

# Addiction & the Brain

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# The Impact of Language

- Addict
  - Addicted to \_
  - Addiction OR
  - Alcoholic or Drug Addict
  - Clean
  - Dirty
  - Drug habit
- Person with a Substance Use Disorder (SUD)
  - Has a \_\_\_\_ use disorder
  - SUD
  - Person with an alcohol use disorder or drug use disorder
  - Negative: Free of illicit substances
  - Positive: Active use
  - Substance use disorder

# The Impact of Language

Drug Abuser	- Person with SUD
Former	- In sustained remission
Maintenance	- Medication -Assisted Treatment (MAT)
Pain Seeker	- Relief / Treatment Seeking
Recreational	- Non-medical use
Reformed	- In remission
Replacement	- MAT
Substance Abuser	- Person with SUD

# Why Do People Take Drugs in The First Place?

## To Feel Good

**To have novel:**

feelings

sensations

experiences

**AND**

to share them



## To Feel Better

**To lessen:**

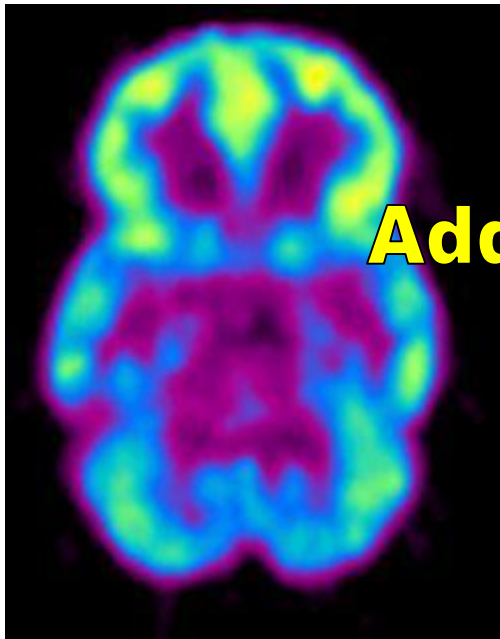
anxiety

worries

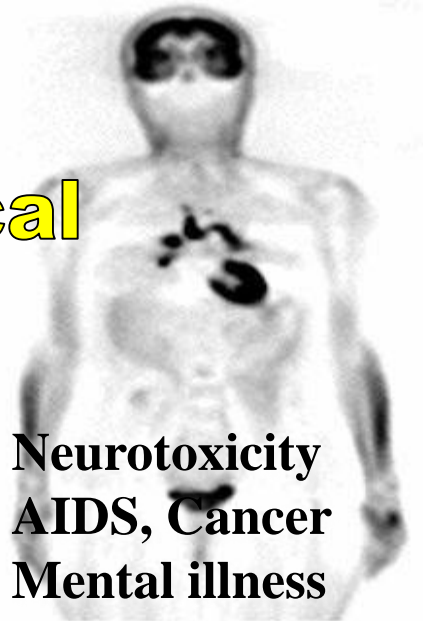
fears

depression

hopelessness



**Addiction**



**Medical**

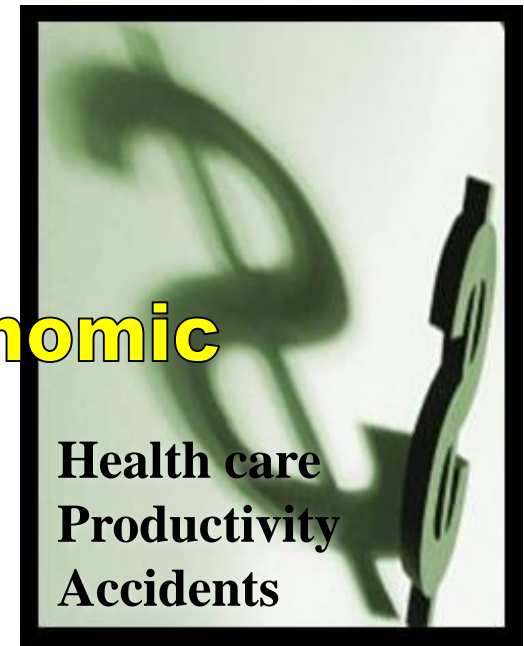
**Neurotoxicity  
AIDS, Cancer  
Mental illness**

**DRUGS**



**Social**

**Homelessness  
Crime  
Violence**

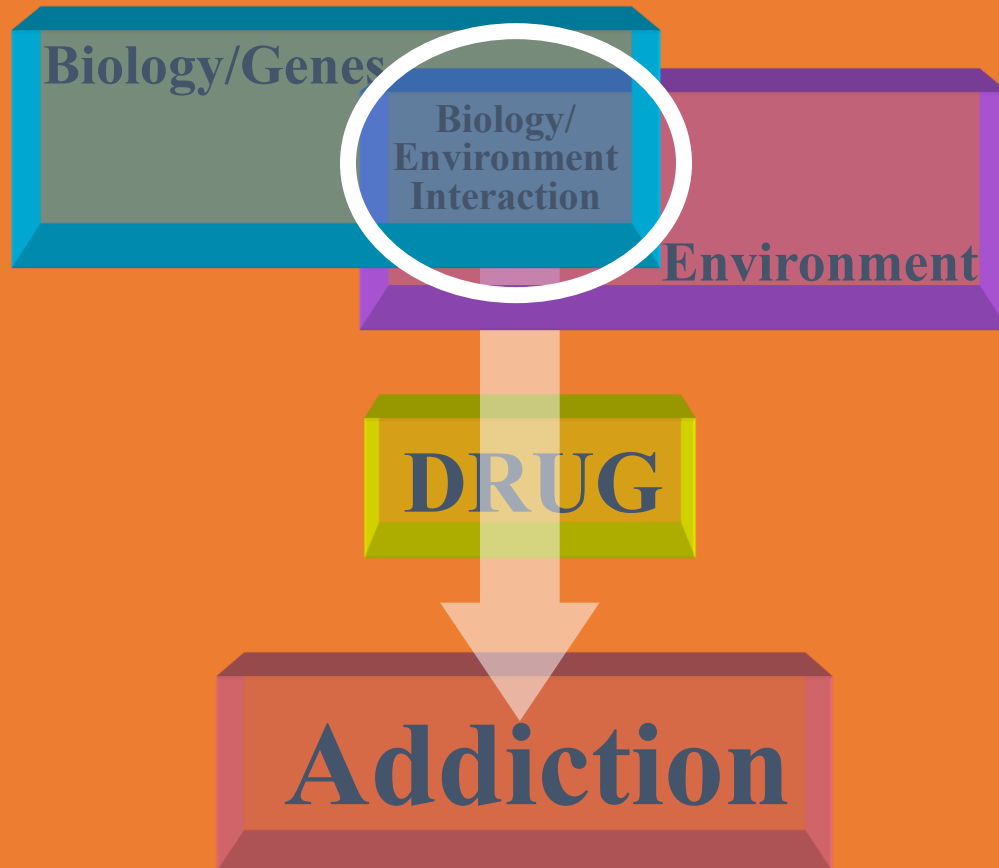


**Economic**

**Health care  
Productivity  
Accidents**

# Key Roles in Vulnerability

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# **Estimated Economic Cost to Society Due to SUDs**

<b>Illegal drugs:</b>	<b>\$193 billion/year</b>
<b>Prescription drug:</b>	<b>\$78.5 billion/year</b>
<b>Alcohol:</b>	<b>\$ 249 billion/year</b>
<b>Tobacco:</b>	<b>\$300 billion/year</b>
<b>Total:</b>	<b>\$820 billion/year</b>

## & The Impact on Families & Children



## MENTAL AND SUBSTANCE USE DISORDERS IN AMERICA: 2016

PAST YEAR, 2016, 12+

Among those with a substance use disorder about:

- 1 IN 3 (37%) struggled with illicit drugs
- 3 IN 4 (75%) struggled with alcohol use
- 1 IN 9 (12%) struggled with illicit drugs and alcohol

Among those with a mental illness about:

