

Addiction & the Brain

Antoine Douaihy, MD

Professor of Psychiatry & Medicine

University of Pittsburgh School of Medicine

Senior Academic Director of Addiction Medicine Services

UPMC-Western Psychiatric Hospital

douaihya@upmc.edu

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:

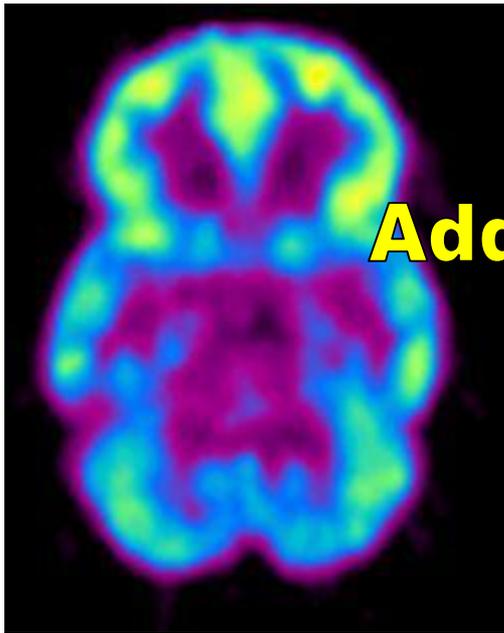
anxiety

worries

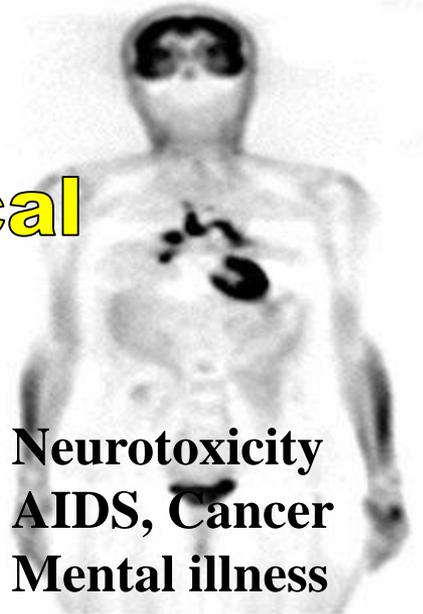
fears

depression

hopelessness



Addiction



Medical

**Neurotoxicity
AIDS, Cancer
Mental illness**

DRUGS



Social

**Homelessness
Crime
Violence**



Economic

**Health care
Productivity
Accidents**

Key Roles in Vulnerability



Estimated Economic Cost to Society Due to SUDs

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

& The Impact on Families & Children



MENTAL AND SUBSTANCE USE DISORDERS IN AMERICA: 2016

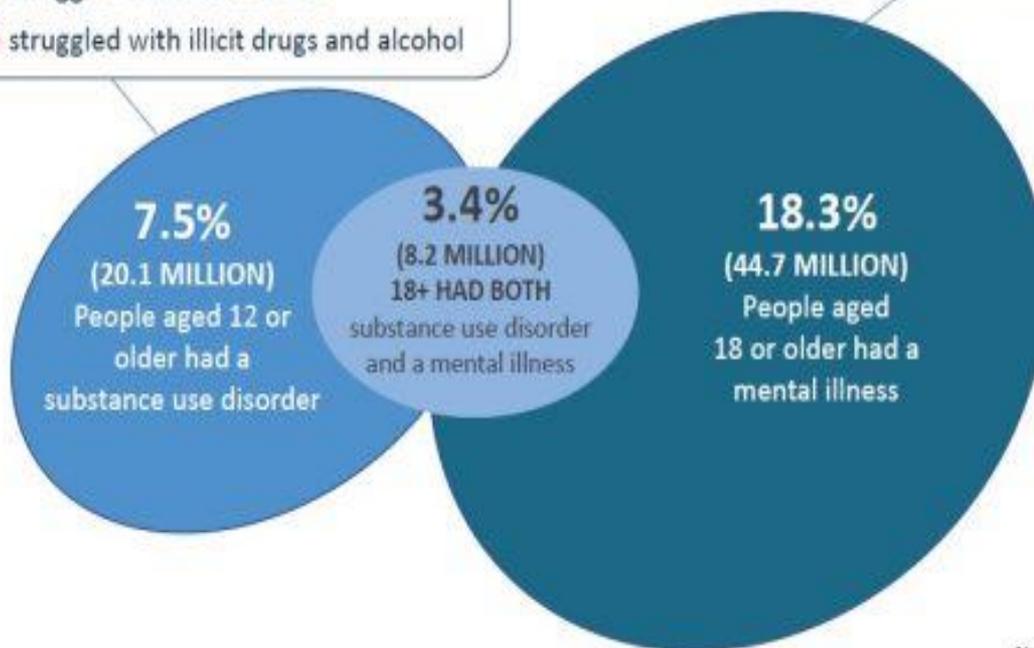
PAST YEAR, 2016, 12+

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:

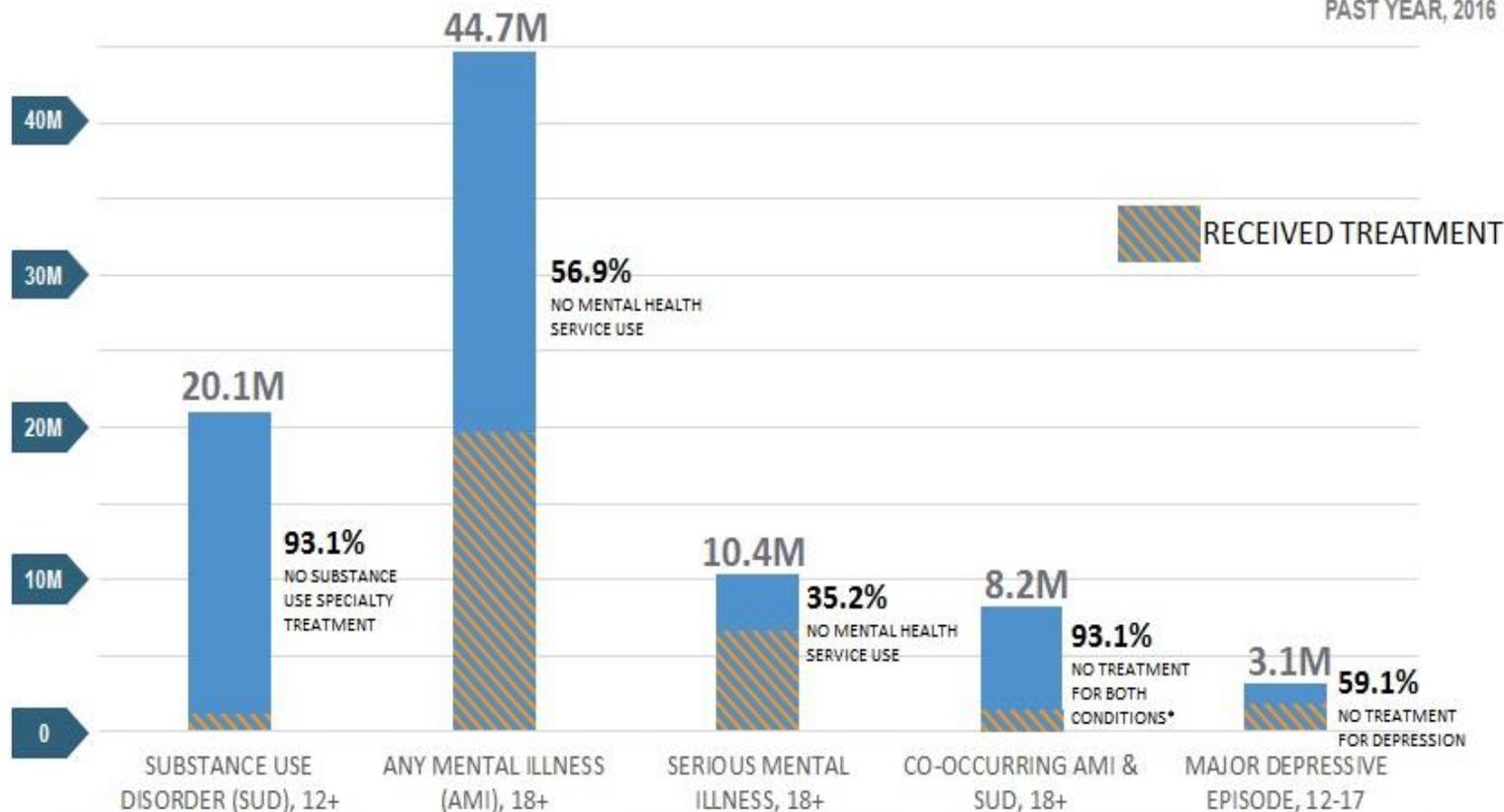
- 1 IN 4 (23%) had a serious mental illness



