

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



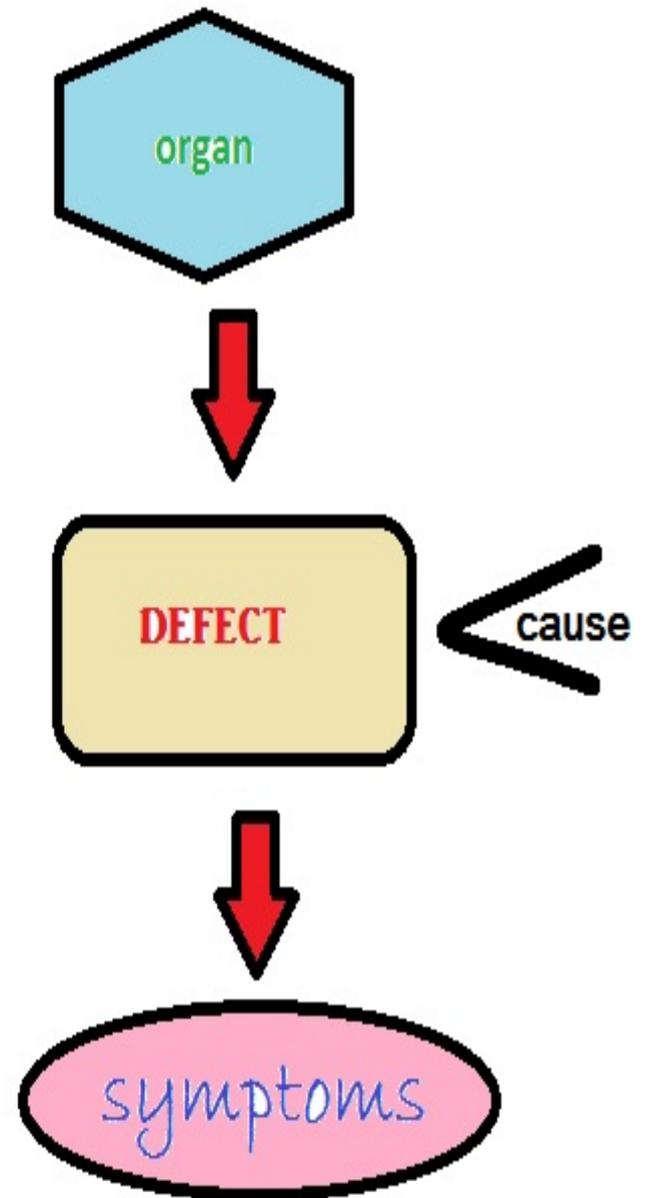
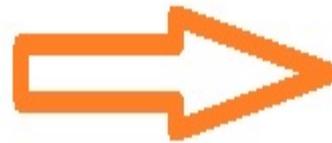
3. 1950s-1970s- Heroin (illicit)
 - African American/Latinos
 - Male > Female



ADDICTION IS A DISEASE...

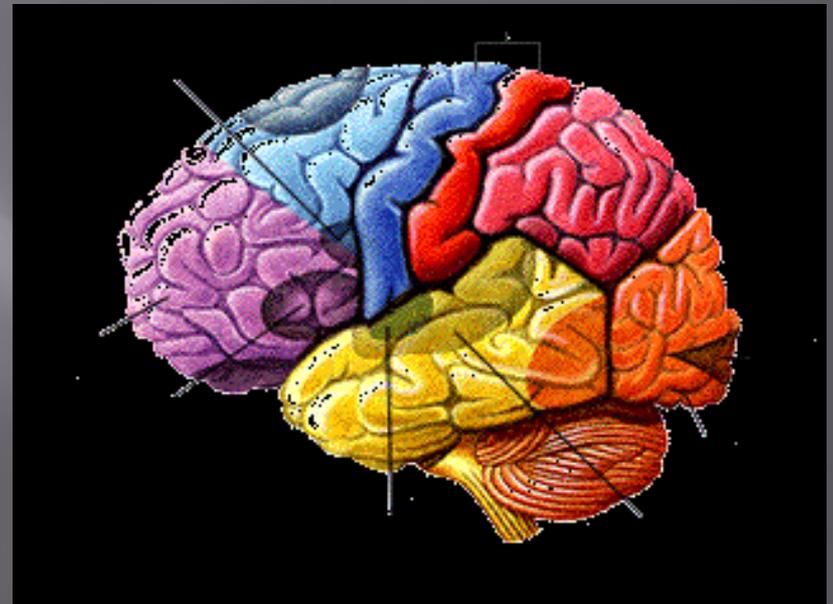
BUT HOW DO WE KNOW??

**THE
DISEASE
MODEL**



Addiction is a brain disease

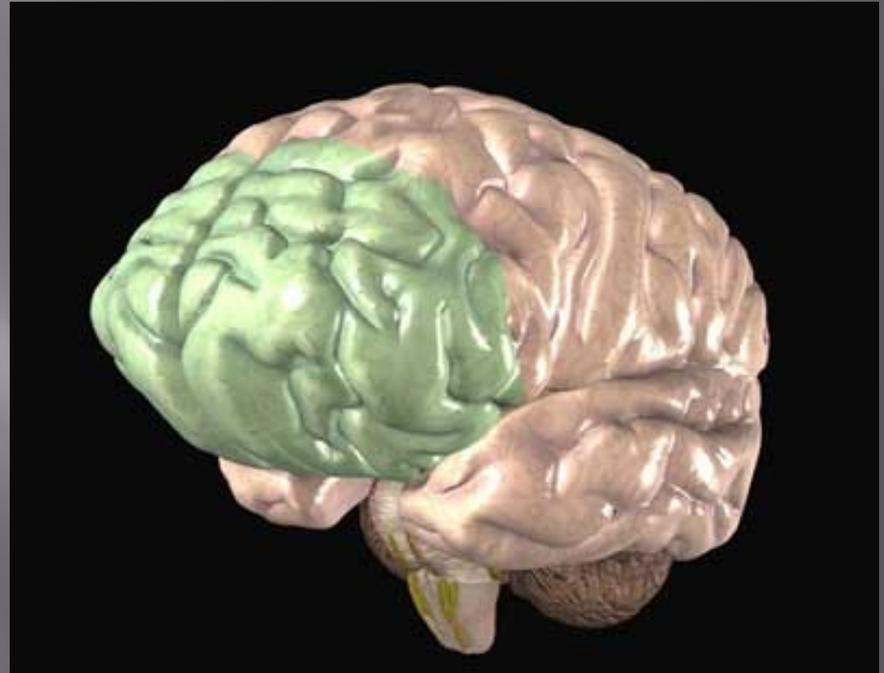
- ▣ The BRAIN is the organ involved in the disease of addiction
- ▣ There are no good tests for brain diseases (at least no inexpensive ones)
- ▣ So people with brain diseases start out at a disadvantage
- ▣ The symptoms of brain diseases are more likely to be labeled as “badness”



organ

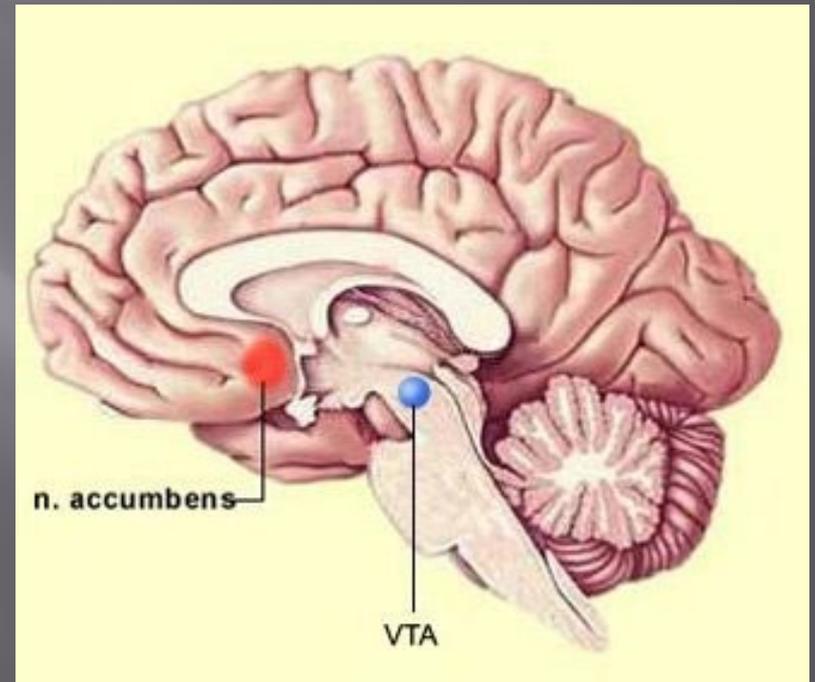
The frontal cortex...

