D·B·H·D·D

Georgia Department of Behavioral Health & Developmental Disabilities

BE D·B·H·D·D
BE COMPASSIONATE
BE PREPARED
BE RESPECTFUL
BE PROFESSIONAL
BE CARING
BE EXCEPTIONAL
BE INSPIRED
BE ENGAGED
BE ACCOUNTABLE
BE INFORMED
BE FLEXIBLE
BE HOPEFUL
BE CONNECTED
BE D·B·H·D·D

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Substance Use Disorders (Addiction) As A Brain Diseases Part 1

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Learning Objectives:

- **Participants will:**
- **1.Recognize the latest neurotransmitter research of substance use disorders to include opioid use disorders;**
- **2. Explain the neurochemical basis of the reward and anti-reward brain systems and their effects on the stress mechanisms of the brain;**
- **3. Describe the neurobiological basis of detachment from human relationships with substance use disorders in the brain.**

The terms addiction and substance use disorder used in this presentation are interchangeable- the term "substance use disorder" is replacing the term "addiction" in an effort to reduce the stigma associated with the experience of a substance use disorder.

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The Pharmacist's Guide To Opioid Use Disorders
ASHP Bookstore

Contributors
Wally Cross R.Ph.,CAC
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Jeff Baldwin Pharm.D.
Kevin McCauley MD
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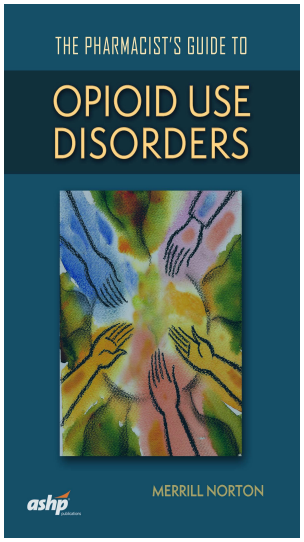

Ordering Info:
ashp.org/opioiddisorders

Amazon.com

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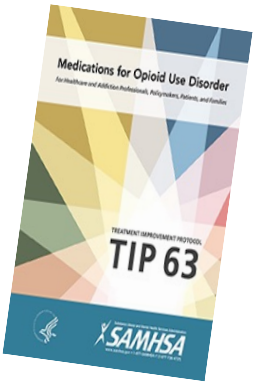
Introduction

- **The goal of treatment for opioid addiction or opioid use disorder (OUD) is remission leading to lasting recovery.**
- **This presentation summarizes TIP 63 content:**
  - **Food and Drug Administration (FDA)-approved medications for treating OUD**
  - **Other evidence-based care to support OUD recovery**
- **The Substance Abuse and Mental Health Services Administration's (SAMHSA) TIPs provide evidence-based, best-practice guidelines for the behavioral health field.**



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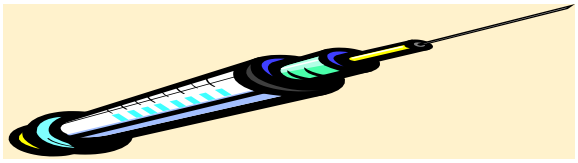

Understanding the Pharmacology of Substance Use Disorders

Dr. Merrill Norton, Pharm.D., D.Ph., CMAC
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New Behavioral Medications App

- BHMEDS-R3 App
- Collaborating TTC: Mid-America ATTC
- Publication Date: November 5, 2019
- The BHMEDS-R3 app is designed as a quick reference for non-prescriber behavioral health professionals and consumers who need general knowledge about medications prescribed for behavioral health conditions. The language has been modified to increase readability for a larger audience and, in keeping with the goal of continuously updating the app content, new medications are added after FDA approval. Download the FREE app from the Google Play or iTunes store.
- Use the BHMEDS-R3 app for the following:
- Browse through different types of behavioral health medications
- Click a medication category icon to learn more details, including brand and generic names
- Use drop-down navigation menus to learn more about medications' purpose, dose and frequency, side effects, emergency conditions, misuse potential, and cautions.
- Access provider tools and other free medication resources

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Session I: Introduction

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My philosophy in addressing addiction in America for the last 30 years of providing education to professionals:

"The science of addiction will reduce the shame and stigma of the addict and their families-thus help them seek help from those who understand the disease."

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This Lecture Will Cover:

- Pharmacology of SUDS
- The Opioids and SUDS
- Assessment & Treatment

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What Is Addiction (Substance Use Disorder) ?

- Substance Use Disorders (Addiction) can be defined as a chronic, relapsing disorders that has been characterized by
- (i) a compulsion to seek and take drugs,
- (ii) loss of control over drug intake, and
- (iii) emergence of a negative emotional state (e.g., dysphoria, anxiety, and irritability) that defines a motivational withdrawal syndrome when access to the drug is prevented.
- The occasional, limited, recreational use of a drug is clinically distinct from escalated drug use, the loss of control over drug intake, and the emergence of compulsive drug-seeking behavior that characterize addiction.
- *Koob GF (2013) Addiction is a reward deficit and stress surfeit disorder. Front. Psychiatry 4:72. doi: 10.3389/fpsyt.2013.00072*
-)

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Challenges

- Which Type of Treatment?
- The Moral Model
- The Biopsychosocial Model
- The Harm Reduction Model
- The Drug Court Model
- Are the Opioid Treatment Programs closed systems? What are the OTP systems doing to educate the healthcare practitioner of the future? Is MAT the only reasonable alternative to long term opioid addiction? Is there a bias against OTPs?
- Does OTPs remove the stigma of addiction or promote it ?
- It will take a multiple types of approaches for successful treatment of opioid addicts
- And this is why…….

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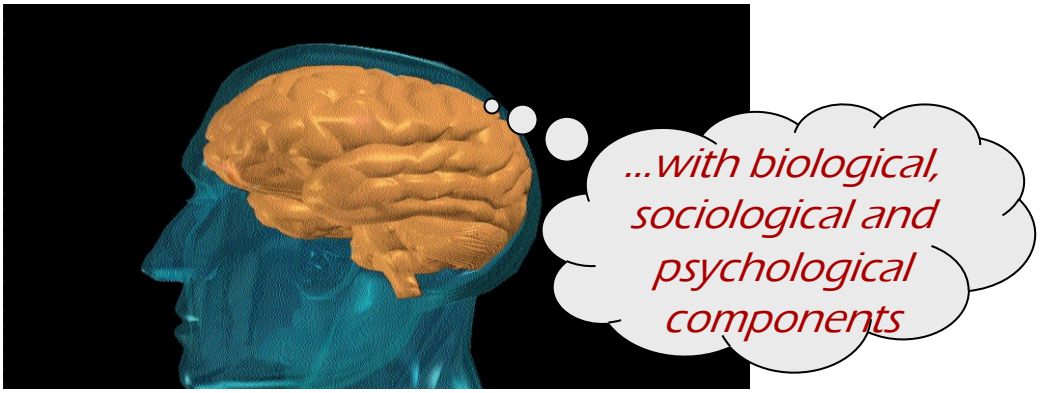
Substance Use Disorders (Addictions) are a Complex Illnesses



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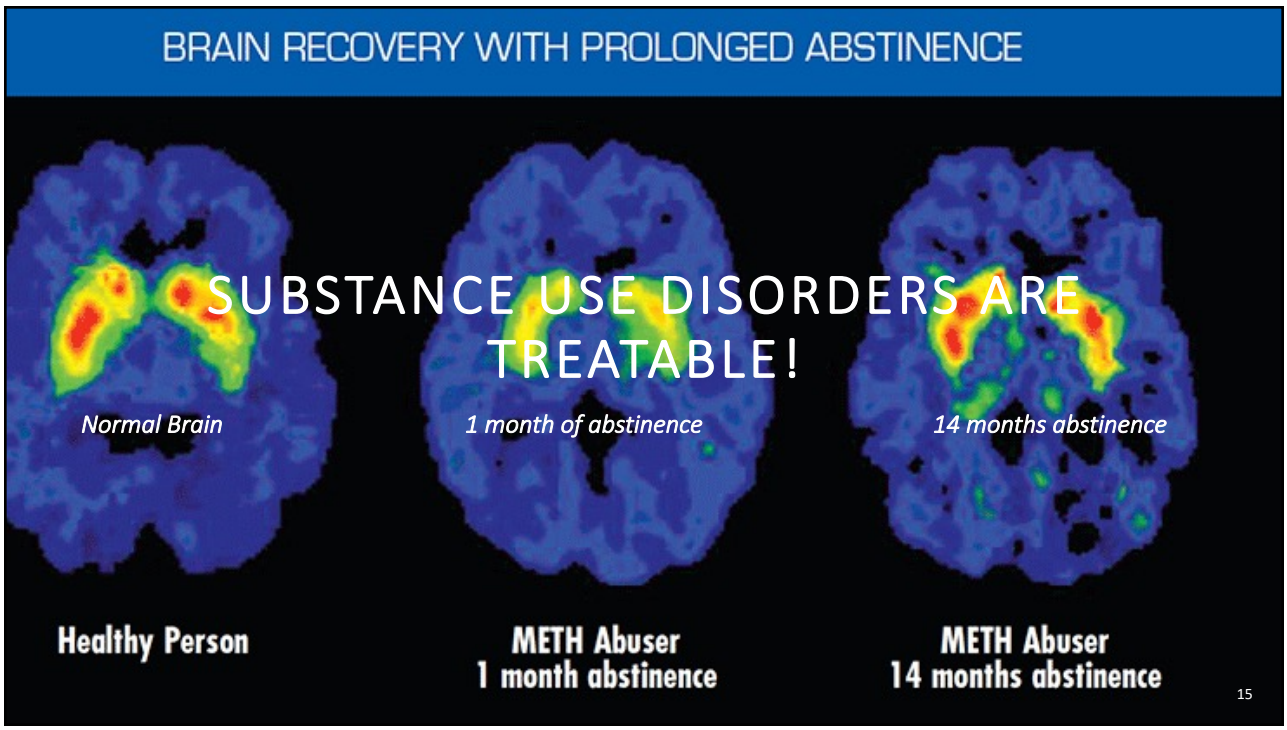

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Neurobiology of Substance Use Disorders 2021

- Substance Use Disorders (SUDS) are increasingly understood as a neurobiological illness where repetitive substance abuse corrupts the normal circuitry of rewarding and adaptive behaviors causing drug-induced neuroplastic changes.
- The addictive process can be examined by looking at the biological basis of substance initiation to the progression of substance abuse to dependence to the enduring risk of relapse.
- Critical neurotransmitters and neurocircuits underlie the pathological changes at each of these stages.
- Enhanced dopamine transmission in the nucleus accumbens is part of the common pathway for the positively rewarding aspects of drugs of abuse and for initiation of the addictive process. γ-Aminobutyric acid, opioid peptides, serotonin, acetylcholine, the endocannabinoids, and glutamate systems also play a role in the initial addictive process.
- Dopamine also plays a key role in conditioned responses to drugs of abuse, and addiction is now recognized as a disease of pathological learning and memory.
- In the path from substance abuse to addiction, the neurochemistry shifts from a dopamine-based behavioral system to a predominantly glutamate-based one marked by dysregulated glutamate transmission from the prefrontal cortex to the nucleus accumbens in relation to drug versus biologically oriented stimuli. This has been called the anti-reward brain.
- This is a core part of the executive dysfunction now understood as one of the hallmark features of addiction that also includes impaired decision making and impulse dysregulation.
- Understanding the neurobiology of the addictive process allows for a theoretical psychopharmacological approach to treating addictive disorders, one that takes into account biological interventions aimed at particular stages of the illness.
- The Neurobiology of Addictive Disorders ,Ross, Stephen MD; Peselow, Eric MD

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Definitions Important to understanding Substance disorders

- **Central Nervous** System-The central nervous system consists of the brain and spinal cord. It is referred to as “central” because it combines information from the entire body and coordinates activity across the whole organism.
- **Psychoactive Substance**-A drug or other substance that affects how the brain works and causes changes in mood, awareness, thoughts, feelings, or behavior. Examples of psychoactive substances include alcohol, caffeine, nicotine, marijuana, and certain pain medicines. Many illegal drugs, such as heroin, LSD, cocaine, and amphetamines are also psychoactive substances. On the street known as uppers, downers, and allrounders.
- **Homeostasis**-Addiction interferes with an important biological process called *homeostasis*. Scientists consider the human body a biological system. All biological systems attempt to maintain a "normal" balance, known as *homeostasis*. The homestasis of the brain is a balance of the pleasure/pain brains, the mood brains, and neurotransmitters that regulate both the pain/pleasure and mood brains.
- **Allostasis**-When the brain has difficulty maintaining homeostatic balance, the wonderfully adaptive brain makes adjustments. It does this by creating a new balanced set-point. The creation of a new balance is called allostasis.