- 1 IN 4 (23%) had a serious mental illness

**7.5%**  
(20.1 MILLION)  
People aged 12 or  
older had a  
substance use disorder

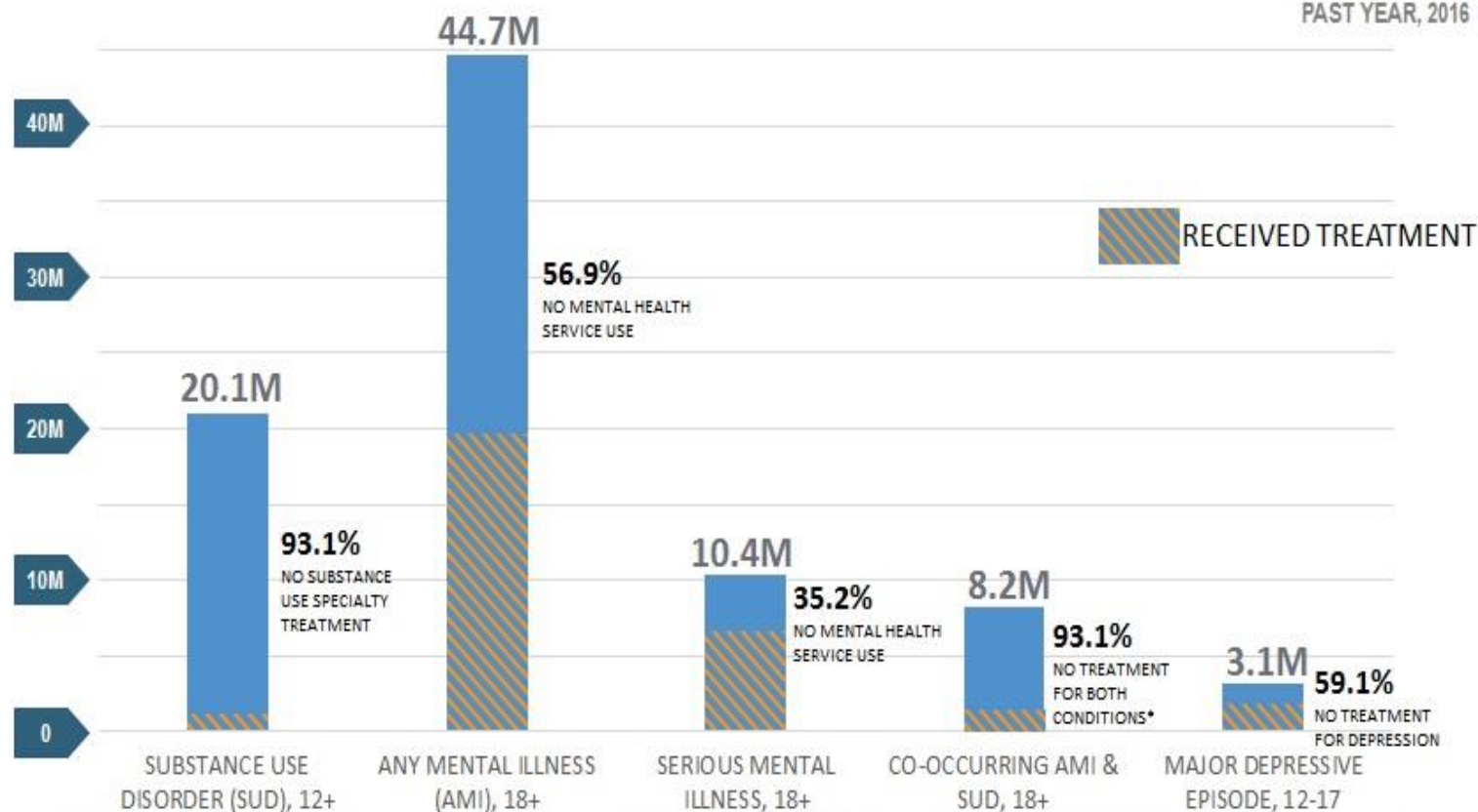
**3.4%**  
(8.2 MILLION)  
18+ HAD BOTH  
substance use disorder  
and a mental illness

**18.3%**  
(44.7 MILLION)  
People aged  
18 or older had a  
mental illness

No statistically different changes from 2015

## DESPITE CONSEQUENCES AND DISEASE BURDEN, MANY DO NOT GET TREATMENT

PAST YEAR, 2016



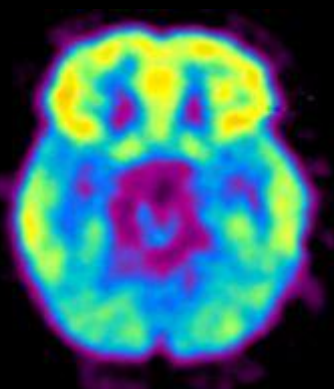
\*Received no substance use treatment at a specialty facility and no mental health services



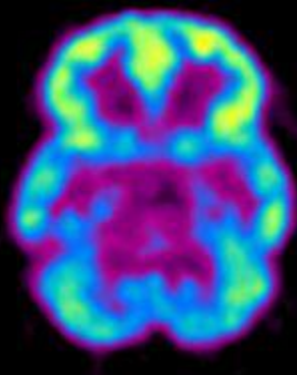
# Addiction is Like Other Chronic Diseases...

- It is preventable
- It is treatable
- It changes biology
- If untreated, it can last a lifetime
- Recurrence and recovery

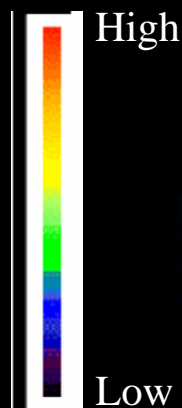
Decreased Brain Metabolism  
in *Drug User*



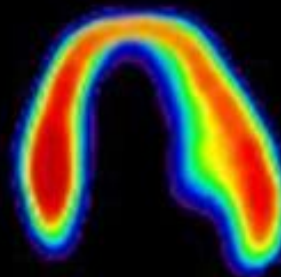
Healthy Brain



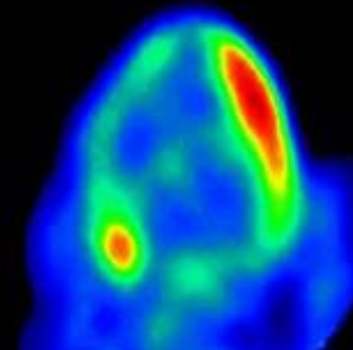
Diseased Brain/  
Cocaine User



Decreased Heart Metabolism  
in *Heart Disease Patient*



Healthy  
Heart

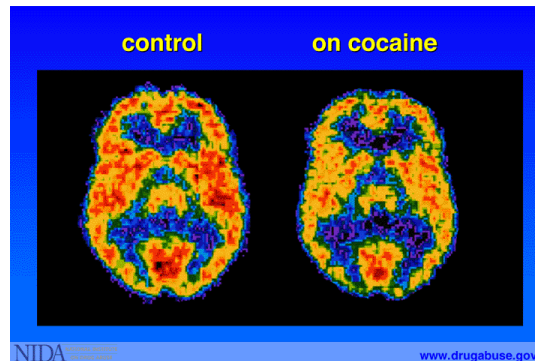


Diseased Heart

*Research supported by NIDA addresses all of these  
components of addiction.*

# Neurobiology of Addiction

- Experimental research has provided a new understanding of addiction and its corresponding treatment
- Addictive drugs can be very damaging to personal, social and economic aspects of lives