- ▣ 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



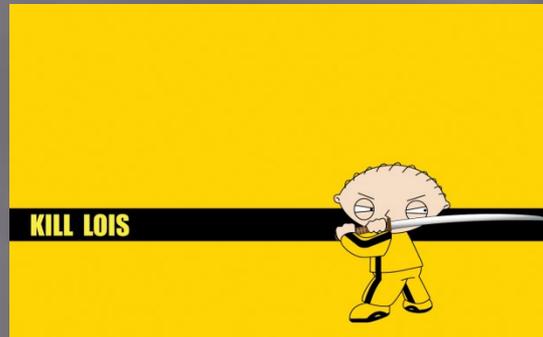
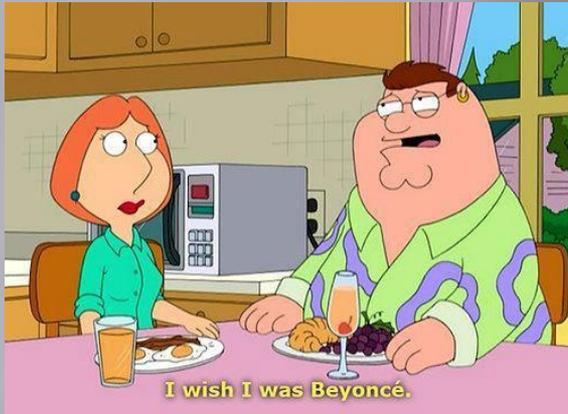
The Midbrain (aka Limbic Brain) is the SURVIVAL brain. It handles:



EAT!!

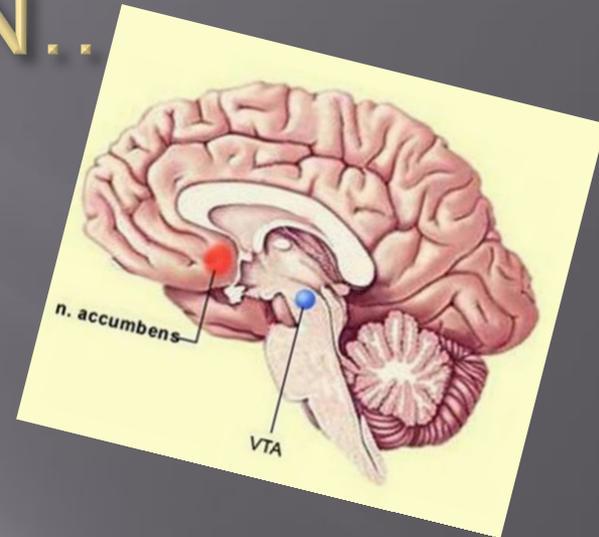
KILL!!

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
- ❑ Drugs are “high dopamine producing agents”



- ❑ Midbrain
- ❑ survival
- ❑ unconscious
- ❑ no free will

Mice get addicted to drugs but...

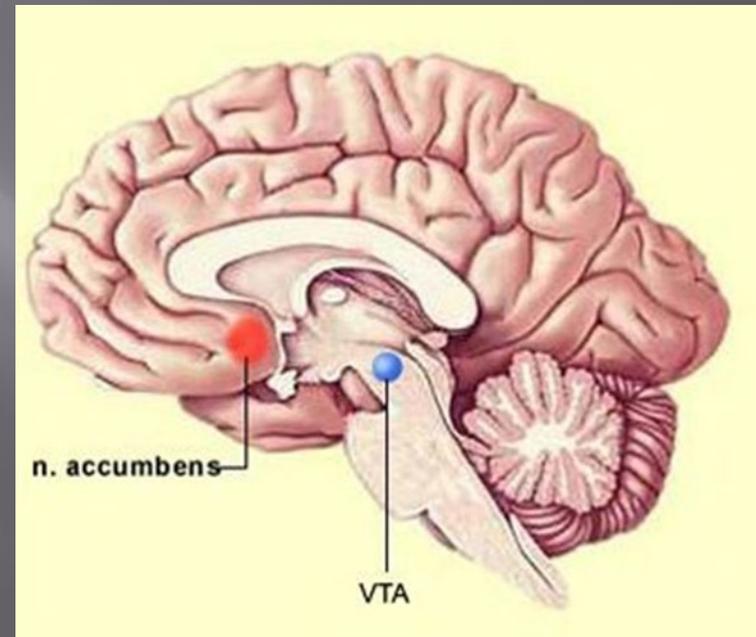
- ❑ Mice don't have morals
- ❑ Mice don't have "Gods"
- ❑ Mice aren't sociopaths
- ❑ Mice don't have bad parents
- ❑ There are no "Mouse Gangs"



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

- ▣ NEW!!! #1 high dopamine producing agent!!!

- ▣ #2 Eat
- ▣ #3 Kill
- ▣ #4 Sex



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

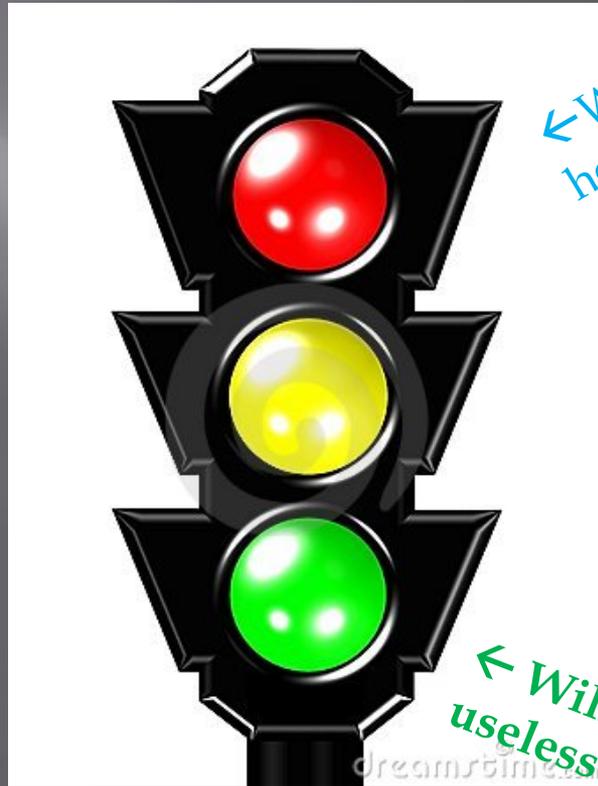


People dying of thirst in the desert will risk losing everything they value for a drink of water → this is the midbrain in action shutting down the frontal cortex in an effort to SURVIVE

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

But what about...

- ▣ “My uncle Marty says he used crystal meth for 10 years and then just stopped and never used again... he says all you need is willpower”



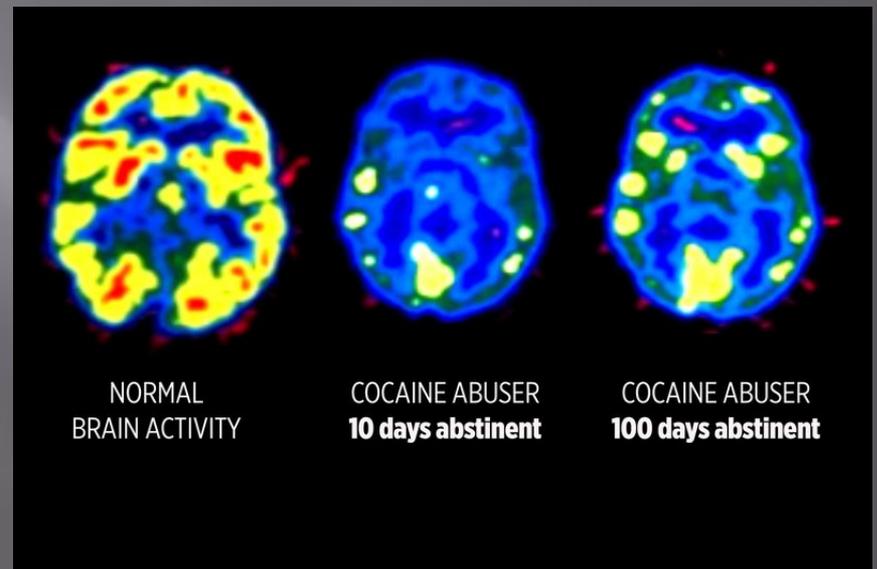
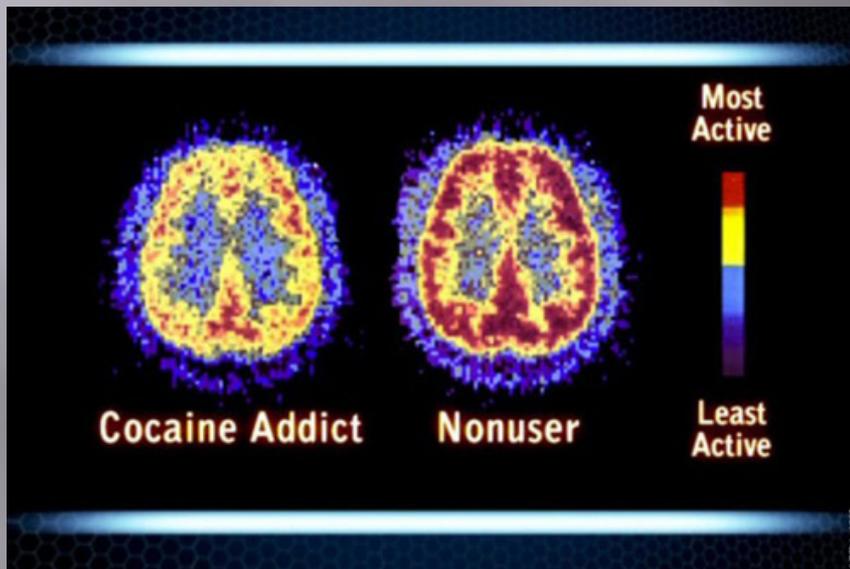
← Will power works here