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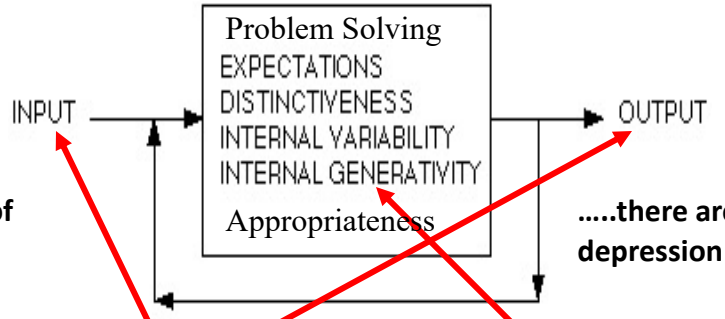
How are human behaviors and neurobiology related?



For every second of stimulation…….

…..there are 3 seconds of depression

Neurobiology and Behavior

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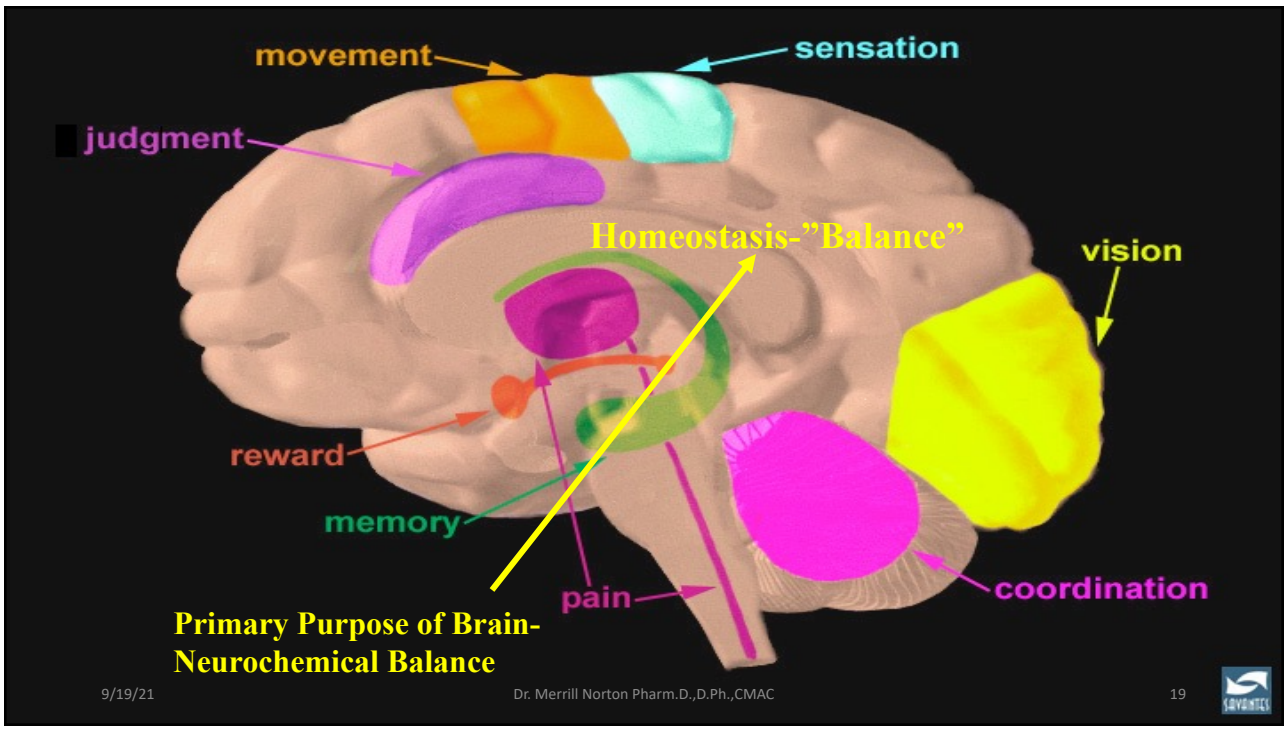

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All Psychoactive Drugs Alter the Homeostasis of the Central Nervous System

- "A major function of the nervous system is to control the relative constancy of the internal environment of the organism. That is, to provide the right chemical environment for living processes to take place. This control of the internal environment is known as homeostasis."
- Psychoactive Drugs disrupt the homeostasis between the pleasure and pain brains.

- *Brown A.G. (1991) The Nervous System and Homeostasis — Interactions with the Internal and External Environments. In: Nerve Cells and Nervous Systems. Springer, London. https://doi.org/10.1007/978-1-4471-3345-2_16*

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Commonly Used Psychoactive Substances

SUBSTANCE	EFFECTS
Alcohol (liquor, beer, wine)	euphoria, stimulation, relaxation, lower inhibitions, drowsiness
Cannabinoids (marijuana, hashish)	euphoria, relaxations, slowed reaction time, distorted perception
Opioids (heroin, opium, many pain meds)	euphoria, drowsiness, sedation
Stimulants (cocaine, methamphetamine)	exhilaration, energy
Club Drugs (MDMA/Ecstasy, GHB)	hallucinations, tactile sensitivity, lowered inhibition
Dissociative Drugs (Ketamine, PCP, DXM)	feel separated from body, delirium, impaired motor function
Hallucinogens (LSD, Mescaline)	hallucinations, altered perception

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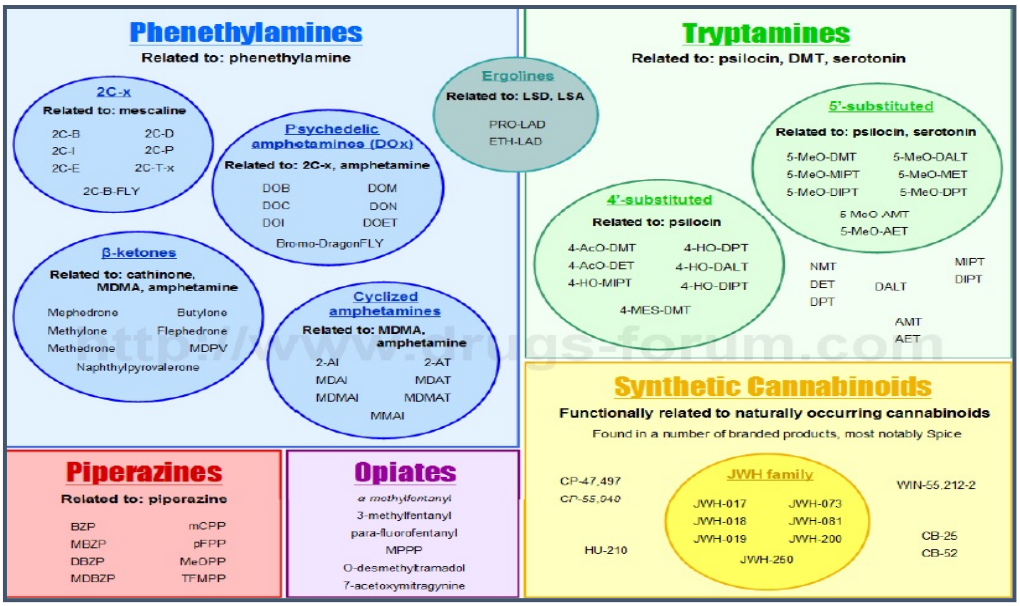
"Designer" Synthetic Psychoactive Substances



SOURCE: http://www.drugs-forum.com.

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Current Gas Station Drugs of Concerns

- Kratom
- Synthetic Marijuana
- Synthetic Opioids
- Delta 8 THC
- Ketamine
- Tianeptine
- Phenibut

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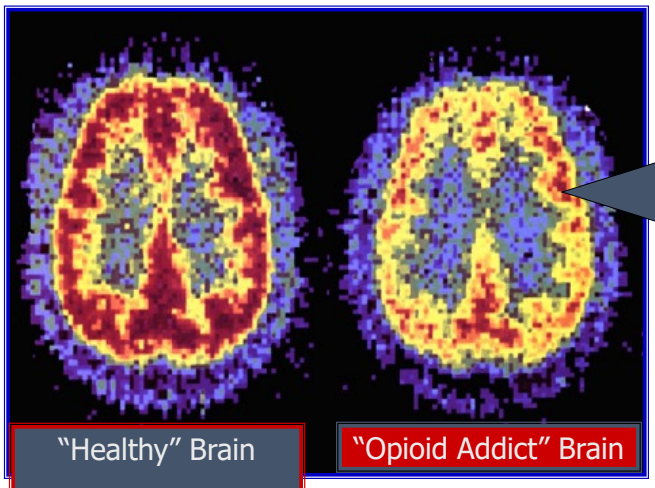
Substance Use Disorders are Brain Diseases



Prolonged Use Changes the Brain in Fundamental and Lasting Ways

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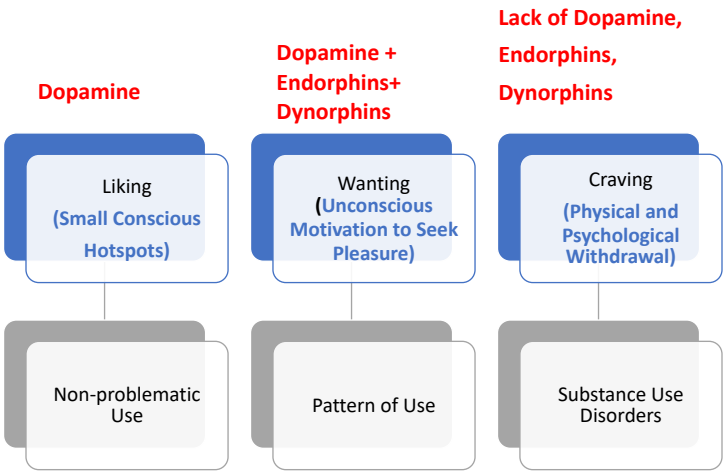
Desire Corresponds with Drug Use



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Routine Substance Use Changes Reward Patterns

Normal Reward Brain Pathways

- Dopamine Release (Happiness & Joy)
- Eventually, the sources (Endorphins, Dynorphins) are depleted
  - Activates Anti-reward brain

Anti-Reward Brain in Substance Use Disorders

- Brain systems in place to limit reward
- Triggered by excessive activity in the reward system
- Glutamate/GABA Release (Pain/Depression/Anxiety)

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Primary Neurochemical Players In SUDS

Dopamine- Pleasure Brain – Reward Brain – *Positive Reinforcement*

"The Accelerator of Pleasure" : Like - Want – Love/Nurture

Glutamate- Pain Brain- Anti Reward Brain- *Negative Reinforcement*

"The Brake of Pleasure" "Pain" – Depression- Anhedonia – Craving

The central nervous system's job is to keep the brain in a balance of positive and negative reinforcement- "homeostasis"

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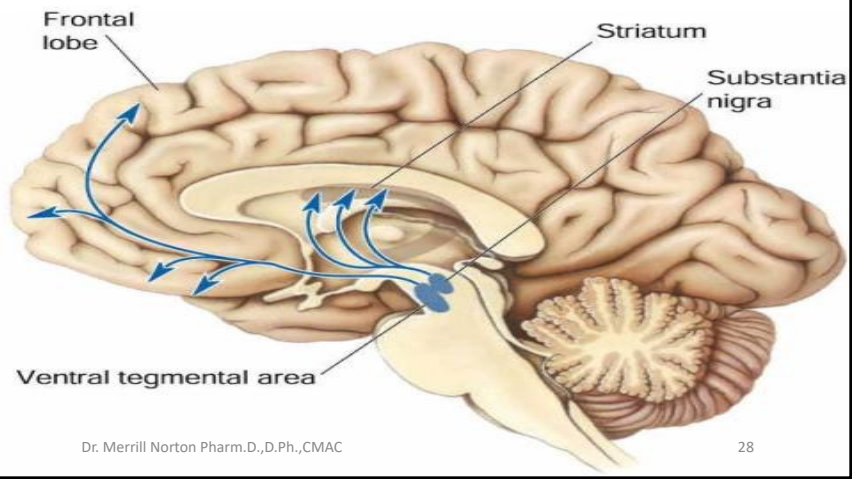
The Pleasure or Reward Brain

Dopamine projection systems

Important for control of reward and reinforcement



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Natural Rewards

- Food
- Sex
- Excitement
- Comfort
- Nurturing
- Bonding (Mammalian Brain)

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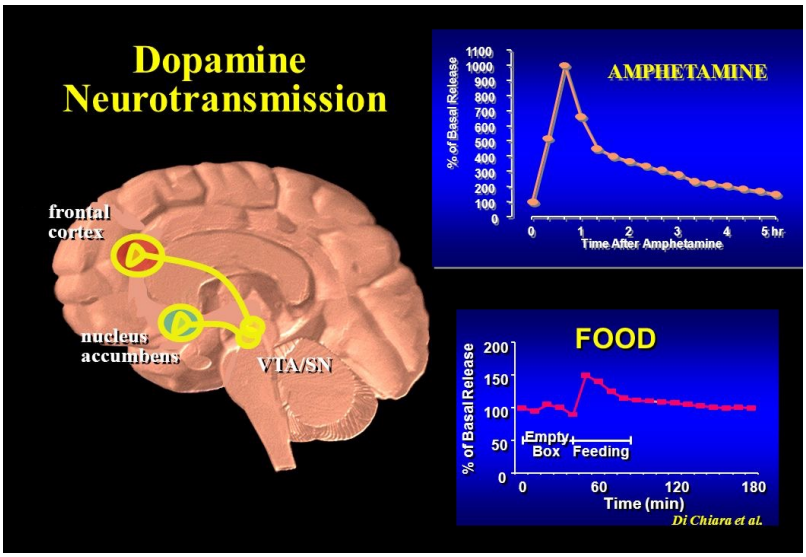

