

THE NEUROBIOLOGY OF ADDICTION: ADDICTION 101

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Why addiction 101

- ▣ As a society we do not treat addiction as a disease
 - Diabetes vs cancer vs addiction
- ▣ There is no such thing as an “opioid” epidemic but rather an “addiction” epidemic that simply changes the primary ‘symptom’ over time

Other “epidemics”

- ▣ **Crack cocaine:** In 1985, cocaine-related hospital emergencies rose by 12 percent, from 23,500 to 26,300. In 1986, these incidents increased 110 percent, from 26,300 to 55,200. Between 1984 and 1987, cocaine incidents increased to 94,000.
- ▣ **Methamphetamine: The Combat Methamphetamine Epidemic Act of 2005 (CMEA)** is federal legislation enacted in the United States on March 9, 2006, to regulate, among other things, retail over-the-counter sales of following products because of their use in the manufacture of illegal drugs: ephedrine, pseudephedrine, phenapropanolamine
- ▣ **Bath Salts:** In October 2011, the DEA used its administrative powers to institute an emergency but temporary one-year ban on the three basic bath-salt chemicals, declaring them Schedule 1 substances. Possession can now lead to a four-year federal felony sentence.

Prior “Opioid” Epidemics

1. Late 1800s: Morphine
 - Mainly middle class
 - Female > Male



2. Early 1900s: Heroin (pharmaceutical grade)
 - First generation Italians, Jews, Irish
 - Male > Female



3. 1950s-1970s- Heroin (illicit)
 - African American/Latinos
 - Male > Female



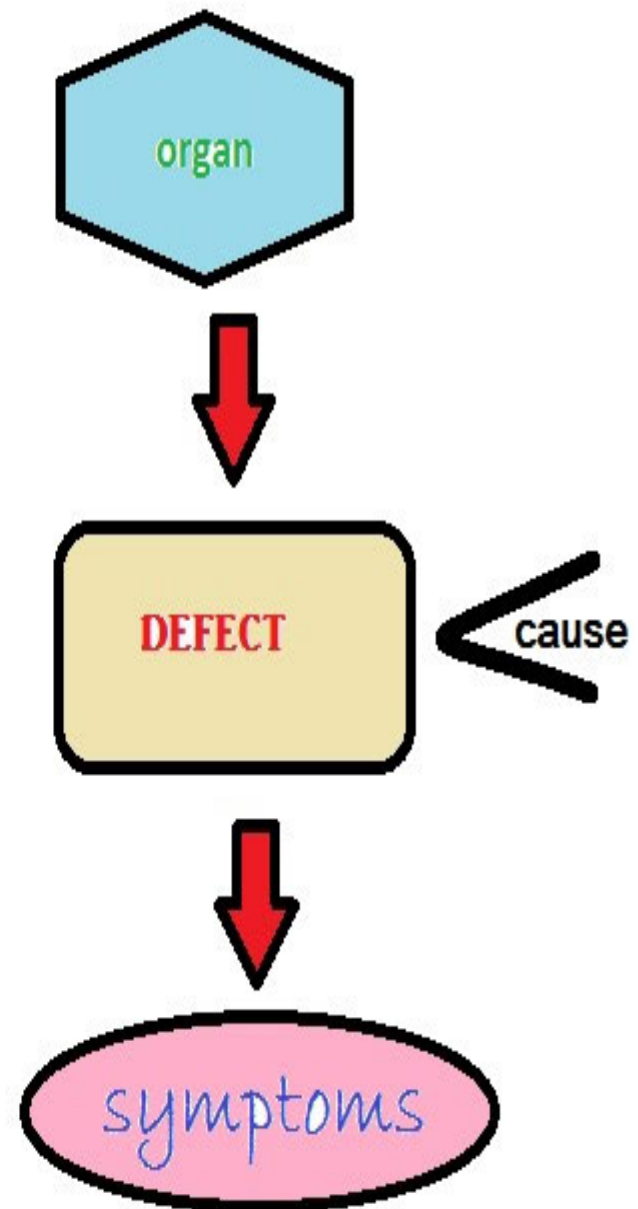
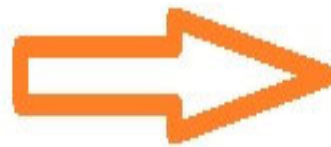
addiction

- ▣ The word "addiction" has existed in the English language for centuries, coming originally from a Latin root meaning "to impose sentence" or "to give over into slavery." The term was usually used to connote a form of self-imposed enslavement, and for many centuries, the widely-held assumption was that addiction was due to weakness of character

ADDICTION IS A DISEASE...

BUT HOW DO WE KNOW??

**THE
DISEASE
MODEL**



Addiction is a brain disease

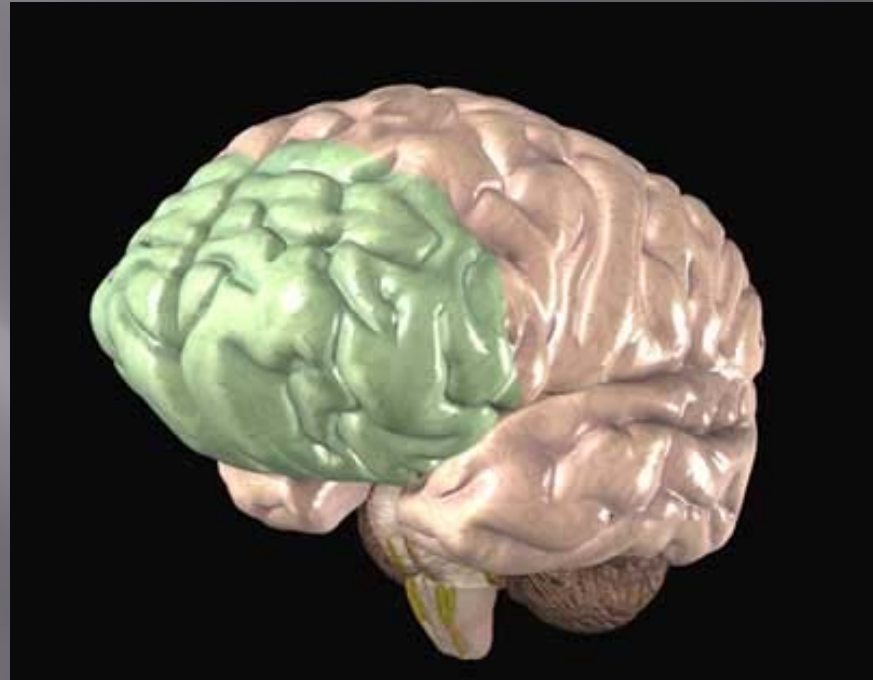
- ❑ The BRAIN is the organ involved in the disease of addiction
- ❑ There are no good tests for brain diseases (at least no inexpensive ones)
- ❑ So people with brain diseases start out at a disadvantage
- ❑ The symptoms of brain diseases are more likely to be labeled as “badness”



organ

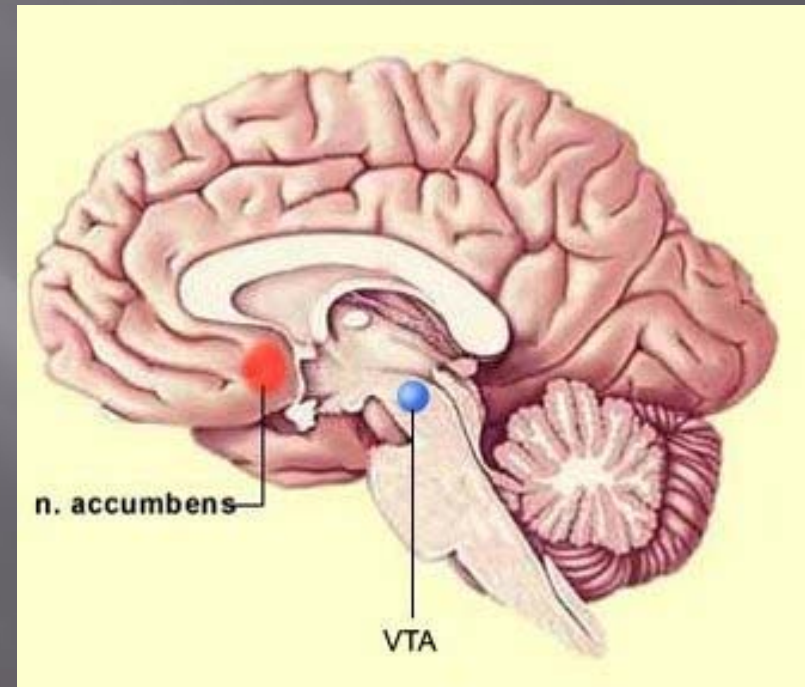
The frontal cortex...