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

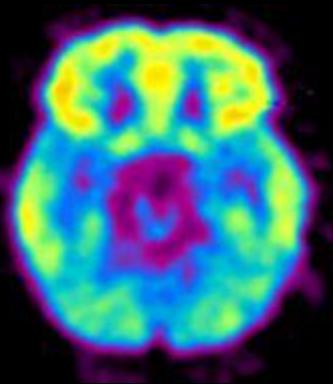


Addiction is Like Other Chronic Diseases...

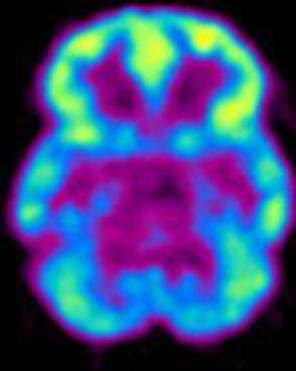
- It is preventable
- It is treatable
- It changes biology
- If untreated, it can last a lifetime
- Recurrence and recovery

Decreased Brain Metabolism
in *Drug User*

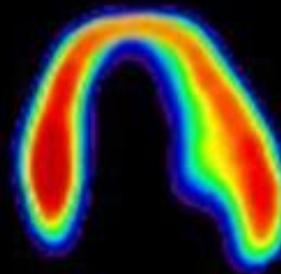
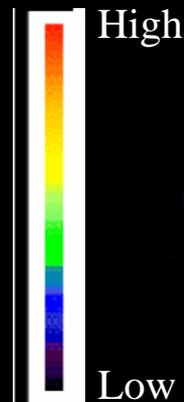
Decreased Heart Metabolism
in *Heart Disease Patient*