- But have also provided an avenue for understanding brain function

## **Frontal Cortex**

**Planning, Strategizing, Logic,  
Judgment**

## **Corpus Callosum**

**Connects Hemispheres  
Creativity and Problem  
Solving**

## **Cerebellum**

**Coordinates muscles/  
movement and thinking  
processes**

## **Thalamus**

## **Nucleus accumbens**

## **Ventral tegmental area**

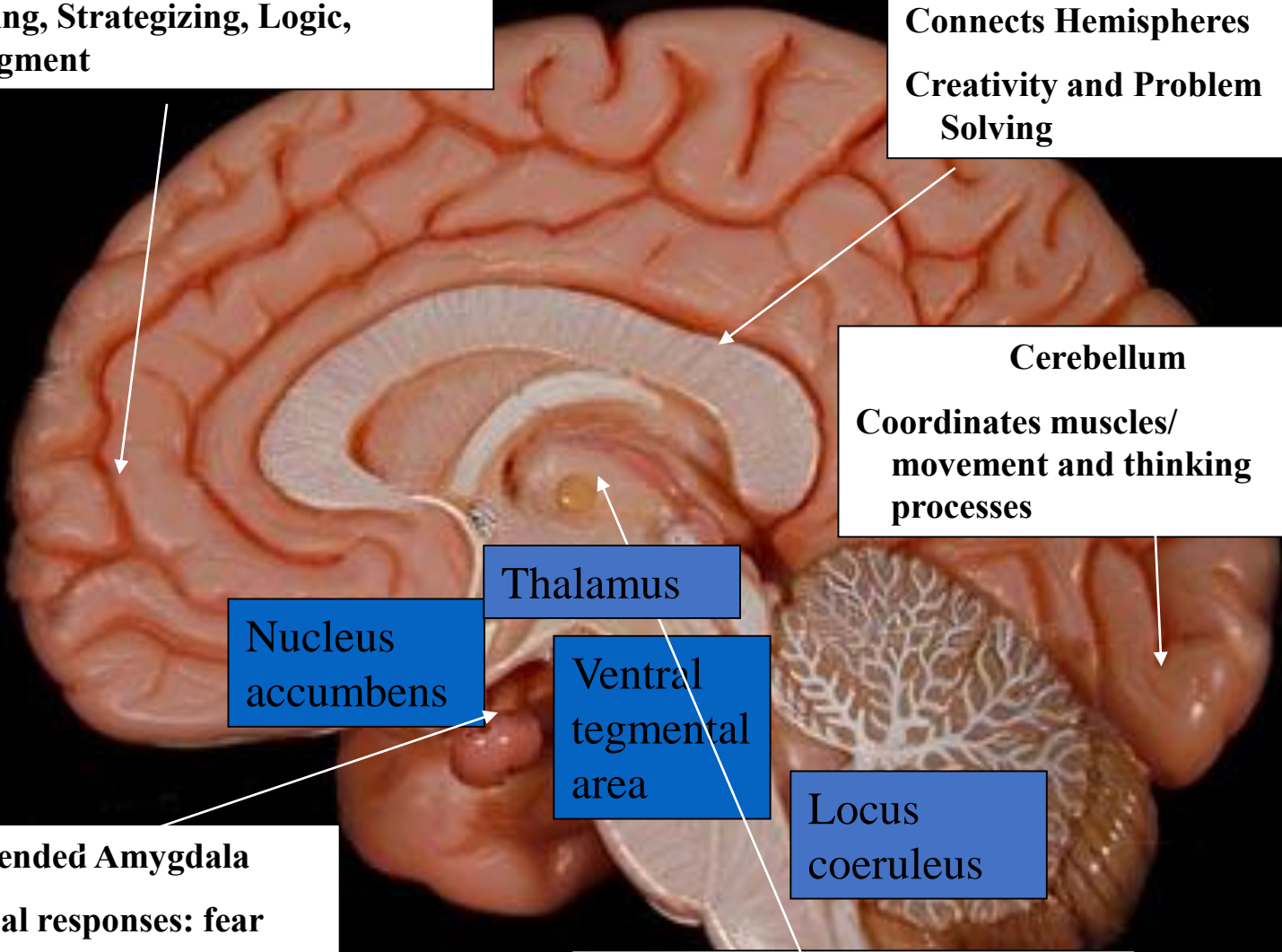
## **Locus coeruleus**

## **Extended Amygdala**

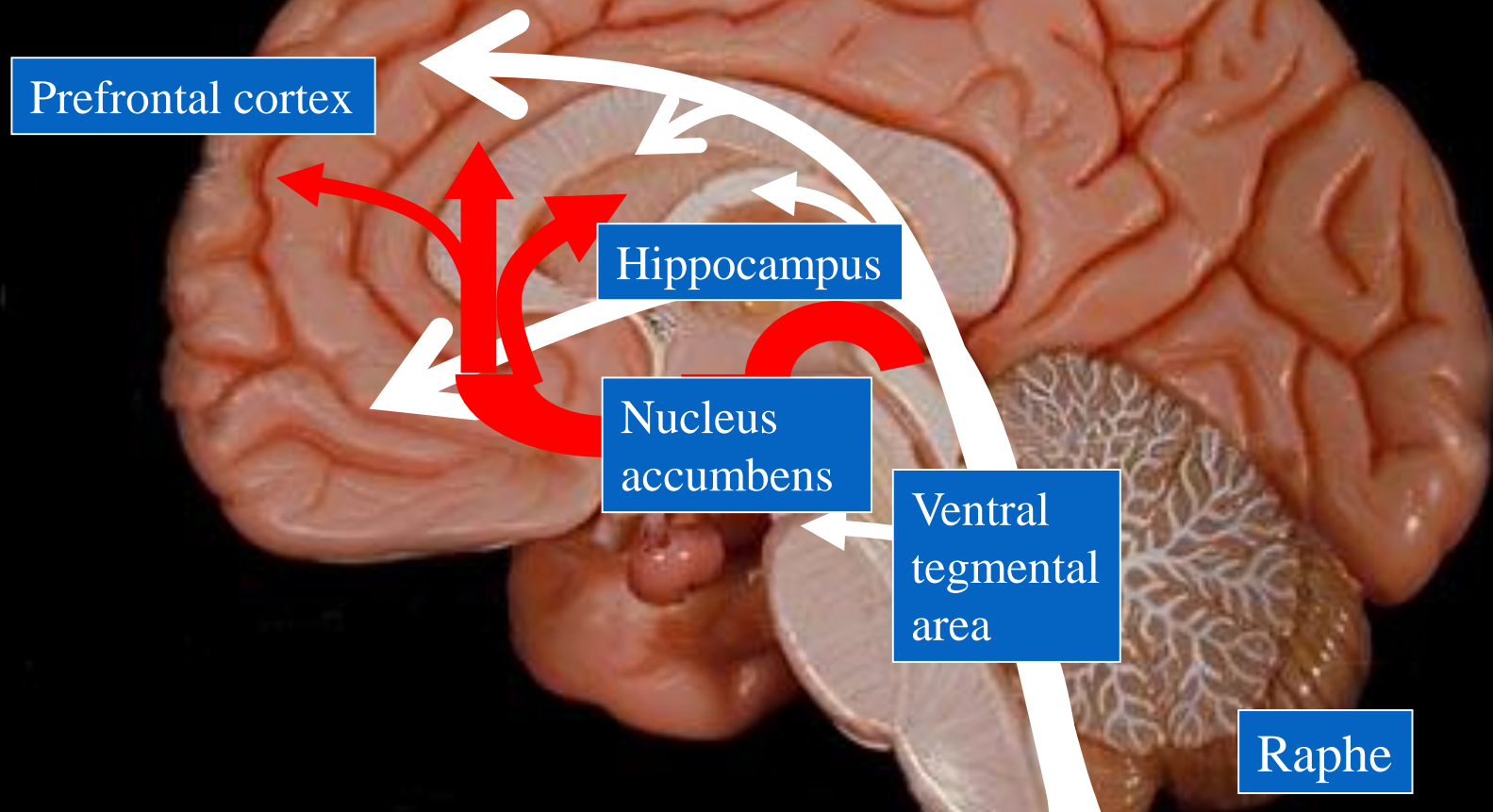
**Emotional responses: fear  
and anger**

## **Hippocampus**

**Forms Memories  
Coordinates thinking processes**



# Dopamine Pathways: Reward, Pleasure, Euphoria, Motor Function, Decision making



Serotonin Pathways: Mood, Memory, Sleep, Cognition

# Reward Pathway

- There is a axonal network in the brain labeled the 'reward pathway'
- This reward pathway is activated by:
  - Food, water and sex, activities (such as sky diving, paragliding etc) and exercise

*This reward pathway is also activated by drugs and alcohol*

# Reward Pathway

The following neurotransmitters act on the reward pathway:

<b>Dopamine</b> <ul style="list-style-type: none"><li>•Receptors: D1, D2</li><li>•Function: pleasure, euphoria, mood, motor function</li></ul>	<b>Serotonin</b> <ul style="list-style-type: none"><li>•Receptors: 5HT3</li><li>•Function: mood, impulsivity, anxiety, sleep, cognition</li></ul>
<b>Cannabinoids</b> <ul style="list-style-type: none"><li>•Receptors: CB1, CB2</li><li>•Function: Pain, appetite, memory</li></ul>	<b>Opioid peptides (Endorphins, Enkephalins)</b> <ul style="list-style-type: none"><li>•Receptors: Kappa, Mu, Delta</li><li>•Function: pain</li></ul>

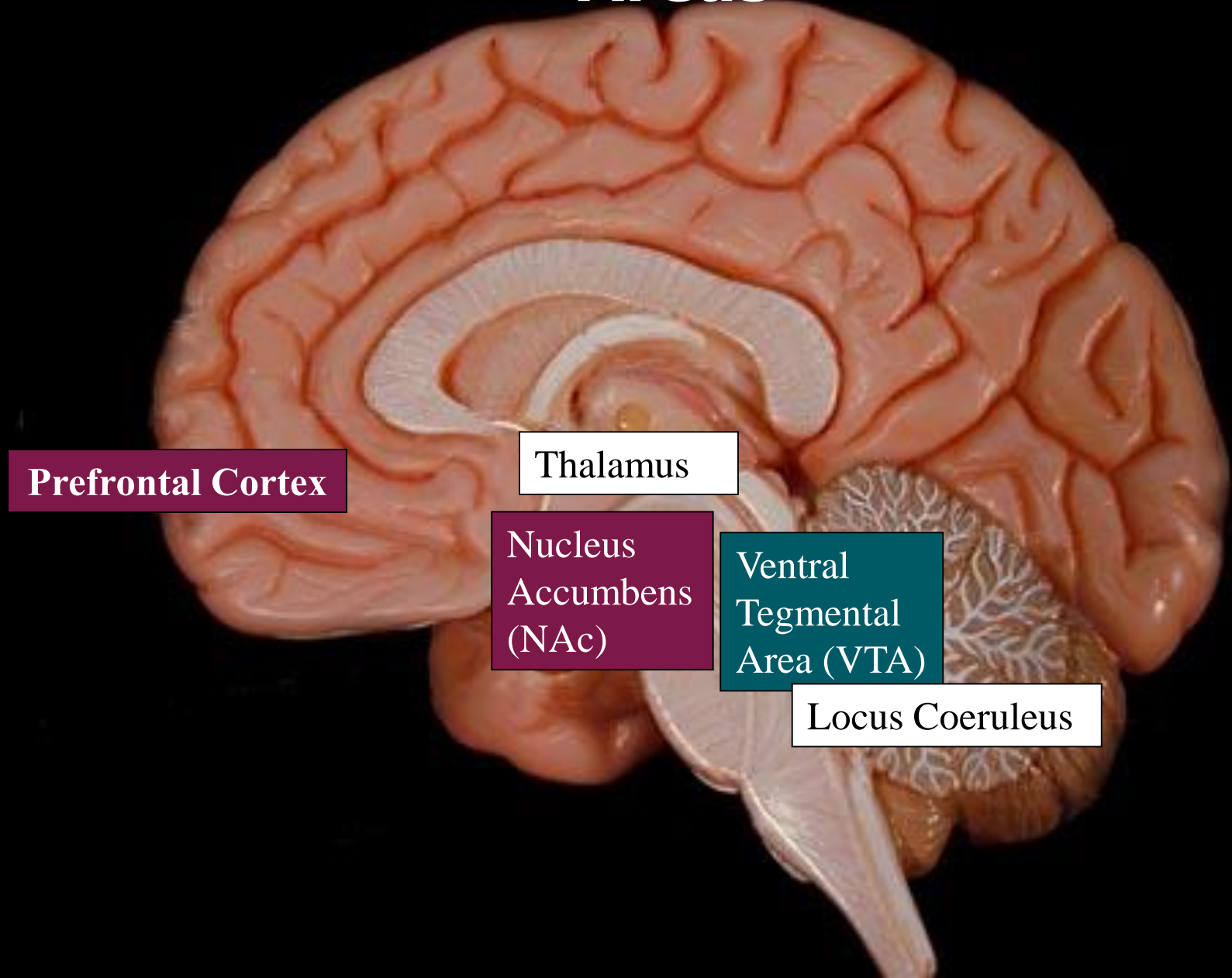
In all rewards, dopamine is the final activation chemical