- ▣ Confers emotional meaning (semantic content) onto objects in the world
- ▣ Seat of the Self and Personality
- ▣ Love, Morality, Decency, Responsibility, Spirituality
- ▣ Conscious “choice”
- Will power



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



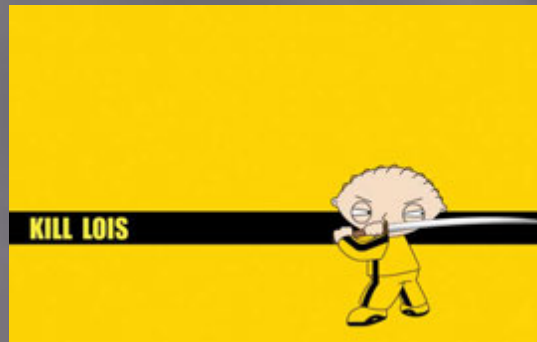
The Midbrain (aka Limbic Brain) is the SURVIVAL brain. It handles:



EAT!!

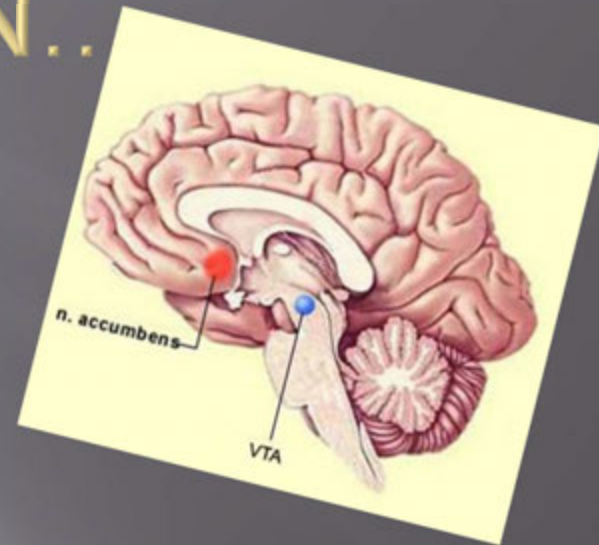
KILL!!

SEX!!!



DRUGS WORK IN THE MIDBRAIN..

- ▣ NOT in the Cortex...
- ▣ (how do we know?)
 - The Olds Experiments
- ▣ Mice preferentially self-administer drugs of abuse like cocaine ONLY to the Reward Centers of the Midbrain



- ▣ Midbrain
- ▣ survival
- ▣ unconscious
- ▣ no free will

Mice get addicted to drugs but...

- ❑ Mice don't have morals
- ❑ Mice don't have "Gods"
- ❑ Mice aren't sociopaths
- ❑ Mice don't have bad parents
- ❑ There are no "Mouse Gangs"



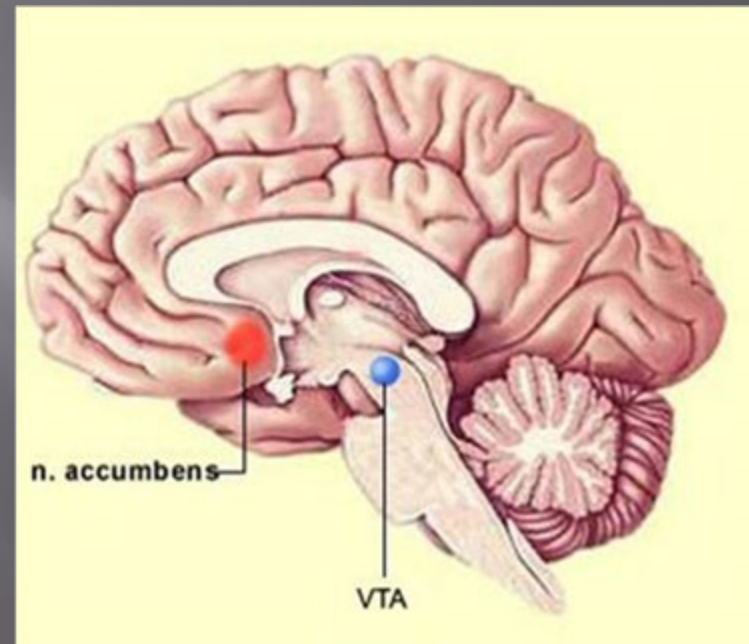
in addition, the drug hijacks the survival hierarchy and is so close to actual survival that it is indistinguishable from actual survival

- ▣ NEW!!! #1 drug!!!

- ▣ #2 Eat

- ▣ #3 Kill

- ▣ #4 Sex



*In addiction, the drug is equated with survival
at the level of the unconscious*



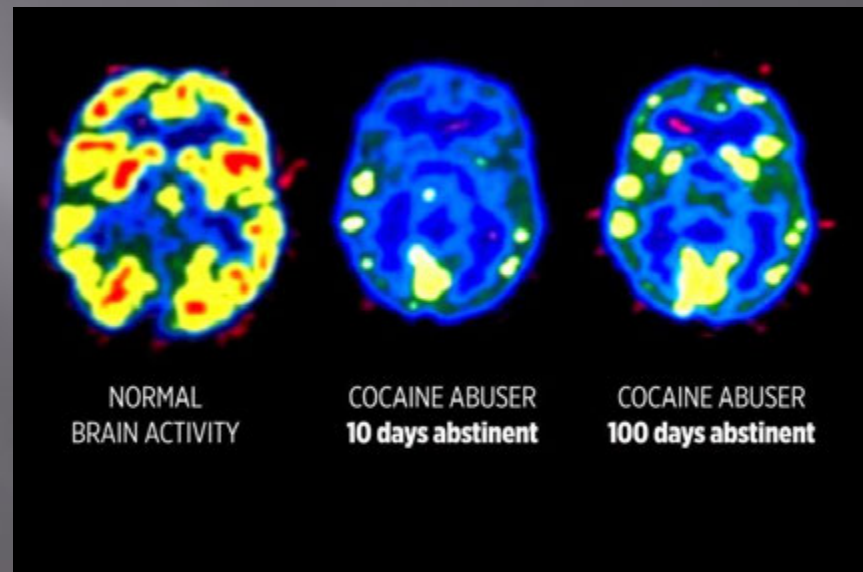
People dying of thirst in the desert will risk losing everything they value for a drink of water → this is the midbrain in action shutting down the frontal cortex in an effort to SURVIVE

(i.e. IN ADDICTION the drug IS survival)