← Will power is useless here

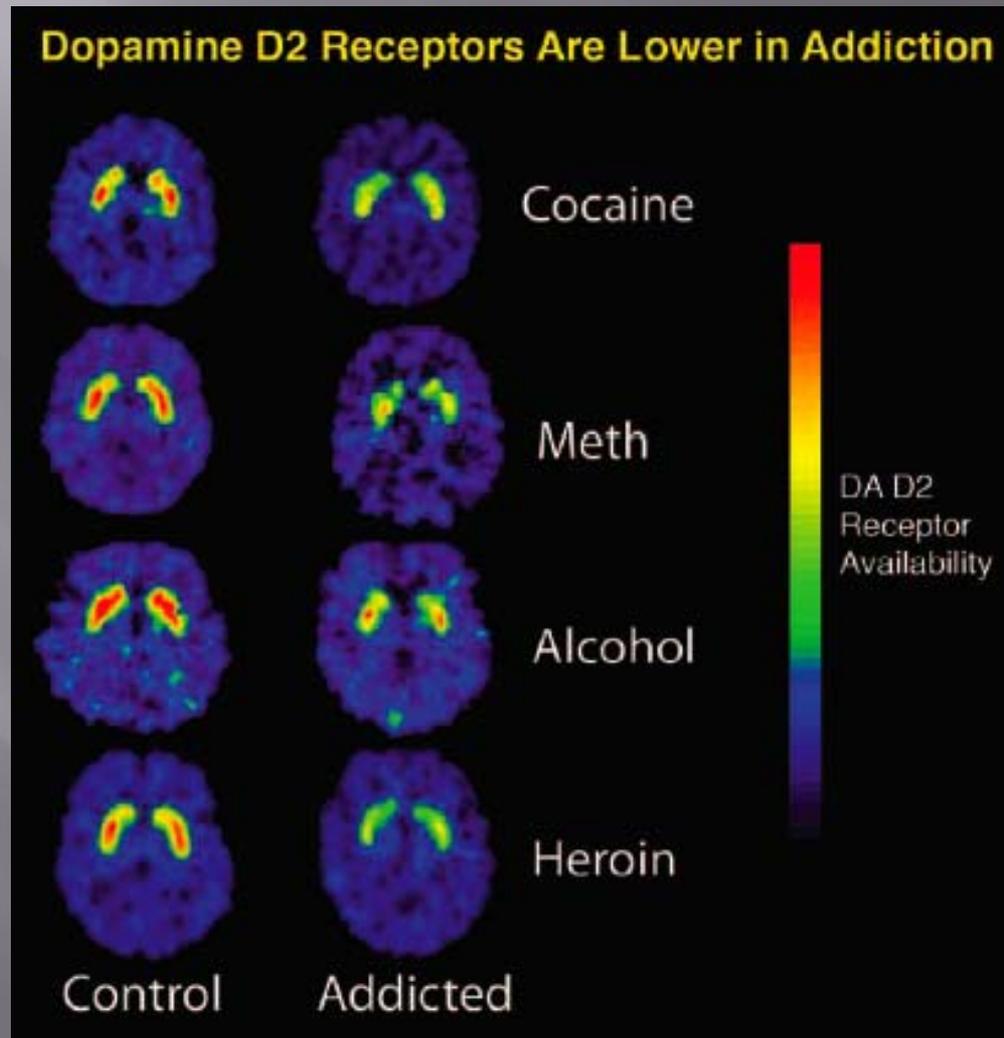
In a PET scan of the brain where the patient is shown their drug of choice

- ▣ 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



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

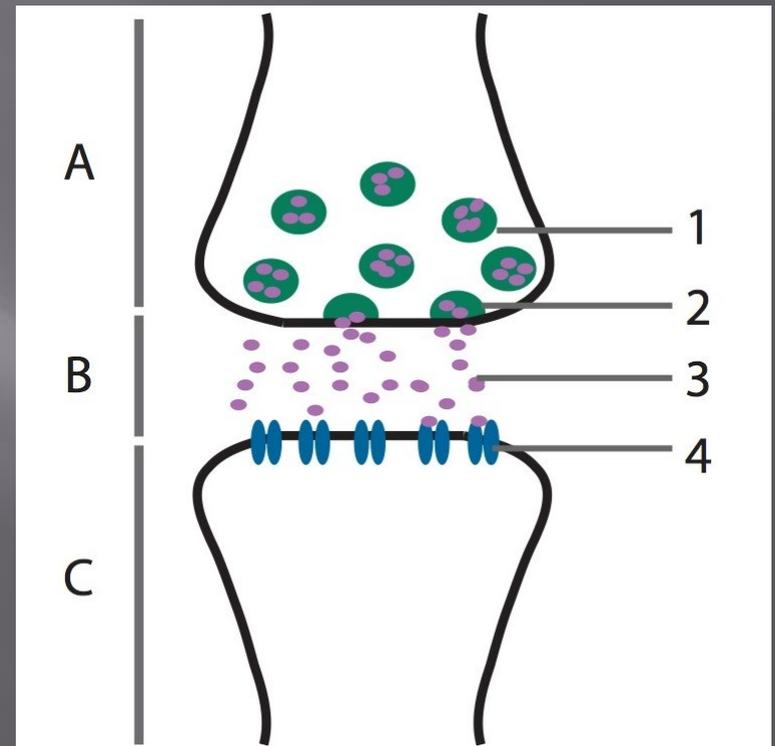
IT IS A BROKEN "PLEASURE SENSE" IN THE BRAIN

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!!!



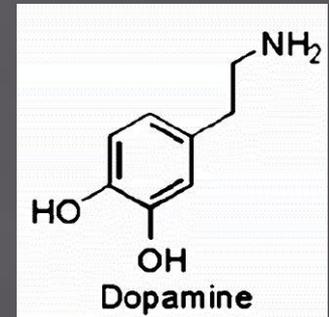
Brain Perceptual Systems (all of them):

- ▣ **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**

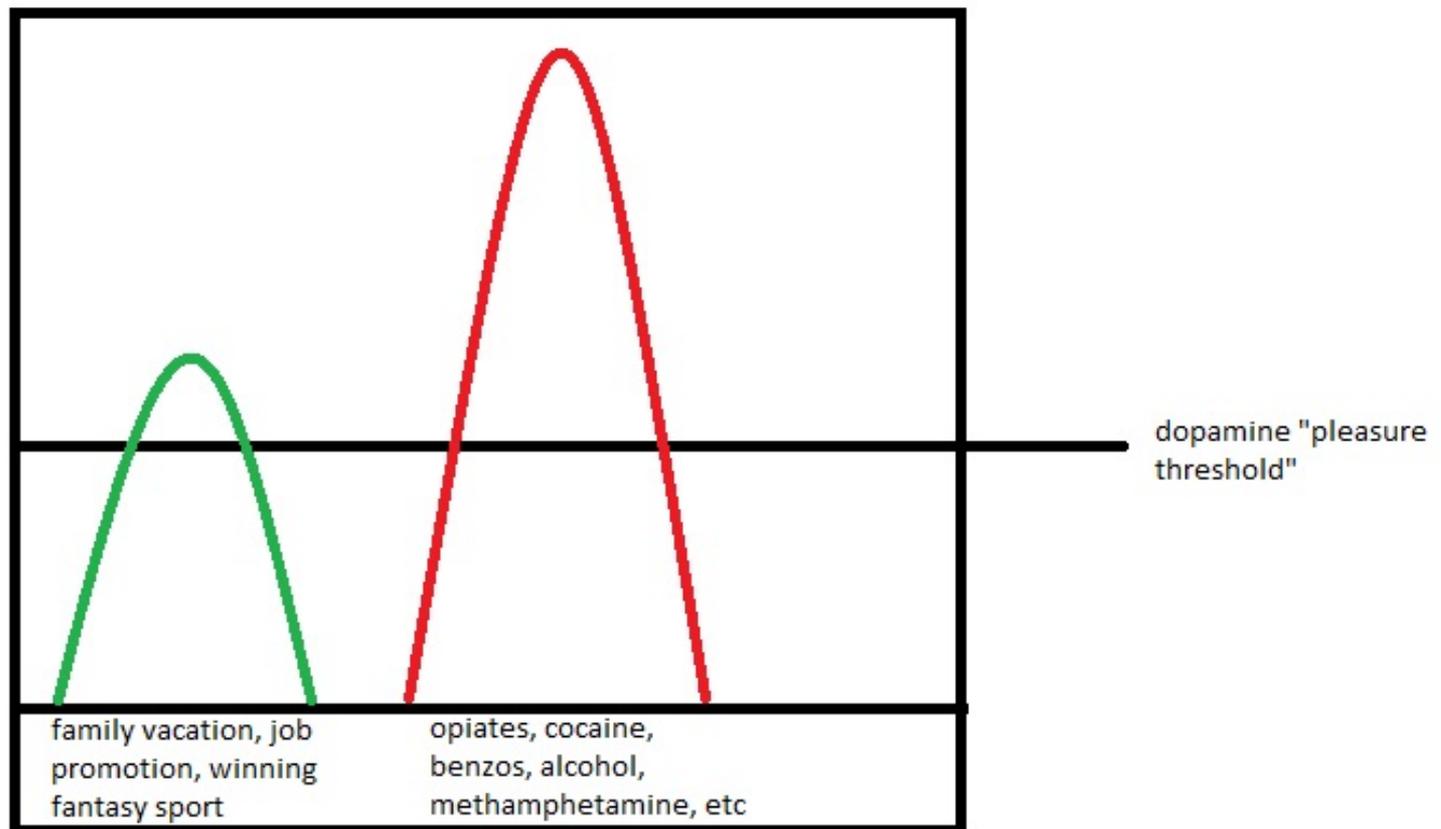
Addiction Neurotransmitter # 1:

Dopamine

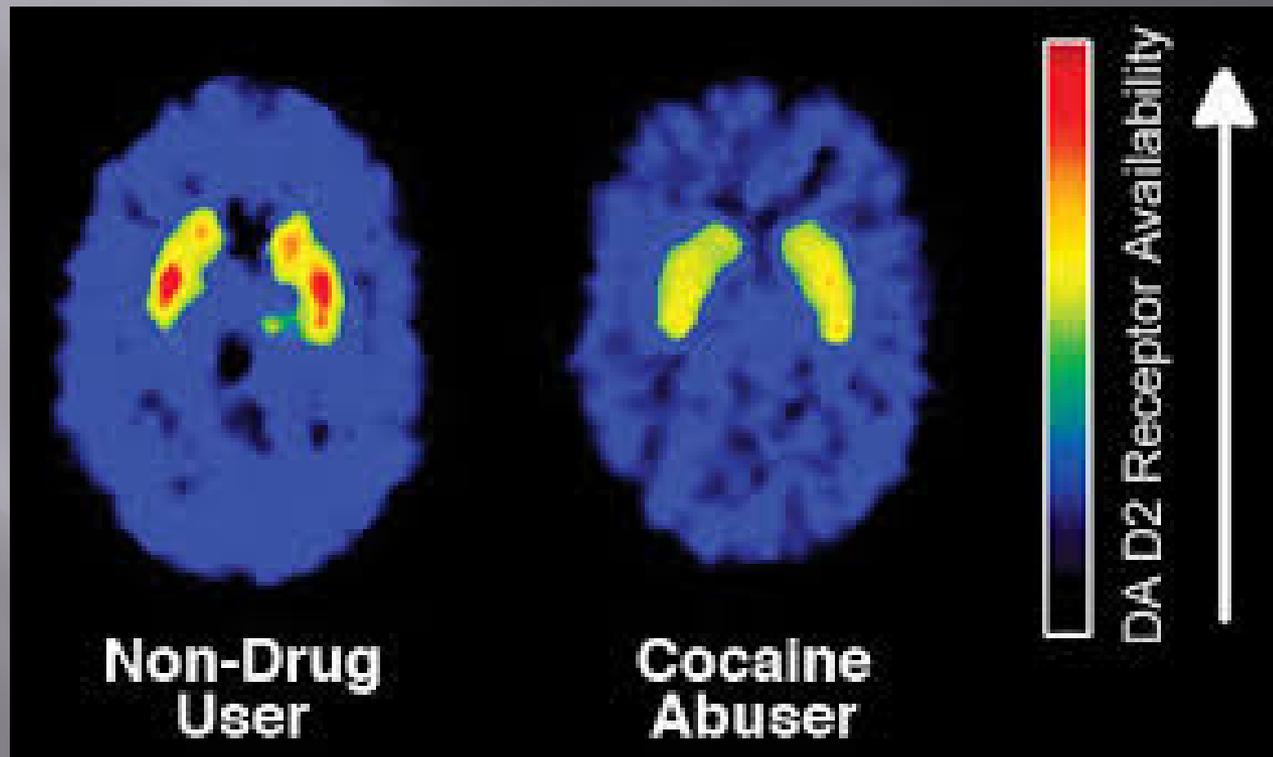
- ▣ • All drugs of abuse and potential compulsive behaviors release Dopamine
- ▣ • Dopamine is first chemical of a pleasurable experience - at the heart of all reinforcing experiences
- ▣ • DA is the neurochemical of salience (it signals survival importance)
- ▣ • DA signals reward prediction error
-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



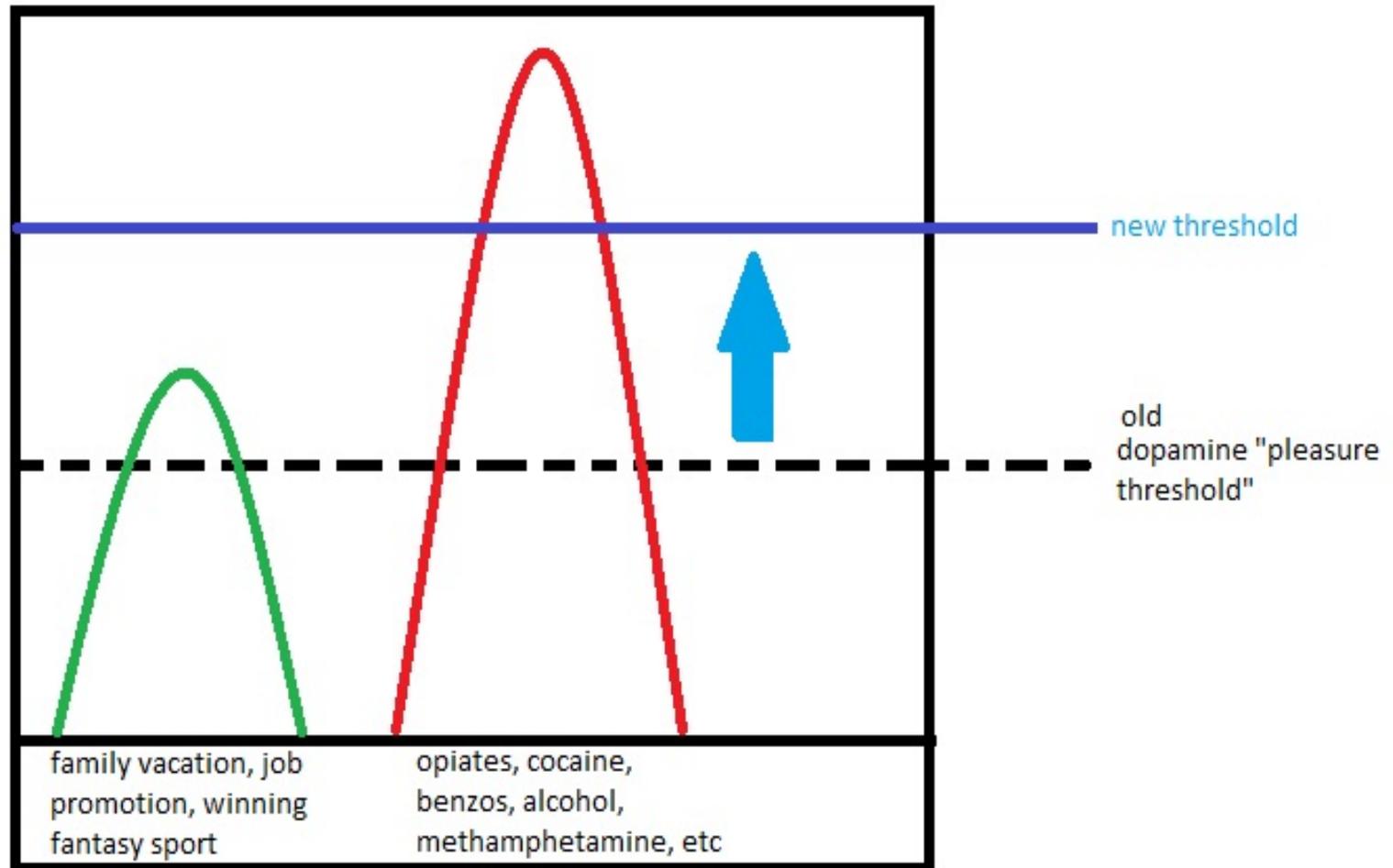
The Brain has a Hedonic "Set Point"