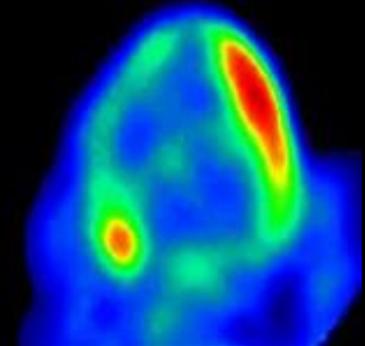
Healthy Brain



Diseased Brain/
Cocaine User



Healthy
Heart

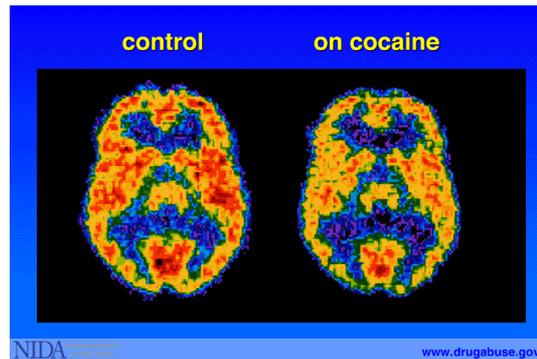


Diseased Heart

*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**

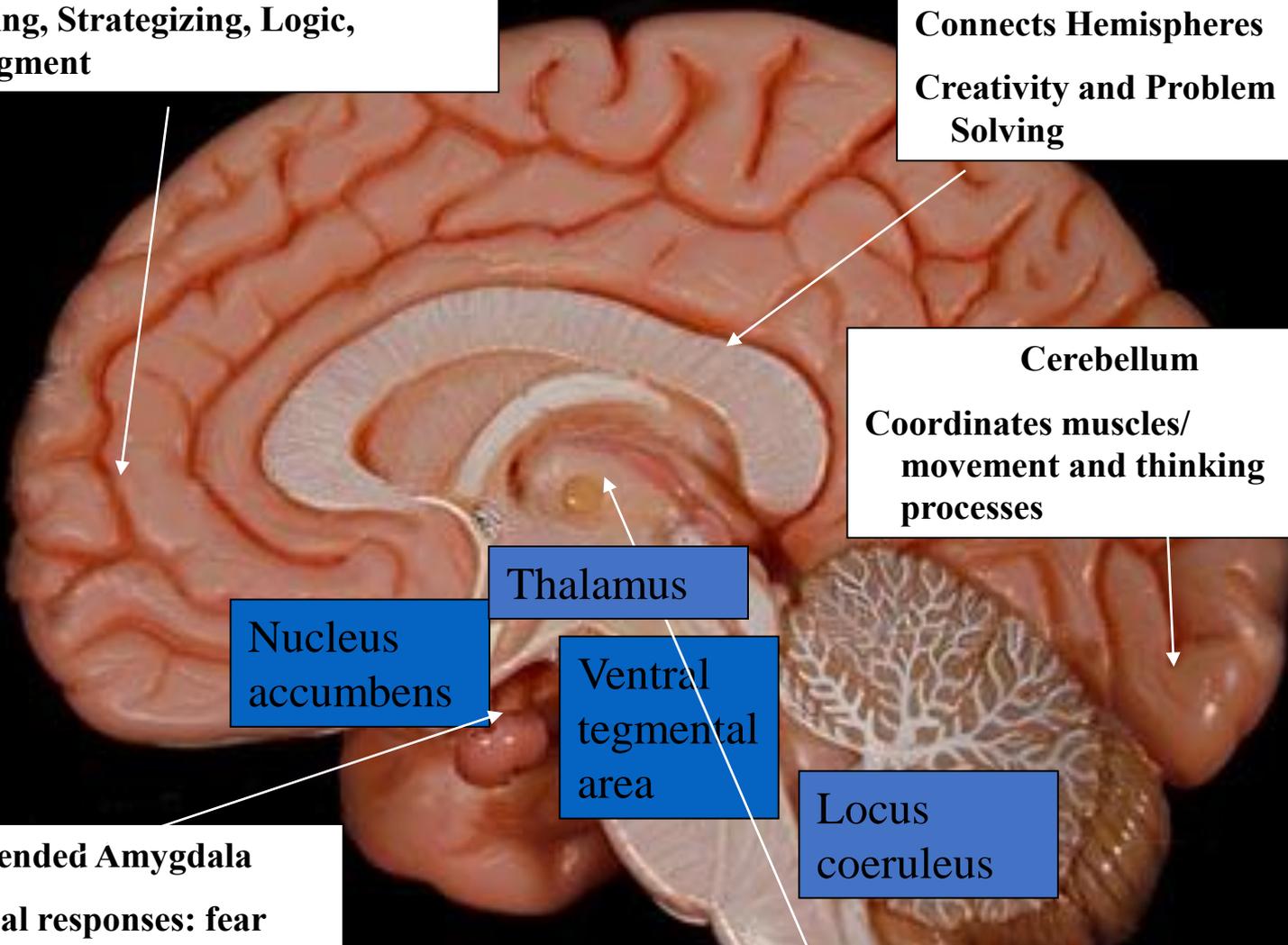
**Locus
coeruleus**

Extended Amygdala

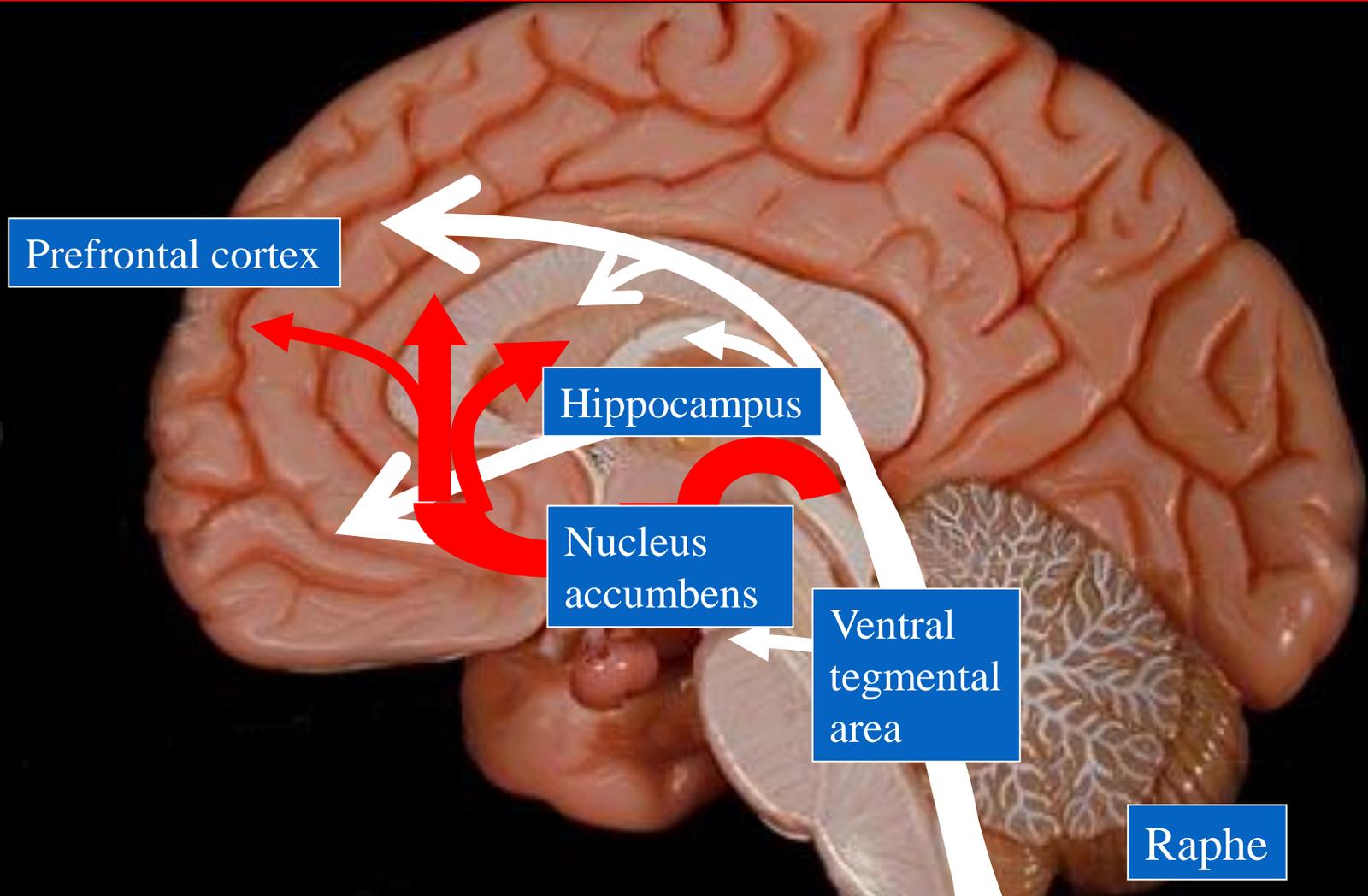
**Emotional responses: fear
and anger**

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:

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

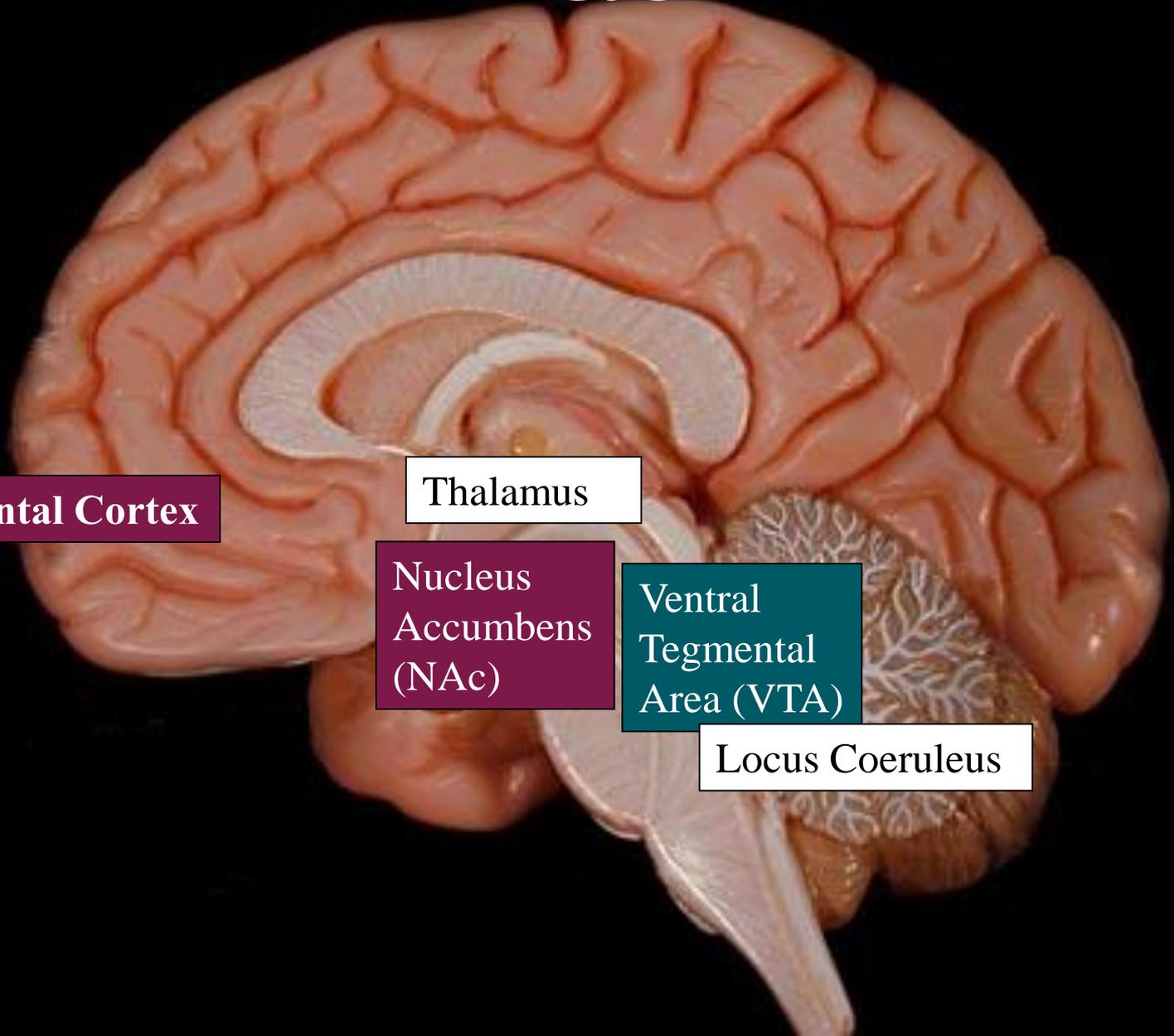
In all rewards, dopamine is the final activation chemical