In a PET scan of the brain where the patient is shown their drug of choice

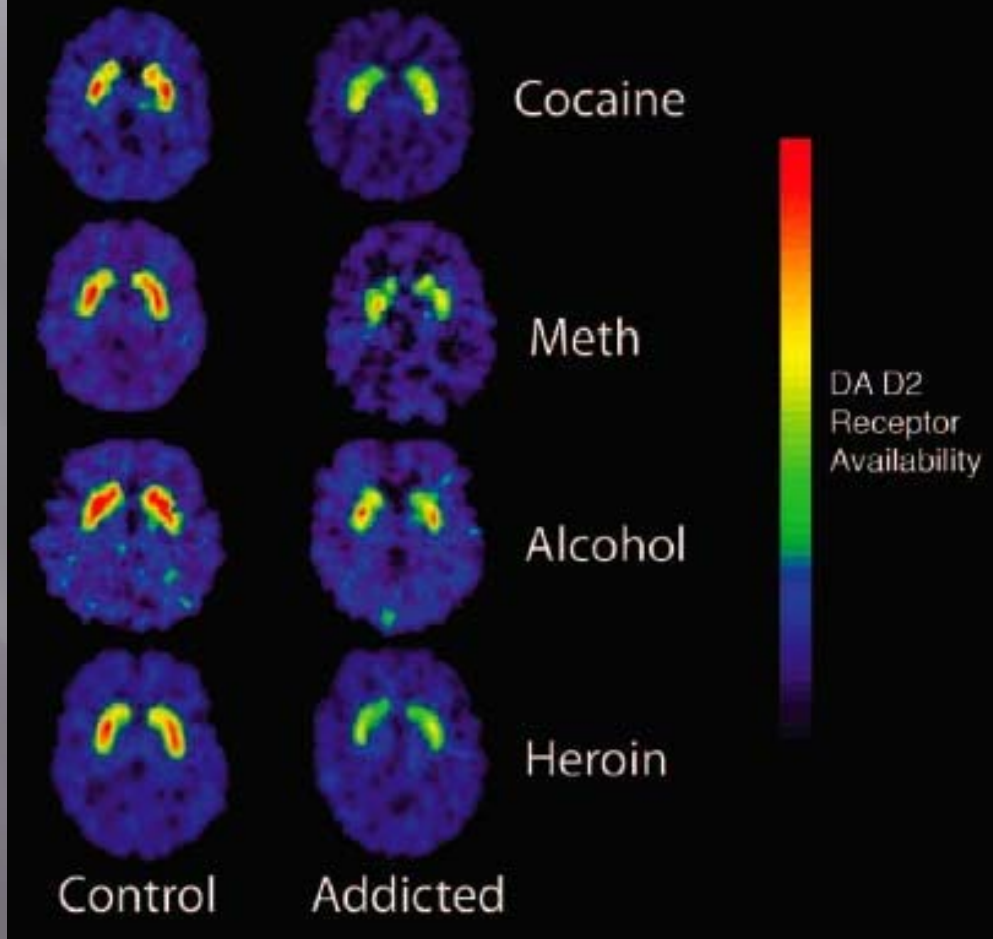
- ▣ The non-addict will show activity in the frontal cortex
 - THINKING about how the drug is “good” or “bad”
- ▣ The addict will show activity in the midbrain and very little activity in the frontal cortex
 - CRAVING/SURVIVAL

Cortex changes



Midbrain changes

Dopamine D2 Receptors Are Lower in Addiction



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

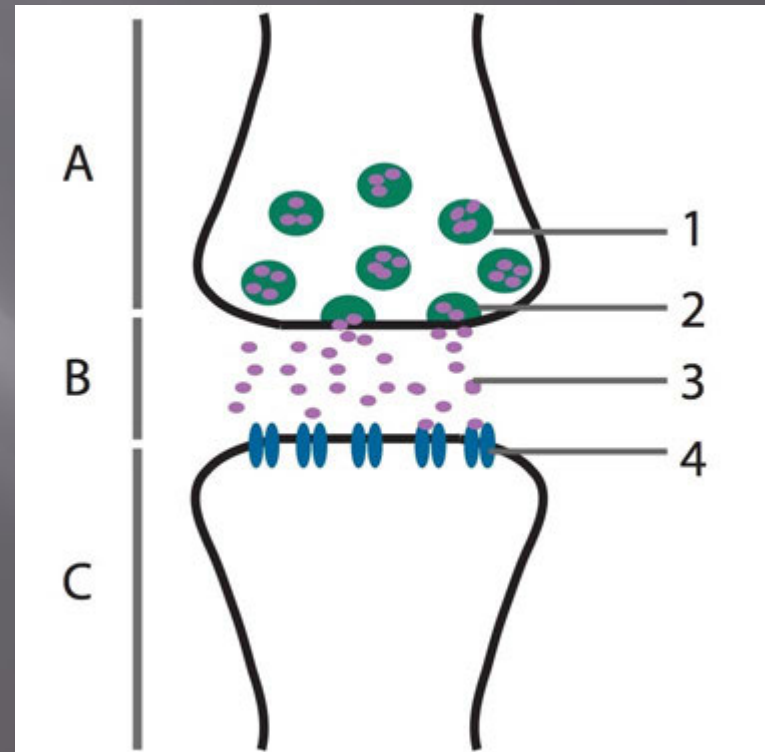
IT IS A BROKEN "PLEASURE SENSE" IN THE BRAIN

DEFECT

HOW THE BRAIN WORKS...

- ▣ A= presynaptic neuron
- ▣ B= synapse
- ▣ C= postsynaptic neuron

- ▣ 1. neurotransmitter(NT) in vesicle
- ▣ 2. NT being released/ taken back up
- ▣ 3. receptor for NT= effects!!!



Brain Perceptual Systems (all of them):

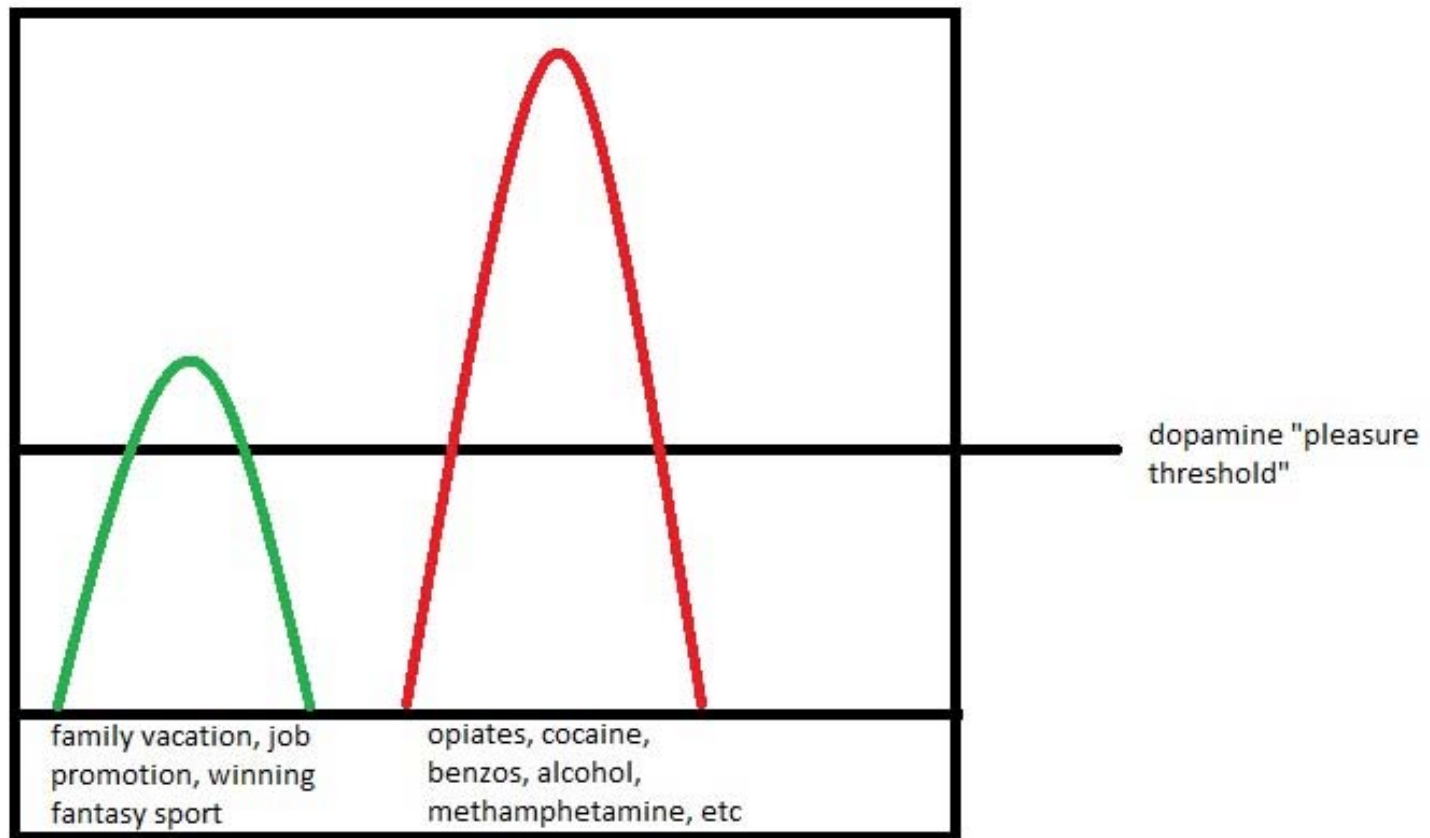
- ▣ **1. Vision**
- ▣ **2. Hearing**
- ▣ **3. Touch**
- ▣ **4. Smell**
- ▣ **5. Taste**
- ▣ **6. Linear Acceleration**
- ▣ **7. Angular Acceleration**
- ▣ **8. Gravity (Proprioception) ← perceptual construct**
- ▣ **9. Blood pO₂ and pCO₂**
- ▣ **10. Pleasure ← perceptual construct**

