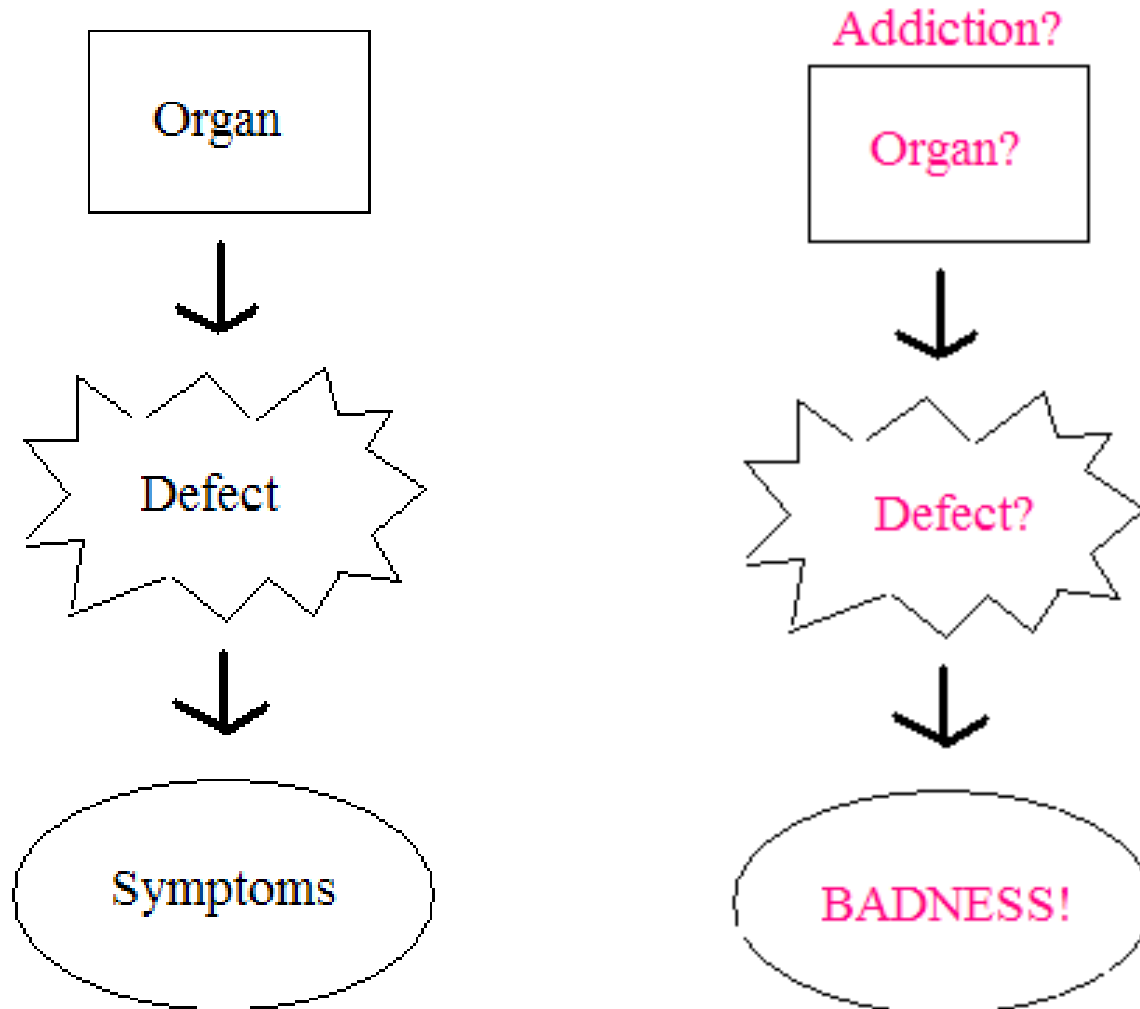
The Disease Model



(a CAUSAL model)

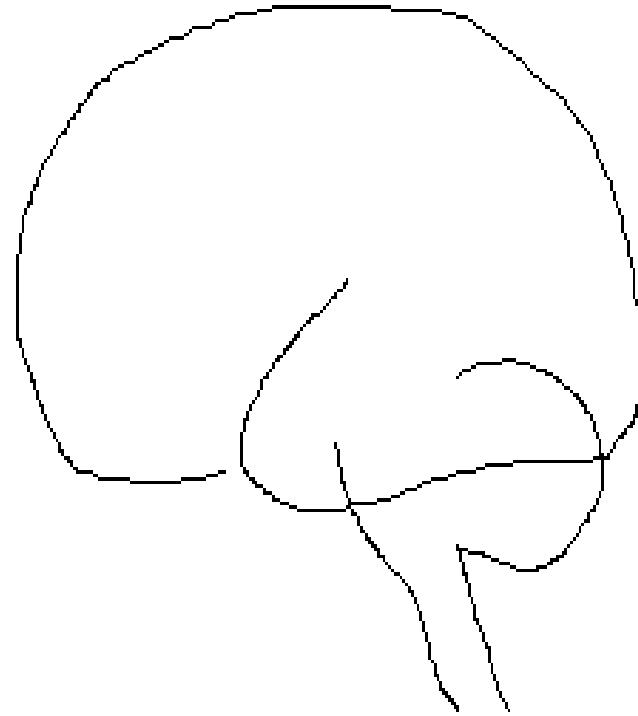


If ever we could fit addiction into this model, then it would win admission into "The Disease Club". . .



Addiction is a BRAIN disease

- *The brain's a HARD organ - very complex and difficult to study*
- *There are no good tests for brain diseases (yet)*
- *So people with brain diseases start out at a disadvantage*
- *The symptoms of brain diseases are more likely to be labeled as "badness"*



the Brain

The Limbic (Emotional) Brain

CORTICAL

(Conscious)

- Prefrontal Cortex (PFC)
- Orbitofrontal Cortex (OCC)
- Anterior Cingulate Cortex (ACC)

SUBCORTICAL

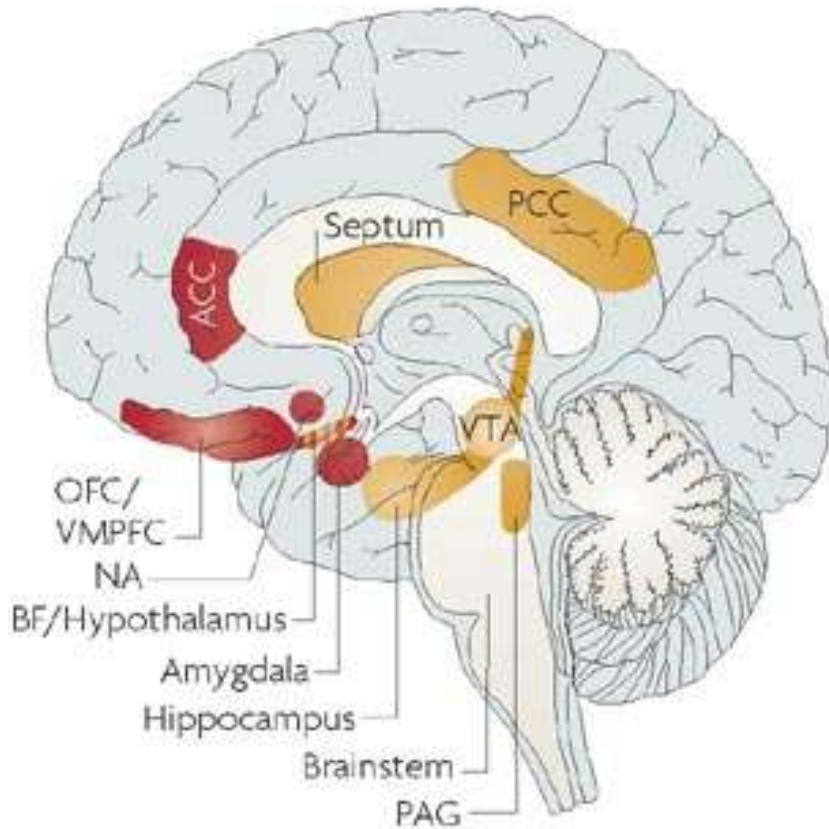
(Unconscious)

- Midbrain
- Ventral Tegmental Area (VTA)
- Nucleus Accumbens (NA)
- Hippocampus
- Amygdala
- Hypothalamus

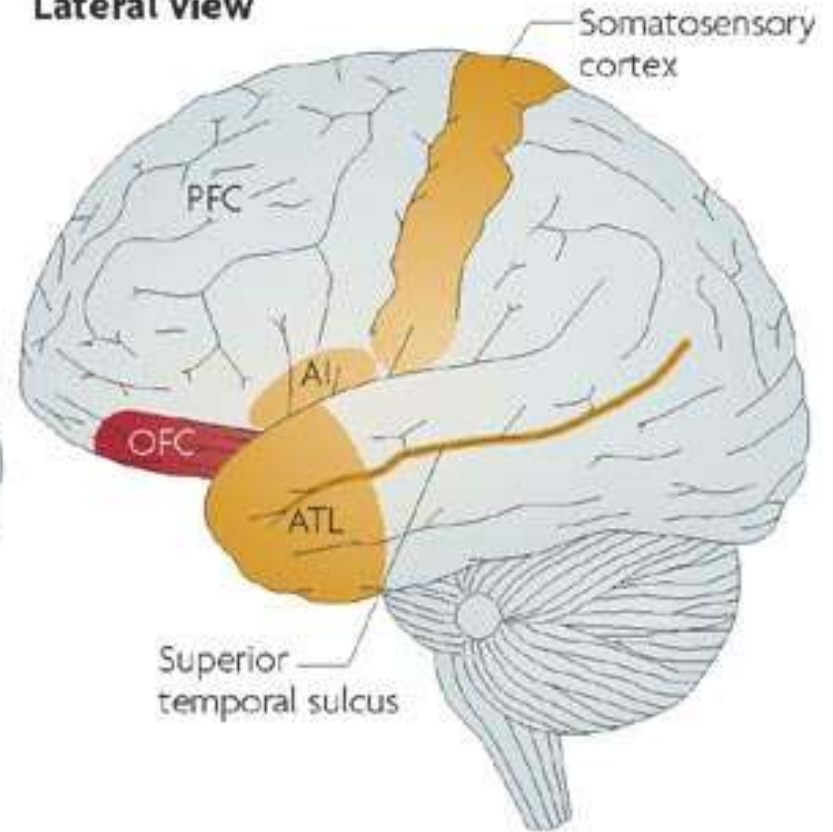
(note: I use the term "midbrain" in the DVD to denote all the