Photo Courtesy of NIDA Neurobiology of Addiction

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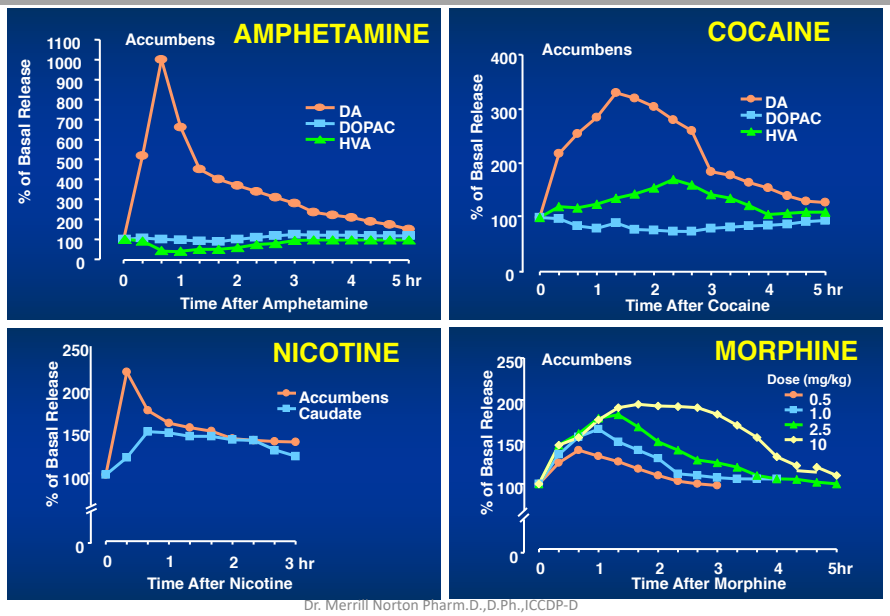
Effects of Drugs on Dopamine Release



Di Chiara and Imperato, PNAS, 1988

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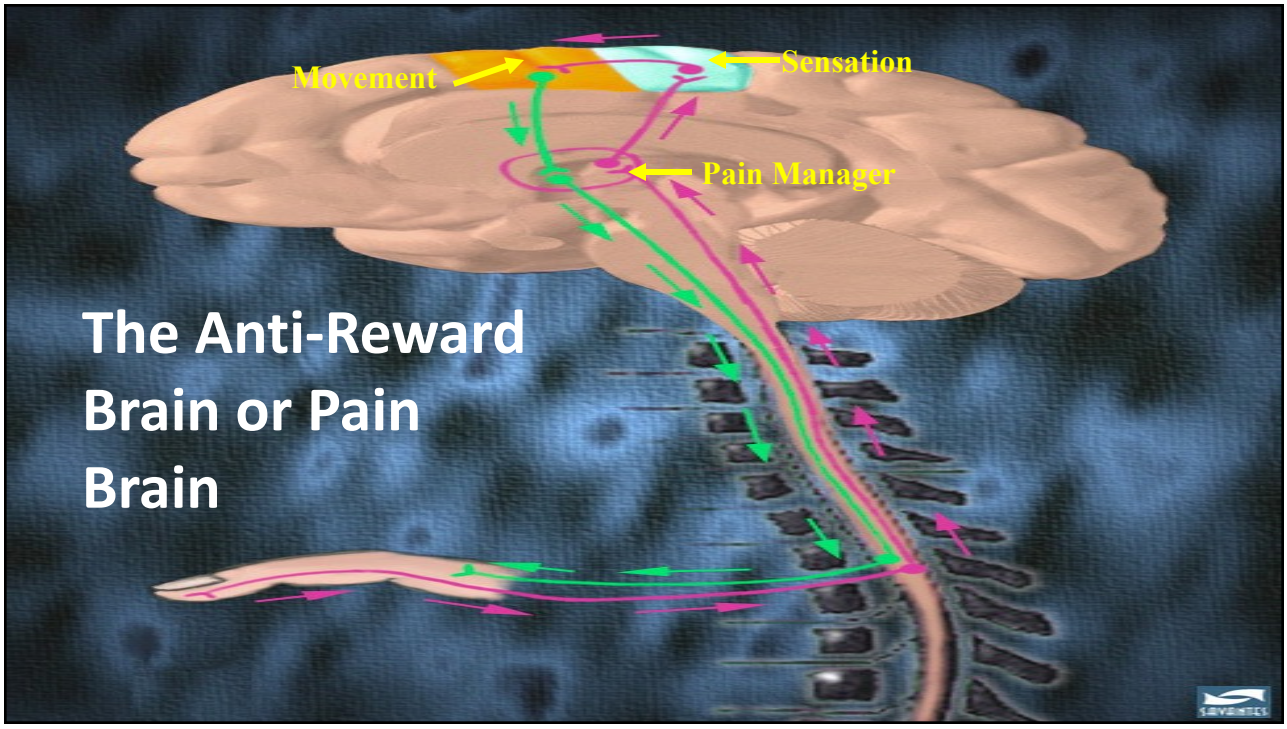

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The Anti-Reward Brain

- 1. A key element of addiction is the development of a negative emotional state during drug abstinence.
- 2. The neurobiological basis of the negative emotional state derives from two sources: decreased reward circuitry function and increased anti-reward circuitry function.
- 3. The anti-reward circuitry function recruited during the addiction process can be localized to connections of the extended amygdala in the basal forebrain.
- 4. Neurochemical elements in the antireward system of the extended amygdala have as a focal point the extrahypothalamic corticotropin-releasing factor system.
- 5. Other neurotransmitter systems implicated in the anti-reward response include norepinephrine, dynorphin, neuropeptide Y, and nociceptin.
- 6. Vulnerability to addiction involves multiple targets in both the reward and anti-reward system, but a common element is sensitization of brain stress systems.
- 7. Dysregulation of the brain reward system and recruitment of the brain anti-reward system are hypothesized to produce an allostatic emotional change that can lead to pathology.
- 8. Nondrug addictions may be hypothesized to activate similar allostatic mechanisms.

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Positive and Negative Reinforcement- Definitions

Positive Reinforcement — defined as the process by which presentation of a stimulus (drug) increases the probability of a response (non dependent drug taking paradigms).

Negative Reinforcement —defined as a process by which removal of an aversive stimulus (negative emotional state of drug withdrawal) increases the probability of a response (dependence-induced drug taking)

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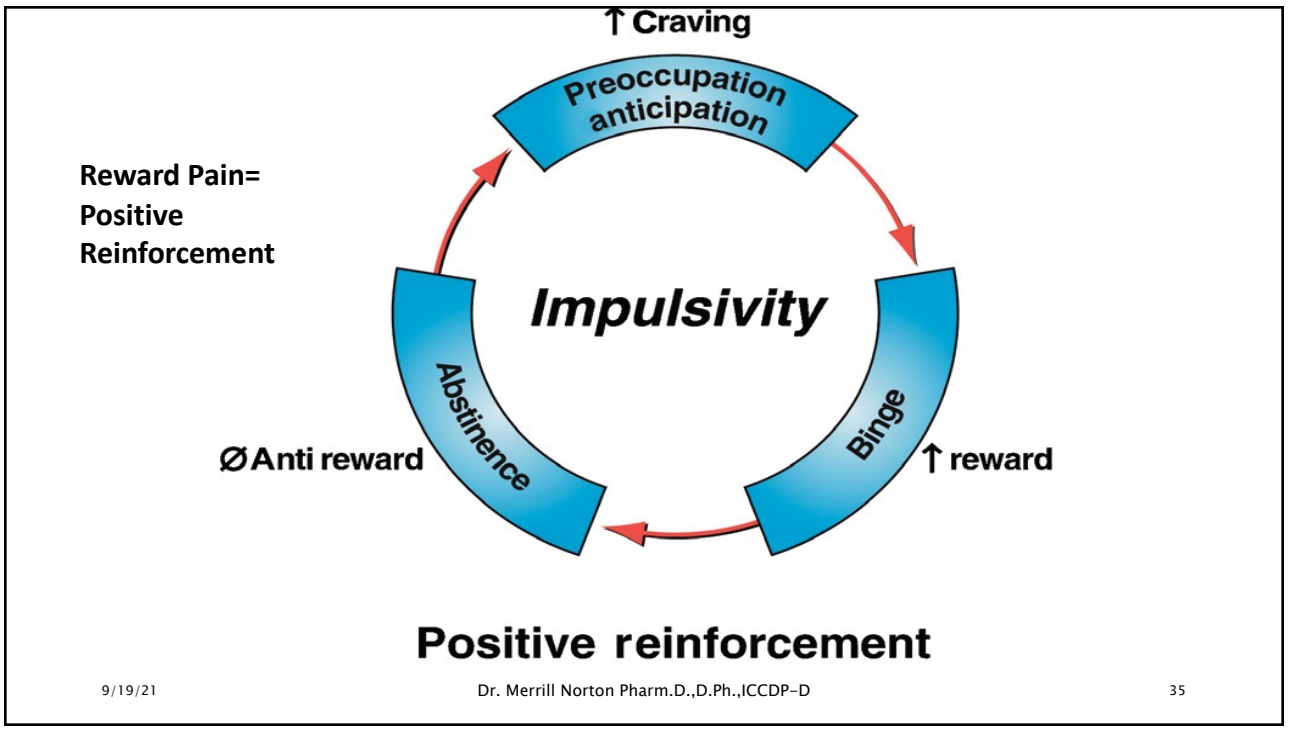

Reward Pain= Positive Reinforcement

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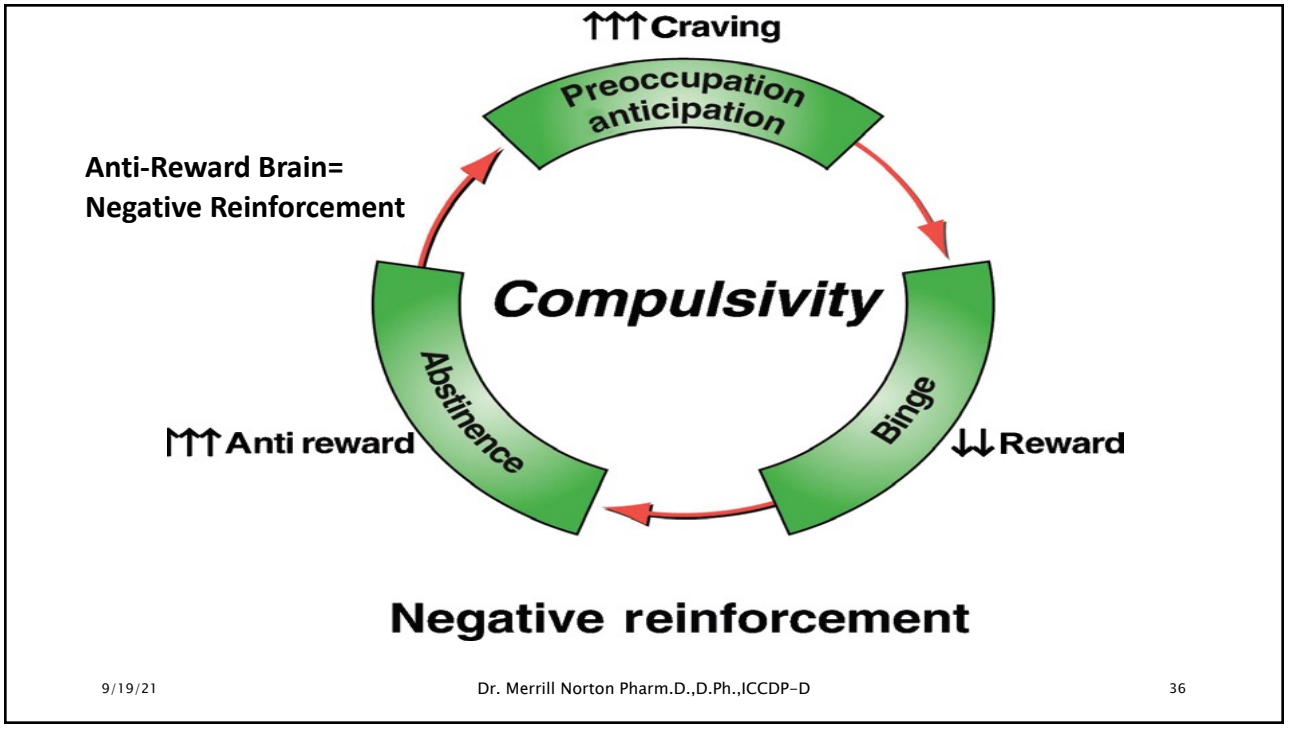

Anti-Reward Brain= Negative Reinforcement

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Neuroadaptation

The more a drug is used, the more the brain gets accustomed to its effects. This can cause long term changes in the nervous system. The begins to change the mesolimbic dopaminergic system circuits.