# Reward Pathway

Neurotransmitters and anatomical sites involved in the acute reinforcing effects of drugs of abuse

<b>Dopamine</b>  Ventral tegmental area, nucleus accumbens	<b>Opioid Peptides</b>  Nucleus accumbens, amygdala, ventral tegmental area
<b>GABA</b>  Amygdala, bed nucleus of stria terminalis	<b>Glutamate</b>  Nucleus accumbens

# Reward Pathway: Brain Areas



# Drug Action & Reward Pathway

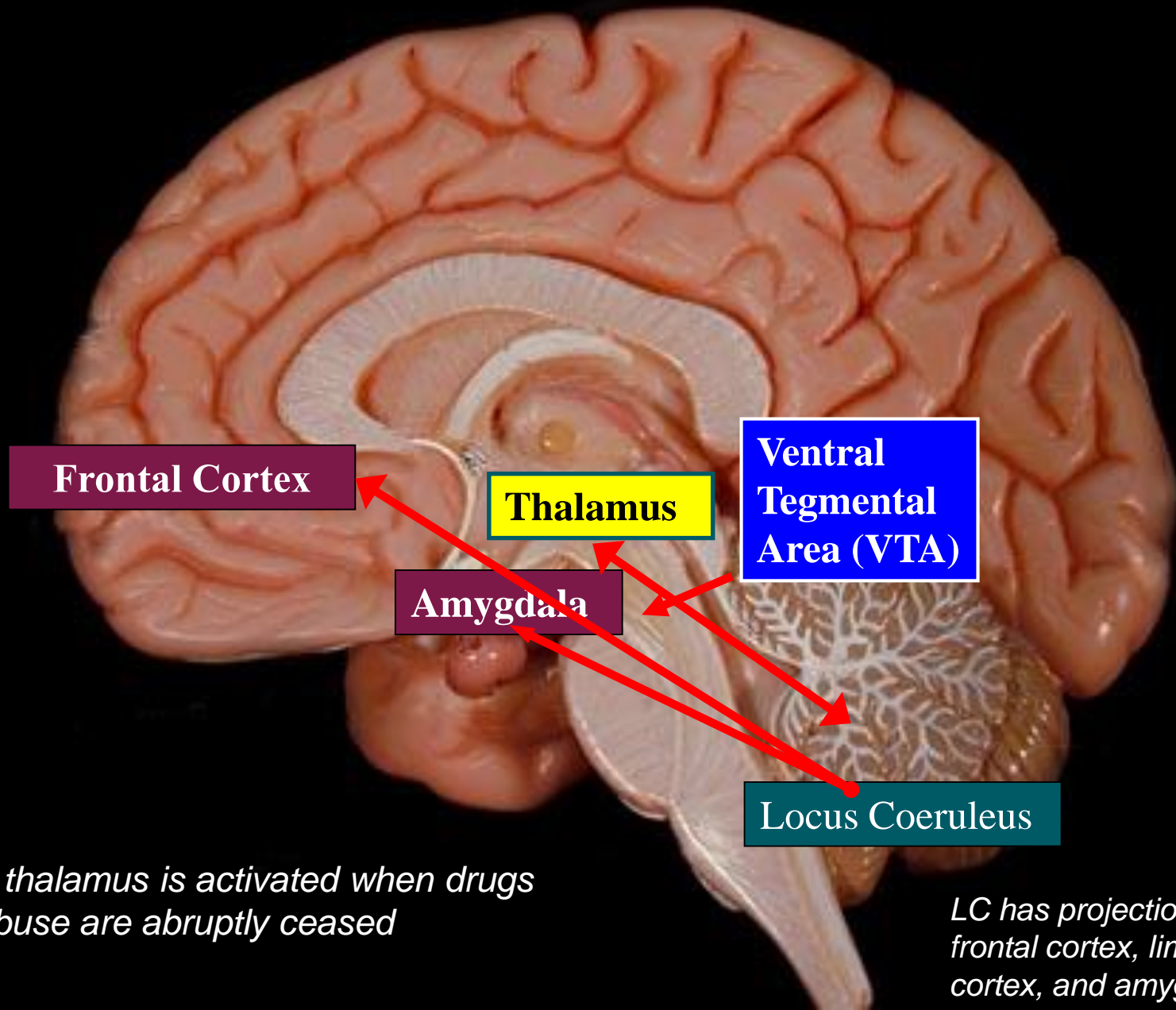
*In summary:*

<b>Alcohol</b> <ul style="list-style-type: none"><li>• Inhibit GABAergic neurons that project to dopaminergic neurons in the VTA</li></ul>	<b>Heroin</b> <ul style="list-style-type: none"><li>• Binds to opioid receptors that inhibit GABAergic neurons that project to dopaminergic neurons in the VTA</li></ul>
<b>Cocaine</b> <ul style="list-style-type: none"><li>• Blocks the function of DAT (by binding to the DAT and slowing transport)</li></ul>	<b>Nicotine</b> <ul style="list-style-type: none"><li>• Activates cholinergic neurons that project to dopaminergic neurons of the VTA</li></ul>

# Withdrawal

- Following a physiological adaptation to the presence of an agent (e.g. drug of abuse), tolerance occurs
- Withdrawal is the result of an abrupt cessation of the drug
- This syndrome involves:
  - disturbance of the autonomic nervous system
  - activation of the thalamus
  - release of corticotrophin releasing factor (CRF)
  - activation of the locus coeruleus (LC)