Reward Pathway

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

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

Reward Pathway: Brain Areas



Prefrontal Cortex

Thalamus

Nucleus
Accumbens
(NAc)

Ventral
Tegmental
Area (VTA)

Locus Coeruleus

Drug Action & Reward Pathway

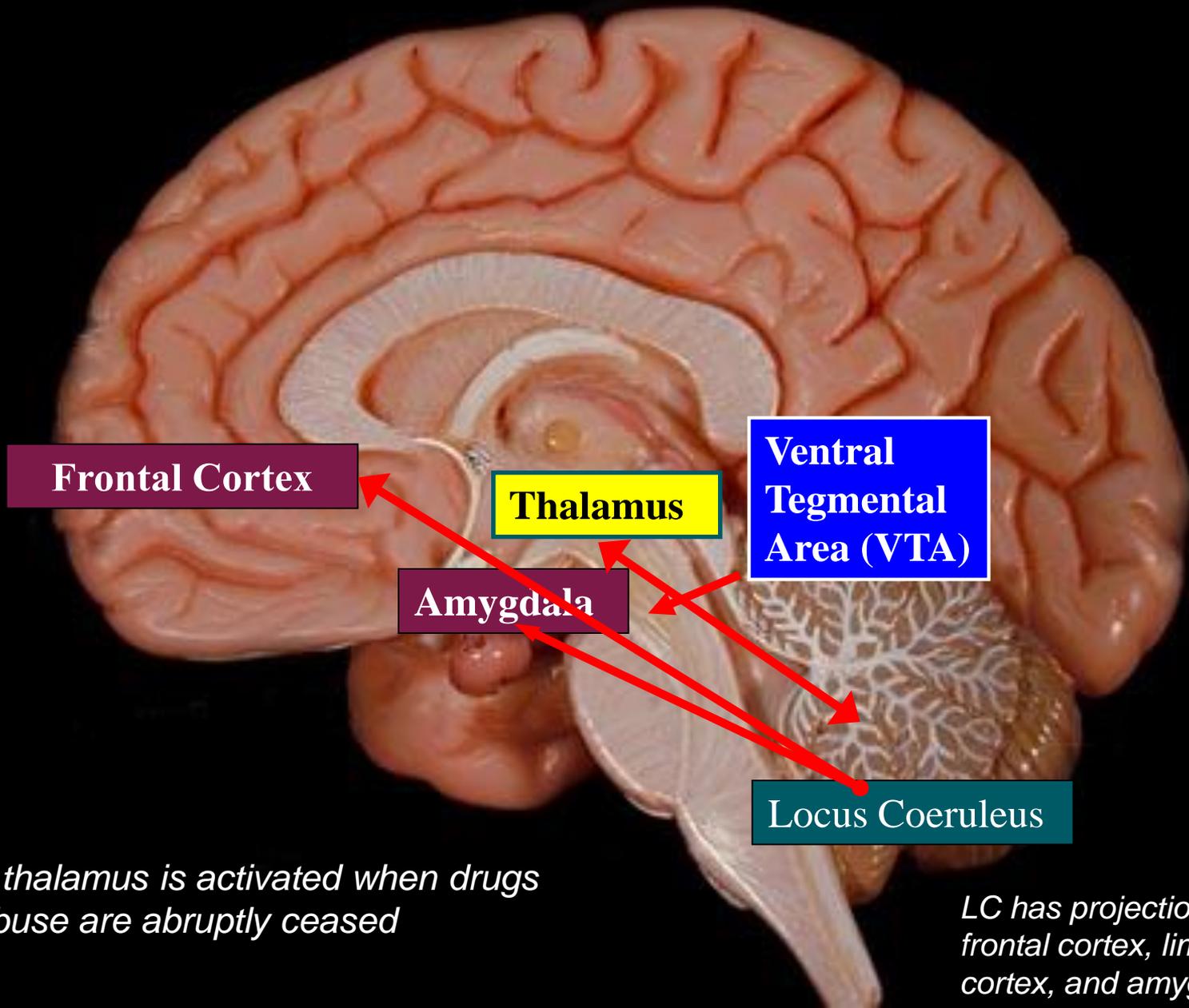
In summary:

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

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)

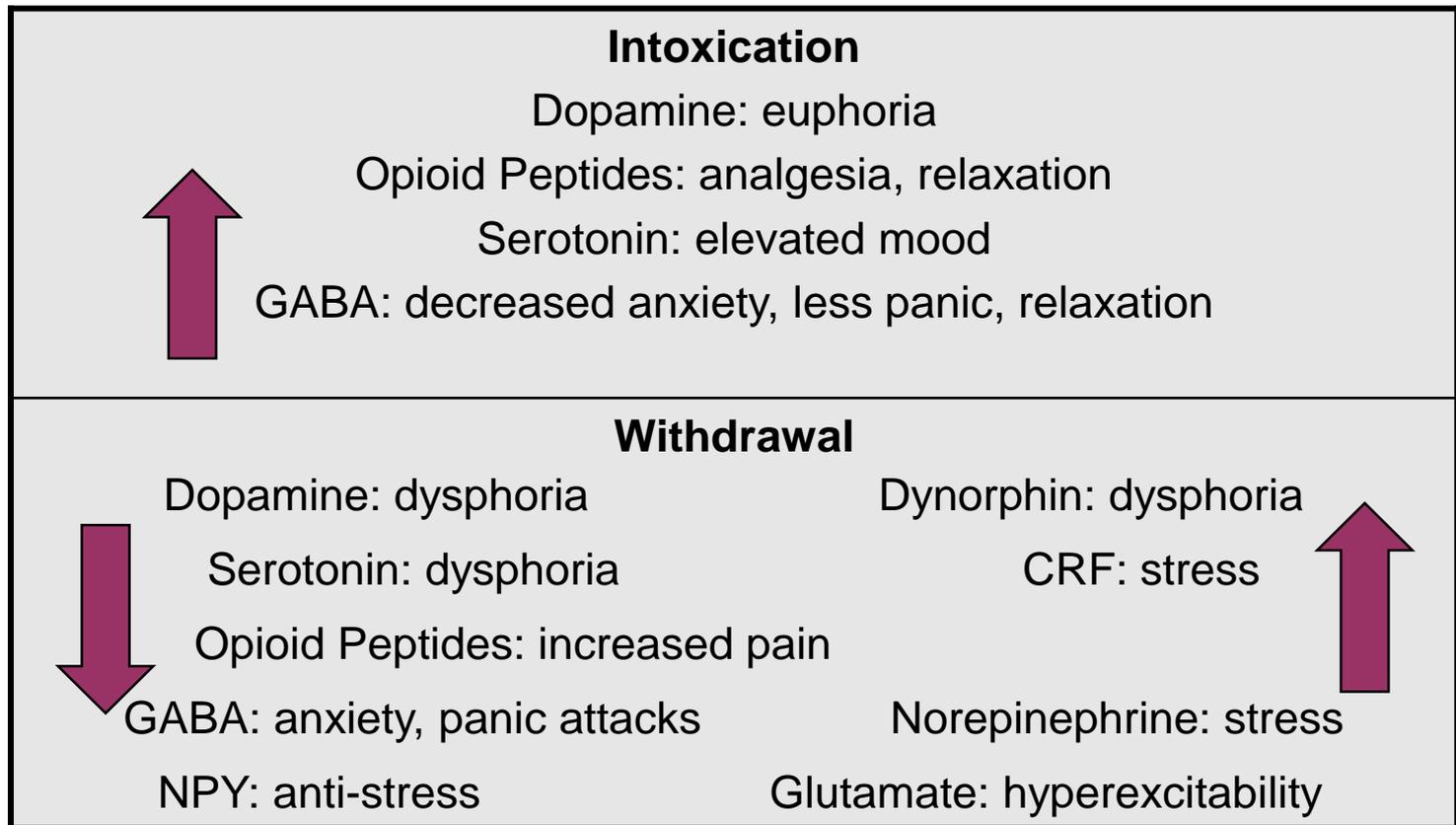
Withdrawal: Brain Areas



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)