Addiction Neurotransmitter # 1: Dopamine

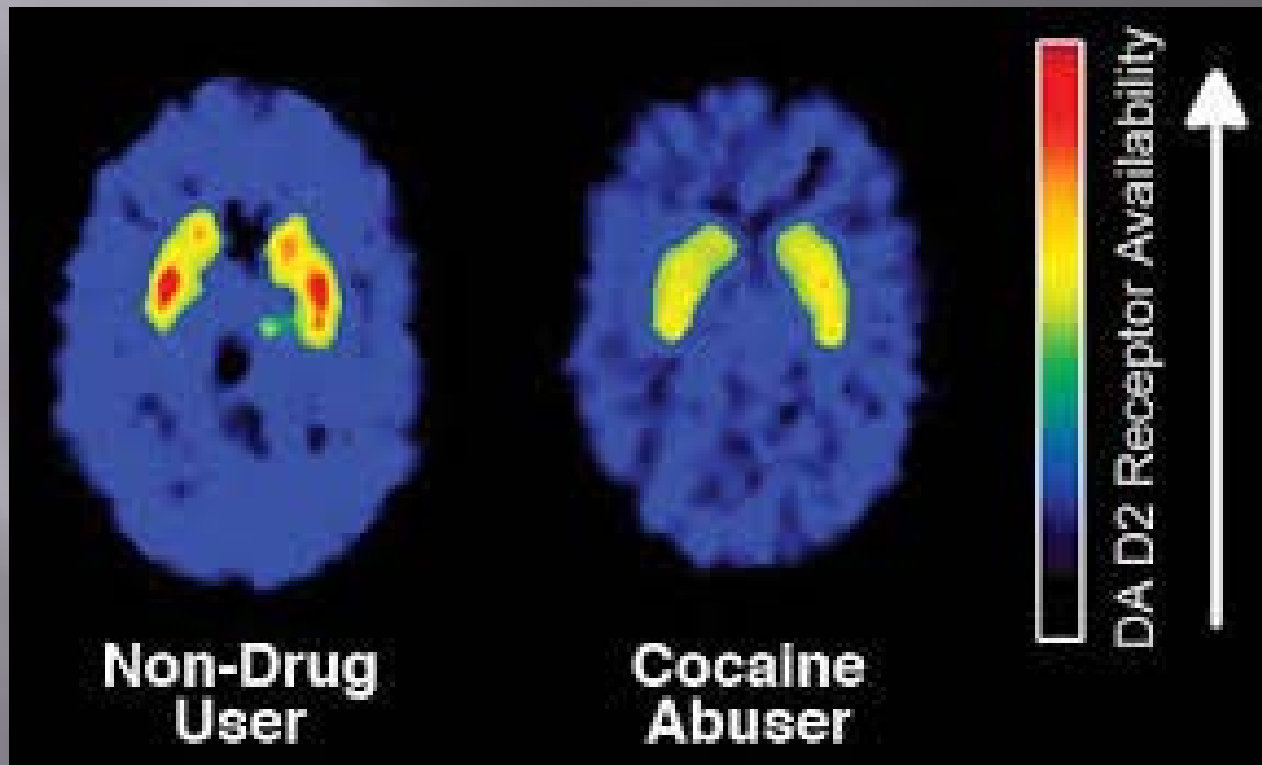
- ▣ • All drugs of abuse and potential compulsive behaviors release Dopamine
- ▣ • Dopamine is first chemical of a pleasurable experience - at the heart of all reinforcing experiences
- ▣ • DA is the neurochemical of salience (it signals survival importance)
- ▣ • DA signals reward prediction error
-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



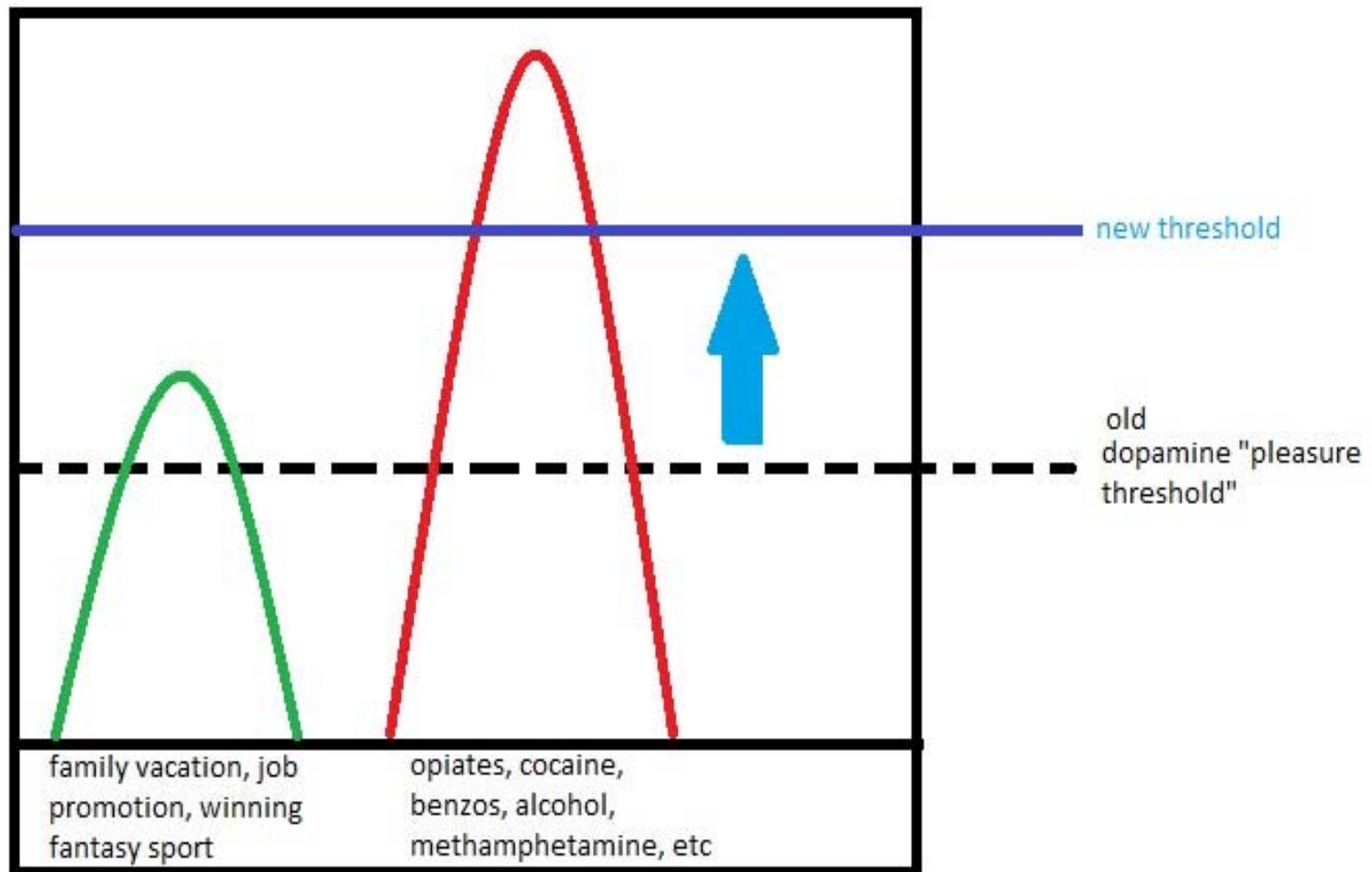
The Brain has a Hedonic "Set Point"