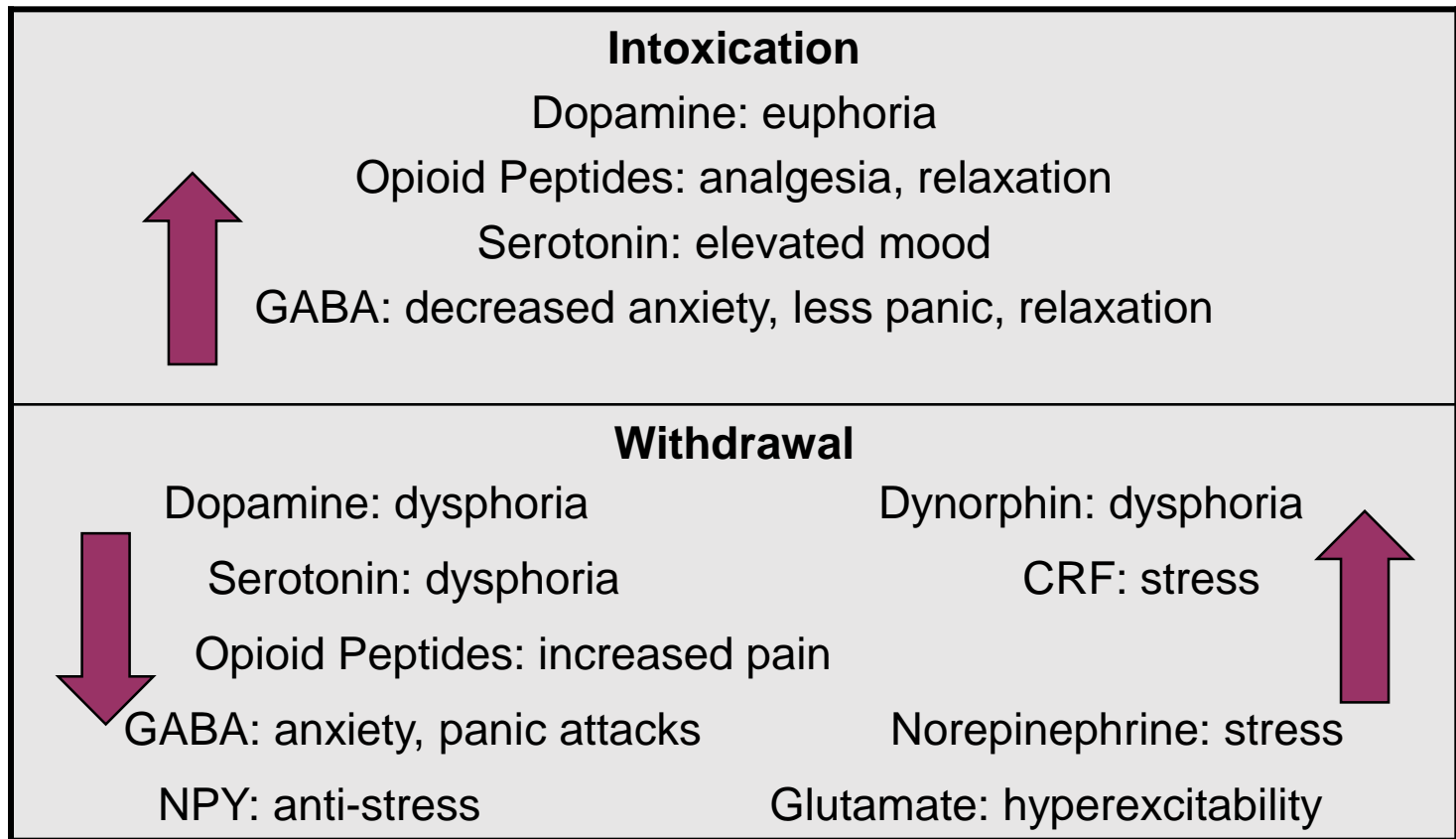
# Withdrawal: Brain Areas



*The thalamus is activated when drugs of abuse are abruptly ceased*

*LC has projections to frontal cortex, limbic cortex, and amygdala*

# Intoxication & Withdrawal: Neurotransmitter Involvement



*Person feels dysphoric, irritable, depressed and angry*

# The Development of Addiction

- The use of the drug of abuse is increased to maintain euphoria or to avoid dysphoria or withdrawal
- The number of receptors gradually increases to counter for the continual presence of the drug of abuse
- The amount of neurotransmitter gradually decreases through *depletion* and *feedback inhibition*
- The reinforcing properties of the drug are thus gradually decreased (tolerance)
- The need for drug to maintain this new homeostasis is therefore increased (dependence begins)

# The Development of Addiction

- The resulting behaviours activate the reward pathway and a relationship is developed and becomes dominant.
- Behavioral repertoire is narrowed and eventually other important behaviors are ignored (e.g. familial, financial)
- The reward and cognitive (decision making systems) are compromised resulting in an imbalance in impulsive behaviours (e.g. violence, crime)

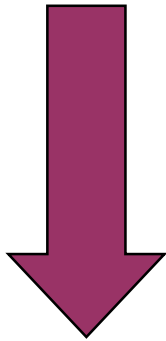
PFC

Amygdala  
NAc

*The neurobiology of the two  
dominant decision-making  
system is altered*

# The Development of Addiction: Long Term Changes

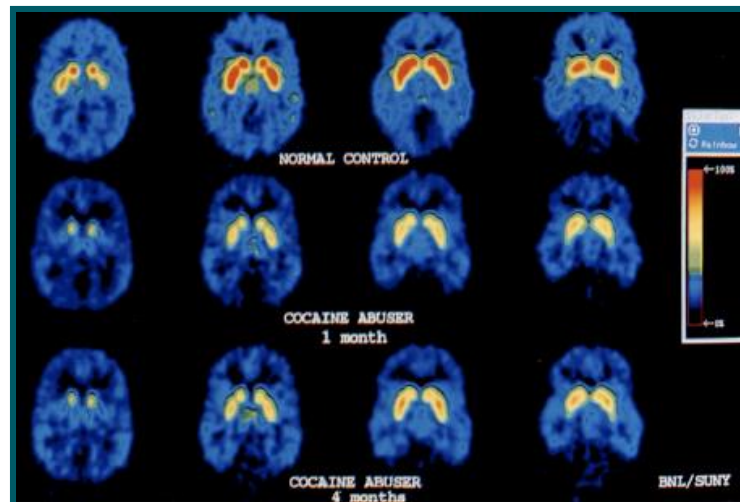
*There is evidence of prolonged drug abuse resulting in both structural and functional brain changes*



Decreases in CREB transcription factor in NAc (and extended amygdala)

Decreases in metabolism in Orbito Frontal Cortex (OFC)

Decreases in dopamine D2 receptor binding (see figure below)

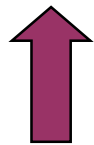


*Volkow et al.  
Synapse 14 (2), 1993, pp. 169-177. © 1993 Synapse.  
Reprinted with permission of  
John Wiley & Sons, Inc.*

# The Development of Addiction: Genetics

Inheritability has been found to range from 40-60%  
Some variability between: gender and substances

*Specifically:*



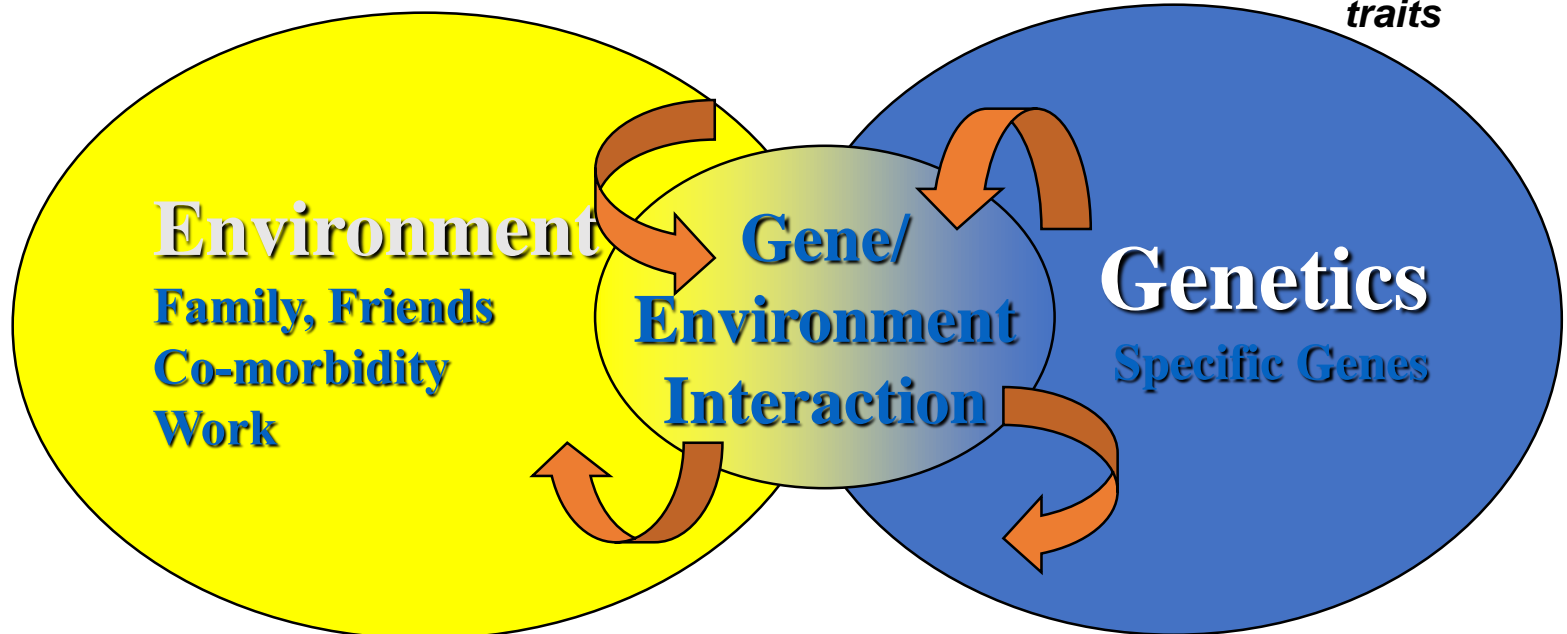
4-fold increased risk in 1st degree relatives



4-fold increased risk also in adopted away children

# The Development of Addiction: Genetics

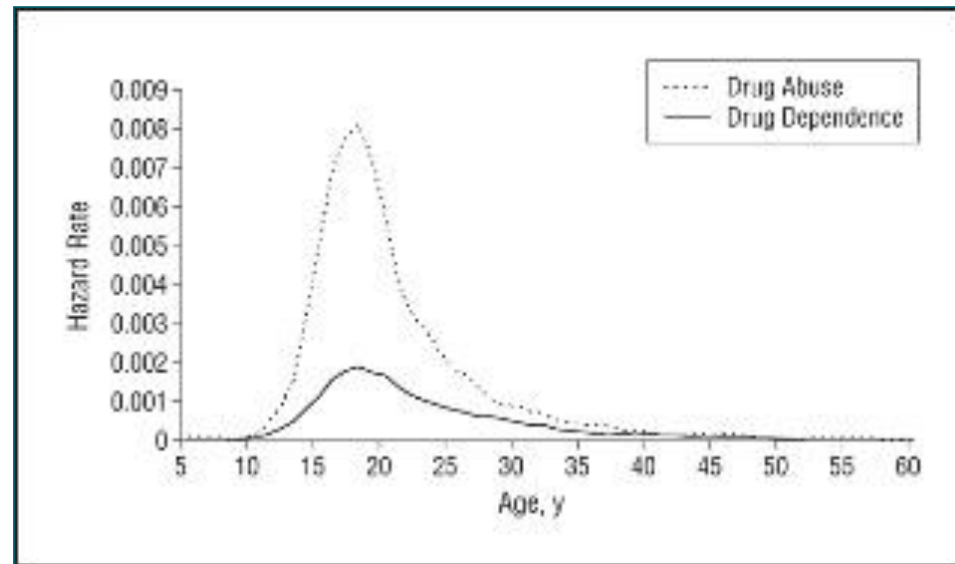
*However,  
behaviors are  
complex genetic  
traits*