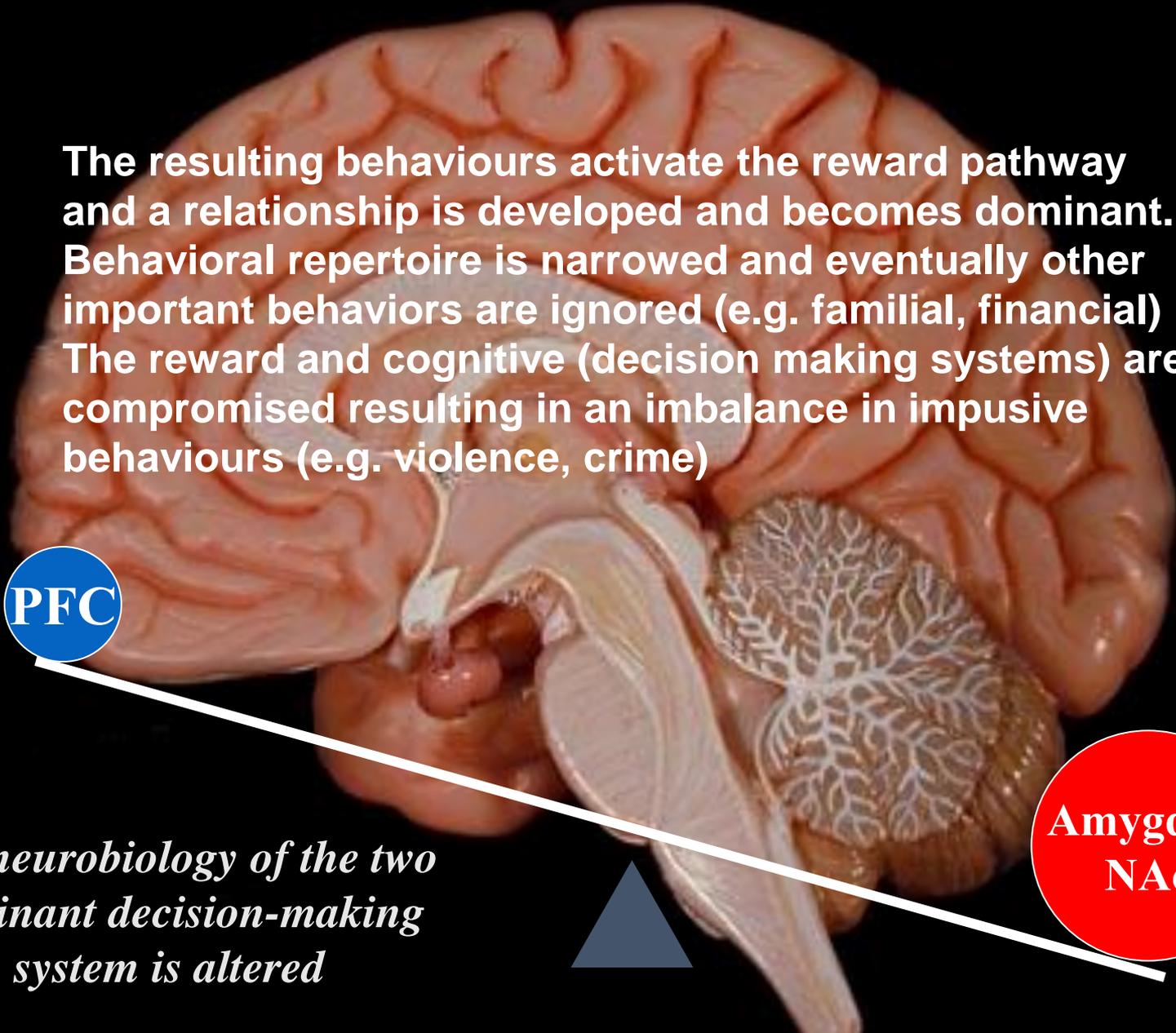
The Development of Addiction

- 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

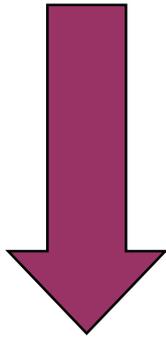
Amygdala
NAc

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



The Development of Addiction: Long Term Changes

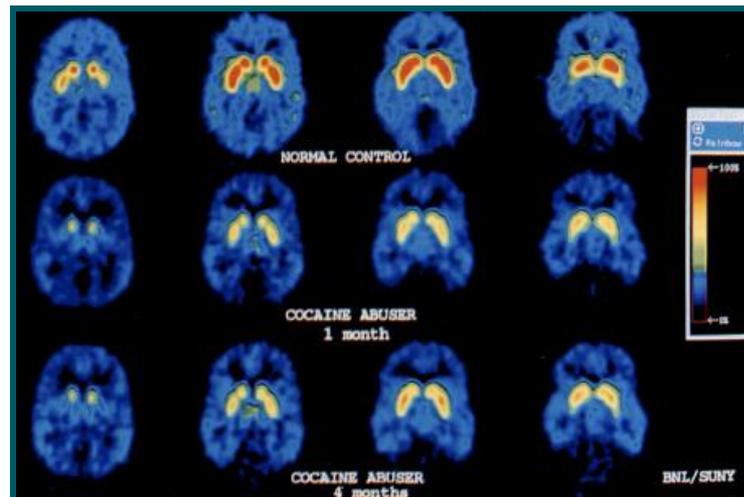
There is evidence of prolonged drug abuse resulting in both structural and functional brain changes



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:



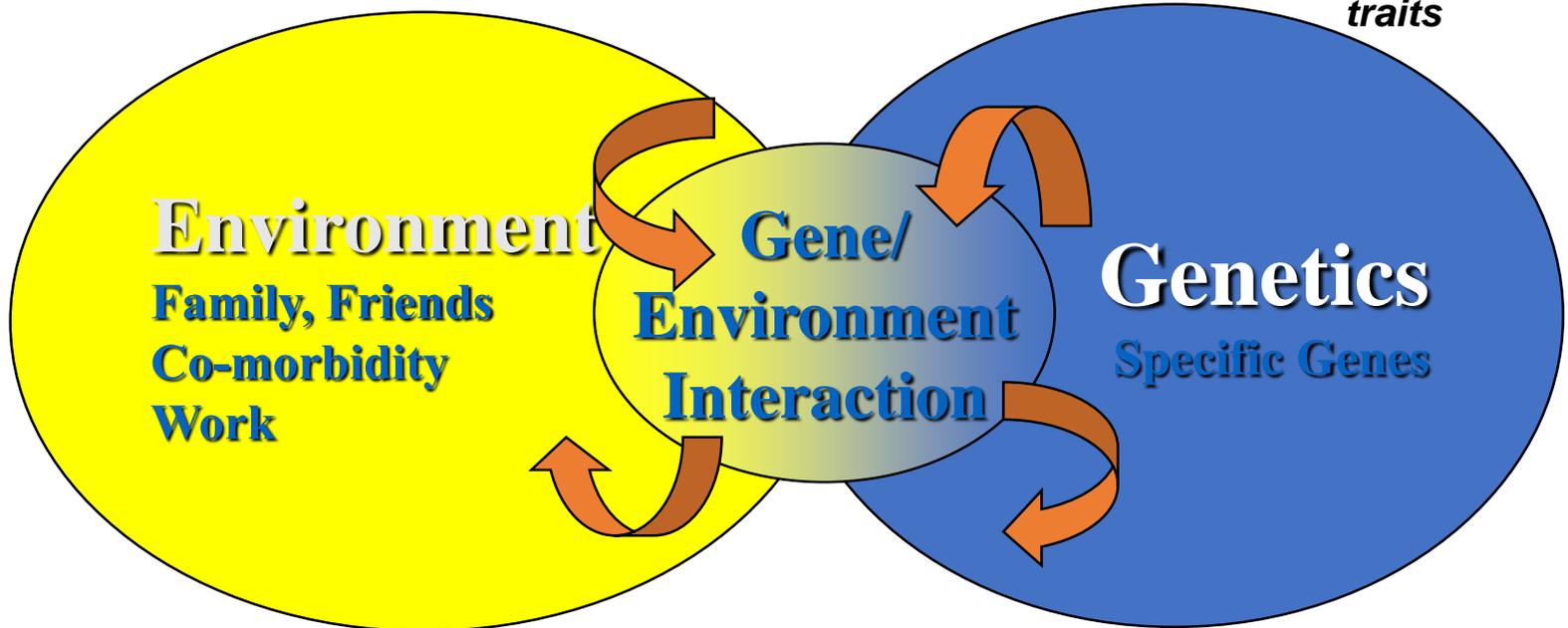
4-fold increased risk in 1st degree relatives