Fewer dopamine receptors means more dopamine needed to feel “normal pleasure”



Increased drug use reset the brain's pleasure "set point"



STRESS: a major player in addiction & relapse

CHRONIC, SEVERE STRESS = \uparrow CRF

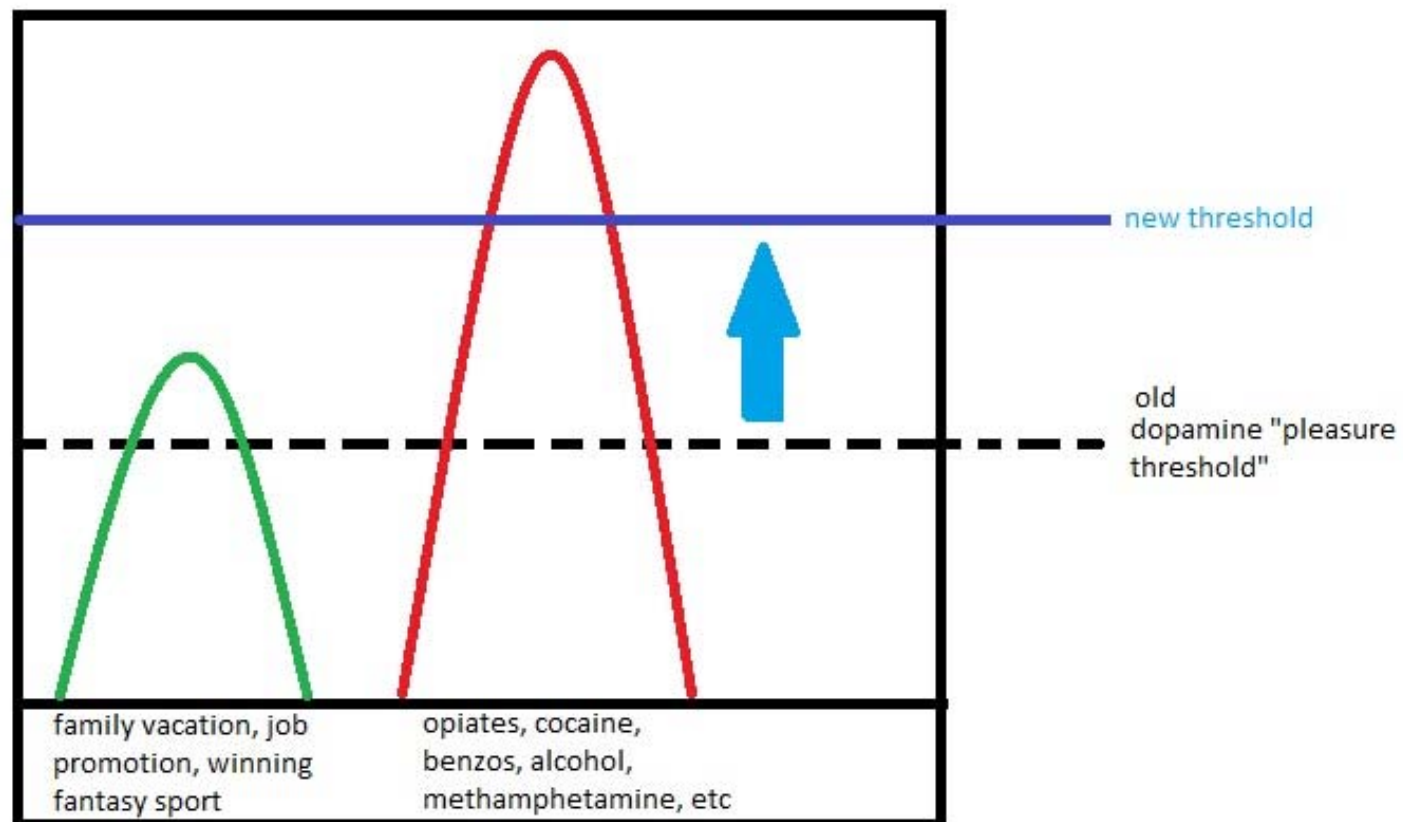
And \uparrow CRF = \downarrow DAD2 receptors

And \downarrow DAD2 receptors = Anhedonia

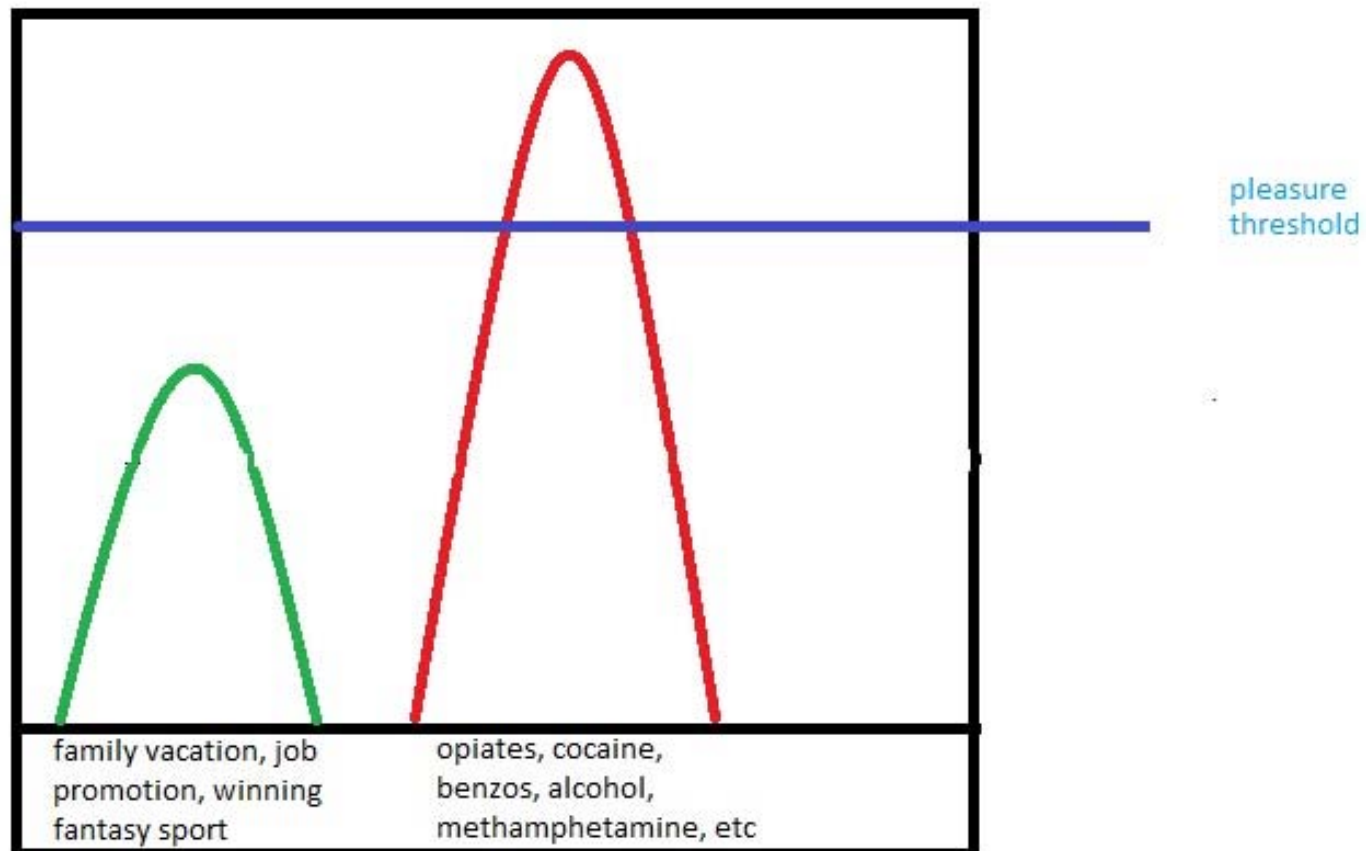
ANHEDONIA: PLEASURE “DEAFNESS”