This ultimately leads to increased tolerance to the drug.

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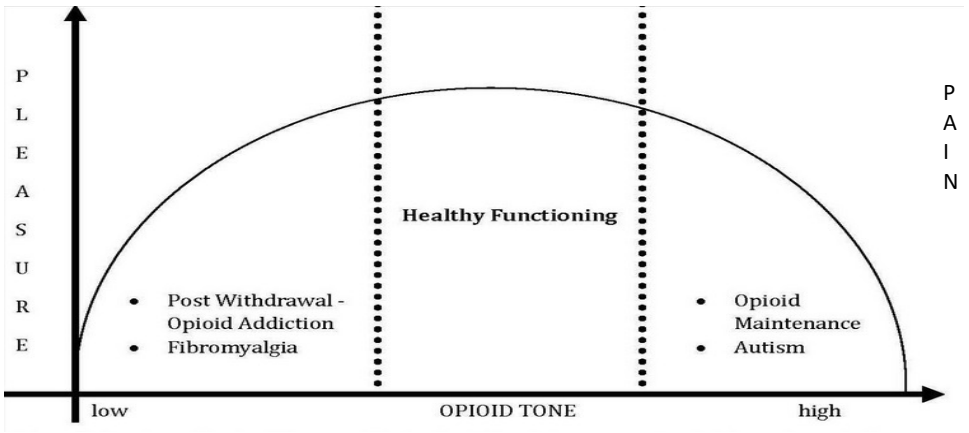

Figure 1. The hypothesized 'inverse U' relationship of pleasure and opioid tone in central nervous system subcortical pathways. The left side of the x-axis corresponds with low opioid tone, associated with post acute withdrawal syndrome and opioid induced hyperalgesia (OIH) after opioid withdrawal and with fibromyalgia. The right side of the x-axis corresponds with high opioid tone, associated with patients maintained on opioid drugs and with autism. Pleasure is at its peak when regulated by human interactions in the band labeled 'healthy functioning.'

Johnson B, Ulberg S, Shivale S, Donaldson J, Milczarski B, Faraone SV. Fibromyalgia, autism, and opioid addiction as natural and induced disorders of the endogenous opioid hormonal system. Discov Med. 2014 Oct;18(99):209-20. PMID: 25336035.

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Fibromyalgia, Autism, and Opioid Addiction as natural and Induced Disorders of the Endogenous Opioid Hormonal System

Conclusions:

- 1. Opioid-maintained patients relate autistically.
- 2. Autism is a hyperopioidergic disorder.
- 3. Fibromylagia is a hypoopioidergic disorder.
- 4. Low opioid tone caused by opioid maintenance or fibromyalgia can usually be reversed with low-dose naltrexone.
- 5. The increase in the incidence of autism may have been caused by the increase in use of opioids for analgesia during childbirth.
- Johnson B, Ulberg S, Shivale S, Donaldson J, Milczarski B, Faraone SV. Fibromyalgia, autism, and opioid addiction as natural and induced disorders of the endogenous opioid hormonal system. Discov Med. 2014 Oct;18(99):209-20. PMID: 25336035.

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Tolerance vs. Reverse Tolerance

Drug/Alcohol effectiveness has decreased due to chronic administration

Consumption of larger quantity of abused substance

more tolerance

- **Larger Dose is needed to achieve same effects**
- **Diminishes over time with abstinence**

The more often you consume drugs and/or alcohol, the greater the positive effects appear to be

More frequent consumption of abused substance

more tolerance

- **Same dose is needed, but more frequently, to achieve same effects**
- **Continues long after the use of alcohol or drug of choice has been stopped**
- **Environmental/social influence**

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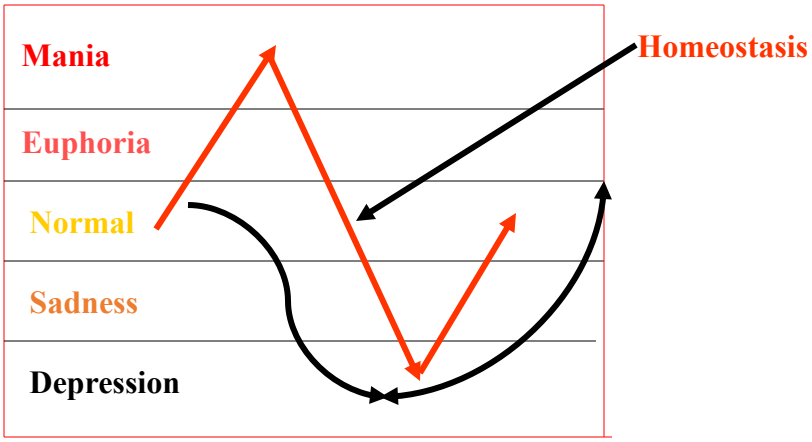
Mood Chart of the Human Brain



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Suicide and SUDS

- **Suicide is the 10th leading cause of death** among all Americans, but it is the third leading cause of death of Americans aged 10-14 and **the second leading cause of death for Americans aged 15-34.** In 2015 alone, 44,193 Americans died of suicide.
- The presence of an alcohol use disorder is confirmed as a distal risk factor for completed suicide, as well as attempted suicide.
- **Approximately 22 percent of deaths by suicide involved alcohol intoxication**, with a blood-alcohol content at or above the legal limit (CDC, 2014b).
- Individuals with a substance use disorder are nearly **6 times as likely** to attempt suicide at some point in their life.

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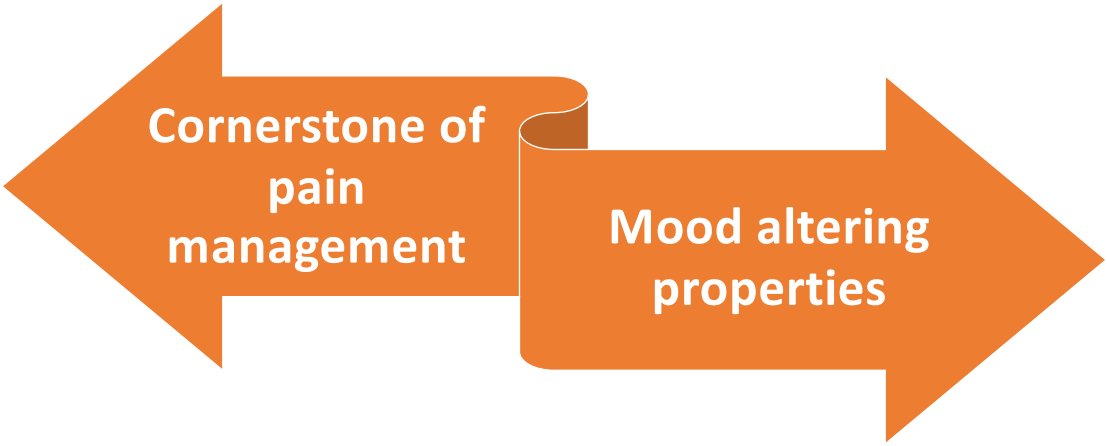
Opioids: Double-Edged Sword



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Might Not Meet Today's FDA Standards

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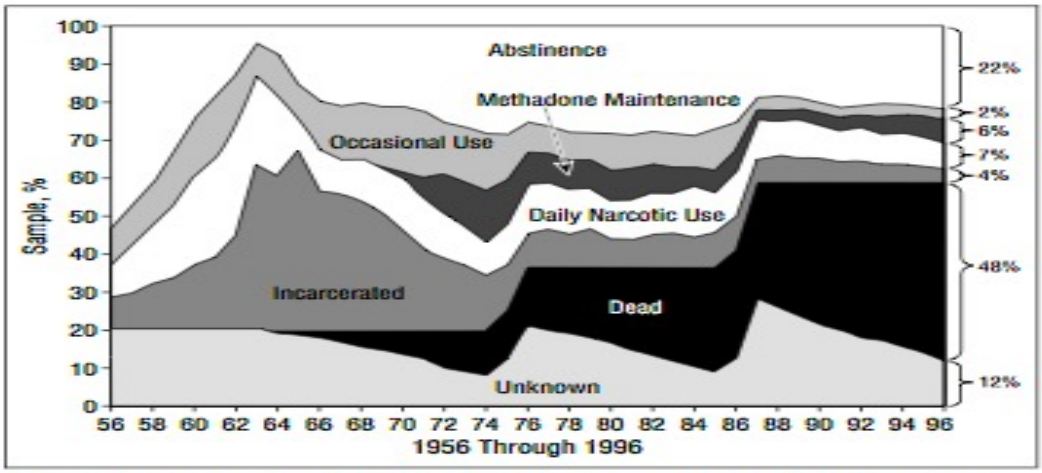
Today's Epidemic Is NOT New News
A 33-year Follow-Up of Narcotics Addicts



The natural history of narcotics addiction among a male sample (N=581).

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Addiction Liability

- ~10% who ever use marijuana become daily users
- Conditional dependence – risk of dependence of those who ever use substance
  - Marijuana 9%
  - Ethanol 15%
  - Cocaine 17%
  - Heroin/Opioids 23%
  - Tobacco 32%

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The Brain's Addiction Network

- The Addiction Process
- The Anti-Reward System**
- The BDNF System**
- The Brain Stress System**
- The Cravings
- The Drugs
- The Genetics
- The Mental Component
- The Neurotransmitters
- The Receptors**
- The Relapse Process
- The Reward System**

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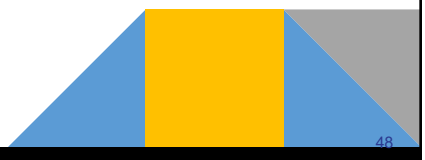
Brain Systems Involved In Addiction For Dummies

- The Anti-Reward System: Pain Brain
- The BDNF System: Mood Brain
- The Brain Stress System: Functionality Brain
- The Cravings: Brain's Desire to Seek Homeostasis
- The Drugs: External Molecules that Change Homeostasis
- The Genetics: Risk Factors that Change Homeostasis



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Brain Systems Involved In Addiction For Dummies

- The Mental Component: The Obsession for the Drug
- The Neurotransmitters: The Essential Eleven
- The Receptors**: Mu, Delta, Kappa, Glutamate, GABA are primary
- The Relapse Process: SUDS is a Chronic Disease
- The Reward System**: The Pleasure Brain

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Addicts Are Addicted to Pain- Not Pleasure

-Merrill Norton

August 2003

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Primary Neurochemical Players In SUDS

- **Dopamine- Pleasure Brain – Reward Brain – *Positive Reinforcement***

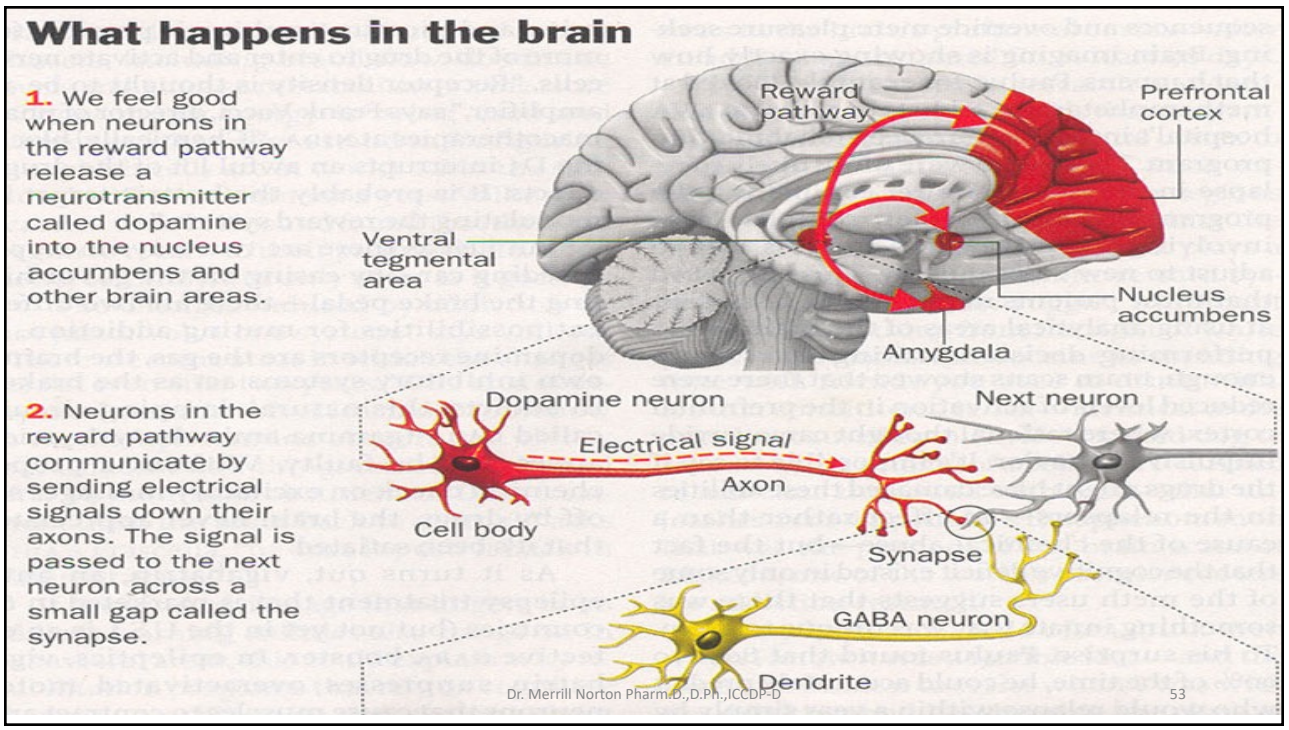
  "The Accelerator of Pleasure" : Like - Want – Love/Nurture