**Genetics May Influence How Neurobiology Interacts With  
Environment**

# The Development of Addiction: Adolescence

*Drug and alcohol problems commence in adolescence*



*Compton et al, 2007, Arch Gen Psychiatry, 64.  
Reprinted with permission*

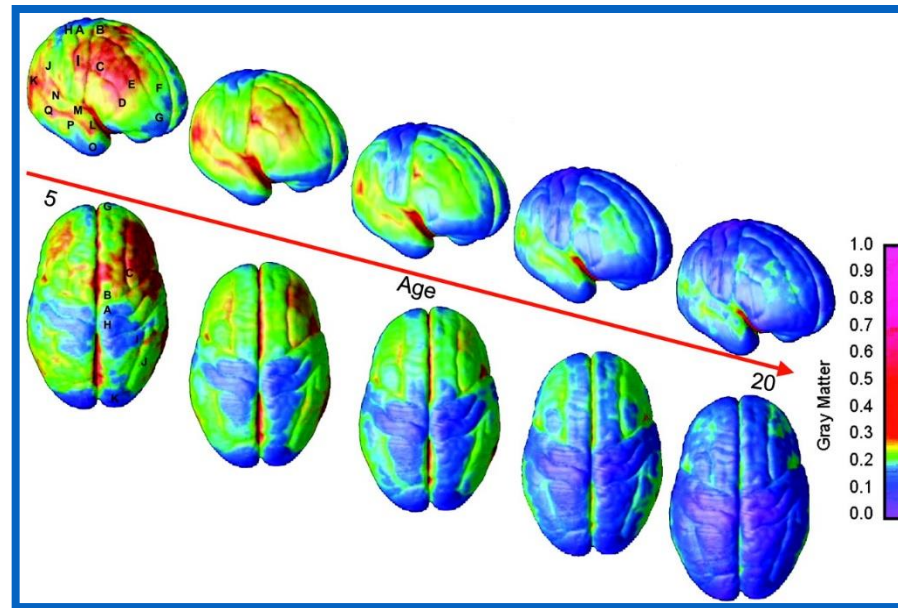
# The Development of Addiction: Adolescence

## *Neuronal Development*

- The back of brain matures first...
  - sensory and physical activities favoured over complex, cognitive-demanding activities
  - propensity toward risky, impulsive behaviors
    - group setting may promote risk taking
  - poor planning and judgment

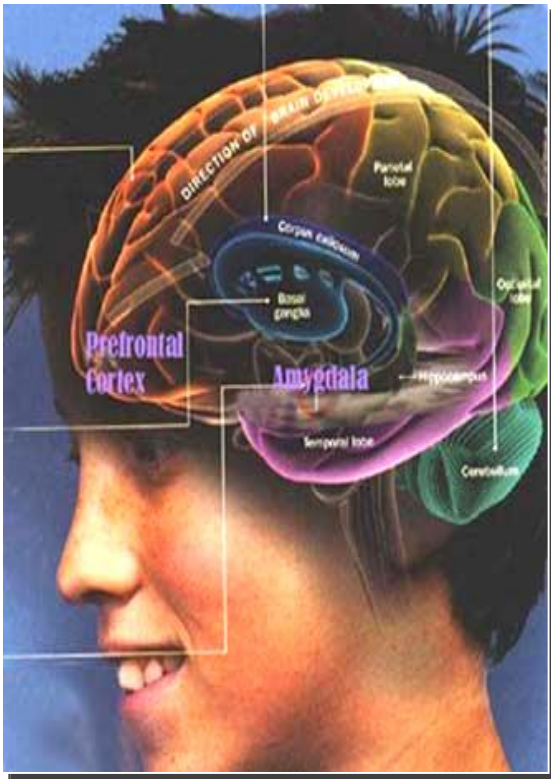
# The Development of Addiction: Adolescence

***Neuronal Development:*** Grey matter maturation moves from back to front



Gogtay et al (2004) PNAS, 101 (21). Copyright 2004, National Academy of Science, U.S.A.

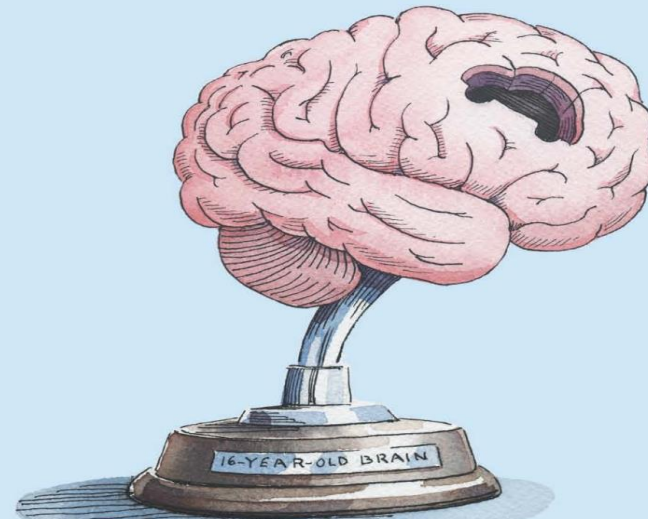
# The Adolescent Brain – “A Work in Progress”



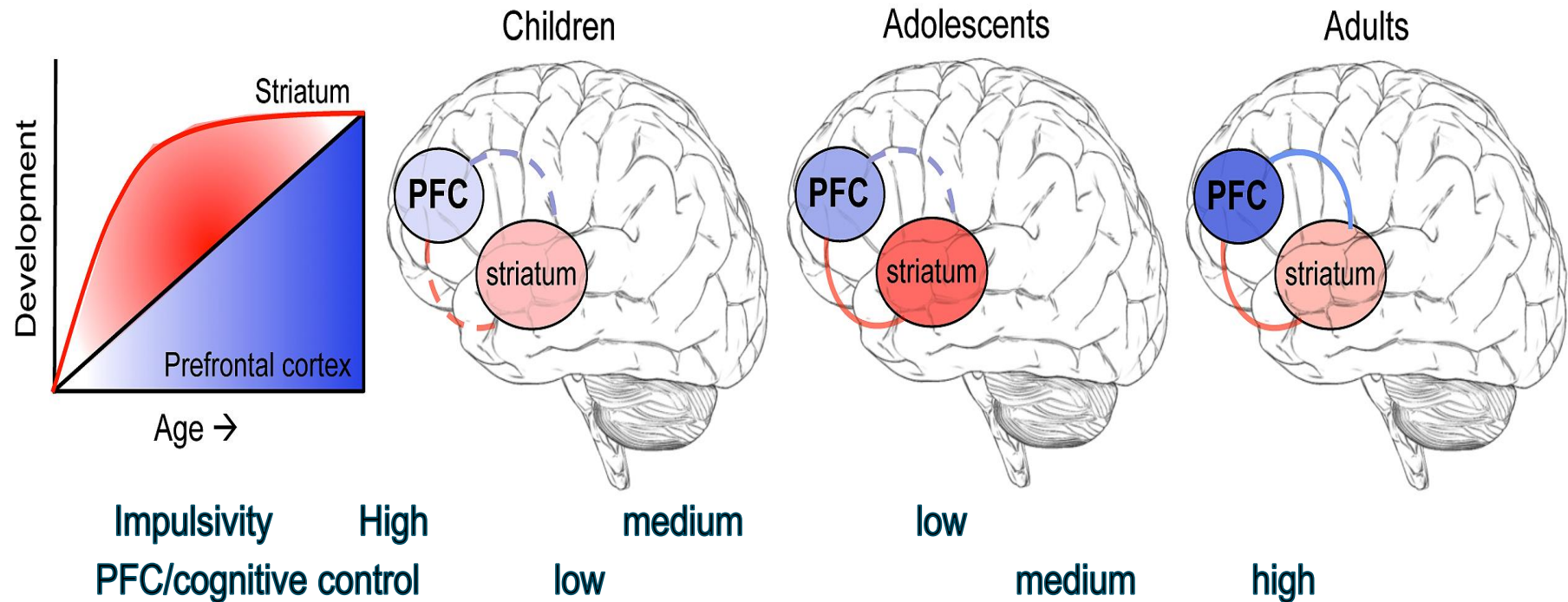
Why do most 16-year-olds  
drive like they're  
*missing a part of their brain?*



BECAUSE THEY ARE.