4-fold increased risk also in adopted away children

The Development of Addiction: Genetics

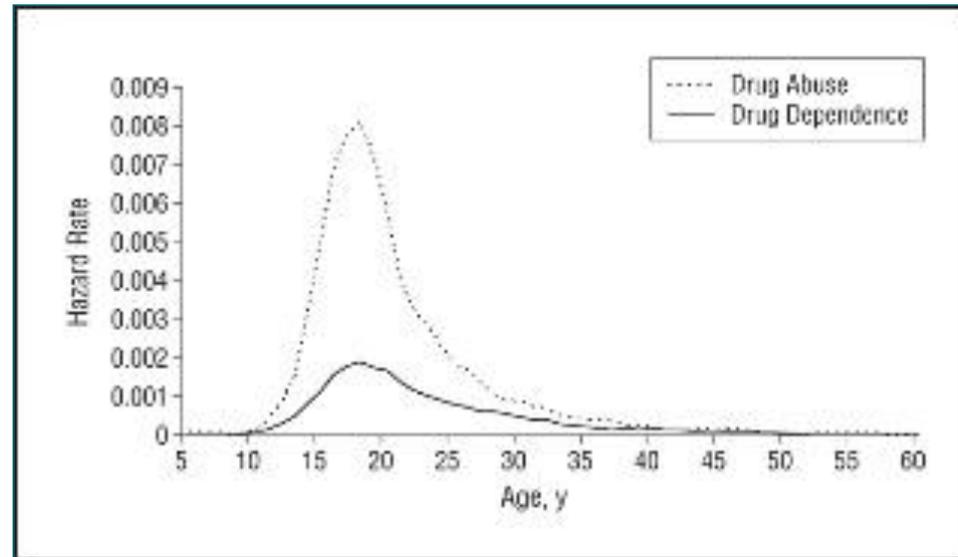
*However,
behaviors are
complex genetic
traits*



**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*

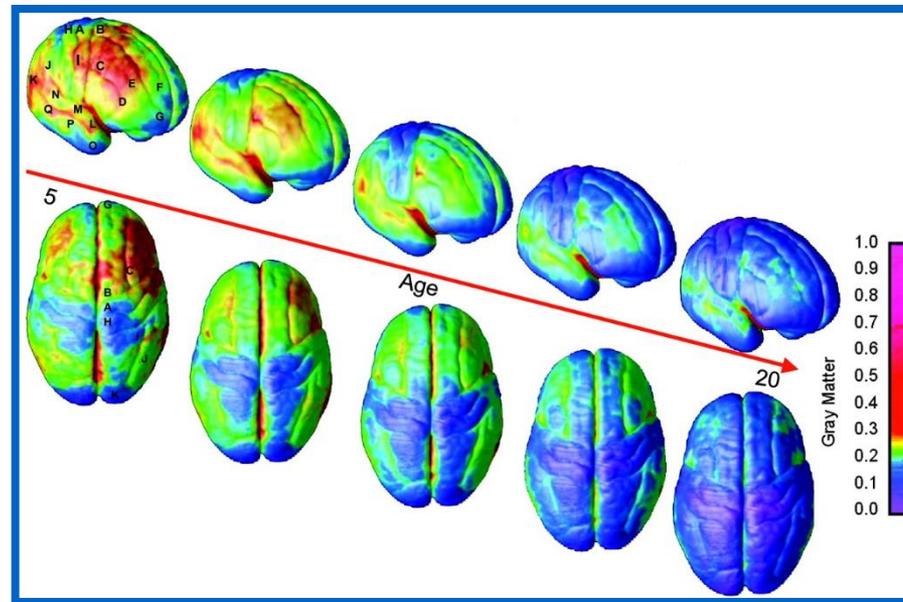
The Development of Addiction: Adolescence

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

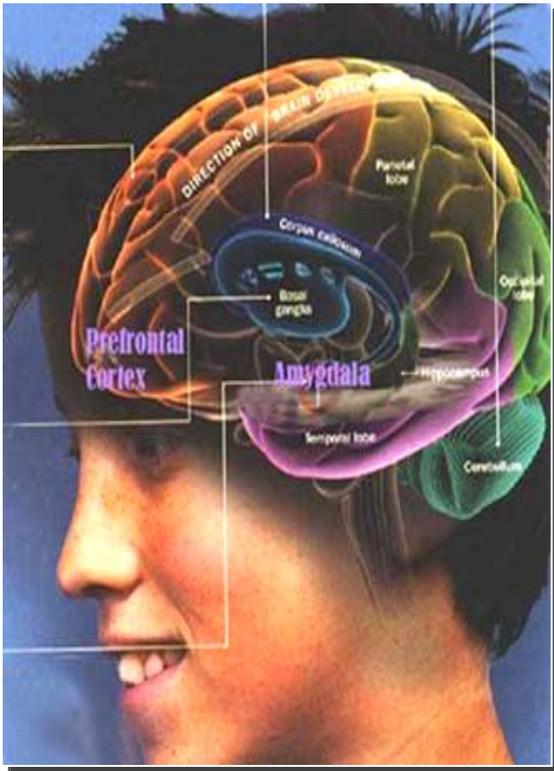
The Development of Addiction: Adolescence

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.