The Key Parts of the Limbic Brain

Medial view

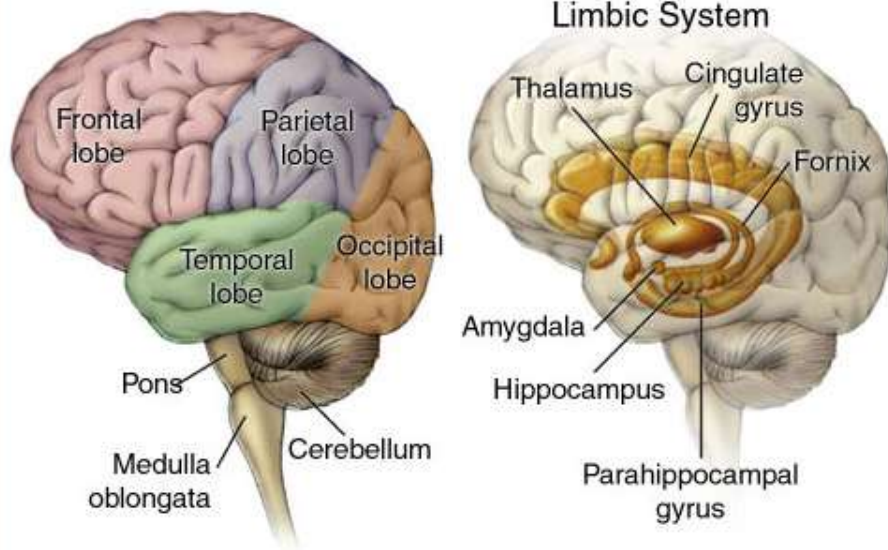


Lateral view



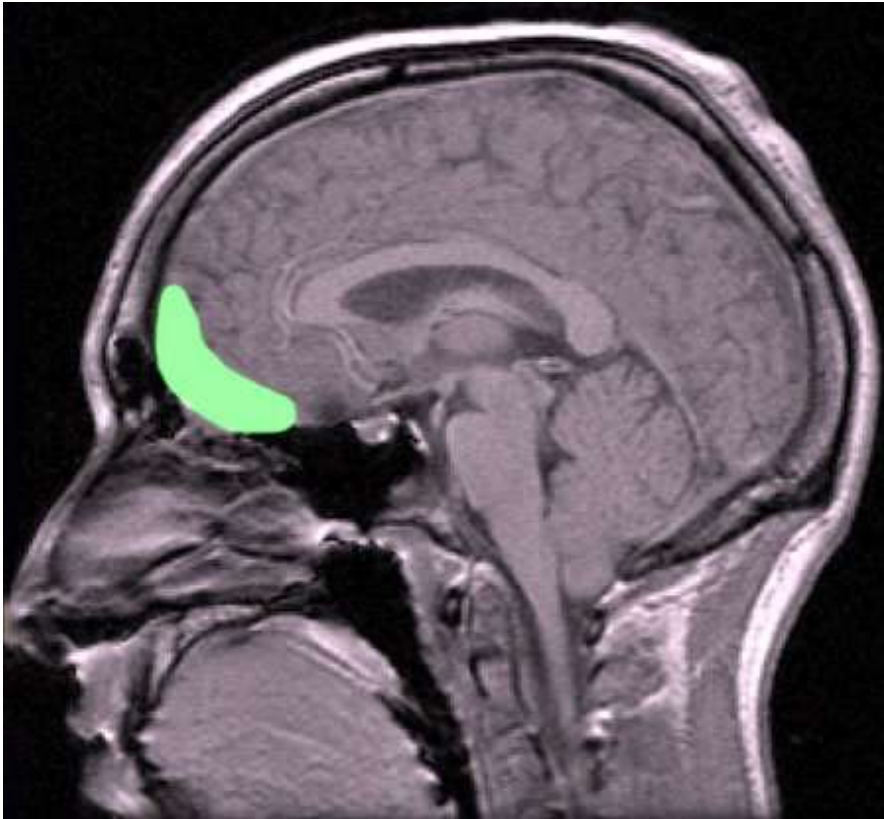
The Frontal Cortex

Anatomy of the Brain



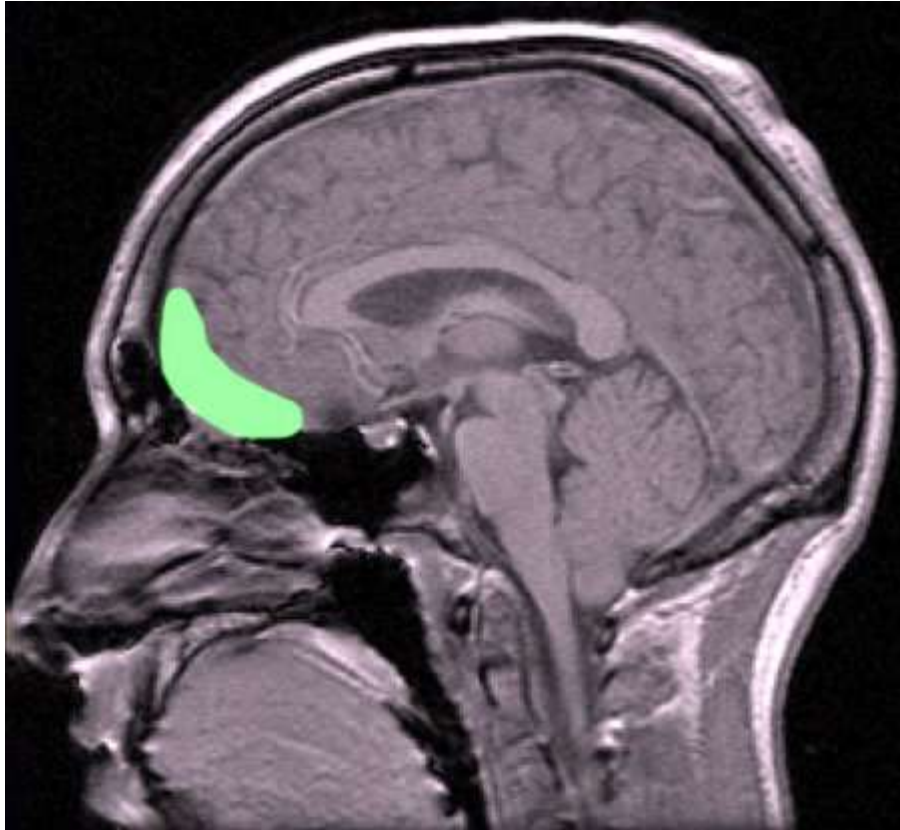
- The “Human” Brain
- Processes judgment, executive decision making,
- Conscious emotions
- Confers emotional meaning onto objects in the world
- Seat of the Self and Personality
- “Love, Morality, Decency, Responsibility, Spirituality”

Orbitofrontal Cortex (OFC)



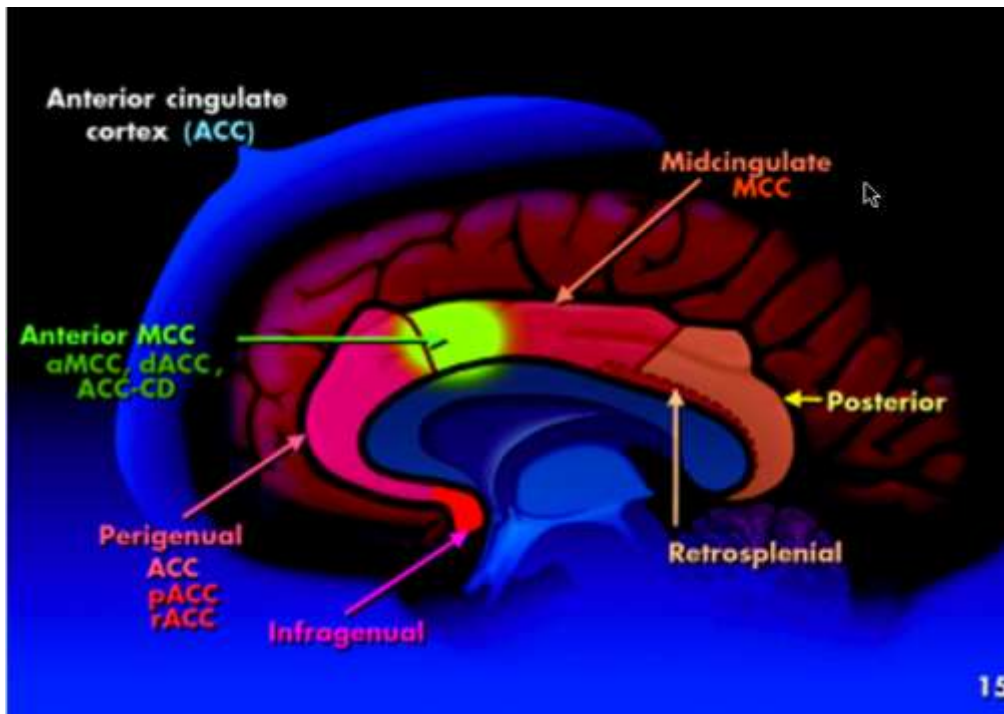
- Decision-making guided by rewards
- Integrates sensory and emotional information from lower limbic structures
- Flexible assignment of value to environmental stimuli to motivate or inhibit choices & actions
- Self-monitoring and social responding

damage to Orbitofrontal Cortex (OFC)



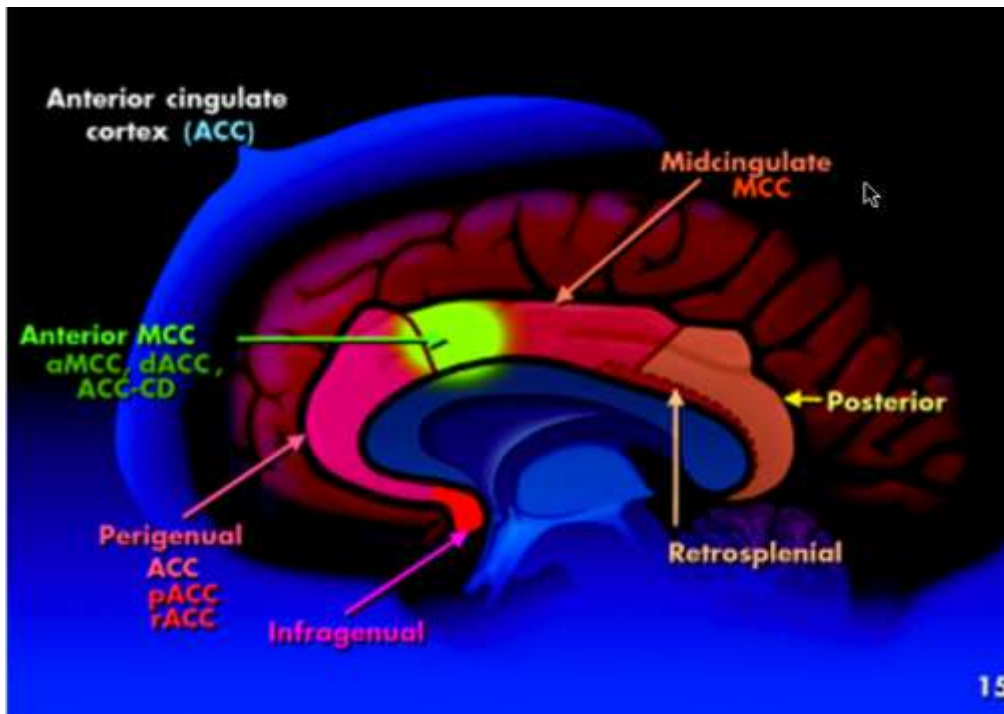
- Causes a loss of a crucial behavioral guidance system
- Responses are impulsive and inappropriate
- Deficits of self-regulation
- Inability to properly assign value to rewards (such as money vs. drugs)
- Tendency to choose small & immediate rewards over larger but

Anterior Cingulate Cortex (ACC)



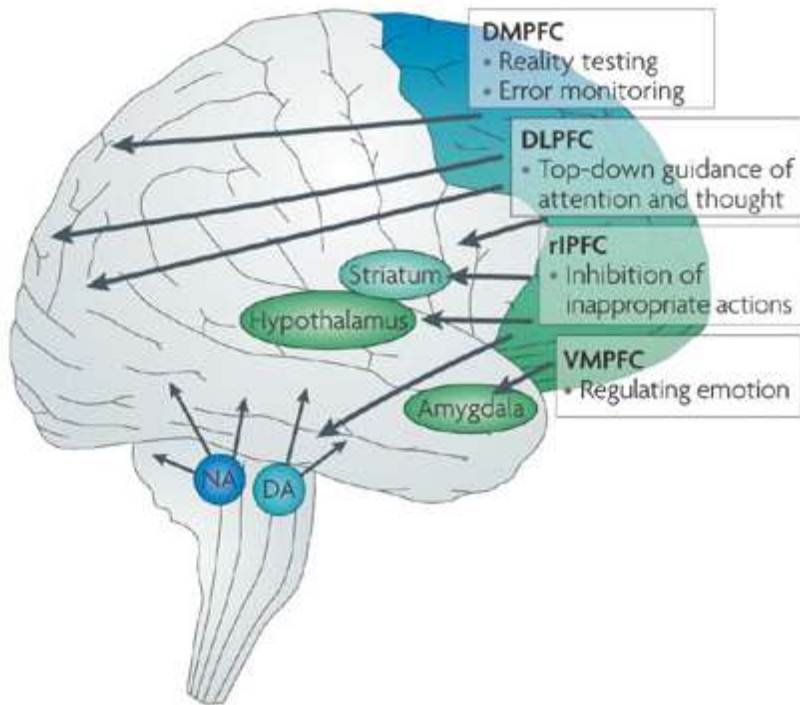
- Works with OFC: decision-making based on reward values
- But also generates new actions based on past rewards/punishments
- Appreciation and valuation of social cues
- MRI: active in tasks

damage to Anterior Cingulate Cortex (ACC)