# Adolescent Brain Development

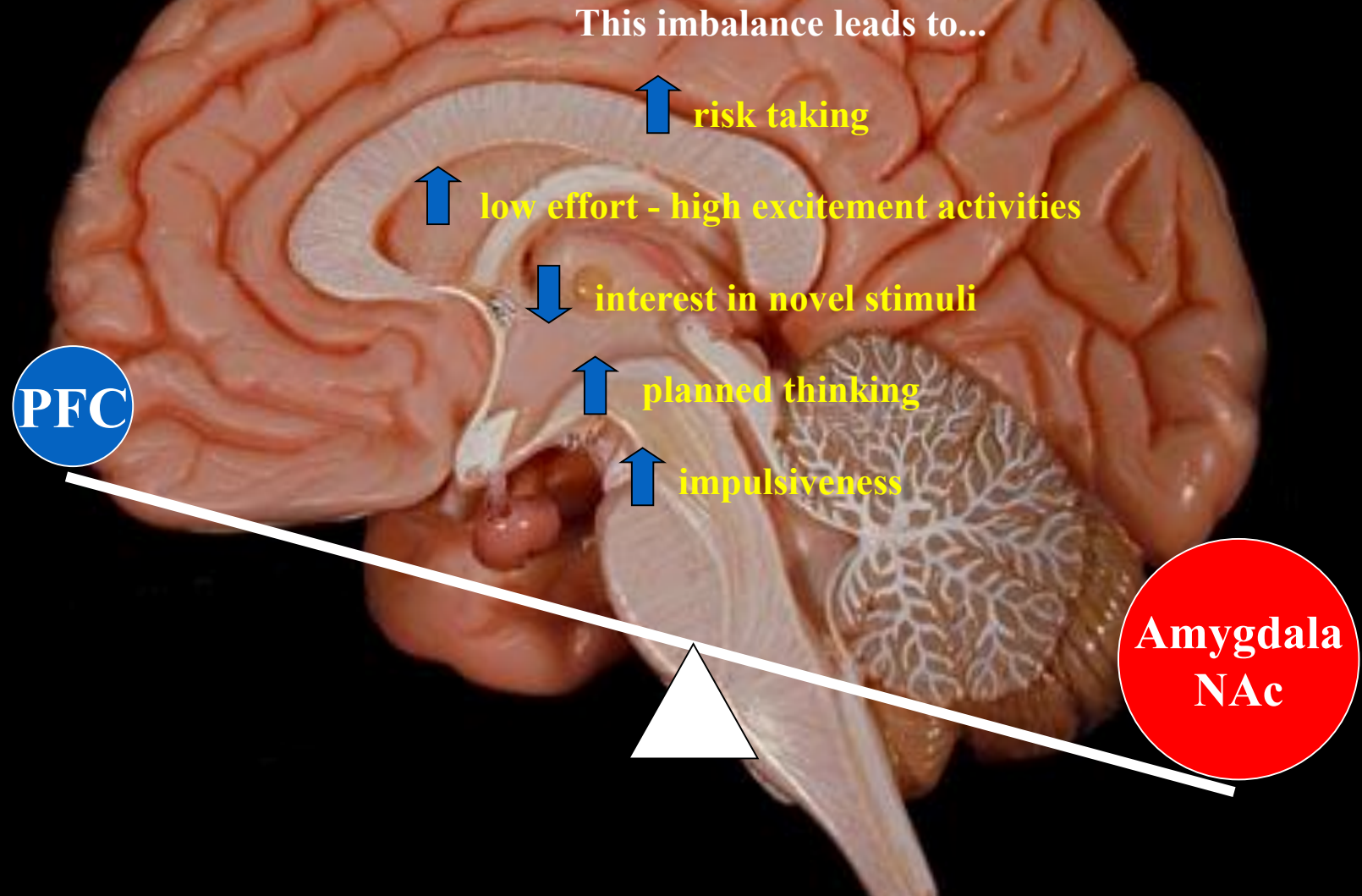


- “ what teens do during their adolescent years – whether it's playing sports or playing video games – can affect how their brains develop”

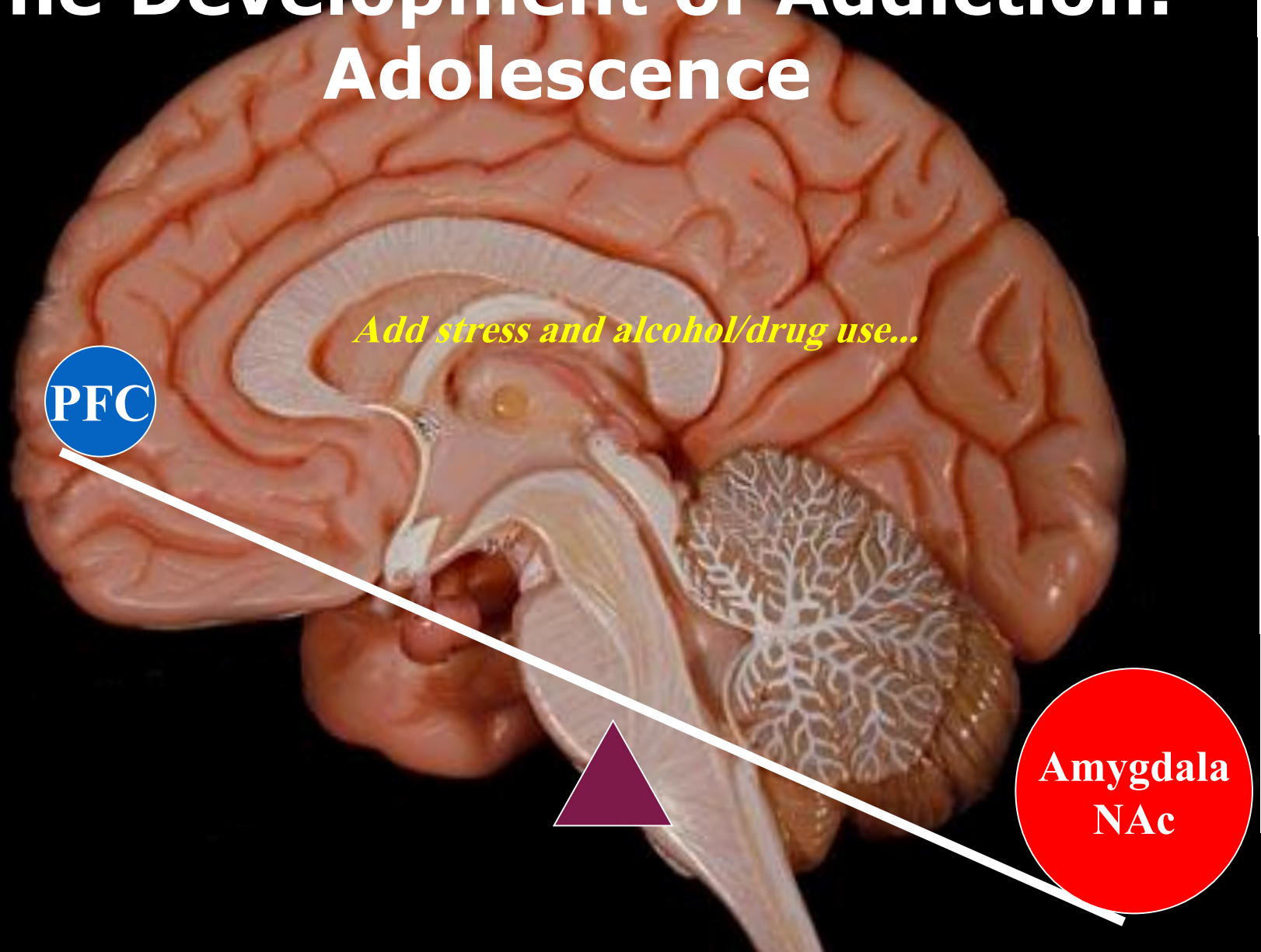
--J Giedd

- Environment and activities during teenage years guide selective synapse elimination (“pruning”) during critical period of adolescent development