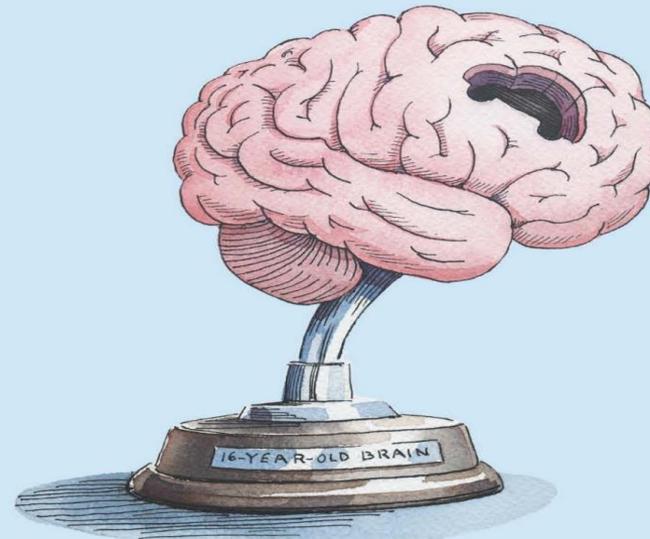
The Adolescent Brain – “A Work in Progress”



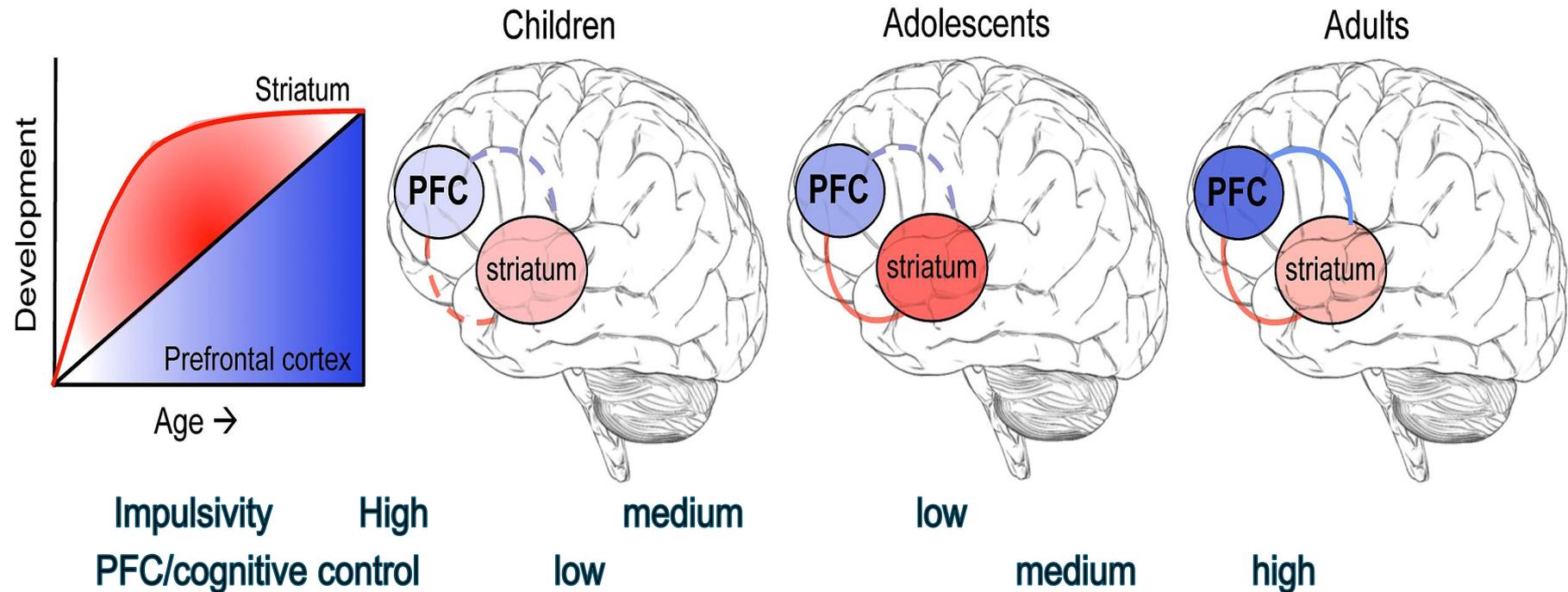
Why do most 16-year-olds
drive like they're
missing a part of their brain?



BECAUSE THEY ARE.



Adolescent Brain Development

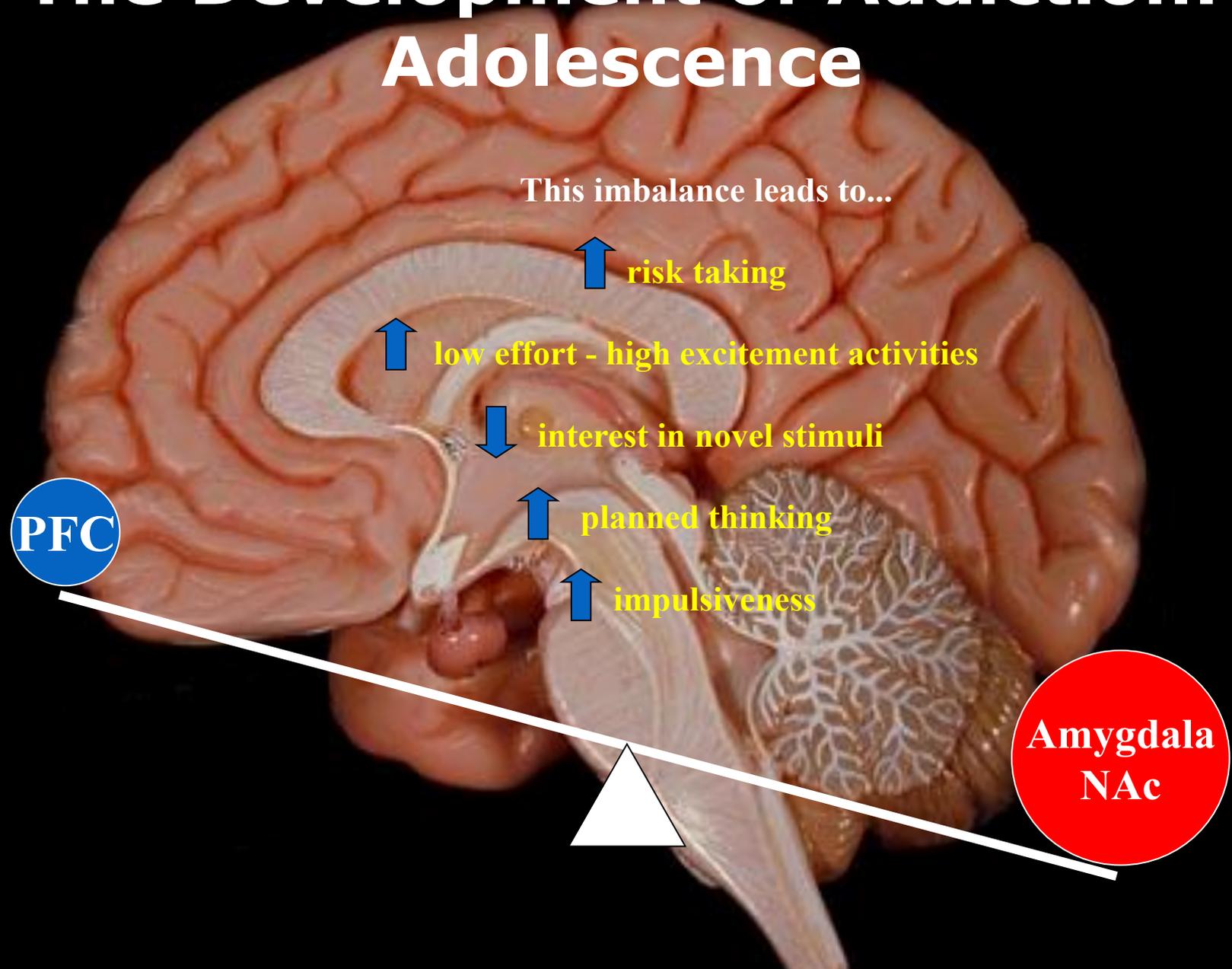


- “ what teens do during their adolescent years – whether it's playing sports or playing video games – can affect how their brains develop”