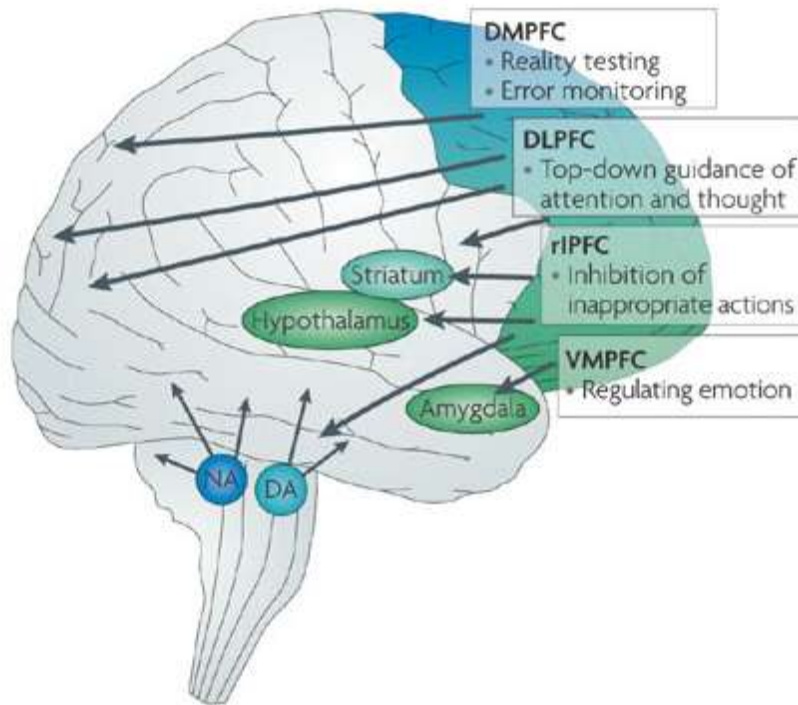
- Just as with OFC damage: causes a loss of a crucial behavioral guidance system
- Inflexibility/Inability to respond to errors in the past with regard to rewards/punishments
- Deficits in social responding due to decreased awareness of social cues

Prefrontal Cortex (PFC)



- Behavioral regulation
- Reflective decision-making
- Inhibition of socially inappropriate actions
- Emotional and sensory integration
- Planning complex behaviors

damage to Prefrontal Cortex (PFC)



- Failure of executive function

Failure of Executive Functioning

- Premature, unduly risky, poorly conceived actions
- Urgency
- Sensation seeking
- Expressed emotions inappropriate to the situation
- Deficits in attention, lack of perseverance
- Rapid responses without reflection or premeditation
- Insensitivity to consequences
- Impulsive choice (increased delay

Conditions associated with deficits in impulsive control

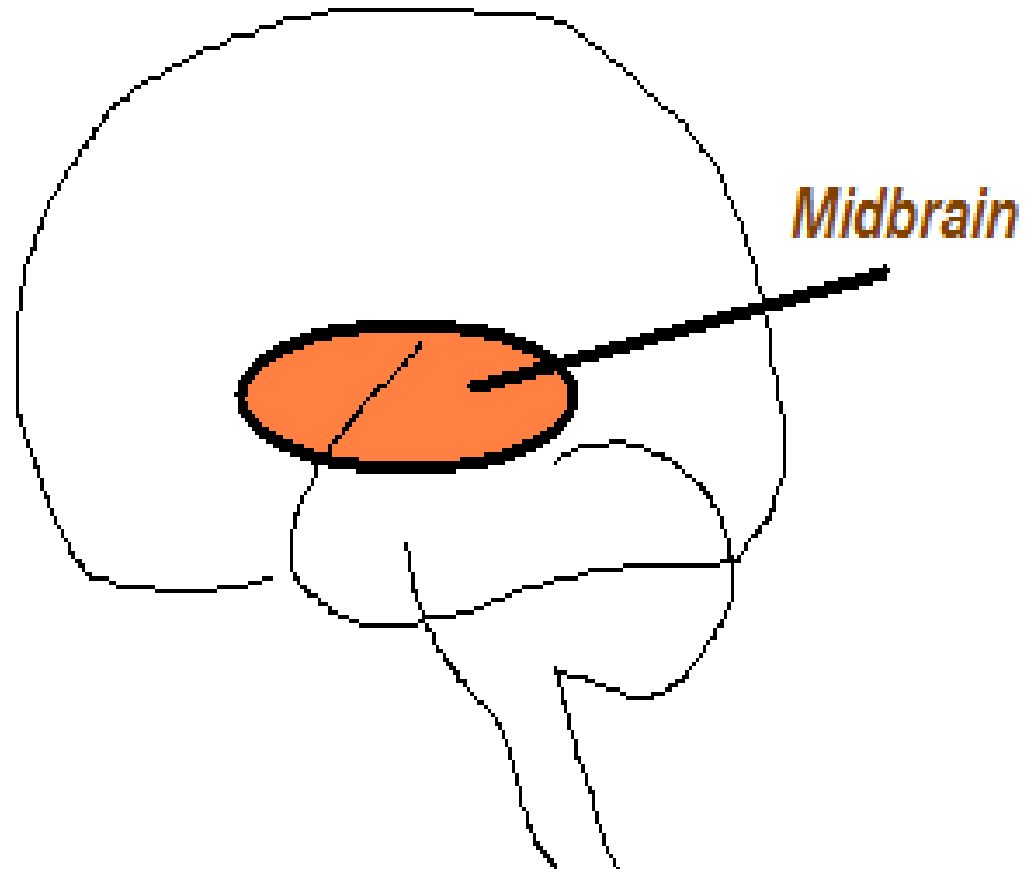
- Adolescence
- Alcohol use disorders
- Substance abuse
- ADHD
- Anti-social personality disorder

But addiction does not begin
in the Frontal Cortex ...

*... addiction begins at a deeper
(and older) part of the brain: the
“Midbrain”*

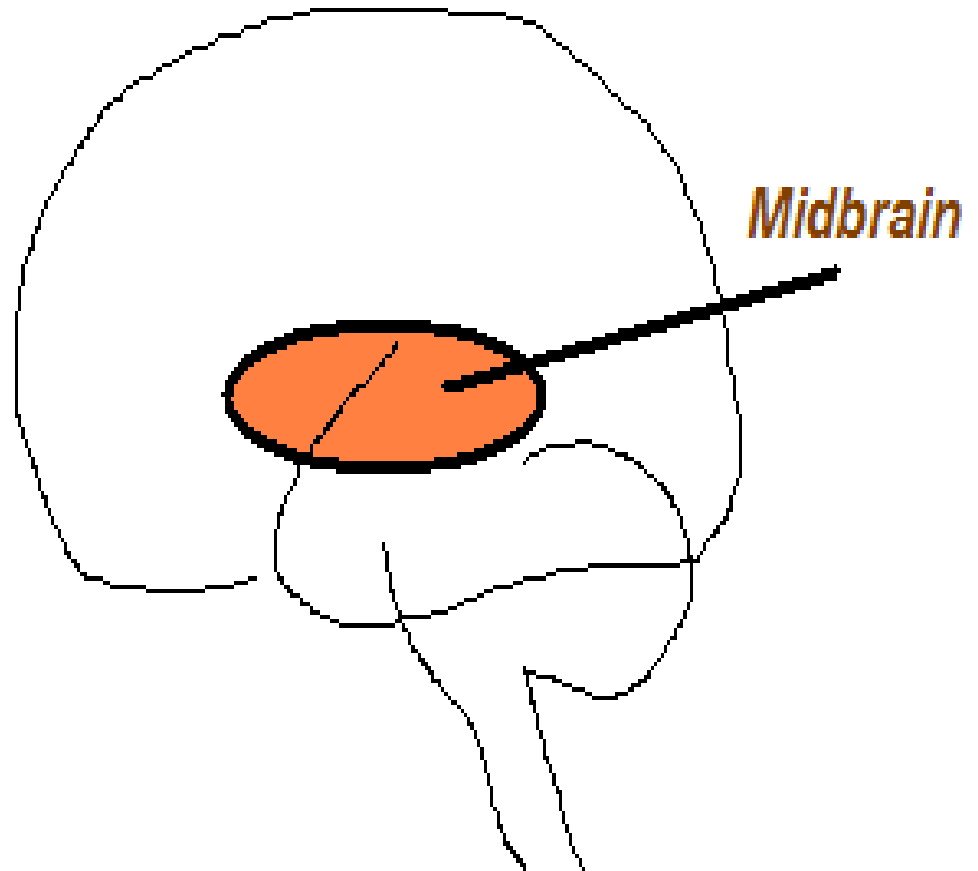
*The Midbrain is the **SURVIVAL** brain*

- Not conscious
- Acts immediately, no future planning or assessment of long-term consequences
- A life-or-death processing station for arriving sensory information



*The Midbrain (aka Limbic Brain)
is your **SURVIVAL** brain. It handles:*

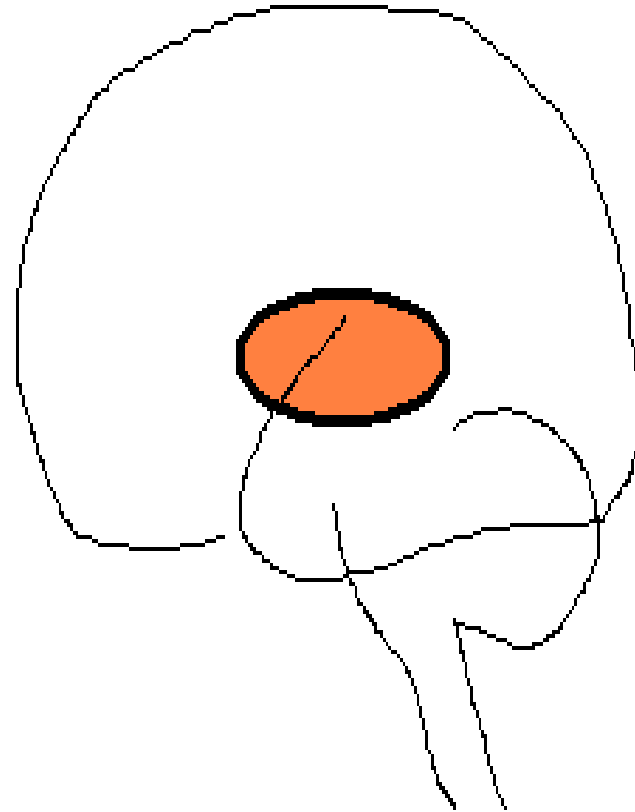
- *EAT!*
- *KILL!*
- *SEX!*



*Drugs work in the **Midbrain***

- *NOT in the Cortex*

*(and how do we know
this? ...)*



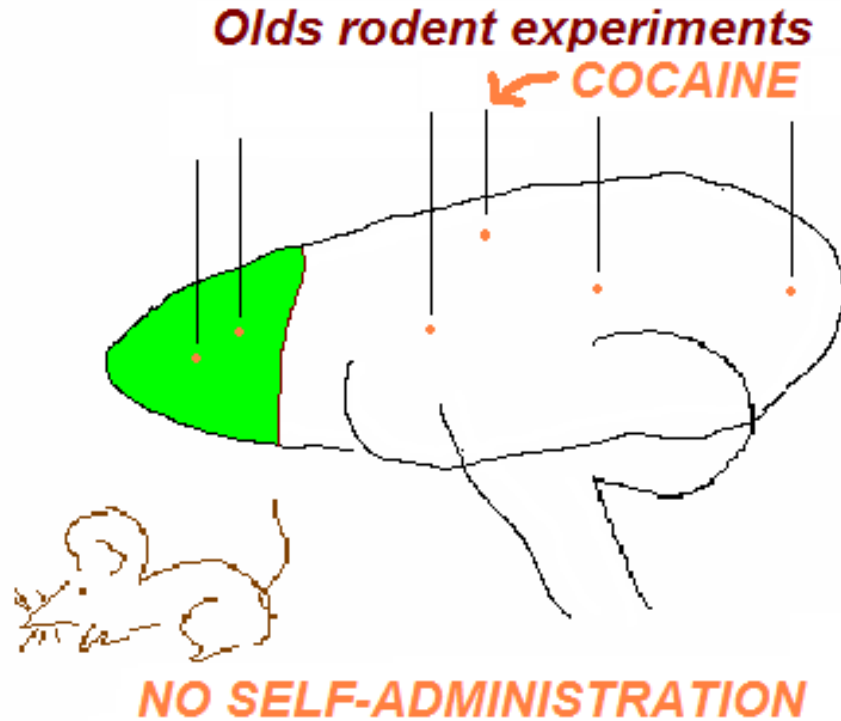
Midbrain
- survival
- unconscious
- no free will