# The Development of Addiction: Adolescence

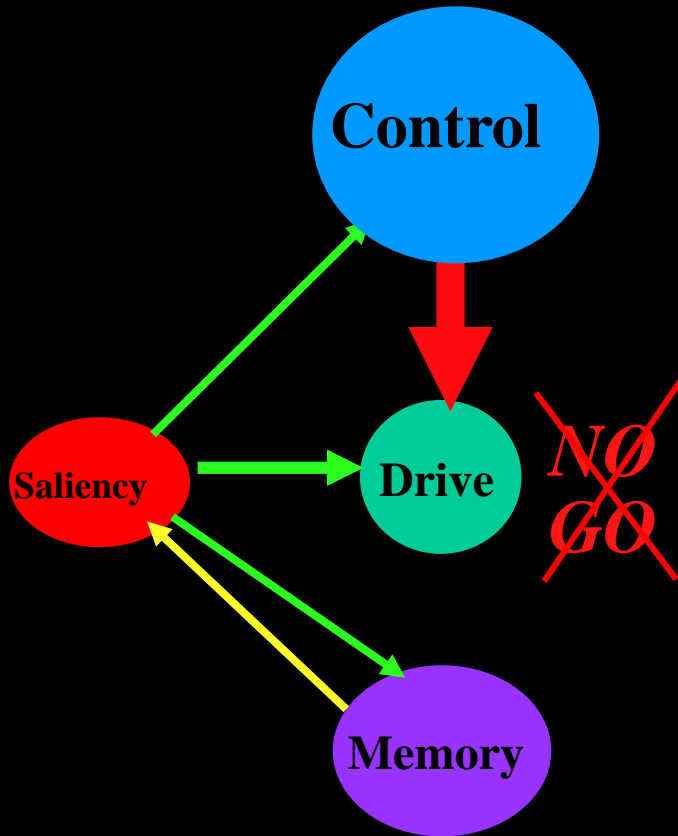


# The Development of Addiction: Adolescence

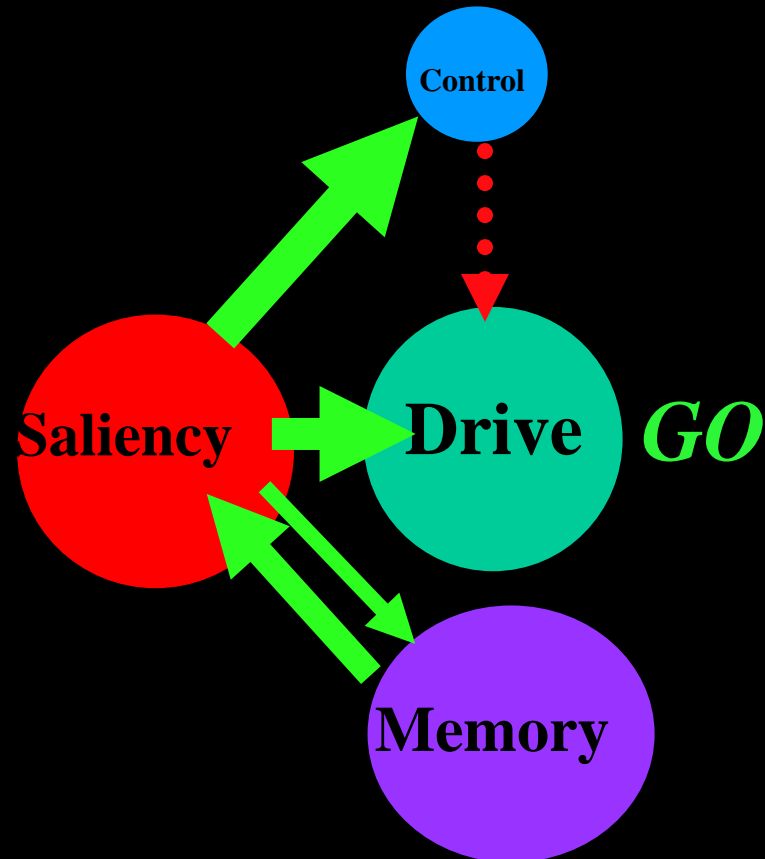


# Why Can't People with SUDs Just Quit?

Non-Addicted Brain



Addicted Brain



## Because Addiction Changes Brain Circuits

# Four “C’s” of SUDs

- Control
  - Early social/recreational use
  - Eventual loss of control
  - Cognitive distortions
- Compulsion
  - Drug-Seeking activities
  - Continued use despite adverse consequences
- Chronicity
  - Natural history is of multiple relapses preceding stable recovery
  - Relapse after years of sobriety is possible
- Craving
- Consequences

# Hitting Bottom

- What is this concept about?
- “Treatment resistant people”
- Putting off treatment
- Denial vs Ambivalence as integral to the process of change
- Use of coercion in addiction treatment
- Irony with the whole concept: Addiction is a chronic and VERY treatable illness;
- People with diabetes and asthma need to “hit rock bottom” to have treatment for their illness to be successful?
- What is the scientific evidence?

# Other Deadly Myths

- Brain and addiction
- Enough “determination” and “willpower” should help people with addictions quit using
- What about tough love?
- Lapse and Relapse = Failure
- Using a drug (medication) to treat a drug problem does not work
- Gateway drugs?
- Addiction gene and addictive personality?
- Drugs damage your brain permanently ?
- Addiction is a “career” for life?

# Too Many Myths to Debunk!

- Treatment doesn't work
- “Addicts” are bad, crazy, stupid, lack of moral fiber—  
“Addicts and Alcoholics” are “separate class” of people!
- There is an addictive personality: NO

## In Fact, It's Even Worse!

- Stigma (against the illness and the person with addiction)
- Prejudice (against the person with addiction)
- Anger and lack of empathy (toward the person with addiction )
- Misunderstanding (about what to do and how to help)

# Facts of Addiction Treatment

- Addiction is a brain disorder
- Chronic medical illnesses, “cancerous” disorders require multiple strategies and multiple episodes of intervention
- Treatment works in the long run
- Treatment is cost-effective

# Treatment of Addiction

*Treatments incorporate medications + Psychosocial interventions + mutual support groups (12-step programs)*

## **Novel medications:**

- Alcohol use disorder:

**Naltrexone:** blocks mu opioid receptor (reduces the rewarding effects of alcohol)

**Acamprosate:** inhibits the release of glutamate thus decreasing excitation (withdrawal) that occurs during withdrawal

# Treatment of Addiction

*Novel medications continued:*

- Opioid use disorder:

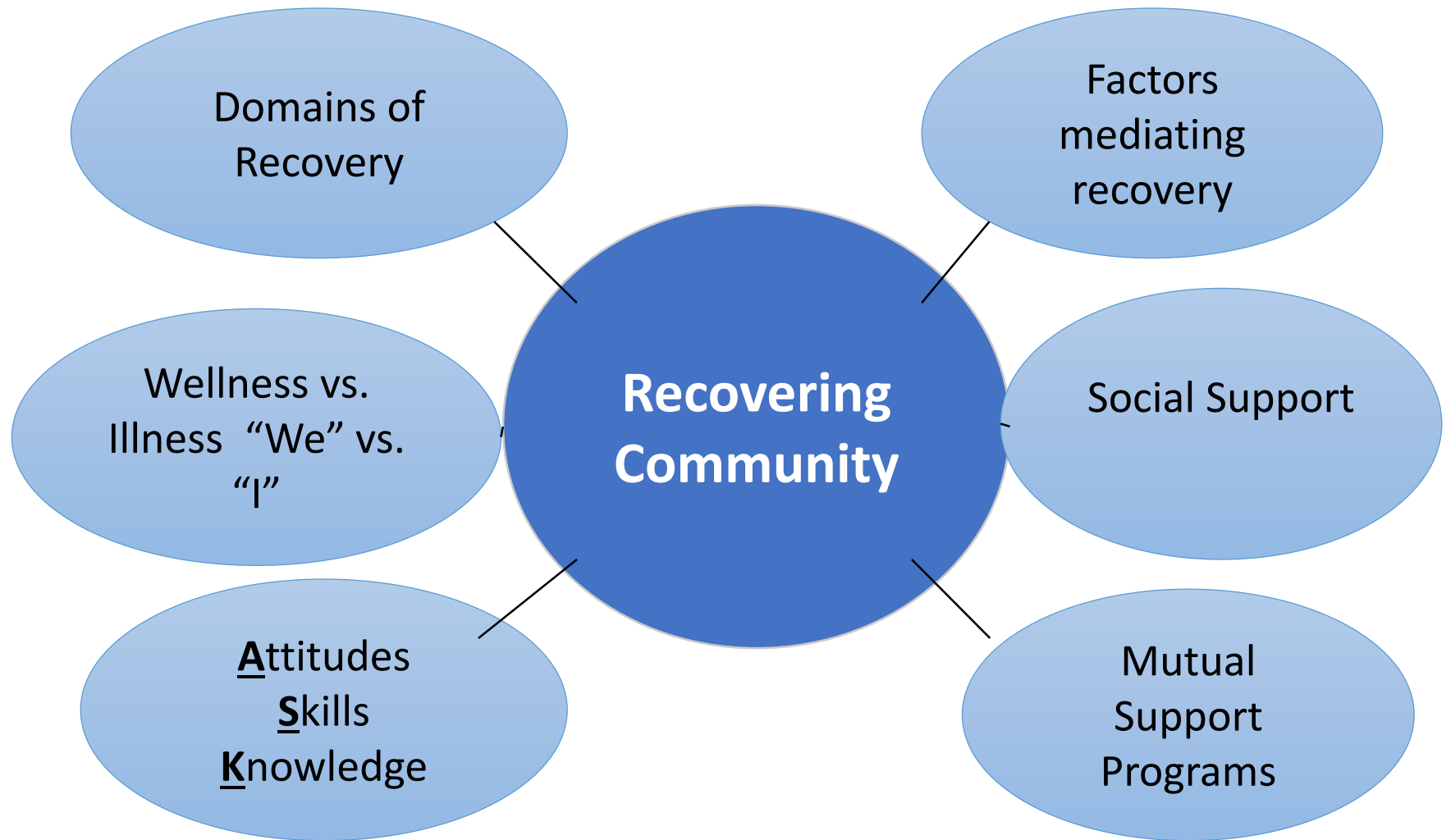
Methadone & buprenorphine: activate opioid receptors; naltrexone as opioid antagonist

- Tobacco use disorder:

NRT: activate nicotinic receptors; varenicline, and bupropion

# Addiction Is Multidimensional

- Addiction is influenced by many factors including biological (neurobiology), social (family, friends, work) and personal (psychological processes relating to addiction).
- Thus while the potential for addiction is related to neurobiology in some degree, situational (social circumstances) factors play a substantial role.
- Indeed, many people use alcohol and drugs and do not become addicted.



# Prevention, Treatment, & Recovery



## Continuum of Care Response



Thanks!