(THE PATIENT IS NO LONGER ABLE TO DERIVE NORMAL PLEASURE FROM THOSE THINGS THAT HAVE BEEN PLEASURABLE IN THE PAST)

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



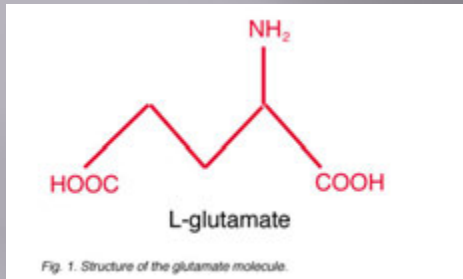
Change in Hedonic Set Point: Old pleasures don't show up



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”

Addiction Neurotransmitter #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 (TRIGGERS, PEOPLE, PLACES AND THINGS)
- ▣ •AND ... GLUTAMATE IS THE NEUROCHEMICAL OF “MOTIVATION” (IT INITIATES DRUG SEEKING)

Relapse

• Three things that are known to evoke relapse in humans:

1. Brief exposure to ANY abusable drug OR compulsive behavior (**DA release and DA receptor down regulation**)
2. Stress (**CRF release and DA receptor down regulation**)
3. Exposure to drug cues (people, places and things!!!) (**GLU release**)

▣ **Now that the midbrain has found what secures **survival**...**

▣ *... how does it motivate the individual to repeat that behavior?*

craving



- Increased stress = increased pleasure threshold = increased need for dopamine = midbrain thinks it is dying = CRAVING
- CRAVING is a physiological response to a neurochemical deficiency resulting in symptoms including sweating, stomach cramps, obsession, increased respirations, etc.
- CRAVING IS THE REASON THE “CHOICE” ARGUMENT FAILS.
 - No person can choose to crave or not.
 - You don't actually have to have drug use for the defective physiology of addiction to be active

symptom

Once Craving sets in, how does it control behavior???

- ▣ The midbrain hijacks the abilities of the frontal cortex...
 - The brain will utilize the most likely reasoning to get the addict to feel like they have to use
 - ▣ Pain (won't cause death)
 - ▣ Anxiety (won't cause death)
 - ▣ Stress (won't cause death)
 - ▣ Specific people or events/reservations (ALWAYS a choice)

Once there is a “reason”, suddenly behaviors become “justified”

- Lying
- Manipulating/stealing
- Reasoning/making excuses
- Rationalization
- Justification

use of 'activating'
substance x
activating number
of uses

gene activated
("turned on")

use of ANY dopamine
releasing substance



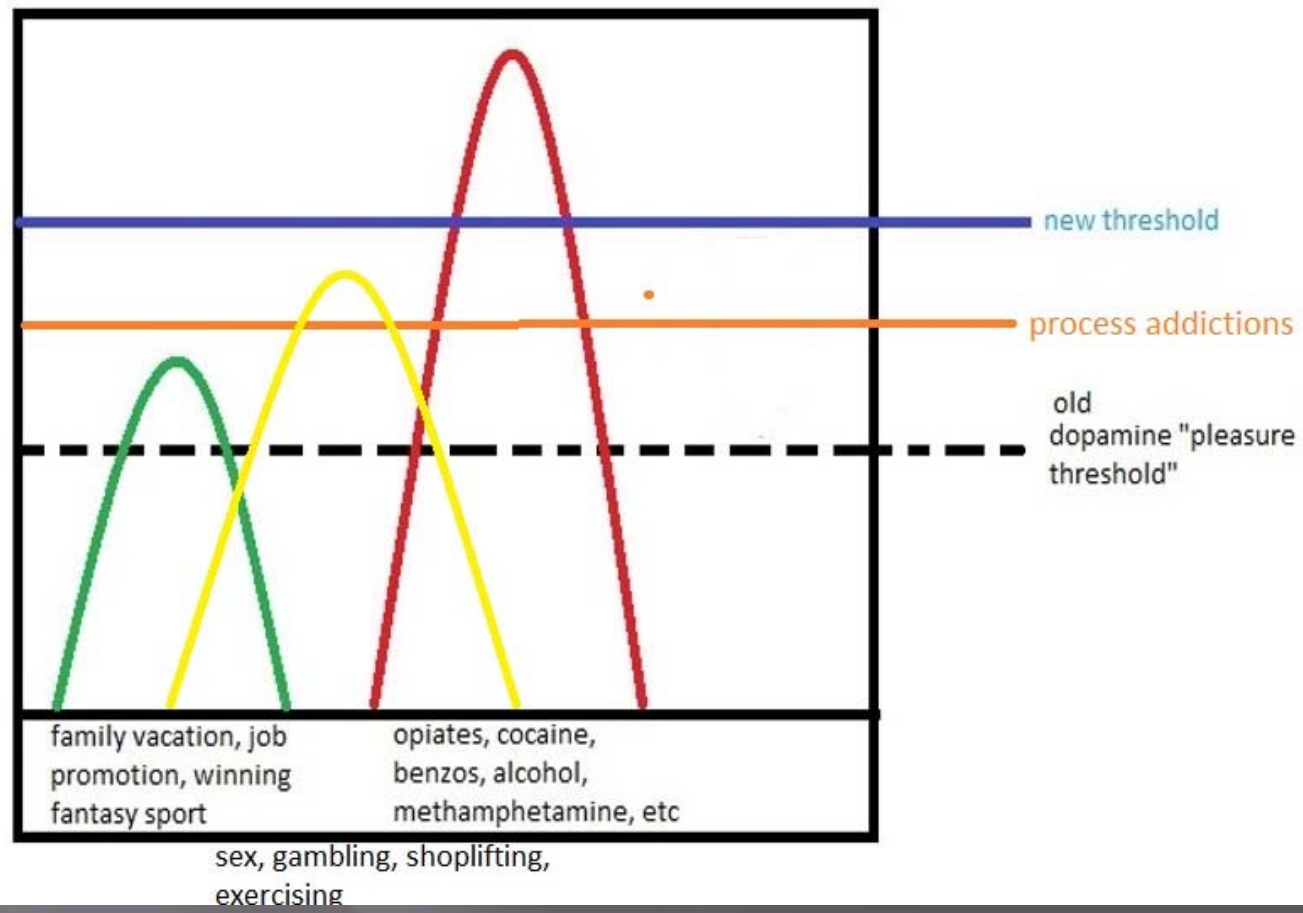
midbrain changes
occur (down regulation
of dopamine
receptors--> increased
threshold for pleasure)