James Olds, PhD (1922 - 1976)



- Discovery of the reward system in the midbrain
- Mice will self-administer electric currents to the Ventral Tegmental Area of the midbrain
- They prefer the electrical stimulation over other survival rewards such as food

Olds experiments:



Mice preferentially self-administer drugs of abuse like cocaine ONLY to the Reward Centers of the Midbrain

- *To the exclusion of all other survival behaviors*
- *To the point of death*

*Ventral Tegmentum
Nucleus Accumbens*



*Midbrain
- survival
- unconscious
- no free will*

Mice get addicted to drugs, but ...

- *Mice don't weigh moral consequences*
- *Mice don't consult their "Mouse God"*
- *Mice aren't sociopaths*
- *Mice don't have bad parents*
- *There are no "Mouse Gangs"*



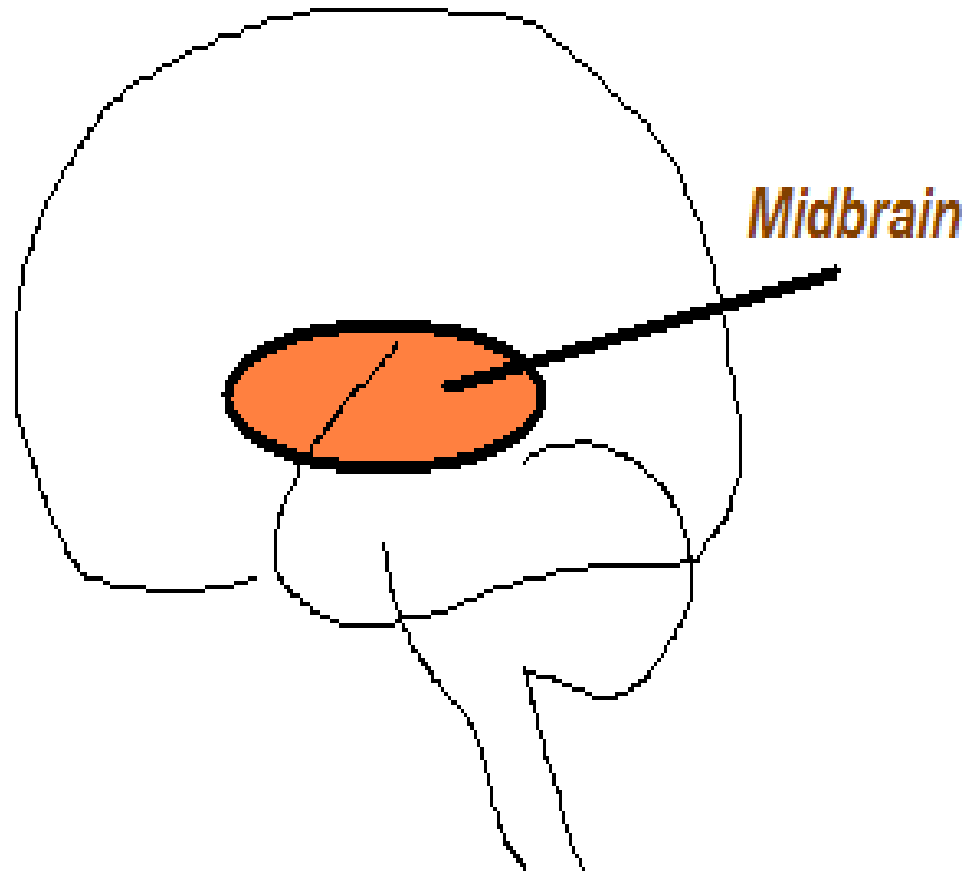
In addiction, the drug hijacks the survival hierarchy and is so close to actual survival that it is indistinguishable from actual survival

***New #1:
DRUG!***

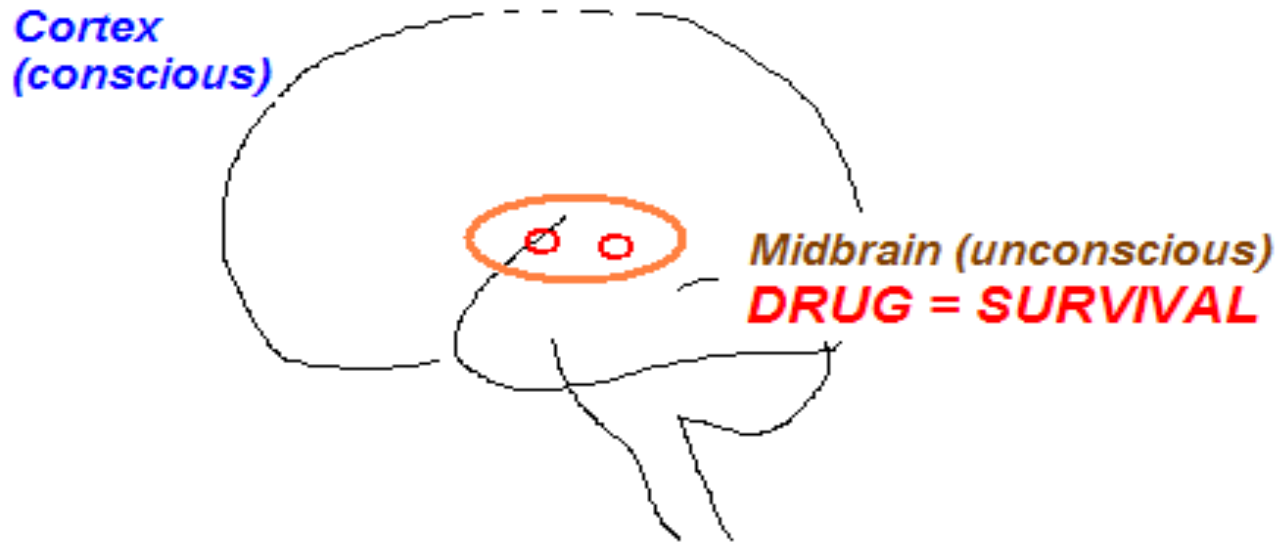
2. EAT!

3. KILL!

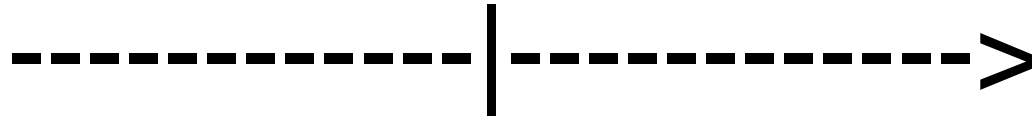
4. SEX !



In addiction, the drug is equated with survival at the level of the unconscious (i.e. the drug IS survival)



In addiction: a line is crossed



NON-ADDICT

(never used drugs)

(experimented in past)

(uses drugs)

(abuses drugs)

ADDICT

DRUG = DRUG

***DRUG =
SURVIVAL***

*Addiction is a disorder in the
brain's Reward (Hedonic) System*

*It is a broken "pleasure sense" in the
brain*

Brain Perceptual Systems (all of them):

- 1. Vision*
- 2. Hearing*
- 3. Touch*
- 4. Smell*
- 5. Taste*
- 6. Linear Acceleration*
- 7. Angular Acceleration*
- 8. Gravity (Proprioception) ← perceptual construct*
- 9. Blood pO₂ and pCO₂*
- 10. Pleasure ← perceptual construct*

Addiction is a disorder of ...

5. ... CHOICE (motivation)
4. ... STRESS (anti-reward system)
3. ... MEMORY (learning)
2. ... PLEASURE (hedonic system)
1. ... GENES (vulnerability)

Five Theories of Addiction

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

Addiction is a disorder of ...

5.

4.

3.

2.

1. ... GENES (vulnerability)

Genetic Vulnerability

- Genetic difference determine “low responders” vs. “high responders” to the effects of alcohol (low responders more likely to become alcoholics)
- There are genetic differences in how people respond to methylphenidate (Ritalin) injections (some like it, some don't care) implying different vulnerabilities
- For addicts, drugs really do “feel” different than they do to non-addicts

COMT gene & Impulsiveness

- COMT (catechol-O-methyltransferase) is an enzyme that breaks down mono-amine neurotransmitters (Dopamine, Norepinephrine and Serotonin)
- Polymorphism at VAL-158-MET gene for COMT influences impulsive decision-making style
- Individuals homozygous for more active 158-VAL allele have an increased tendency to choose immediate over delayed rewards
- This is an example of genetic variation that contributes to impulsivity and may increase risk of addiction

Addiction is a disorder of ...

5.

4.

3.