- **Glutamate- Pain Brain- Anti Reward Brain- *Negative Reinforcement***

  "The Brake of Pleasure" "Pain" – Depression- Anhedonia – Craving

The central nervous system's job is to keep the brain in a balance of positive and negative reinforcement- "homeostasis"

52


What happens in the brain
1. We feel good when neurons in the reward pathway release a neurotransmitter called dopamine into the nucleus accumbens and other brain areas.
Reward pathway
Prefrontal cortex
Ventral tegmental area
Nucleus accumbens
Amygdala
2. Neurons in the reward pathway communicate by sending electrical signals down their axons. The signal is passed to the next neuron across a small gap called the synapse.
Dopamine neuron
Next neuron
Electrical signal
Axon
Cell body
Synapse
GABA neuron
Dendrite
Dr. Merrill Norton Pharm.D.,D.Ph.,ICCDP-D
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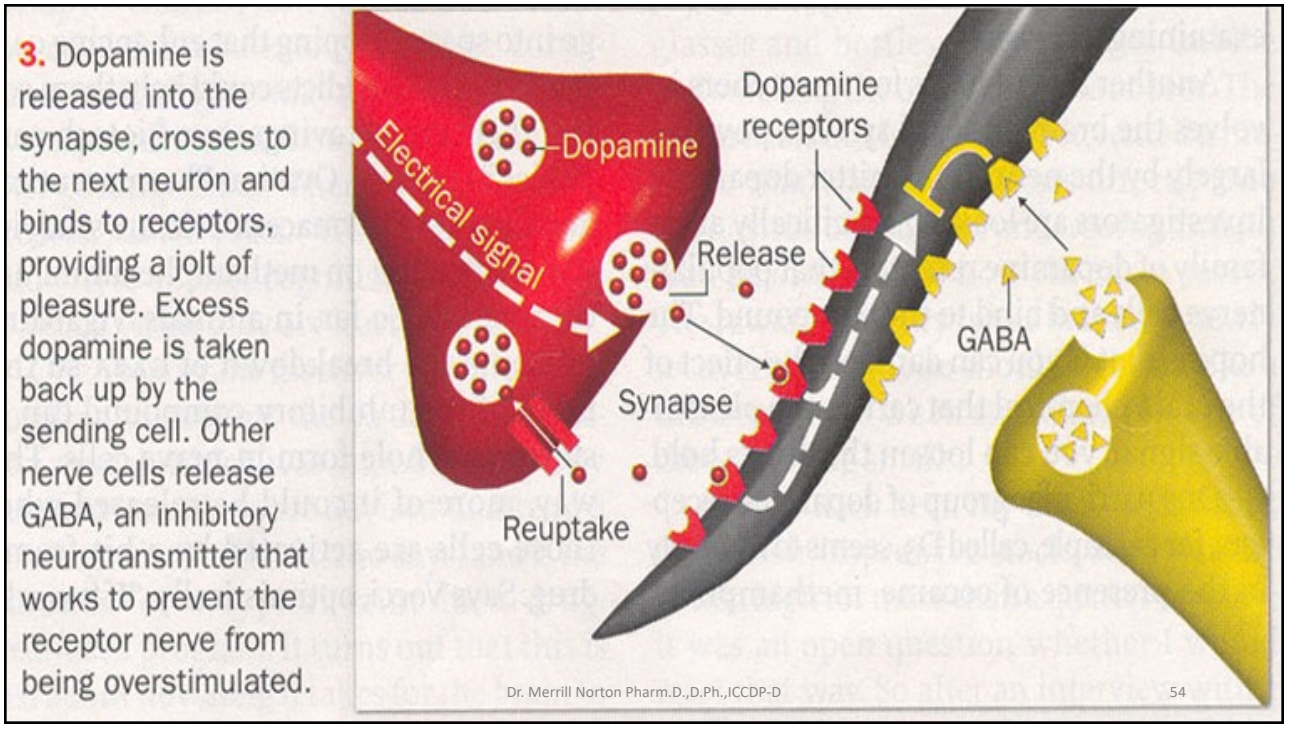
3. Dopamine is released into the synapse, crosses to the next neuron and binds to receptors, providing a jolt of pleasure. Excess dopamine is taken back up by the sending cell. Other nerve cells release GABA, an inhibitory neurotransmitter that works to prevent the receptor nerve from being overstimulated.
Dopamine
Electrical signal
Dopamine receptors
Release
GABA
Synapse
Reuptake
Dr. Merrill Norton Pharm.D.,D.Ph.,ICCDP-D
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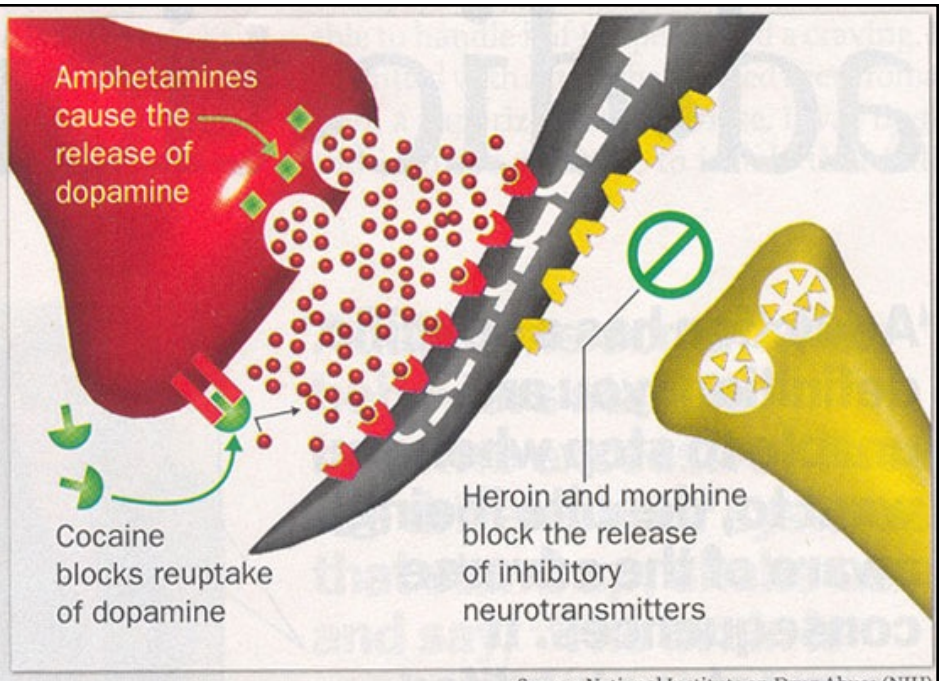
4. Addictive substances increase the amount of dopamine in the synapse, heightening the feeling of pleasure. Addiction occurs when repeated drug use disrupts the normal balance of brain circuits that control rewards, memory and cognition, ultimately leading to compulsive drug taking.



Source: National Institute on Drug Abuse (NIH)
TIME Diagram by Kristina Dell, Meg Massey and Joe Lertola

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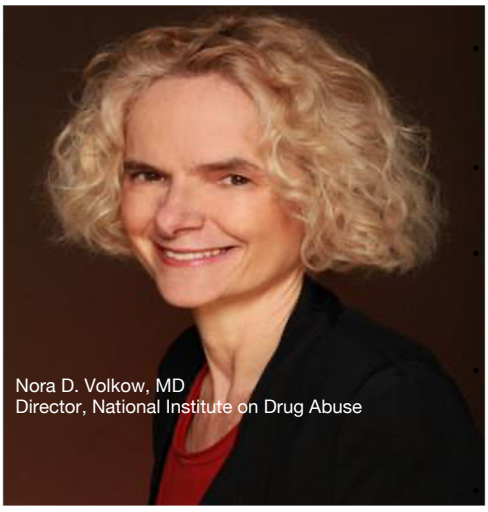
Dopamine and SUDS



- **Drugs of abuse cause supraphysiologic increases in extracellular dopamine in the striatum that correlate with subjective feelings of being "high"**
- **PET scan studies: impaired striatal dopamine signaling due to decreased DAD2 receptors**
- **fMRI scan studies: brain activation abnormalities in striato-cortical pathways that regulate reward, self-control, and affect**
- **Overlap in brain circuitry underlying addiction and disorders such as binge eating and pathological gambling**
- **Other brain chemicals matter, too (glutamate, GABA, endogenous opioid and cannabinoids)**

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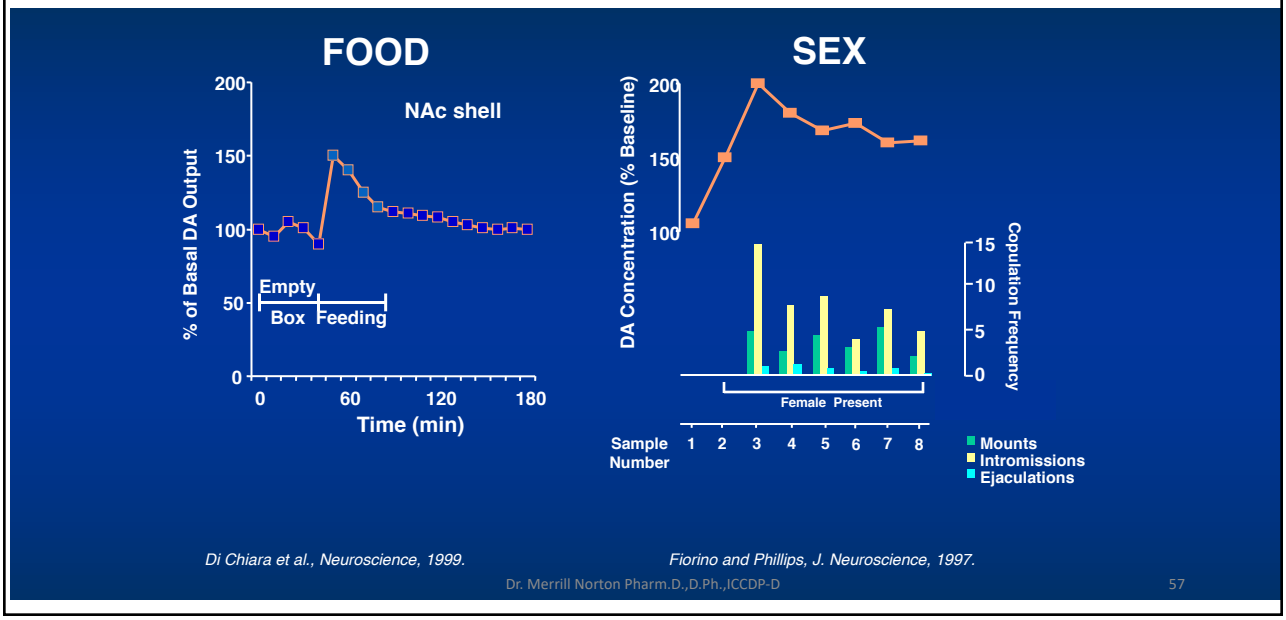
Natural Rewards Elevate Dopamine Levels



Di Chiara et al., Neuroscience, 1999.

Fiorino and Phillips, J. Neuroscience, 1997.