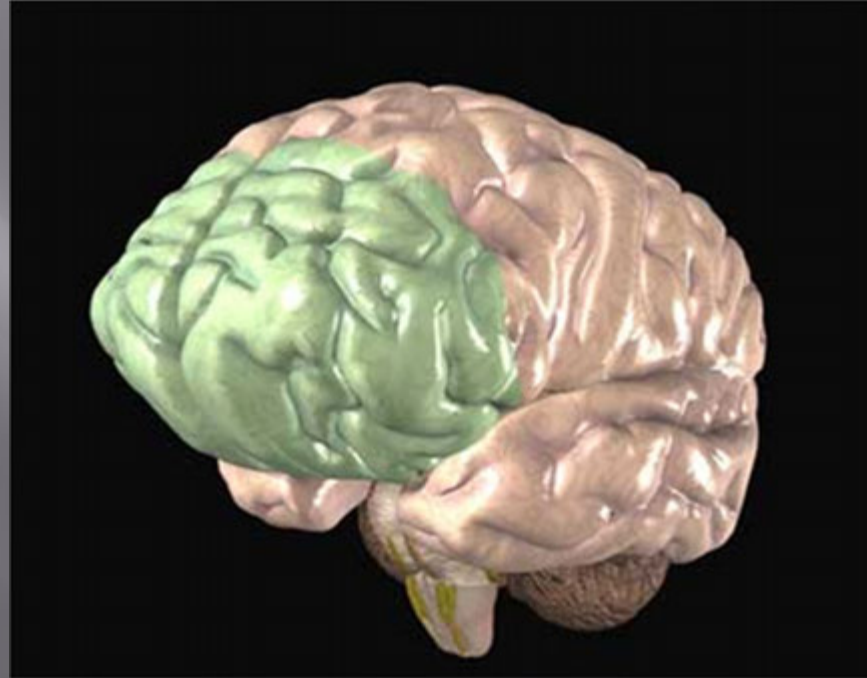
gene
present



A word about process addictions



The Goal of treatment-
regardless of the drug
or length of use is to
RESTORE THE
CORTEX



How do we restore
the Frontal Cortex?

Hierarchy of treatment: summarized

- ▣ Treat most acute medical issues first
- ▣ Detox
- ▣ (quiet the midbrain with medication or abstinence)
- ▣ Restore cortex

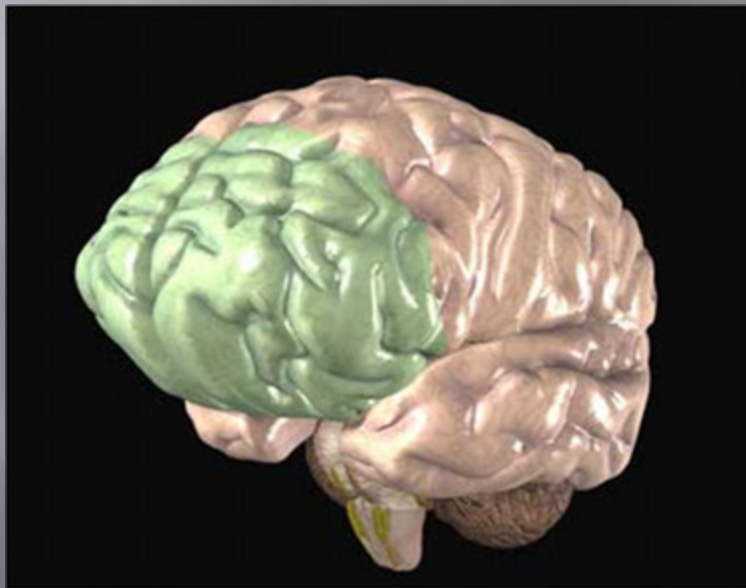
Restoration of the Cortex

- ▣ To give the addict workable, credible tools to proactively manage stress and decrease craving
 1. COPING SKILLS
 2. STRESS RELIEF
 3. SOCIAL SUPPORTS
 4. SAFE ENVIRONMENT
- ▣ For each individual addict, find the thing which is more emotionally meaningful than the drug- and displace the drug with it
 - ▣ 1. SPIRITUAL GROWTH
 - ▣ 2. PERSONAL DEVELOPMENT

THE DIVISION OF LABOR...