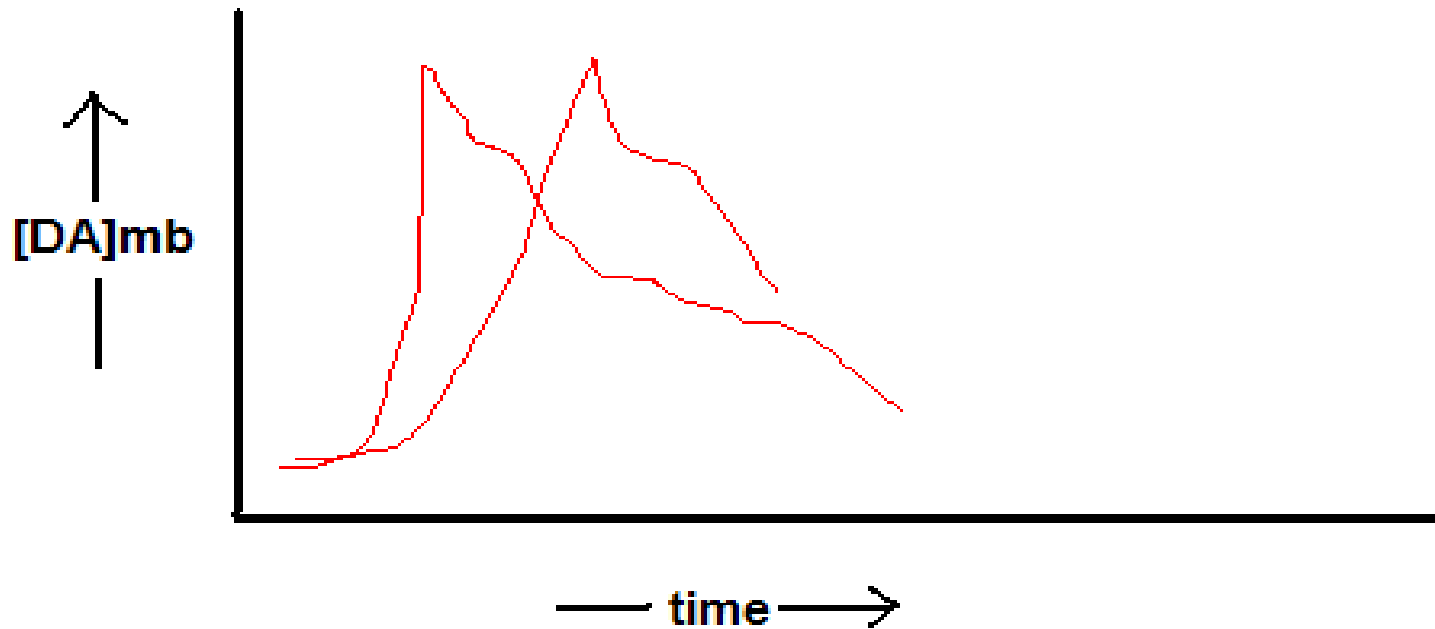
2. ... PLEASURE (hedonic
system)

1. ... GENES (vulnerability)

Addiction Neurochemical #1: Dopamine

- All drugs of abuse and potential compulsive behaviors release Dopamine
- Dopamine is first chemical of a pleasurable experience - at the heart of all reinforcing experiences
- DA is the neurochemical of saliency (it signals survival importance)
- DA signals reward prediction error
- Tells the brain this is “better than expected”

Drugs cause Dopamine Surges in the midbrain reward system



The Full Spectrum of Addiction

- Alcohol & Sedative/Hypnotics
- Opiates/Opioids
- Cocaine
- Amphetamines
- Entactogens (MDMA)
- Entheogens/Hallucinogens
- Dissociants (PCP, Ketamine)
- Cannabinoids
- Inhalants
- Nicotine
- Caffeine
- Anabolic-Androgenic Steroids
- Food (Bulimia & Binge Eating)
- Sex
- Relationships
- Other People
(“Codependency,” Control)
- Gambling
- Cults
- Performance
(“Work-aholism”)
- Collection/Accumulation
(“Shop-aholism”)
- Rage/Violence
- Media/Entertainment

Addiction is a disorder of ...

5.

4.

3. ... MEMORY (learning)

2. ... PLEASURE (hedonic system)

1. ... GENES (vulnerability)

Addiction Neurochemical #2: Glutamate

- The most abundant neurochemical in the brain
- Critical in memory formation & consolidation
- All drugs of abuse and many addicting behaviors effect Glutamate which preserves drug memories and creates drug cues
- And ... glutamate is the neurochemical of “motivation” (it initiates drug seeking)

DOPAMINE (DA) (Glu)

- All drugs of abuse and potential compulsive behaviors INCREASE DA
- Reward salience
- Reward Prediction Error
- “this is important!”
- “I really want this!”
- Rostral (up toward the nose) projections:

PFC < NA < VTA

GLUTAMATE

- All drugs of abuse and potential compulsive behaviors EFFECT Glu
- Drug memories
- Drug seeking
- “OK, I’ll remember”
- “Fine, go and get it”
- Caudal (down toward the tail) projections:

PFC > NA

Relapse

- Three things that are known to evoke relapse in humans:
 1. Brief exposure to drug itself (DA release)
 2. Exposure to drug cues (GLU release)
 3. Stress (CRF release)

(example of a dangerous relapse-triggering behavior:
talking about drugs (cues) with other newly-sober
addicts in treatment (stressed) while smoking (DA

Addiction is a disorder of ...

5.

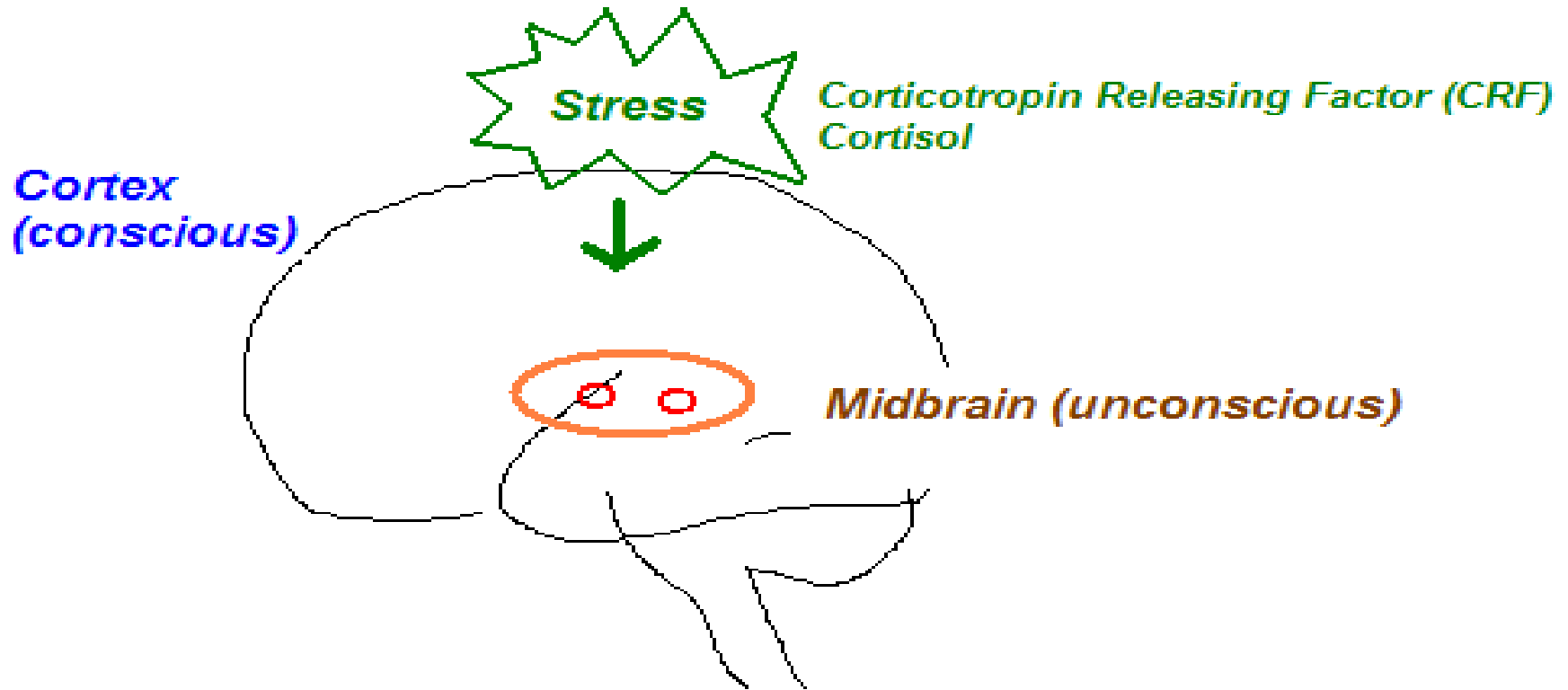
4. ... STRESS (anti-reward system)

3. ... MEMORY (learning)

2. ... PLEASURE (hedonic system)

1. ... GENES (vulnerability)

STRESS : a major player in addiction & relapse



We all face stress, yes . . .

But we don't all:

- Face the same *severity* of stress
- Face the same *pattern* of stress
- Have the functioning *coping mechanisms*
- Come to the table with the *same brain*

CHRONIC, SEVERE STRESS = ↑CRF

and ↑ CRF = ↓DAD2 receptors

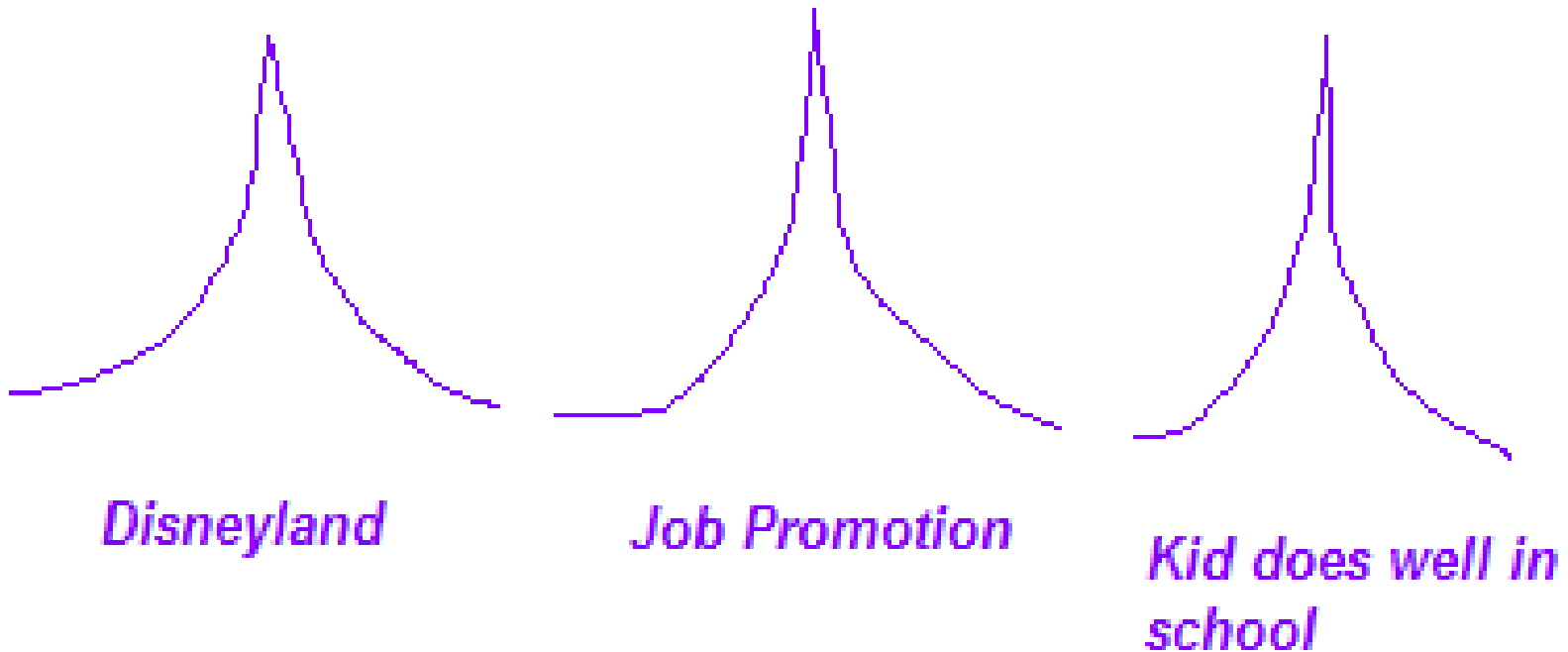
and ↓DAD2 receptors = Anhedonia

Anhedonia: Pleasure “deafness”