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

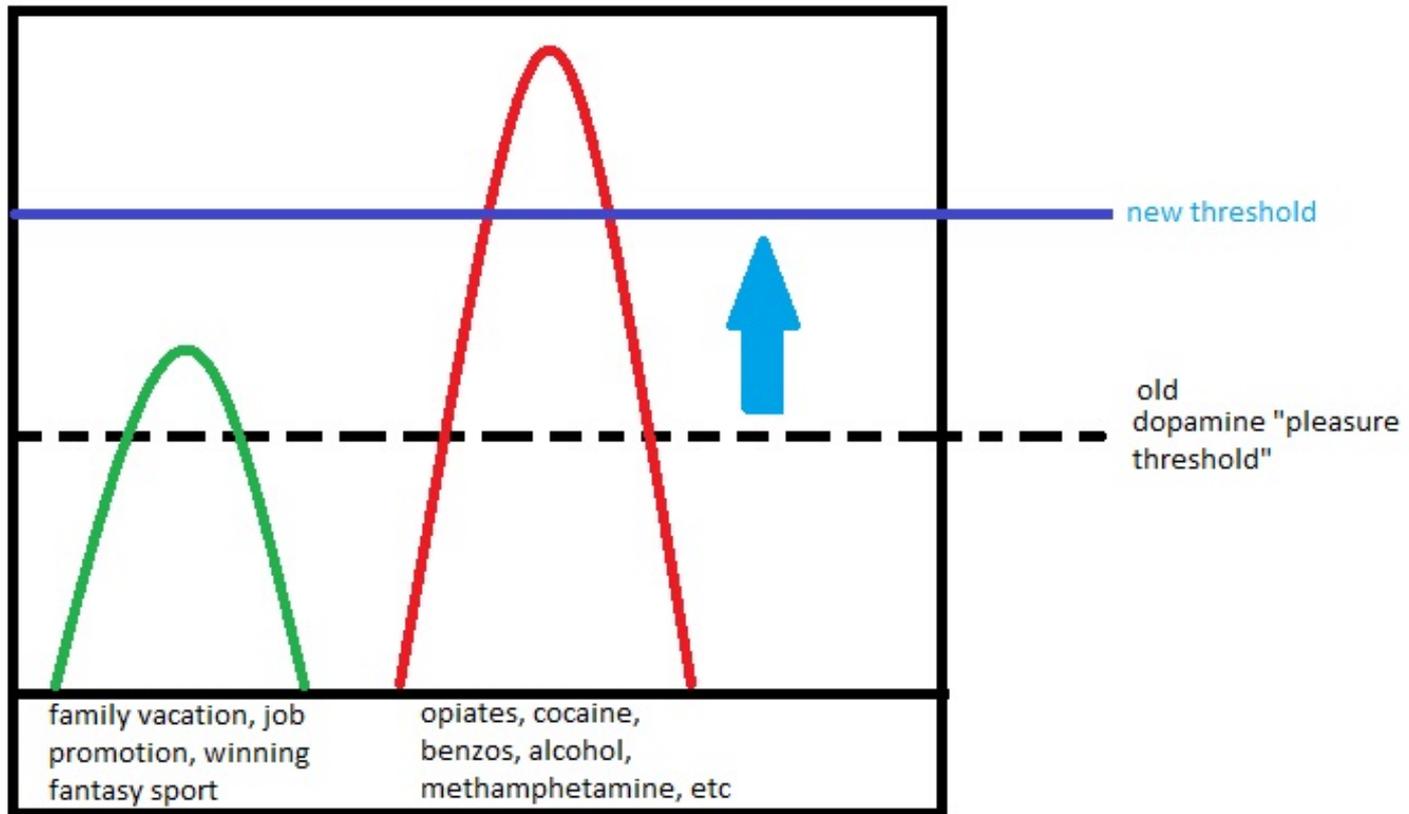
And \uparrow CRF = \downarrow DAD2 receptors

And \downarrow DAD2 receptors = Anhedonia

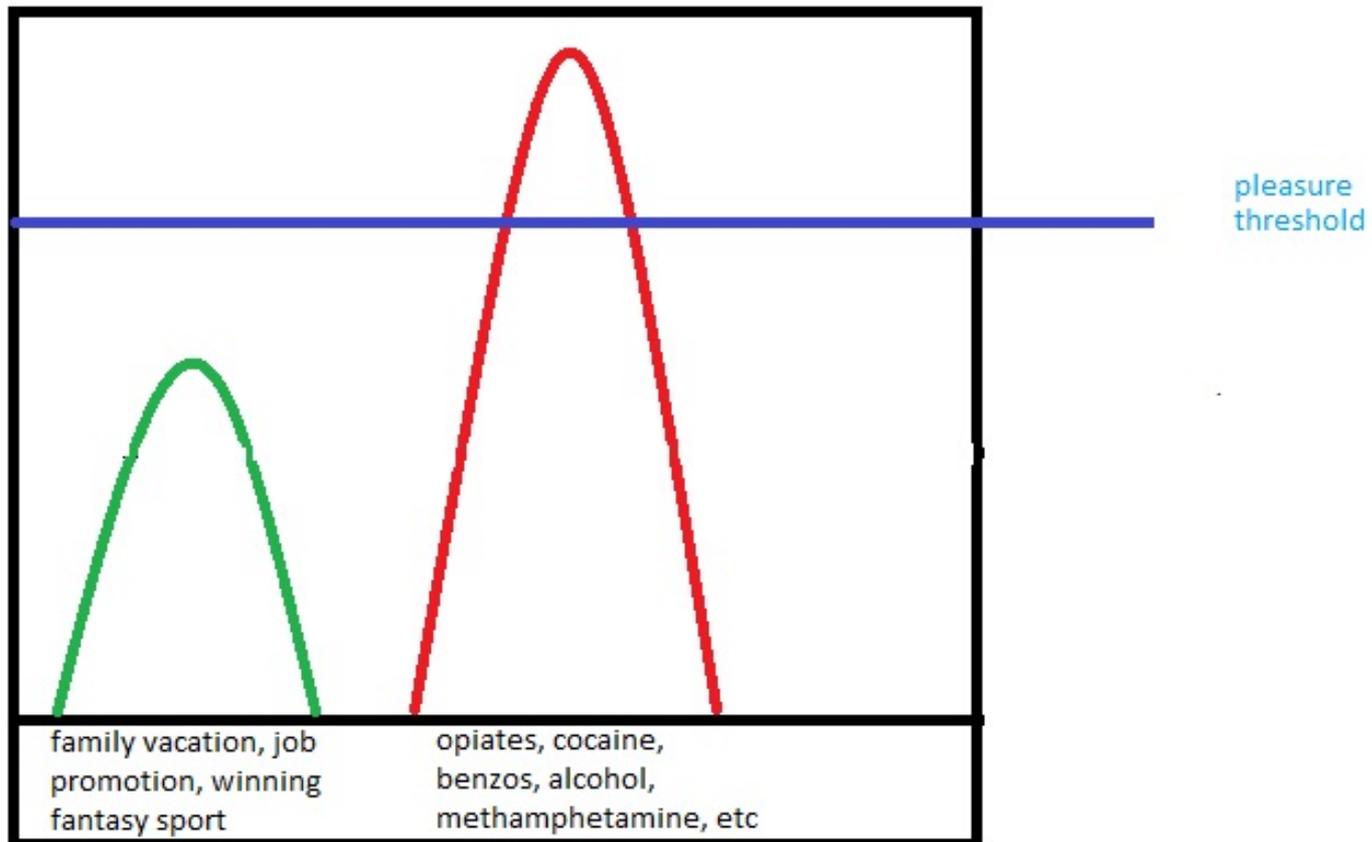
ANHEDONIA: PLEASURE “DEAFNESS”

(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”

use of 'activating'
substance x
activating number
of uses

gene activated
("turned on")

use of ANY dopamine
releasing substance

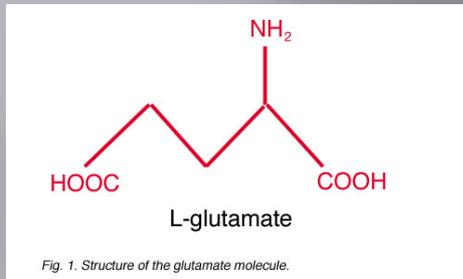


midbrain changes
occur (down regulation
of dopamine
receptors--> increased
threshold for pleasure)

gene
present



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

Ok... but what about the cortex

- ▣ “If you don’t use it, you lose it”
- ▣ If you want to learn to play an instrument or develop big biceps you must CONTINUALLY practice/workout otherwise progress can be lost
- ▣ The same is true for life skills- coping, stress relief, problem solving, other-centeredness/spirituality
- ▣ EVERY TIME THE MIDBRAIN ‘TURNS ON’ THE CORTEX ‘SHUTS OFF’ RESULTING IN A WEAKING OVER TIME