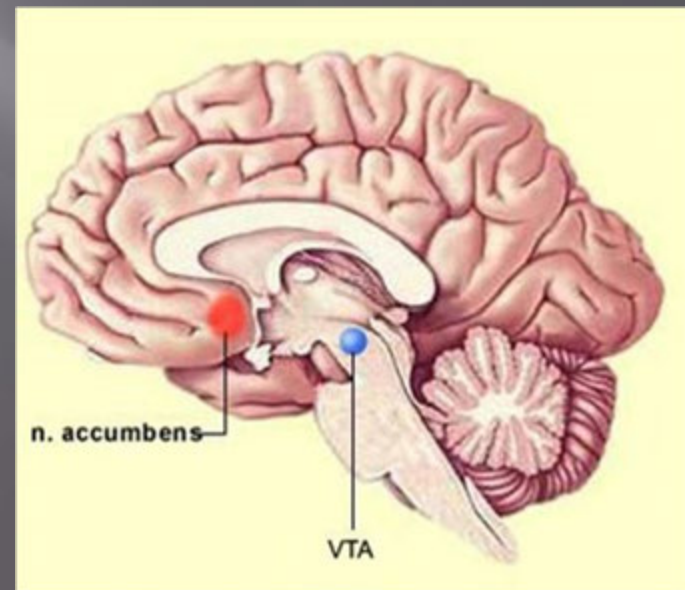
AA/BEHAVIORAL
THERAPY WORK HERE

- ▣ Frontal cortex =
emotional meaning

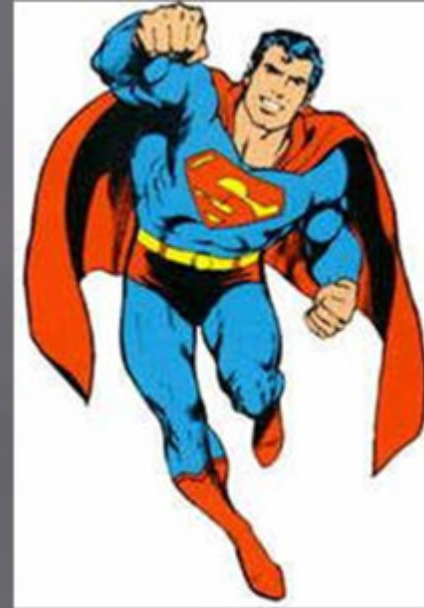


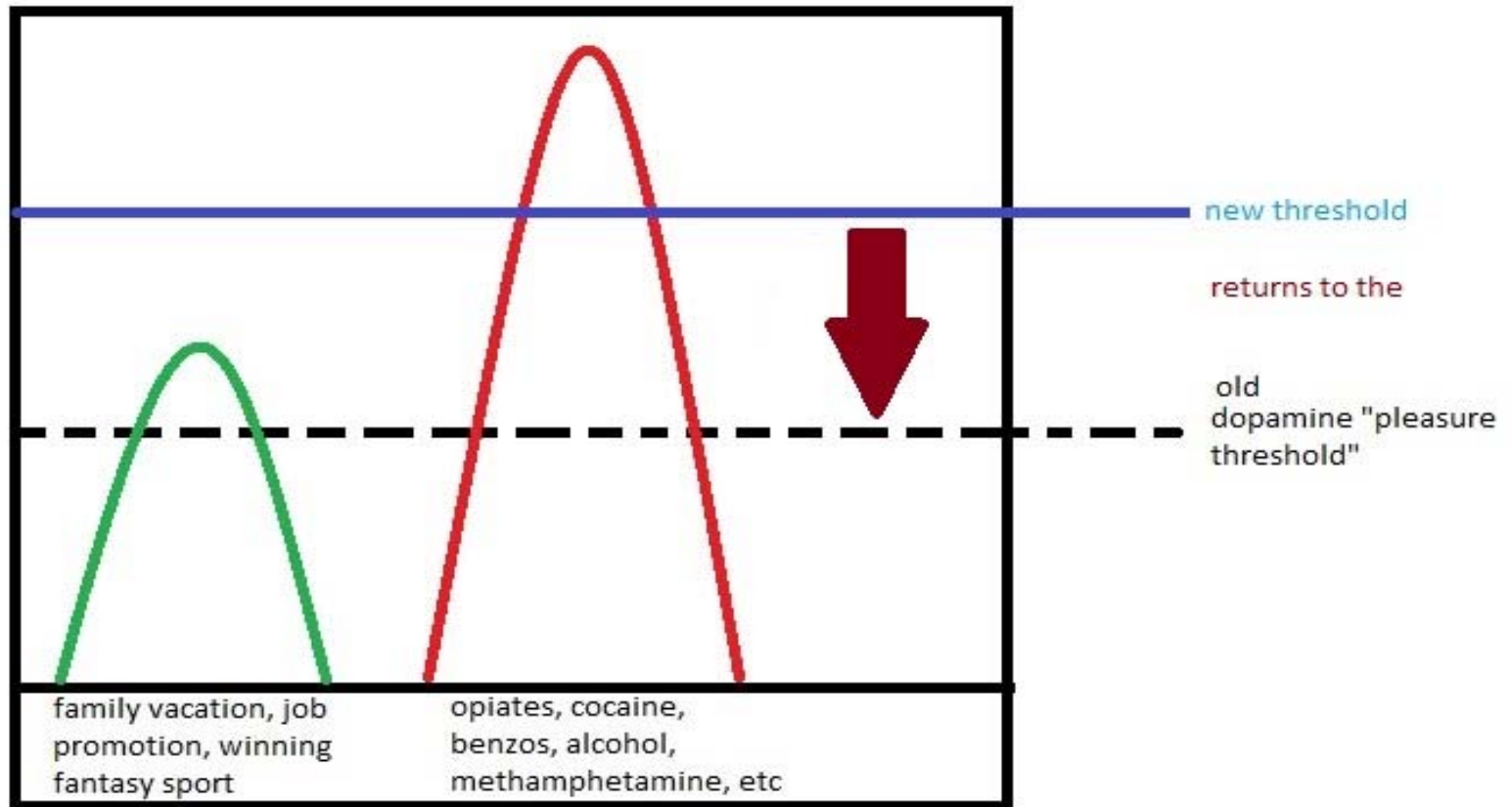
DRUGS/MEDICATIONS
WORK HERE

- ▣ Midbrain =
survival/craving



With the installation of coping mechanisms (A.A.), the Cortex comes back "on-line" and Free Will returns... even during periods of craving (midbrain activity)

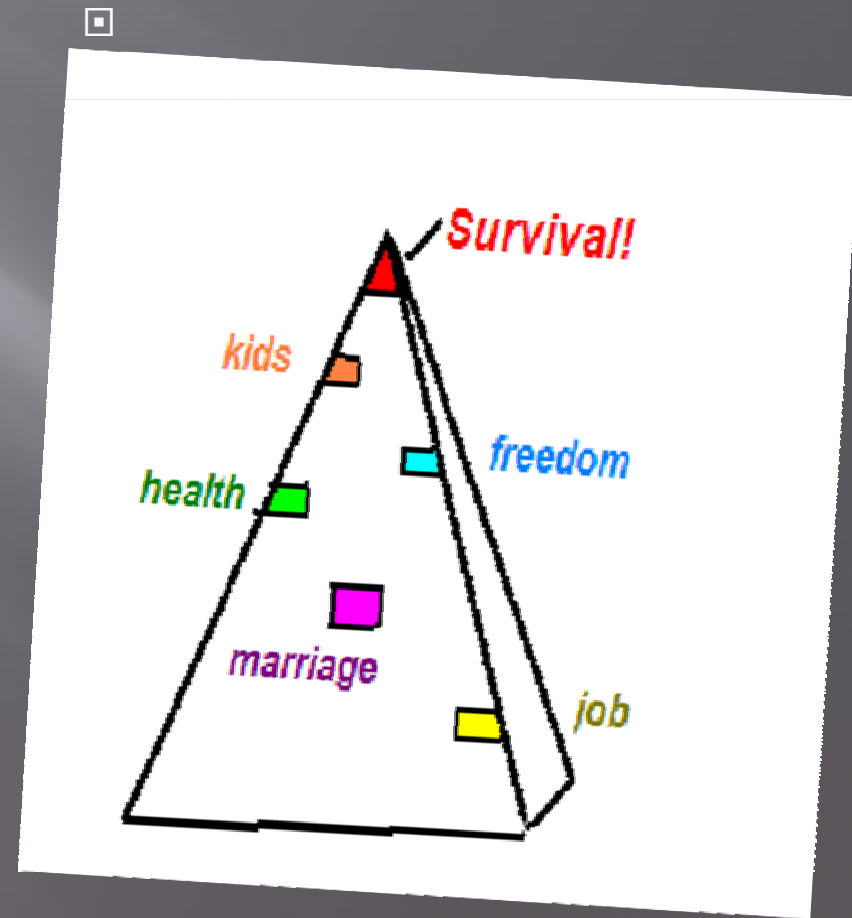




- *This will happen slowly over time with just abstinence- most don't make it
- *It will happen more quickly with work on the cortex
- *Work on the cortex can often be more effective with medication as a tool

Punishment won't stop
drug use because the drug is
survival

- • Nothing's higher than survival
- • No threat matches loss of survival
- • The addict must first secure survival before attending to anything else
- • And the survival imperative exists at the level of the unconscious



Role of Medication in Addiction treatment practices



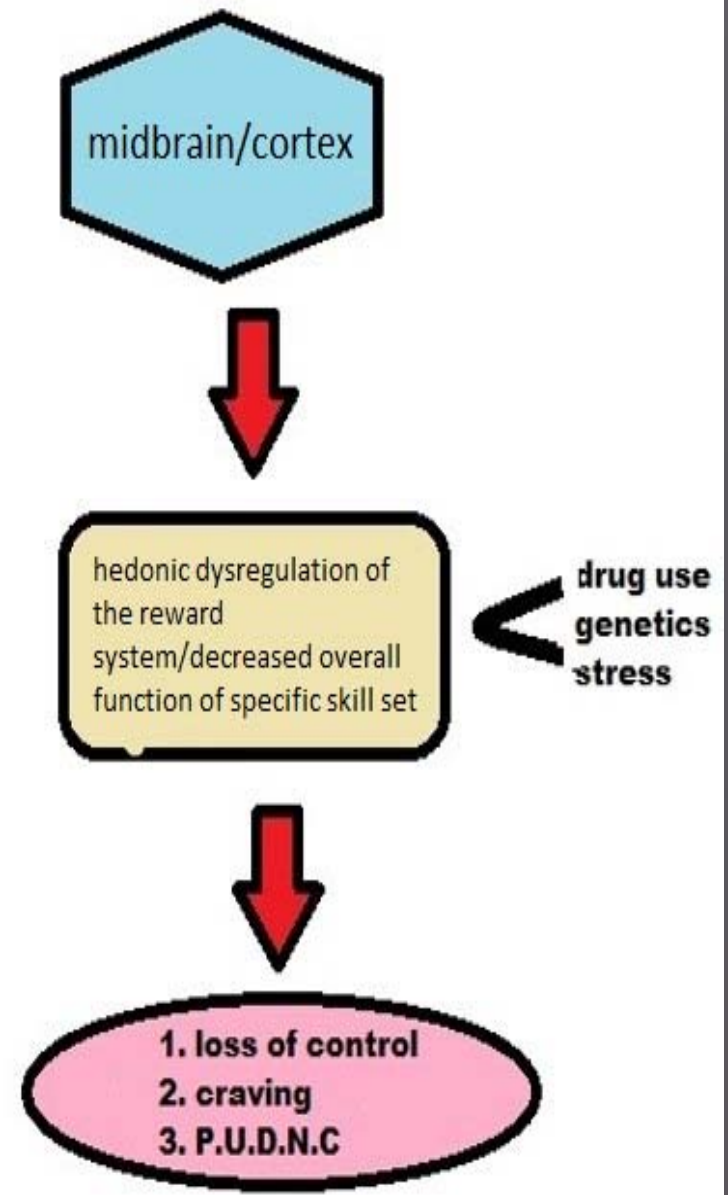
DEFINITION OF ADDICTION

- ▣ 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 IS A DISEASE...

BUT HOW DO WE KNOW??

**THE
DISEASE
MODEL**



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