*(the patient is no longer able to derive
normal*

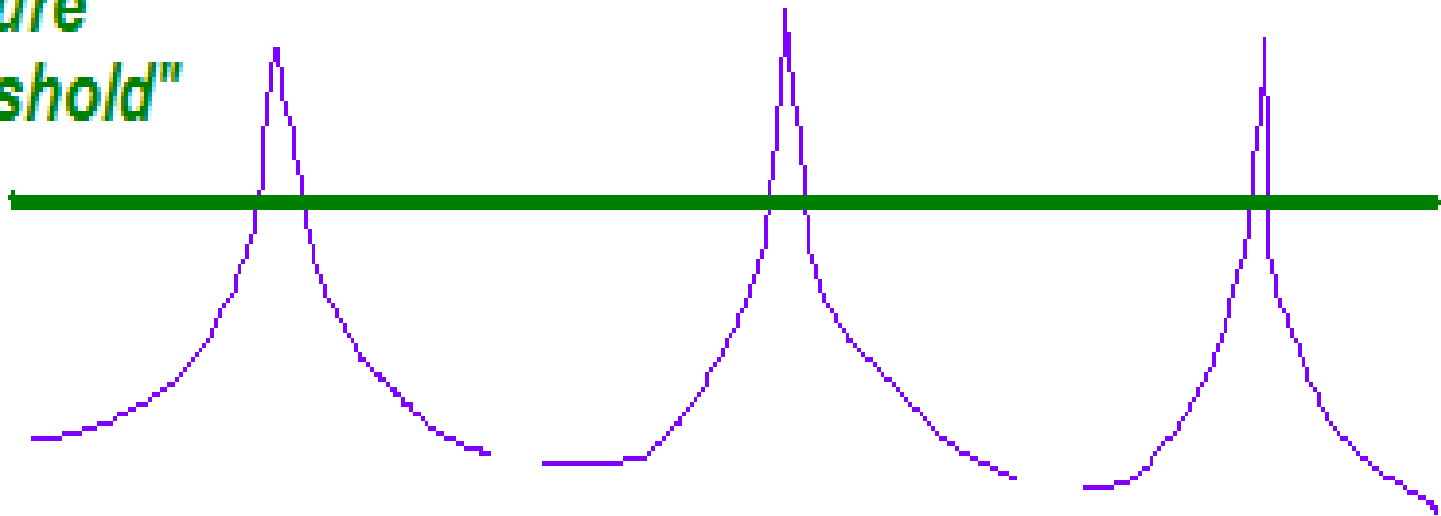
*pleasure from those things that have been
pleasurable in the past)*

*Stress change the brain's ability to process **Dopamine** (pleasure)*



The Brain has a Hedonic “Set Point”

***Pleasure
“Threshold”***

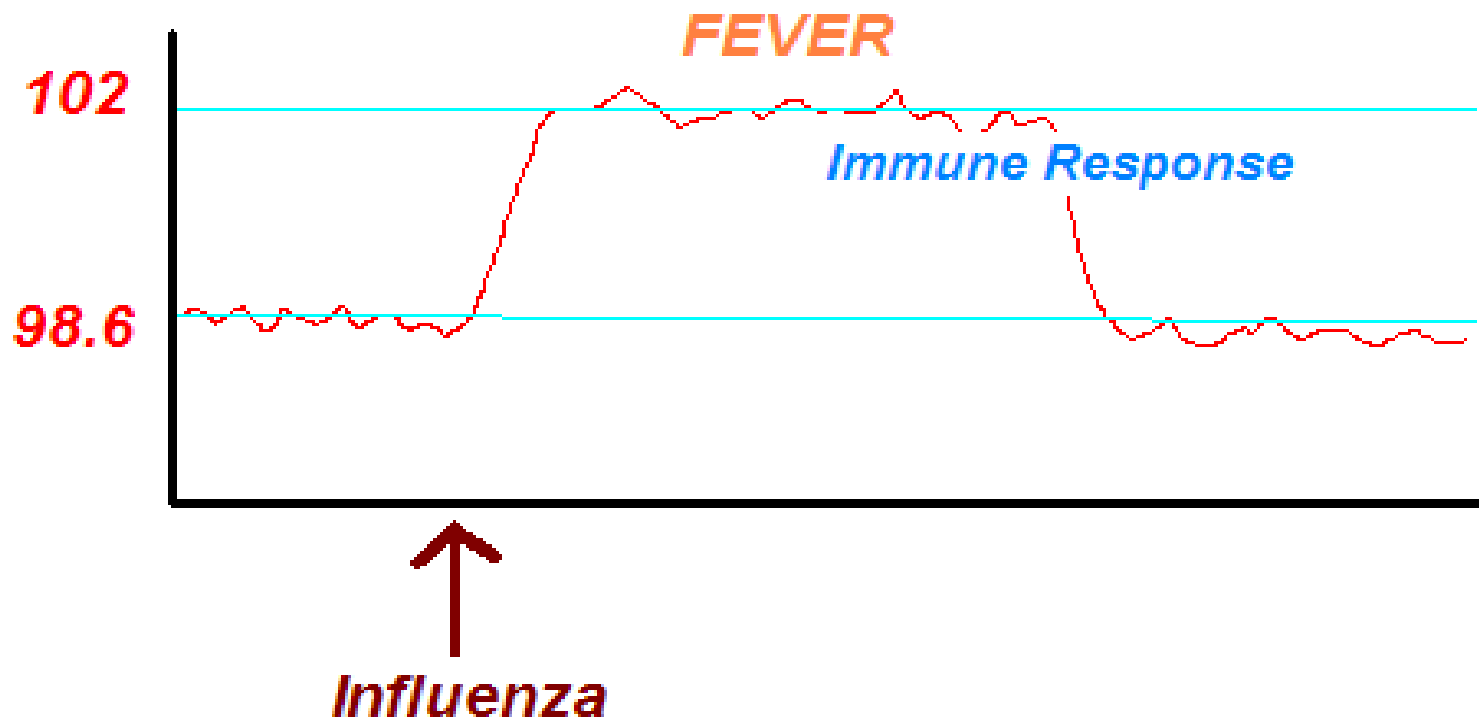


Disneyland

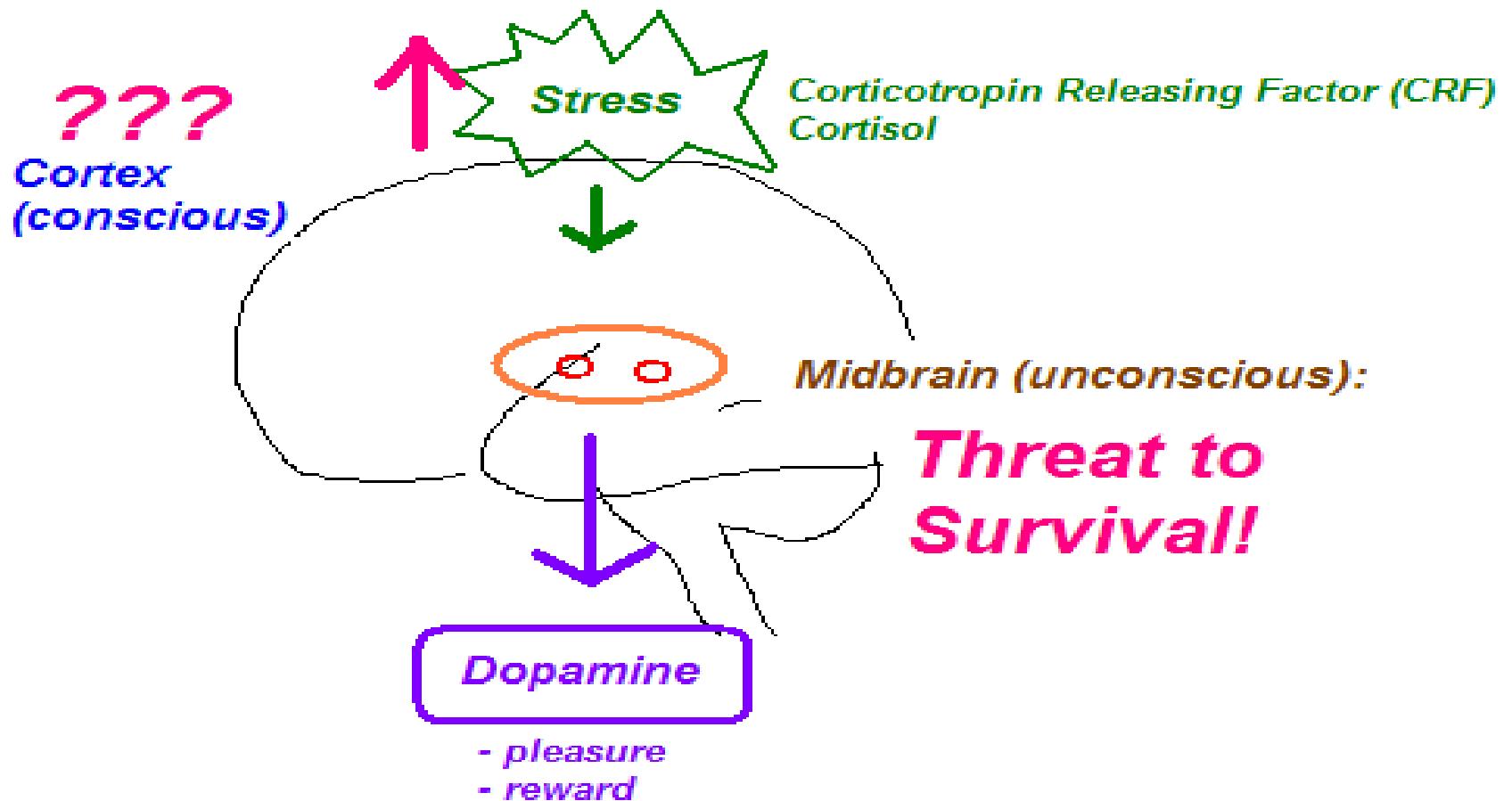
Job Promotion

*Kid does well in
school*

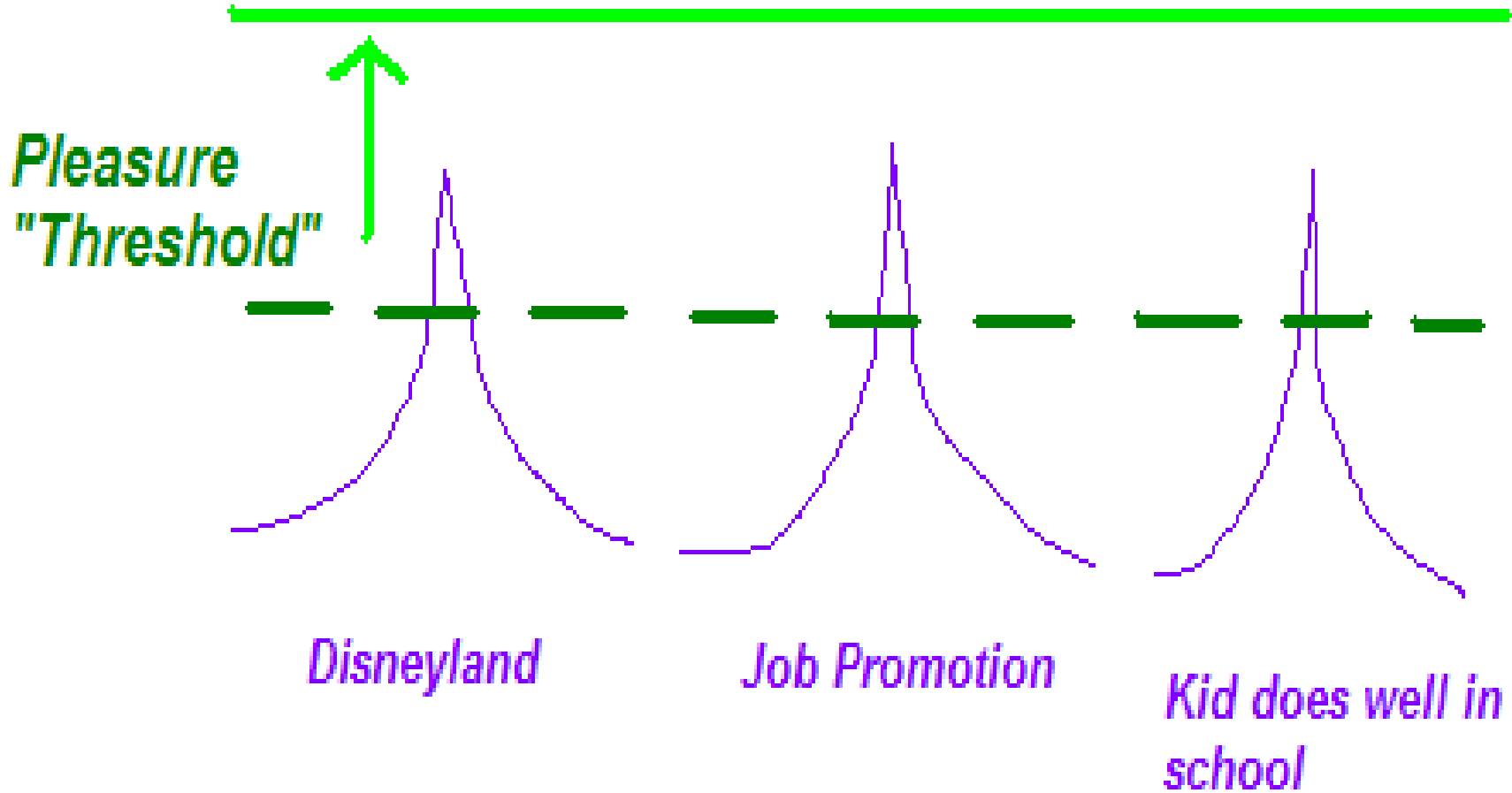
Another “set point” in the brain . . .