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

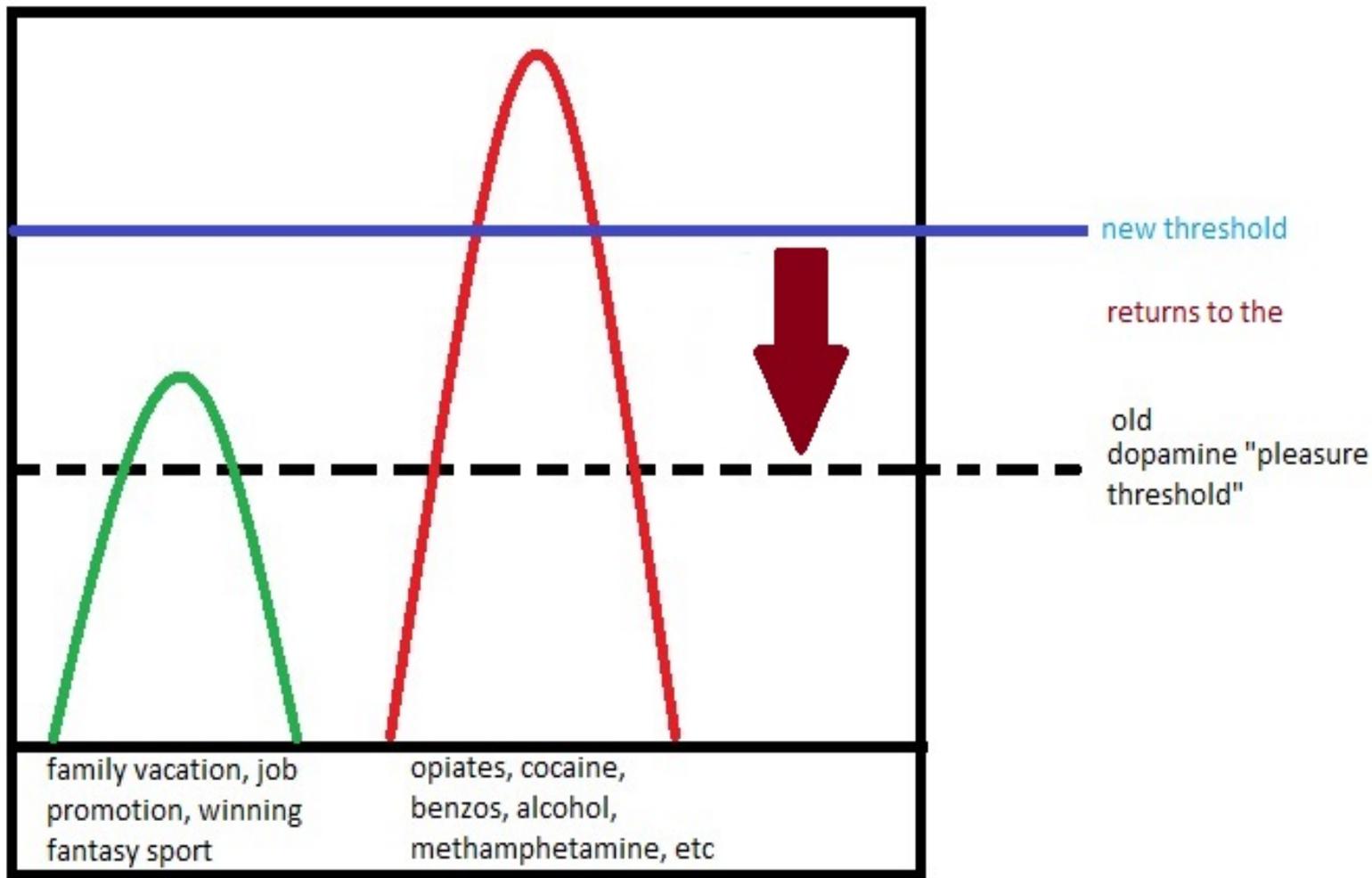


Once the behaviors become habits, the behaviors themselves become the disease

- ▣ The need for instant gratification
 - ▣ And subsequent inability to wait or practice
- ▣ Needing a pill or chemical for EVERYTHING
 - while OTC sleep medications have few addictive properties, the BEHAVIOR of needing something to make the body do what it should naturally learn to do, IS addictive
- ▣ Looking for reasons to avoid recovery related behaviors and activities
 - ▣ Seeking reasons to use

Returning of the threshold

- ▣ Over time the dopamine receptors will regenerate or up regulate
 - With JUST abstinence- up to a year
 - ▣ That is a whole year of not feeling 'normal' or 'enjoying anything'
 - ▣ Why most people who don't work a program will say they had 'clean time' generally lasting less than a year
 - With simultaneous development of the cortex and spirituality- 3 months



family vacation, job promotion, winning fantasy sport

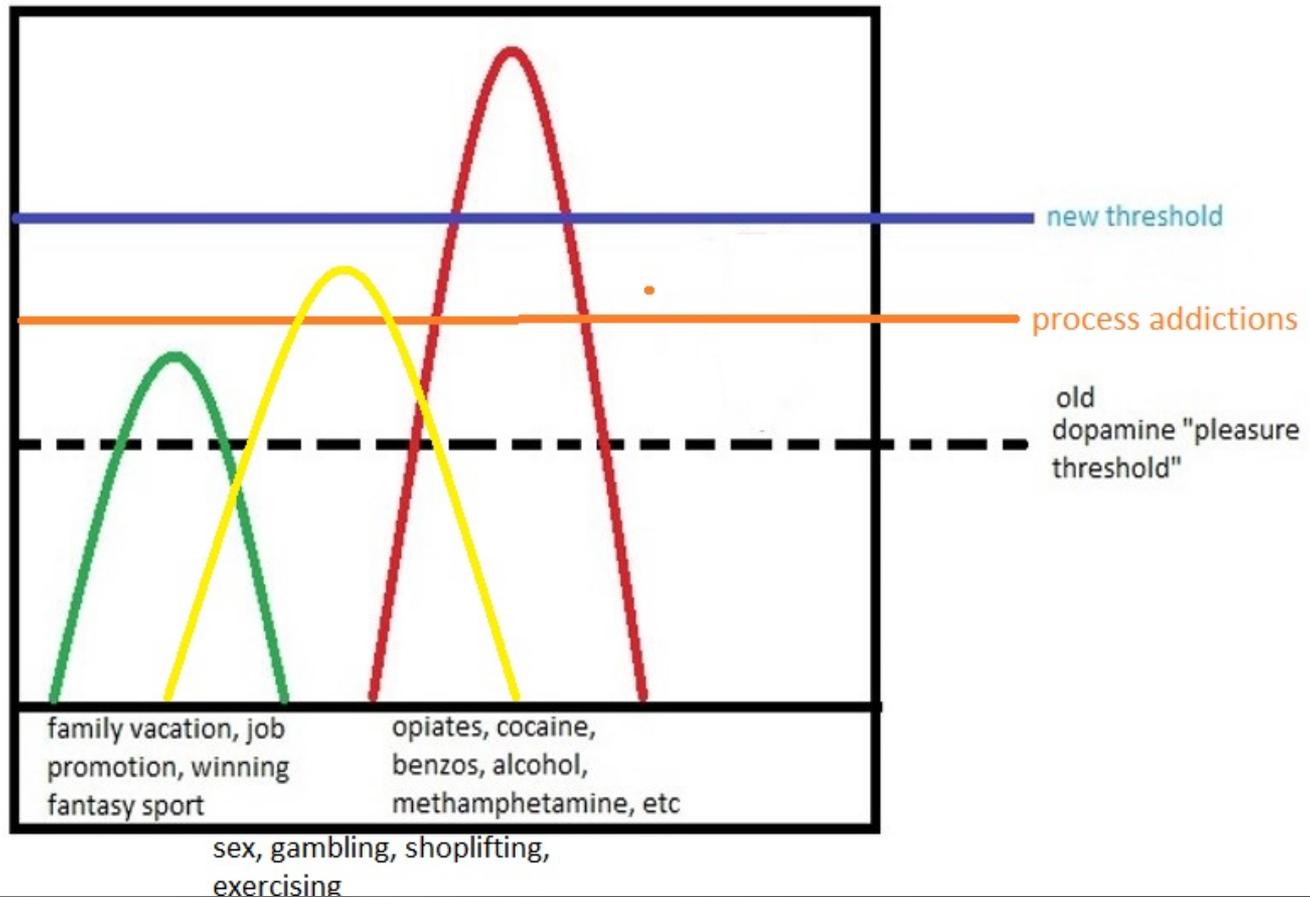
opiates, cocaine, benzos, alcohol, methamphetamine, etc

new threshold

returns to the

old dopamine "pleasure threshold"