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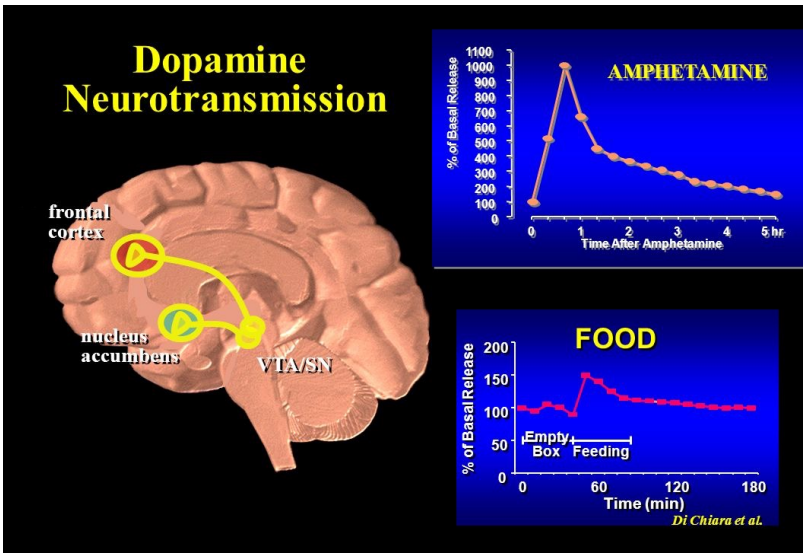

Photo Courtesy of NIDA Neurobiology of Addiction

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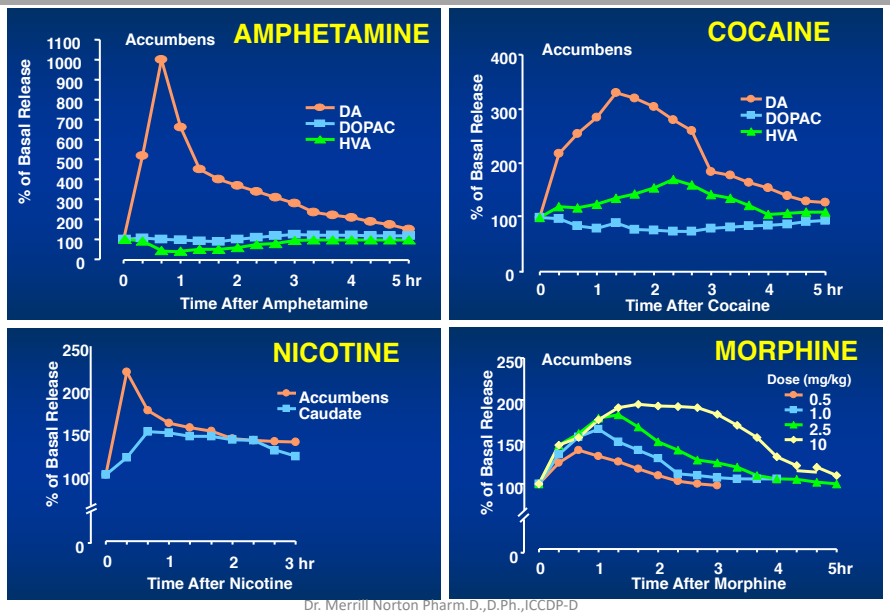
Effects of Drugs on Dopamine Release



Di Chiara and Imperato, PNAS, 1988

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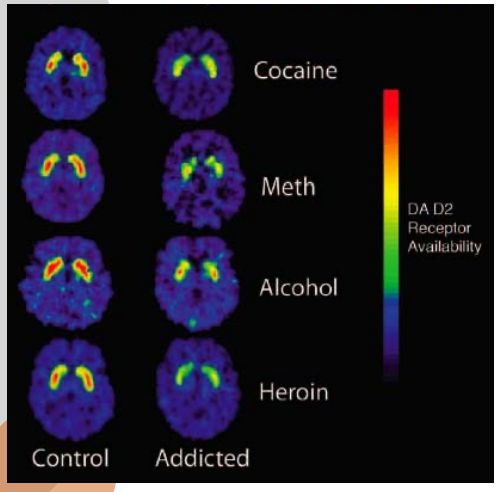
Dopamine D2 Receptors are Lower in Addiction



Repeated drug exposure changes brain function. Positron emission tomography (PET) images are illustrated showing similar brain changes in dopamine receptors resulting from addiction to different substances - cocaine, methamphetamine, alcohol, or heroin. The striatum (which contains the reward and motor circuitry) shows up as bright red and yellow in the controls (in the left column), indicating numerous dopamine D2 receptors. Conversely, the brains of addicted individuals (in the right column) show a less intense signal, indicating lower levels of dopamine D2 receptors.

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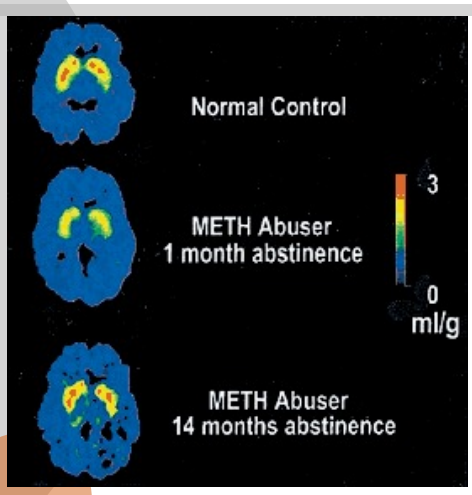
Methamphetamine User Recovery



Depleted dopamine transporter levels in methamphetamine abusers show recovery after prolonged abstinence.

In these brain scans, high dopamine transporter levels appear as red, while low levels appear as yellow/green.

Dr. Nora Volkow, Director of NIDA
National Institute on Drug Abuse

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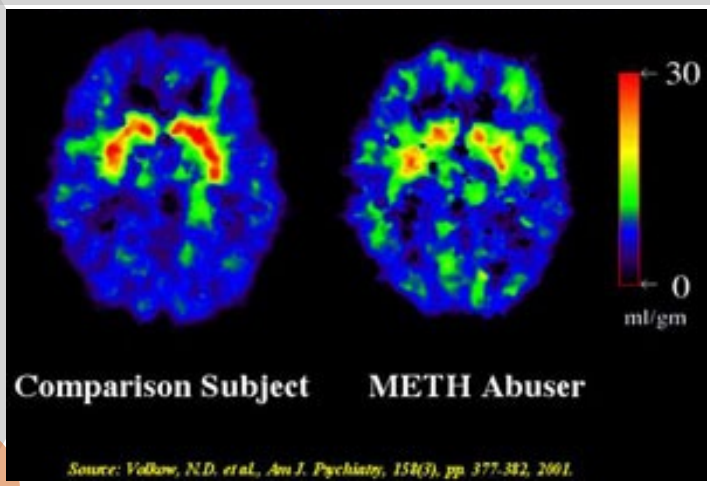
Loss of Dopamine Neurons After Heavy Methamphetamine Use



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Dynorphin, Dysphoria, and Dependence: the Stress of Addiction

Charles Chavkin and George F Koob

The hypothesis that the dynorphin-kappa opioid receptor system may be a key component of the neuroplasticity associated with *stress-induced mood disorders*

and the 'dark side' of addiction (withdrawal-negative affect stage) continues to gain preclinical and clinical experimental support.

The endogenous kappa opioid peptides derived from prodynorphin encode the dysphoric, anxiogenic, and cognitive disrupting responses to behavioral stress exposure.

(Bruchas et al, 2010; Carroll and Carlezon, 2013)

Neuropsychopharmacology **41**, 373-374 (January 2016) | doi:10.1038/npp.2015.258.

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Theory of Euphoria Opioid Receptors

- Five classes of opioid receptor
  - Mu(μ), Delta(δ), Kappa(κ), Nociceptin Subtypes (σ, ε receptors
- Subtype of μ, δ, κ receptor
- Structural characteristics** (The more charateristics- the higher addiction liability)
  - Typical G-protein-coupled receptor
    - Seven hydrophobic region
    - Three intracellular loops
    - Three extracellular loops
    - Intracellular carboxy-terminal tail
    - Extracellular amino-terminal tail

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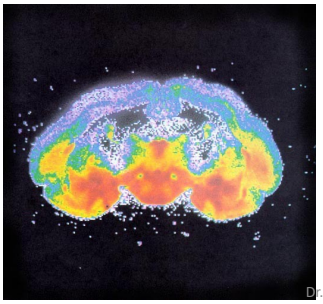
Opioids Receptors

Receptor	High affinity ligands
mu	β-endorphin, enkephalins
delta	enkephalins
kappa	dynorphins



- Opioids act at all opioid receptors, but with different affinities
- Distributed throughout brain and spinal cord, especially in limbic areas
- Some overlap but quite distinct localizations

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Opiates/Opioids Potency

- **Opiates(Opium Poppy Extracts/Modifed Extracts)**
- **Morphine(Various) = 1.0**
- **Codeine(Tylenol #3) = 0.4**
- **Opium(Paregoric) = 0.8**
- **Diacetylmorphine(Heroin) = 1.5**
- **Hydrocodone(Vicodin) = 3.0**
- **Oxycodone(Oxycontin,Percodan) = 4.0**
- **Hydromorphone(Dilaudid) = 5.0**

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Opioid Potency

- Meperidine(Demerol) = 1.0
- Propoxyphene(Darvon) = 0.7
- Pentazocine(Talwin) = 0.5
- L acetyl alpha methadol(LAAM)= 2.0
- Methadone (Dolophine) = 3.0
- Levomethadyl acetate HCl (Orlaam) = 3.0
- Fentanyl(Sublimase) = 50.0
- Sufentanyl(Various) = 100.0
- Alpha Sufentanyl (Various) = 200.0

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Opioid Receptors "Dynamite with Lit Fuse"

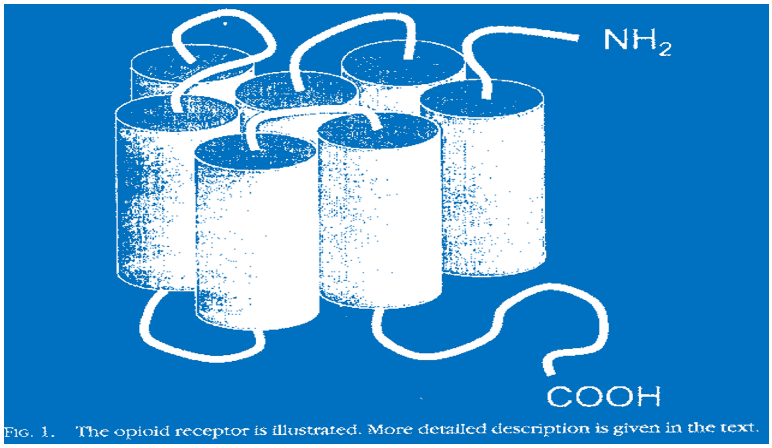

FIG. 1. The opioid receptor is illustrated. More detailed description is given in the text.

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The "Dynamite" of Opioids

Aspirin (1 stick)	Codeine (1 stick)	Hydrocodone (3 sticks)
Morphine (4 sticks)	Fentanyl (21 sticks)	

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Nature of Substance Use Disorders(Addiction)

- **Loss of control**
- **Harmful Consequences**
- **Continued Use Despite Consequences**

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Three "C's" of Substance Use Disorders (Addiction)

Control
- Early social/recreational use
- Eventual loss of control
- Cognitive distortions ("denial")

Compulsion
- Drug-seeking activities
- Continued use despite adverse consequences

Chronicity
- Natural history of multiple relapses preceding stable recovery
- Possible relapse after years of sobriety

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Substance Use Diorders (Addiction) Risk Factors

- Genetics
- Young Age of Onset
- Childhood Trauma (violent, sexual)
- Learning Disorders (ADD/ADHD)
- Mental Illness
  - Depression
  - Bipolar Disorder
  - Psychosis

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Substance Use Disorders (Addiction) As A Brain Diseases
Part 2

Merrill Norton Pharm.D.,D.Ph.,CMAC
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Addition Counselor Emeritus
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Georgia Department of Behavioral Health
& Developmental Disabilities

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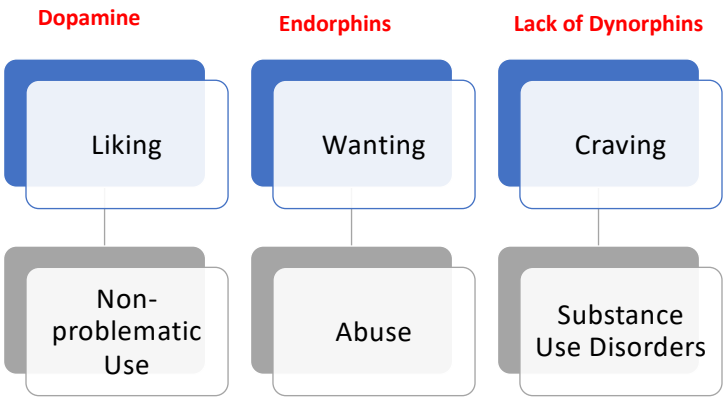
Desire Corresponds with Drug Use