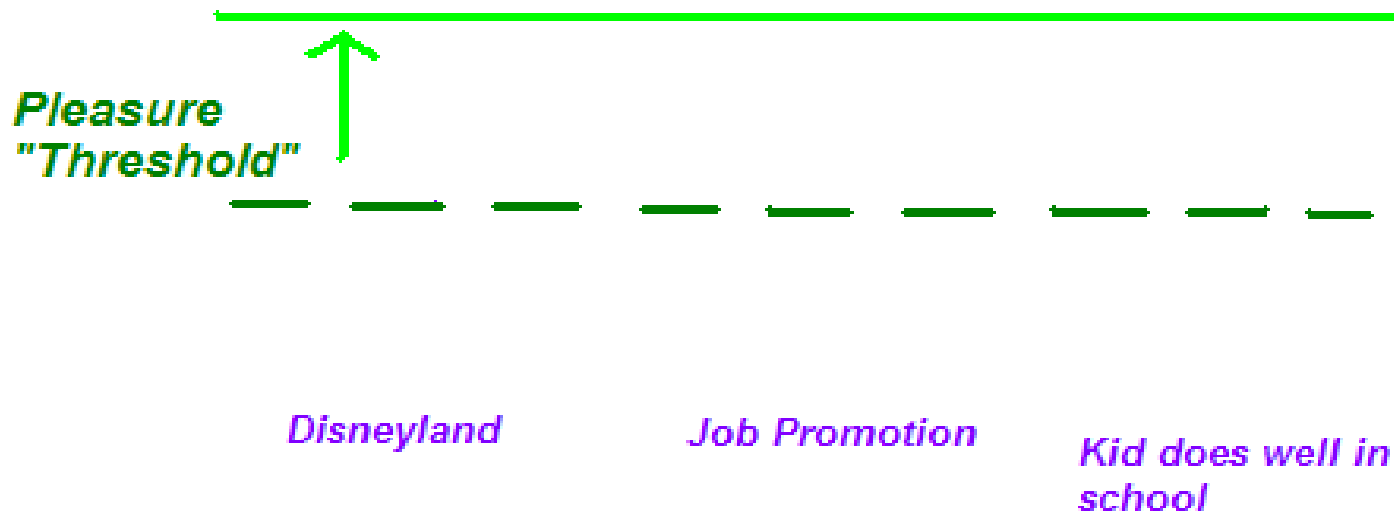
The Dopamine System changes in conditions of severe, chronic stress



High stress hormone levels reset the brain's pleasure "set point"



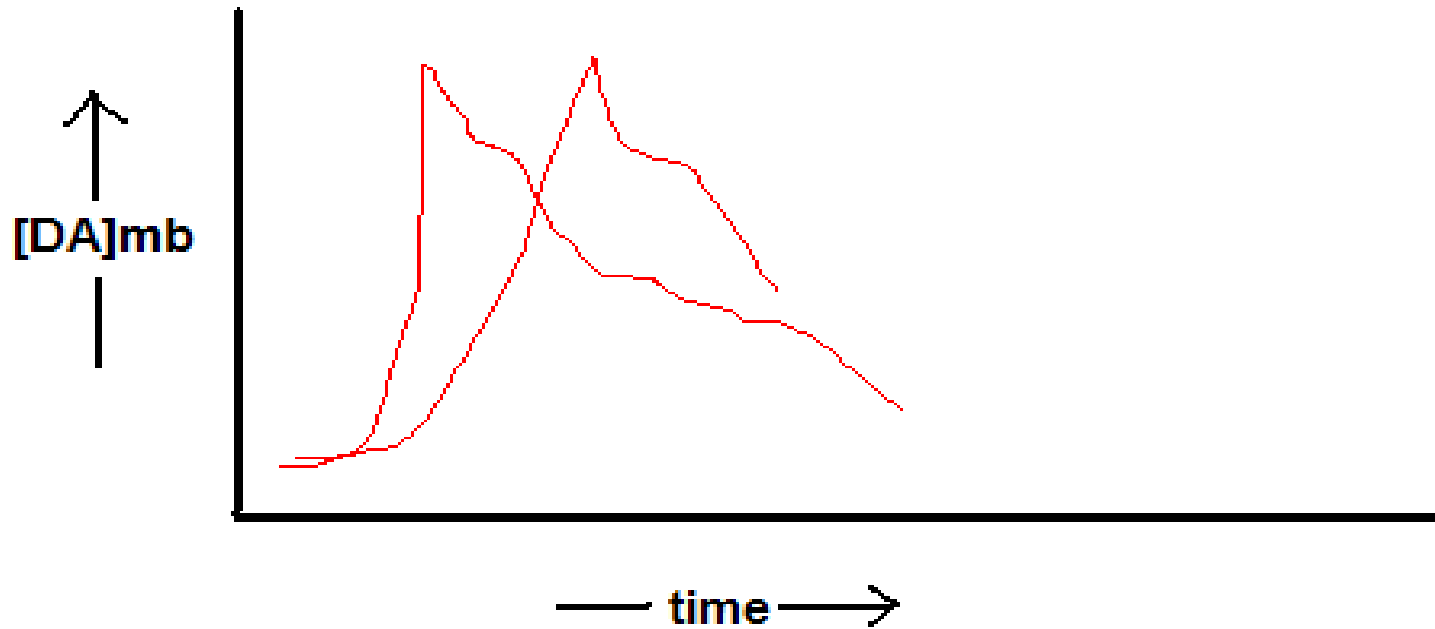
Change in Hedonic Set Point: Old pleasures don't show up



Anhedonia: Pleasure “deafness”

- *The patient is no longer able to derive normal pleasure from those things that have been pleasurable in the past*
- *Addiction is a stress-induced “hedonic dysregulation”*

Drugs cause Dopamine Surges in the midbrain reward system



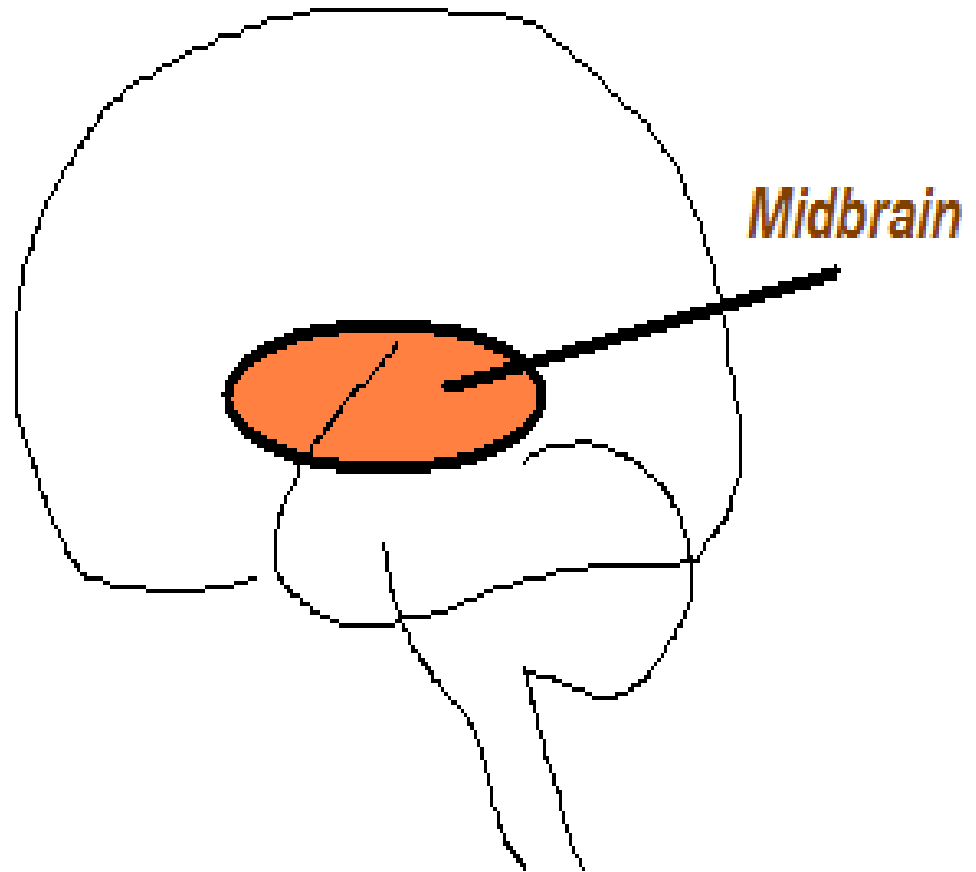
In addiction, the drug hijacks the survival hierarchy and is so close to actual survival that it is indistinguishable from actual survival

**New #1:
DRUG!**

2. *EAT!*

3. *KILL!*

4. *SEX !*



Addiction is a disorder of ...

5. ... CHOICE (motivation)
4. ... STRESS (anti-reward system)
3. ... MEMORY (learning)
2. ... PLEASURE (hedonic system)
1. ... GENES (vulnerability)

The hypofrontal/craving brain state represents and imbalance between 2 brain drives

Cortico-Striatal Circuit

- “STOP!”
- Organized, Attentive
- Sensitive to consequences
- Well-planned
- Socially appropriate