A word about process addictions



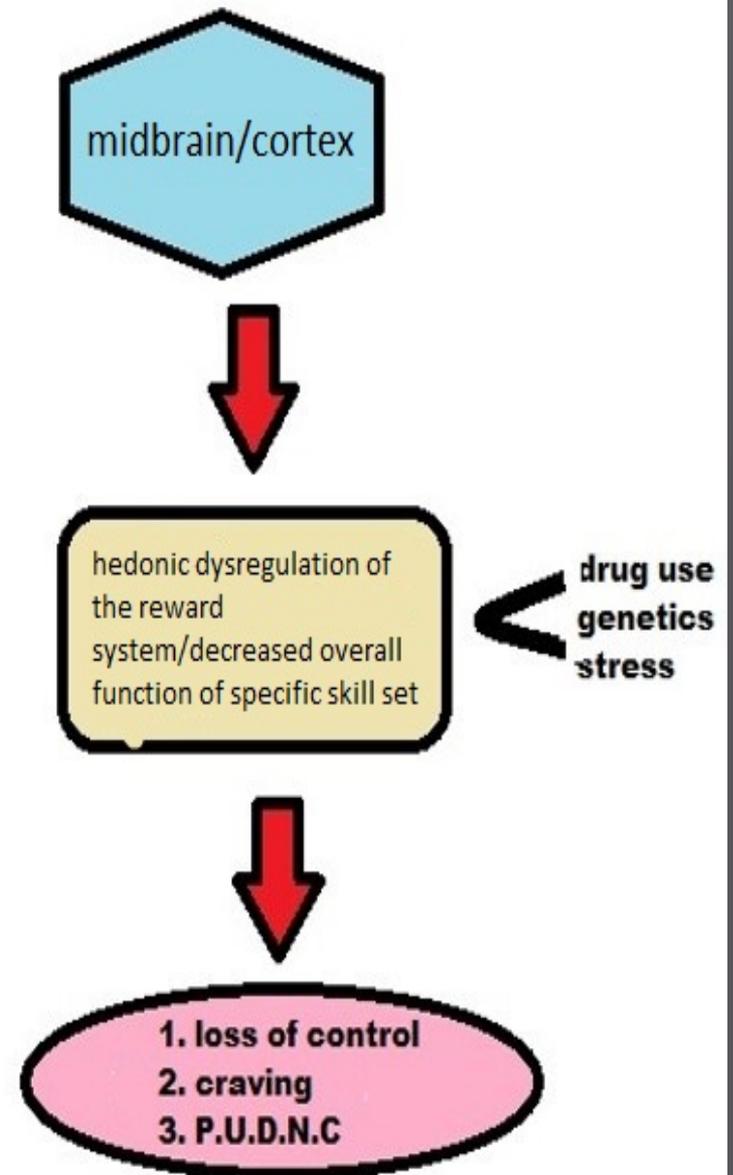
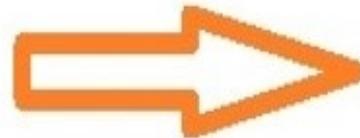
DEFINITION OF ADDICTION

- ▣ 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**

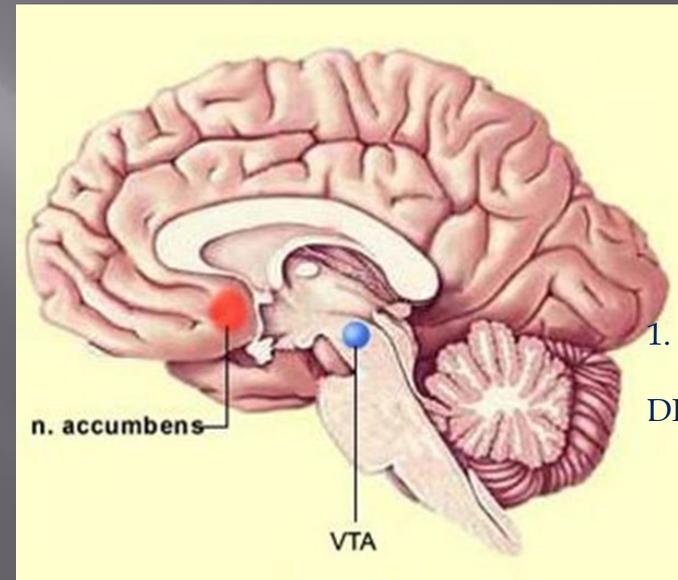


Hierarchy of treatment: summarized

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

The principles of treatment BEYOND DETOX (THE MOST IMPORTANT PART!!!!)

- ▣ • We have to change the misperception of the hedonic aspects of the drug (thinking the drug gives us pleasure)
- ▣ • we must change the attribution of survival salience to the drug on the level of the unconscious

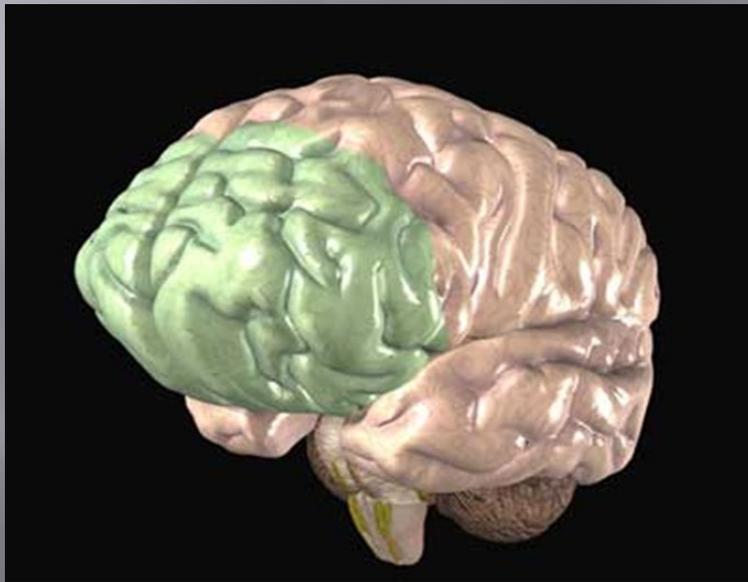


1. Midbrain
(unconscious)
DRUG= SURVIVAL

THE DIVISION OF LABOR...

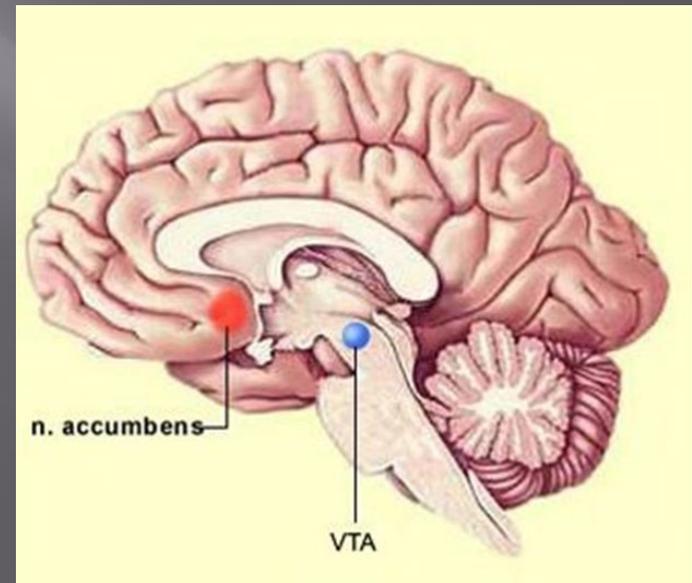
AA/BEHAVIORAL
THERAPY WORK HERE

- ▣ Frontal cortex =
emotional meaning



DRUGS/MEDICATIONS
WORK HERE

- ▣ Midbrain =
survival/craving



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



How do we restore
the Frontal Cortex?

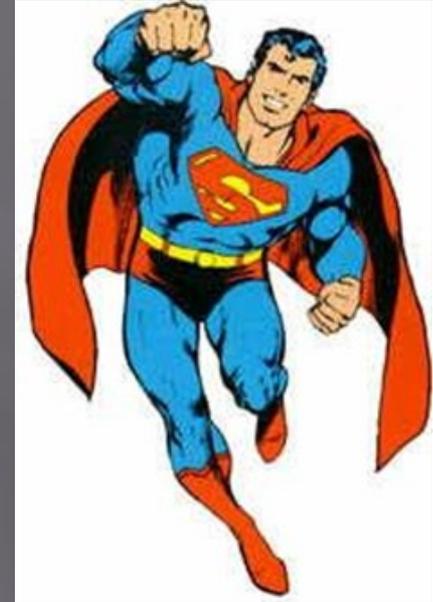
Principles of treatment

- ▣ • 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
- ▣ We must help them find personal meaning in other things
- ▣ We must help them develop emotional relationships with healthy PEOPLE
- ▣ We must help them develop a sense of self INDEPENDENT OF THE DRUG

The Two Tasks of Addiction Treatment:

- ▣ 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

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)



Personal growth, psychic change

12-STEP PROGRAMS

- ▣ “spiritual growth for dummies”

COUNSELING

- ▣ “how to make a donut”

Role of Medication in Addiction treatment practices



THERE ARE MULTIPLE MEDICATIONS WE USE

ALCOHOL (ANTICRAVING)

- ANTABUSE
- CAMPRAL
- NALTREXONE-
VIVITROL

OPIATES

(HARM REDUCTION VS.
MEDICATION ASSISTED
TREATMENT)

- ▣ -SUBOXONE-
SUBUTEX
- ▣ -METHADONE
- ▣ -NALTREXONE-
VIVITROL

Alcohol

- ▣ Antabuse- disulfiram. Interacts with alcohol to induce profuse nausea and vomiting
 - Good for short term use but negative reinforcement does not have long term success (patient will stop taking the medication before they stop drinking)
- ▣ Anticraving medications
 - Decreased drinking is still drinking and still activating midbrain/ deactivating cortex
 - May have use with binge drinkers or early stage relapse

alcohol

- ▣ Naltrexone binds to opioid receptors and may decrease some of the positive rewards from alcohol
- ▣ Does not have a role in withdrawal
- ▣ The pathways by which **Campral works** are still a subject of research. However, it seems to help reduce cravings by reducing the positive response to drinking and reducing cravings
- ▣ Does not have a role in withdrawal