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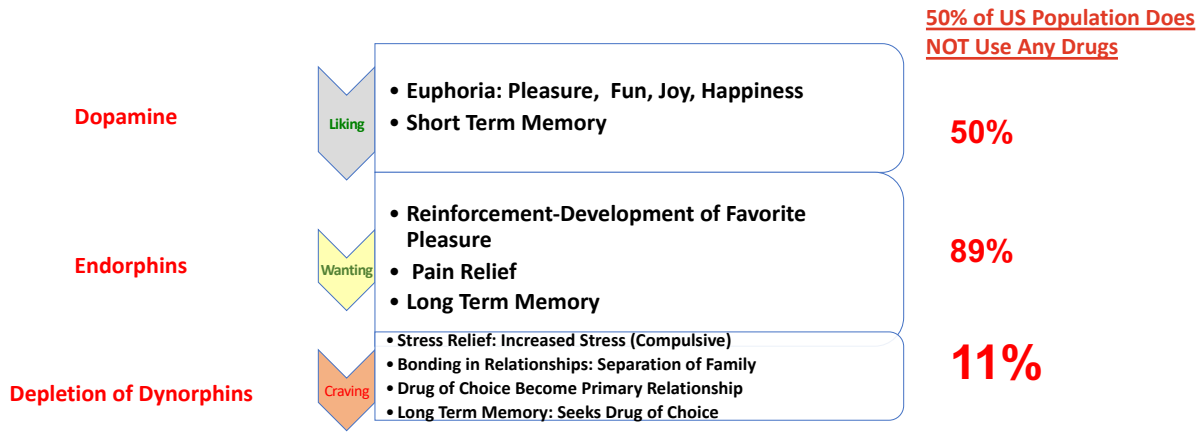
Desire Corresponds with Drug Use



SAMHSA NSDUH Survey June 2015

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The Full Spectrum of Compulsive Disorders

- 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," Over-exercise)
- Collection/Accumulation ("Shop-aholism")
- Rage/Violence
- Media/Entertainment

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"The Essential Eleven"

- Norepinephrine /Epinephrine-stimulant,anger,fear,anxiety,fight,flight
- Serotonin-depressant,sleep,calm,pleasure
- GABA-relaxant,stress reduction,seizure threshold
- Endorphins-pain relief,pleasure
- Acetylcholine-involutary actions,memory,motivation
- Histamine-memory, cognition
- Anandamide-memory,new learning,calmness
- Glutamate-organization of brain signaling,memory,pain
- Dopamine-perception,movement,pleasure
- PIP- loving of one's self,others,GOD
- Dynorphins- stress management, bonding

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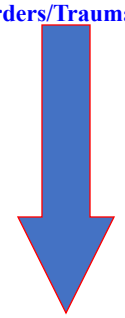
Human Doing

Substance Use Disorders/Trauma



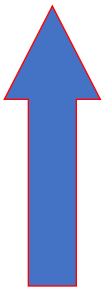
Depletion may take less than 12 months
Trauma only takes seconds to alter these neurtransmitters

Neurotransmitters of Substance Use Disorders

Dynorphins
PIP
Dopamine
Glutamate
Acetylcholine
Histamine
Anandamide
Endorphins / Enkelphins
GABA
Serotonin
Epinephrine / Norepinephrine

Human Being

Recovery



Replenishment may take 5 to 7 years

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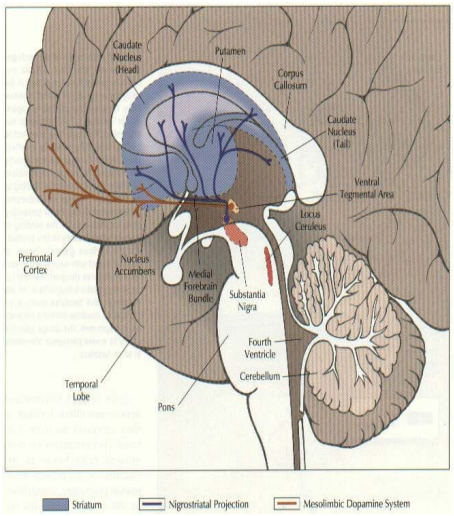
MESOLIMBIC DOPAMINE SYSTEM



- **Circuit #1 Use- Dopamine-mu**
  - **Relief/Like**
    - **Pleasure**/Pain circuit
      Meso-accumbens
- **Circuit #2 Pattern of Use-Endorphins-delta**
  - **Repeat/Want/Reinforcement**
    Desire and urge circuit
    Basolateral n. of amygdala
- **Circuit #3 Stress Relief- Kappa- Addiction**
- **Dynorphin A/B**
  - **Need/Bonding/ (Depletion=Craving)**
  - Pathologic desire & demand circuit
  - Periaqueducal gray of brain stem
  - Stimulation of the periaqueductal gray matter of the midbrain activates enkephalin-releasing neurons that project to the raphe nuclei in the brainstem.
  - Enkephalin (endogenous opioid neurotransmitter), binds to mu opioid receptors.

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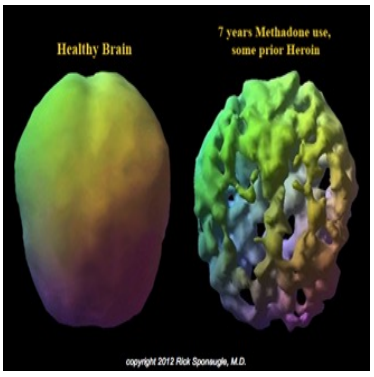
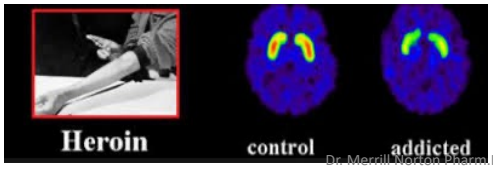
Substance Use Disorder Effects on the Brain

- Long term SUD can lead to areas of the brain "going dark" or the creation of a functional hole in the brain, other areas of the brain will begin to shrink.





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Why Do Individuals with Substance Use Disorders (Addictions) Refuse to Get Better and Run Away from Any Type of Help

Two primary reasons for resistance to seek help for addictions has been discovered recently:

Shame- the stigma of being an addict or alcoholic in this culture is one of the most shaming experiences that an individual exposes themselves and their families to in their lifetime;

The Depletion of the Dynorphin system as a result of the disease process of addiction.

This short presentation will explain both of these powerful events.

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What Does Shame and the Loss of the Dynorphins Do to the Substance Use Disordered (Addicted) Individual?

Shame simply causes the individual to not seek help from anyone-"I can do this all by myself" is the theme of this life-in reality the failure to control one's drinking and using causes tremendous internal shame that creates an inability to ask for help for their addiction without severe consequences occurring first;

The loss of the dynorphin system as a result of an addiction causes an individual to lose their natural bonding to those individuals and situations that the person is connected(family, church, community, close friends). They will deceive, lie, hide, and simply not respond to these individuals concerning their drinking or drugging.

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Definitions Related To Substance Use Disorders

- **Stigma:**
- Erving Goffman, traditionally the best-respected authority on the subject of stigma, defined stigma as *"an attribute that is deeply discrediting" and described the stigmatized individual as "a discredited person facing an unaccepting world"* (Goffman, 1963).
- **Guilt:**
- The uncomfortable feeling we often experience when we have done something wrong ; Guilt is based on a failure of doing ; Guilt involves a violation of standards.

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Definitions Related To Substance Use Disorders

- **Unhealthy Shame:**
- The pervasive feeling that who we are, rather than what we have done, is condemnable, and therefore we are unworthy, unlovable, and defective. Unhealthy shame sufferers have taken on the shame that rightfully belongs to another. Children of addicted parents are an example of this type of shame.

- **Healthy Shame:**
- A balance between knowing what is morally right or wrong and having remorse for our actions and taking responsibilities for our mistakes.

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Impact of Substance Use Disorders on Individuals and Families

- Shame
- Negativism
- Isolation
- Inconsistency in relationships
- Denial
- Miscarried expression of anger
- Self-medication
- Unrealistic expectations
- Unwilling to ask for help

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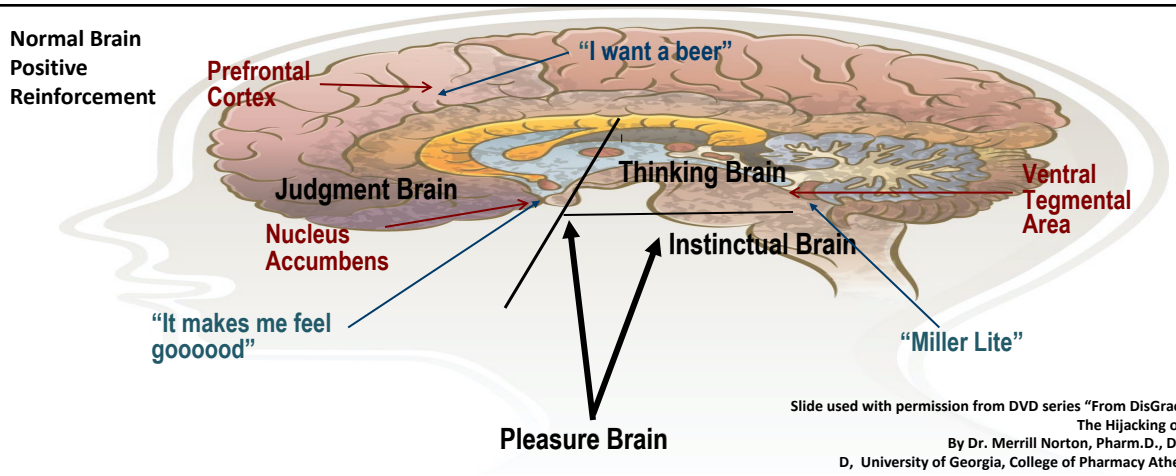

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By Dr. Merrill Norton, Pharm.D., D.Ph., ICCDP-D, University of Georgia, College of Pharmacy Athens, Georgia

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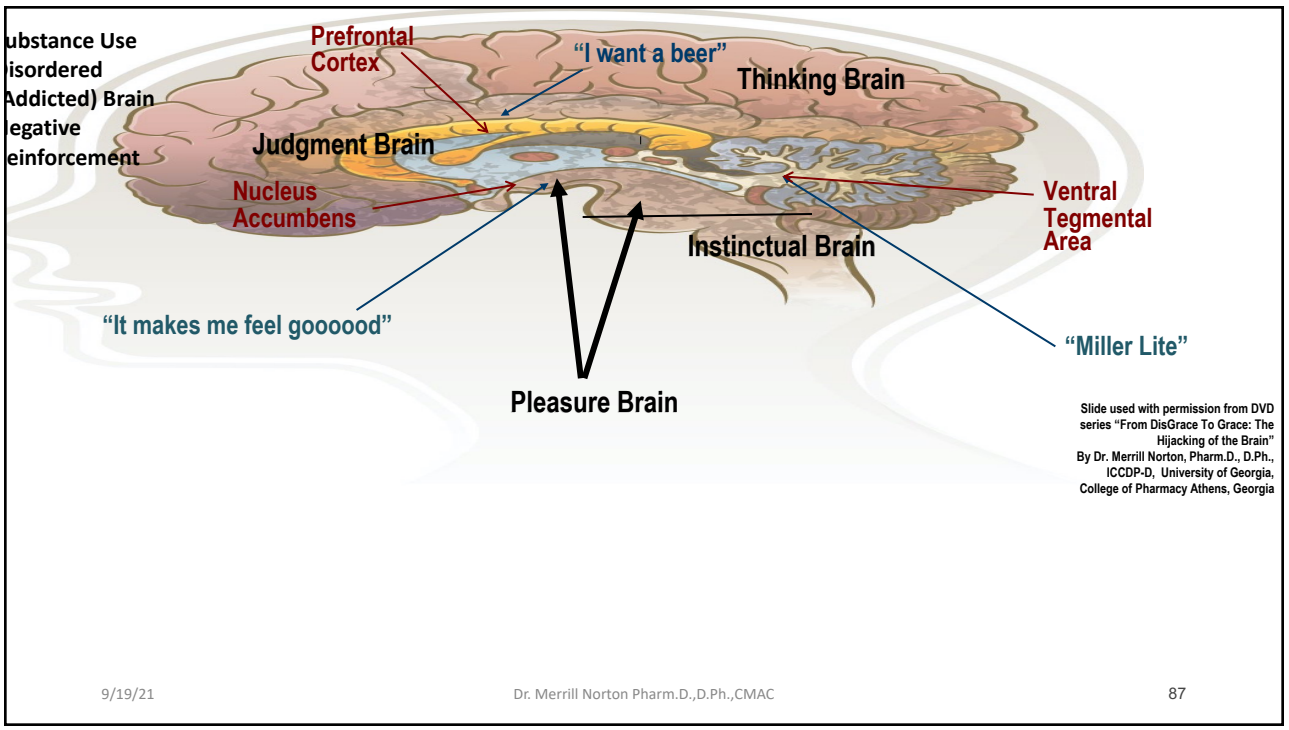
ubstance Use
isordered
Addicted) Brain
egative
einforcement
Prefrontal Cortex
"I want a beer"
Thinking Brain
Judgment Brain
Nucleus Accumbens
Ventral Tegmental Area
Instinctual Brain
"It makes me feel goooood"
"Miller Lite"
Pleasure Brain
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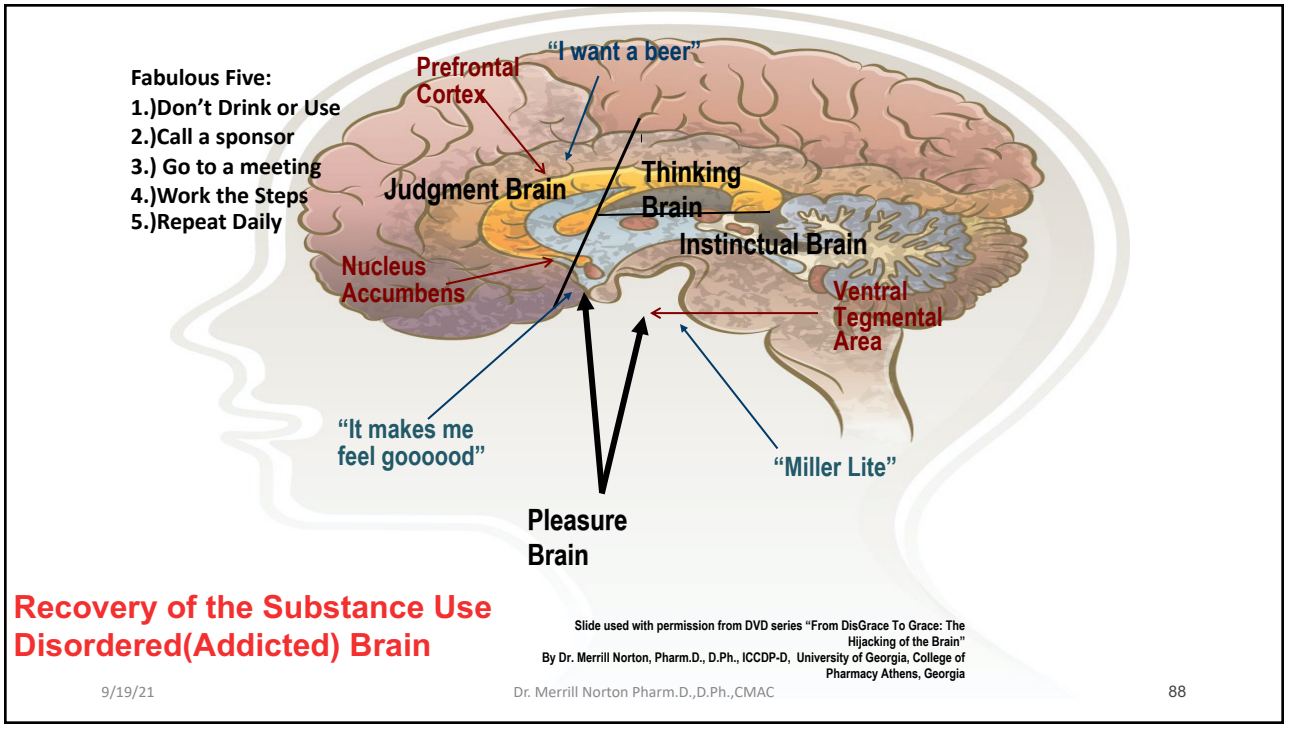
Fabulous Five:
1.)Don't Drink or Use
2.)Call a sponsor
3.) Go to a meeting
4.)Work the Steps
5.)Repeat Daily
Prefrontal Cortex
"I want a beer"
Judgment Brain
Thinking Brain
Instinctual Brain
Nucleus Accumbens
Ventral Tegmental Area
"It makes me feel goooood"
"Miller Lite"
Pleasure Brain
Recovery of the Substance Use Disordered(Addicted) Brain
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The Changing of the Brain's Communication Highway