THERE'S TOO LITTLE OF THIS

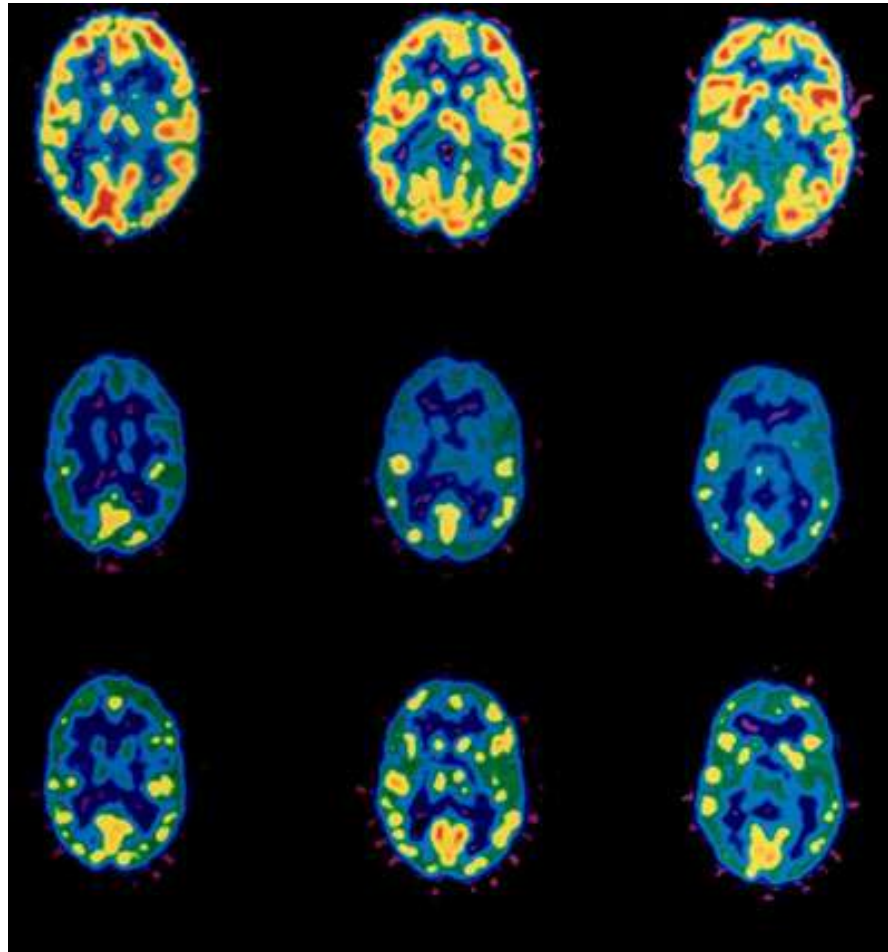
Amygdalar-Cortical Circuit

- “GO!”
- Impulsive
- Non-reflective
- Poorly conceived
- Socially inappropriate

THERE'S TOO MUCH OF THIS

HYPOFRONTALITY:

***during craving states the cortex actually
shuts off***



The ventro-medial Prefrontal Cortex (vmPFC)

- Bechara: research on patients with vmPFC lesions
- “Myopia for the future,” cognitive impulsiveness
 - prefer immediate but disadvantageous rewards over delayed rewards advantageous in the long run
 - guided primarily by immediate prospects and insensitive to pos or neg future consequences
 - deny or are unaware of the problem
 - preferred low immediate punishment over higher immediate punishment with greater advantage over time
- vmPFC pts similar to Substance Abusing patients on MRI

Craving / Drug Seeking

- Not quite as conscious as deliberative acts
- More automatic - like driving a car home from work without really thinking about it
- “I was vaguely aware that what I was doing was not too smart”
- “There I was again with a drink in my hand thinking that this time things would be different”
- A “ruminative,” emotional and involuntary process that many would describe as a form of suffering

Why the “Choice Argument” fails

...

- It fails to take into account **CRAVING**
- The “Choice Argument” measures addiction only by the addict’s external **behavior**
- It ignores the inner **suffering** of the patient
- You don’t actually have to have drug use for the defective physiology of addiction to be active
- The addict cannot choose to not **crave**

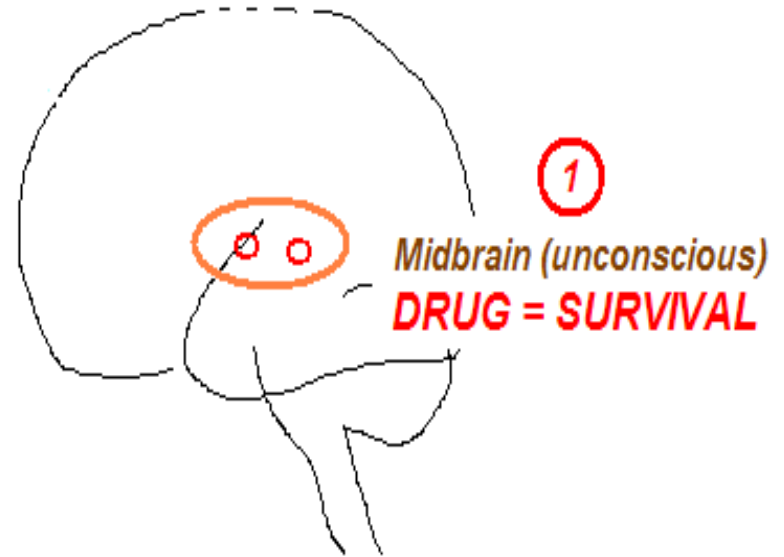
*How do we restore
the Frontal Cortex?*

Addiction Part One:

- *Misperception of the hedonic aspects of the drug*

And

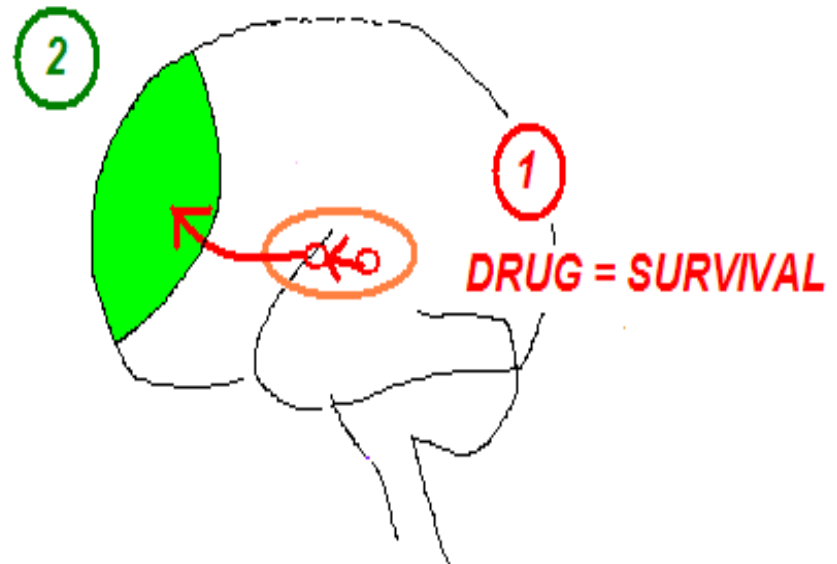
- *Attribution of survival salience to the drug on the level of the unconscious*



Addiction Part Two:

- *The drug takes on personal meaning*
- *The addict develops an emotional relationship with the drug*
- *The addict derives their sense of self and exerts agency through the drug*

DRUG = EMOTIONAL MEANING

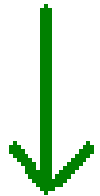


The Two Tasks of Addiction Treatment:

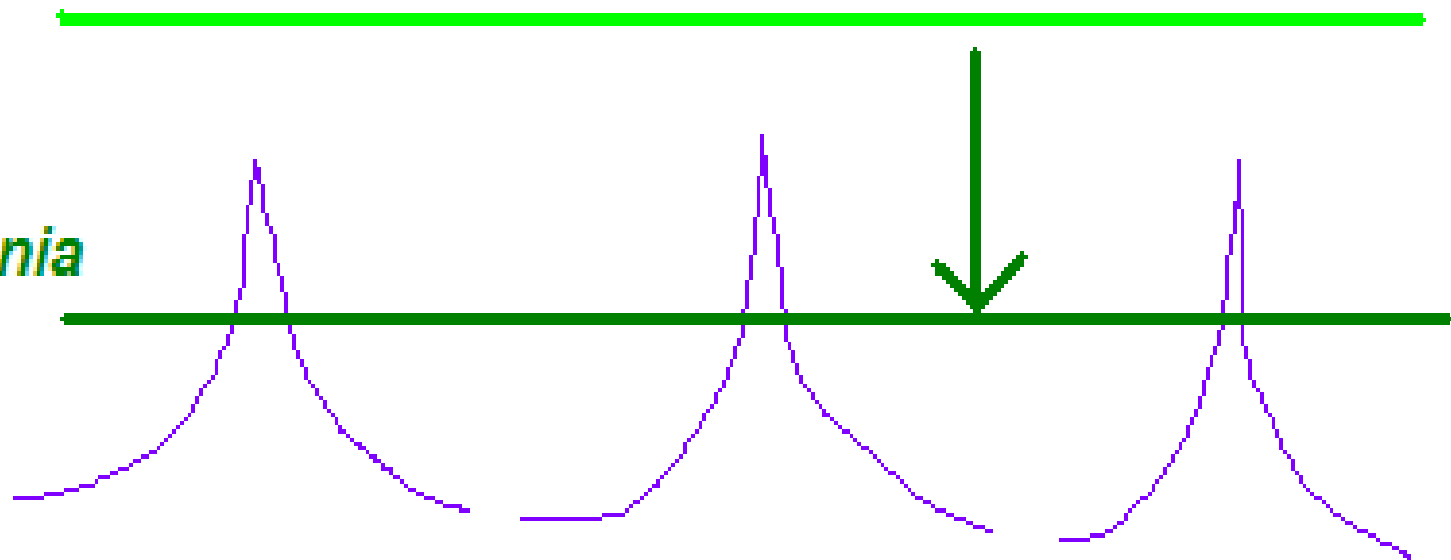
- 1. To give the addict workable, credible tools to proactively manage stress and decrease craving*
- 2. For each individual addict, find the thing which is more emotionally meaningful than the drug - and displace the drug with it*

Then . . .

Anhedonia



Hedonia



Disneyland

Job Promotion

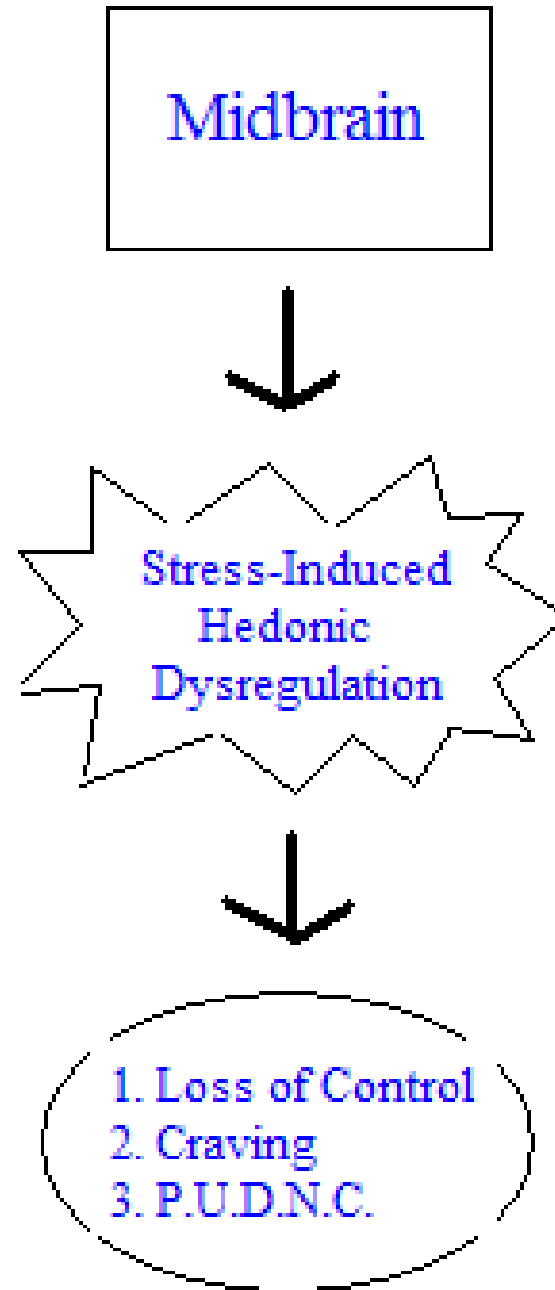
Kid does well in school

Definition of Addiction:

Addiction is a dysregulation of the midbrain dopamine (pleasure) system due to unmanaged stress resulting in symptoms of decreased functioning, specifically:

- 1. Loss of control*
- 2. Craving*
- 3. Persistent drug use despite negative consequences*

***Addiction
fits the
“Disease
Model!”***



Questions?

References available on request

Please contact:

Kevin McCauley

The Institute for Addiction Study

(435) 659-6293

kevintmccauley@hotmail.com

Please also see: www.addictiondoctor.com