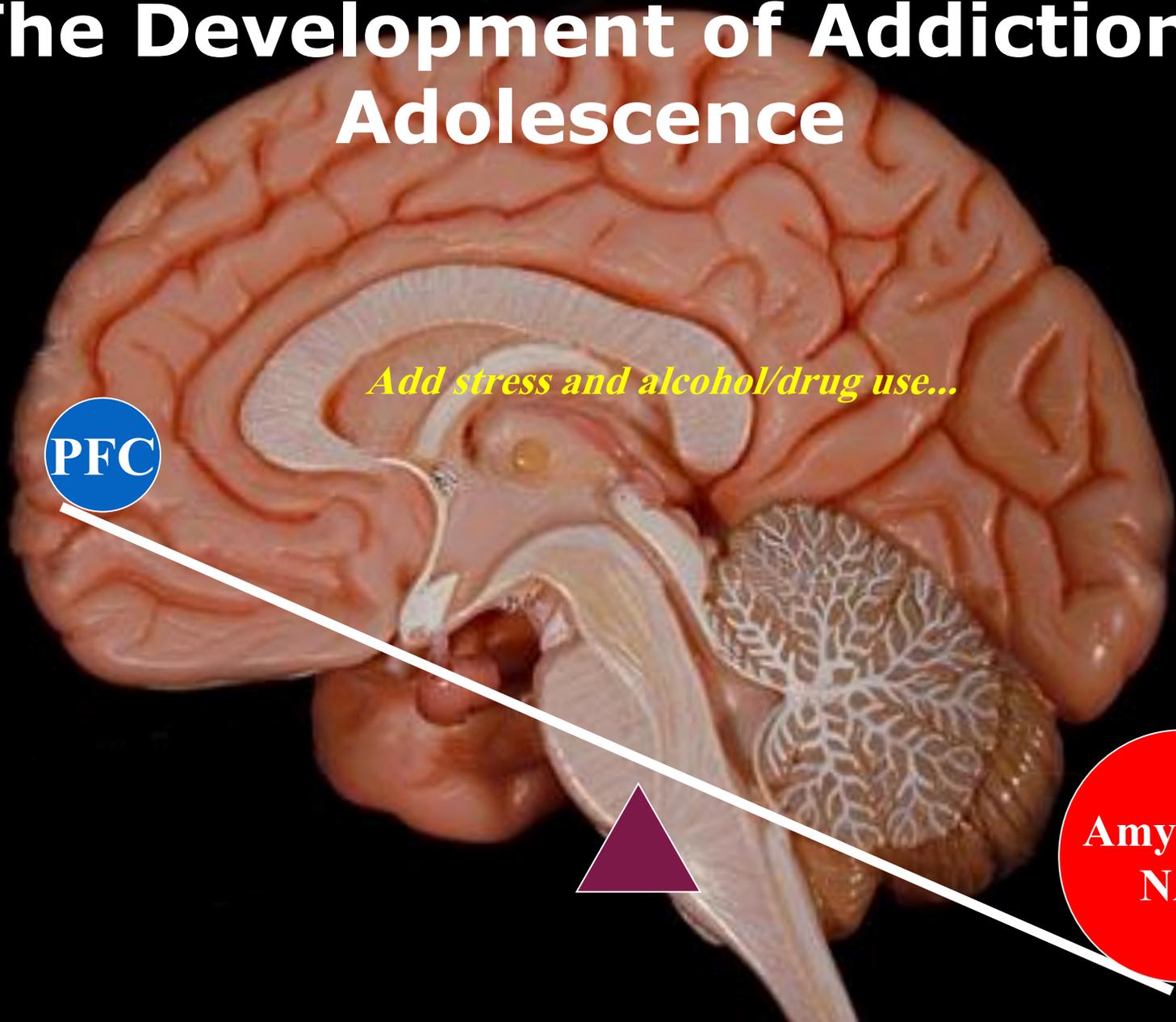
--J Giedd

- 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



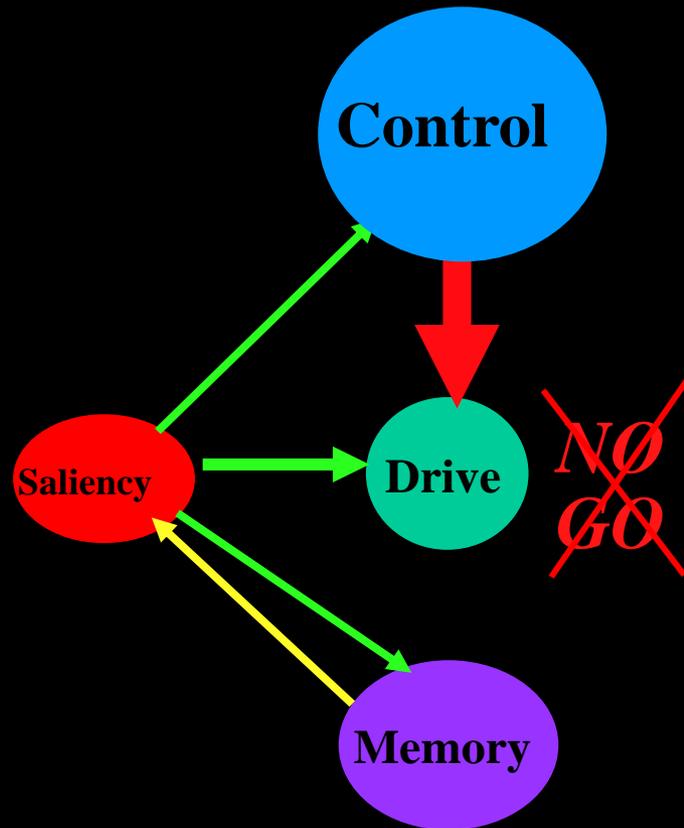
Add stress and alcohol/drug use...

PFC

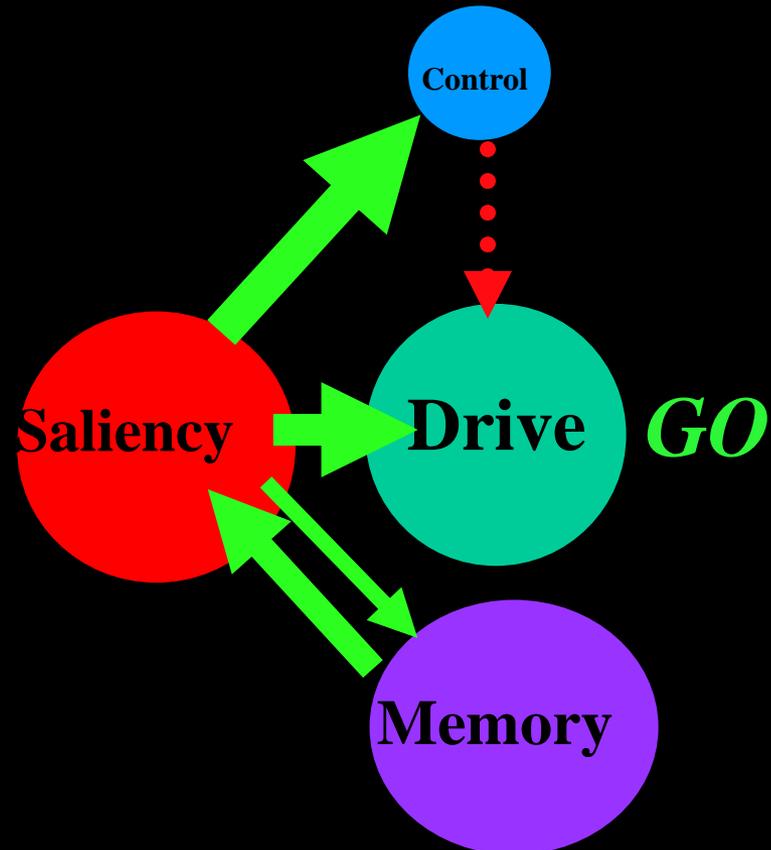
Amygdala
NAc

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.

**Recovering
Community**

Domains of
Recovery

Factors
mediating
recovery

Wellness vs.
Illness "We" vs.
"I"

Social Support

Attitudes
Skills
Knowledge

Mutual
Support
Programs

Prevention, Treatment, & Recovery



Continuum of Care Response



Thanks!