Opioid system:

- The **mu subtype** appears to be a key in opiate addiction: for mice lacking this receptor, morphine is no longer rewarding or reinforcing.
- Neuroimaging studies suggest that alterations in mu receptor level may be fundamental to addiction. Increased receptor levels in the anterior cingulate was found in recently abstinent humans addicted to cocaine or opiates; which may reflect elevated mu opiate receptor levels or decreased endogenous opioid levels leading to craving.
- Roles for **kappa** and **delta** opiate receptors in addiction are also evident. Unlike mu receptors, kappa receptor stimulation reduces dopamine function in the NAcc. This may possibly result in dysphoria. In animal models, delta antagonists can reduce self-administration of alcohol, suggesting that this receptor also plays a key role in reinforcement.

overdose

- ▣ The predominant cause of morbidity and mortality from pure opioid overdoses is respiratory compromise. Less commonly, acute lung injury, status epilepticus, and cardiotoxicity occur in the overdose setting

Drug replacement vs. drug blocking

- ▣ Buprenorphine and methadone bind to opiate receptors for a long time and release a steady stream of dopamine, preventing withdrawal and cravings for opiates
- ▣ Vivitrol and naltrexone bind to opiate receptors and INHIBIT the release of dopamine while also prohibiting other opiates from binding and causing a release of dopamine/euphoria.
 - Because there is NO opiate in this drug there is NO risk of diversion, abuse, dependence, withdrawal
 - This will block ALL opiates, even if they are used for pain
 - This will not block or prevent the use of non-opiate drugs and alcohol
 - The opiate antagonists (eg, naloxone, nalmefene, naltrexone) antagonize the effects at all four opiate receptors

Opiate replacement medications

METHADONE

- ▣ A complete opioid agonist
- ▣ At therapeutic doses can block other opioids from binding
- ▣ Very long half life
- ▣ Can affect liver/heart
 - Monitoring
- ▣ Can only be given for opioid dependence at a State approved clinic!!
 - rx for PAIN ONLY

BUPRENORPHINE

- ▣ A partial agonist/antagonist
- ▣ Will partially block receptors even at low doses
- ▣ Can be given in outpatient office setting OR a clinic with daily dosing/monitoring
- ▣ Long half life

Harm reduction

- ▣ Similar to the concept of sugar free candy in Diabetes
- ▣ **Can be used alone (won't work for long) OR in combination with behavioral therapy (psychic change)**



A chemical will not cure chemical dependency

- ▣ Medication should be used to stabilize the midbrain so that the work can be done in the cortex
- ▣ Without the constant spike of dopamine throughout the day, the threshold will come back to a level closer to normal
- ▣ Relying on a medication alone will likely result in relapse

COMBINATION THERAPY (THE ULTIMATE TOOLBOX)

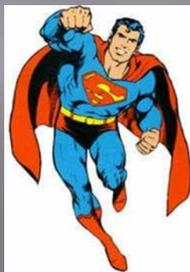
-ALLOWING THE MIDBRAIN TO 'REST' BUT SIMULTANEOUSLY STRENGTHENING THE FRONTAL CORTEX

-ALLOWING THE BEHAVIORAL AND EMOTICOMENTAL TOOLS TO DEVELOP AND BE PRACTICED IN A "LESS STRESSFUL" ENVIRONMENT (THE BRAIN)

▣ APPROPRIATE USE:

- Recovery setting where the medication is on the bottom of the priorities

- Using the medication as a "carrot" to get addict to participate in activities that would otherwise be the antithesis of the addicted mind



▣ INAPPROPRIATE USE:

- As the ONLY tool

- As the most important tool

- Allowing the individual to prioritize the drug over recovery practices



A CHRONIC DISEASE

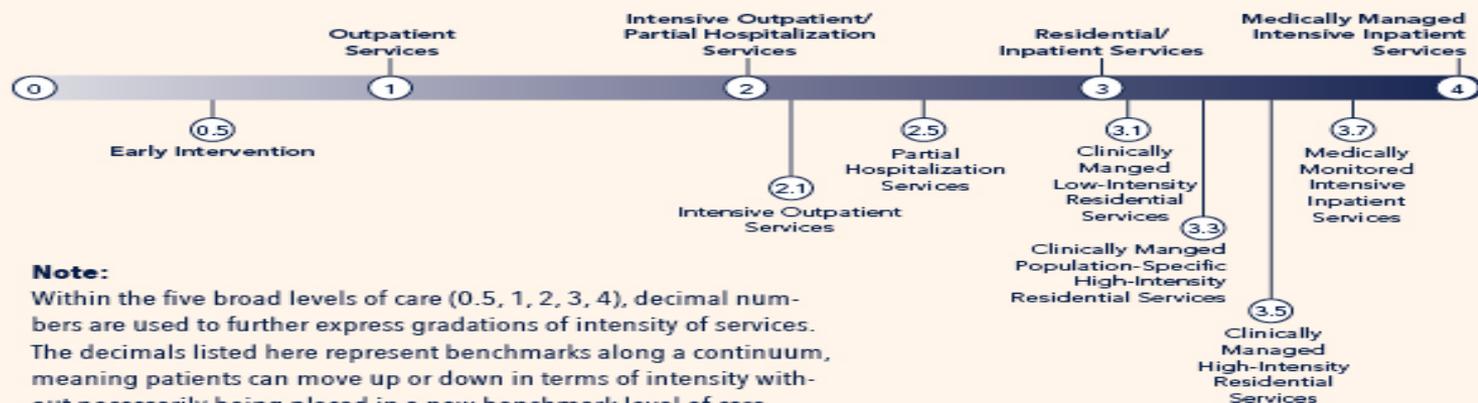
- ▣ Chronic diseases are CHRONIC
- ▣ RELAPSING & REMITTING
- ▣ We focus on the ACUTE phase
- ▣ Need to be looking at the long term
 - ▣ Studies with Physicians show 5 year monitoring has success >90%

AT A GLANCE: THE SIX DIMENSIONS OF MULTIDIMENSIONAL ASSESSMENT

ASAM's criteria uses six dimensions to create a holistic, biopsychosocial assessment of an individual to be used for service planning and treatment across all services and levels of care. The six dimensions are:

1	DIMENSION 1	Acute Intoxication and/or Withdrawal Potential Exploring an individual's past and current experiences of substance use and withdrawal
2	DIMENSION 2	Biomedical Conditions and Complications Exploring an individual's health history and current physical condition
3	DIMENSION 3	Emotional, Behavioral, or Cognitive Conditions and Complications Exploring an individual's thoughts, emotions, and mental health issues
4	DIMENSION 4	Readiness to Change Exploring an individual's readiness and interest in changing
5	DIMENSION 5	Relapse, Continued Use, or Continued Problem Potential Exploring an individual's unique relationship with relapse or continued use or problems
6	DIMENSION 6	Recovery/Living Environment Exploring an individual's recovery or living situation, and the surrounding people, places, and things

REFLECTING A CONTINUUM OF CARE



Treatment in the global sense

- ▣ All inclusive
 - Current models are 'piecemeal' and HIPPA laws make communication amongst facilities difficult
 - ▣ Residential, PHP, IOP, OTP, transitional housing, psychiatric and general medical services should be under one 'umbrella'
 - Start with abstinence and/or MAT and then move to address the triggers
 - ▣ Grief/trauma assessment and treatment should be offered to ALL patients with addiction
 - ▣ Coping skills
 - ▣ Social services

Eliminating the stigma

- ▣ Addiction is a disease
 - Don't call it a disease but then treat it like bad behavior
 - ▣ Healthcare professionals with addiction issues should be TREATED not terminated.
 - ▣ Pregnant patients should be encouraged to get help, not threatened with legal action if they don't
 - ▣ Addicts need firm, clear boundaries without engagement in drama
 - If YOU are judging them, THEY are feeling judged
 - Judged people just shut down

A word about marijuana

- ▣ THC releases dopamine... just like alcohol, opiates, cocaine, benzodiazepines, etc
 - It will awaken the 'tiger' and trigger the inability to cope without chemicals and put the addict in a position of needing stronger chemicals to deal with larger stressors, ultimately leading back to the drug of choice
 - The "marijuana maintenance plan" used as a 'recovery tool' is a nonsensical approach created BY addicts FOR addicts
- ▣ THC is no more 'dangerous' to a NONaddict than prescription medication or alcohol
 - Some evidence supporting its use in some medical conditions

Family disease

- ▣ Addiction is a family disease
 - The addicts behaviors affect everyone in the family
 - The family becomes ADDICTED to the addict
 - ▣ Family treats the addict like the addict treats drugs (constantly thinking about them, adjusting their lives according to the addict, etc...)
 - This process occurs in the same place in the brain and needs to be treated the same
 - Alanon, naranon, individual counseling for family members

Prevention...

- ▣ The truth is that we will never treat this disease to extinction
- ▣ We need to develop tools to prevent it.
- ▣ We can look at current treatment and utilize those strategies to help prevent it
- ▣ Addiction is an adolescent disease, so we must start there

Questions????

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