- 1.) Alcohol, Marijuana, Rx medications alter the receptors and neurotransmitters with any use; it happens like this:
- 2.) The person experiences euphoria from the release of dopamine (excessive amounts) when they drink or use a drug;
- 3.) The brain records this pleasurable experience in short term memory-"this was a good time";
- 4.) If the person begins to repeat the pleasurable experience, the dopamine becomes depleted, the brain attempts to stabilize the chemistry by using another set of chemicals, the endorphins, to reset the brain back to normal; but this attempt just creates a need for more of the drug-tolerance and withdrawal;
- 5.) If the persons continues to use (thinking that they can get back to normal), the brain activates a third set of chemicals, the dynorphins, to keep the brain's communication highway open.

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The Changing of the Brain's Communication Highway

- 6.) The dynorphins are responsible for many things in the brain, one of the most important is stress reduction created by intimate relationships (family, friends, church,etc.) A long term memory system is activated.
- 7. As the person continues to use the drug, the dynorphins are depleted over time, making normal relationships less important.
- 8. As the depletion of the dynorphins continues, the brain will begin to substitute the drug of abuse for the brain's natural dynorphin.
- 9.) The brain becomes "hijacked" using the drug of abuse as the primary relationship of importance, instead of the normal relationships in the person's life. This is addiction.
- 10.) Once the hijacking occurs-it is irreversible-addiction is a chronic disease process.

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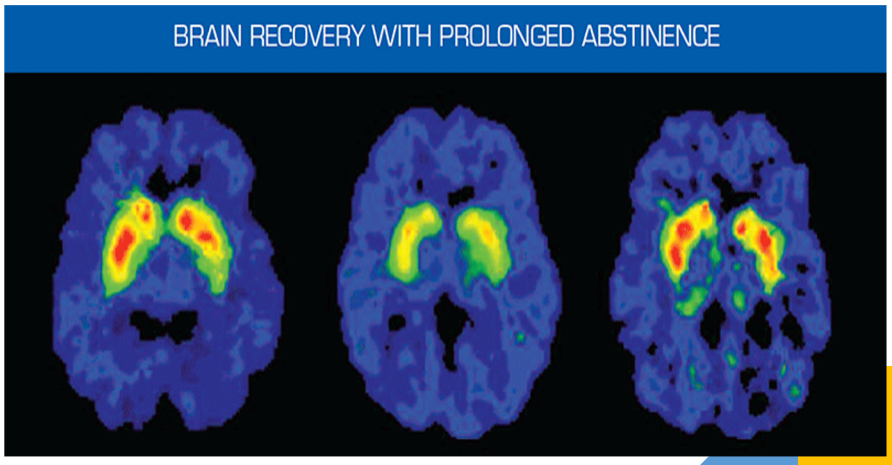
Substance Use Disorders(Addiction) are Treatable and So Is Shame!



Normal Brain 1 month of abstinence 14 months abstinence

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Resources for Assisting Client Heal From Their Shame

- ***Shame: The Power of Caring*** **by Gershen Kaufman**
- ***Shame and the Self*** **by Francis Broucek**
- ***Shame and Pride*** **by Donald Nathanson**
- ***Shame, Exposure and Privacy*** **by Carl Schneider**
- ***Shame and Neurosis*** **by Helen Block Lewis**
- ***The Use of the Creative Therapies in Treating Depression,*** **Shelia Rubin**
- ***Shame and Countertransference*** **by Sheila Rubin**
- ***Shame and Guilt*** **by Jane Middleton-Moz**
- ***Letting Go of Shame*** **by Ronald & Patricia Potter-Effron**
- **Healing the Shame That Binds You by John Bradshaw**
- **The Family by John Bradshaw**

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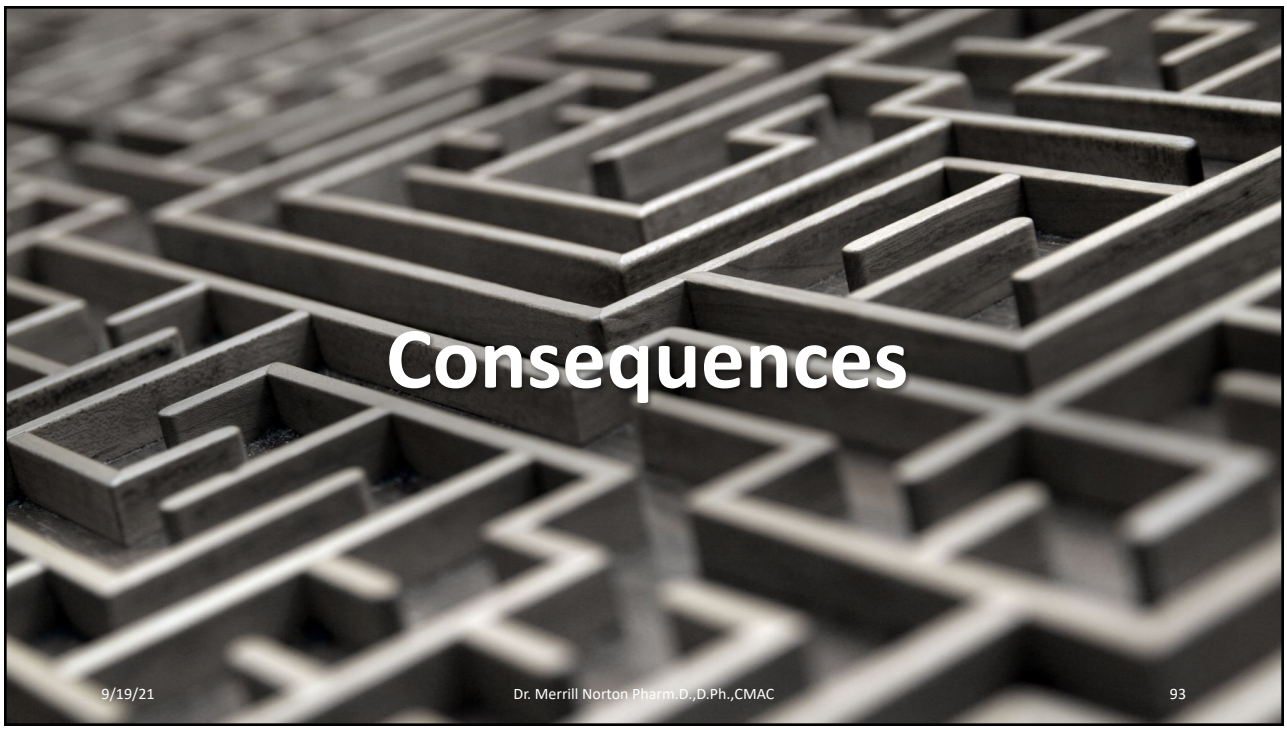

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Overdosing- #1 Issue

- In the events of an opioid overdose, medical professionals and in some cases law enforcement administer naloxone, commonly referred to as naloxone.
- The CDC reports that for every overdose death in the U.S., a person taking opioids on average will overdose nine times. While overdose deaths can occur anytime, the most high-risk individuals are those using escalating doses of drugs and those using a combination of drugs such as opioids and benzodiazepines.
- CDC Morbidity and Mortality Weekly report for 2020 states that over 100,000 lives has been saved by Naloxone since 1999

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Narcan® (naloxone)

- Narcan knocks the opioid off the opioid receptor
- Only blocks opioid receptors; no opioids = no effect
- Not harmful if no opioids in system
- *Temporarily* takes away the "high," giving the person the chance to breathe
- Narcan works in 1 to 3 minutes and lasts 30 to 90 minutes
- Narcan can neither be abused nor cause overdose
- Only known contraindication is sensitivity, which is very rare
- Narcan can cause withdrawal symptoms such as:
- nausea/vomiting
- diarrhea
- Chills

muscle discomfort

disorientation

combativeness

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Withdrawal # 2 Issue

The onset of withdrawal symptoms vary among users.

Those who use heroin once a day experience peak withdrawal effects within 36-48 hours of there last administered dose.

Symptoms such as pain, restlessness and vomiting go away within in 7-10 days.

Medication assisted treatments (MAT) is recommended by SAMHSA for withdrawal.

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Withdrawal Timeline

- **8 - 12 hrs:** tremors, sweats, irritability, runny nose & eyes

→

48 - 72hrs: symptoms worsen; pupil dilation, piloerection, anorexia

→

Long-lasting effects: hypersensitivity to pain, anhedonia

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Opioid Withdrawal Syndrome

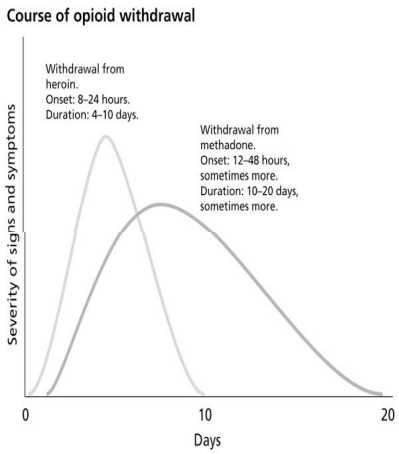

Image source: NSW Department of Health (2007) NSW Drug and Alcohol Withdrawal Clinical Practice Guidelines

- **Increased pain**
- **Agitation, poor sleep**
- **Dysphoria**
- **Dilated pupils**
- **Increased BP, PR, RR**
- **Sweaty, ⇧urine**
- **Diarrhea, abdominal cramps**
- **Nausea, vomiting**

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Cravings # 3 Issue

- Craving: memory of rewarding aspects of drug use superimposed on a negative emotional state
  - Compels drug-seeking in dependent individuals
- 3 Types of Cravings
  - Withdrawal induced
  - Cue-induced
  - Drug-induced

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Options of Pharmacological Treatment

1. Methadone
   - Full μ agonists
   - Once/day dosed
   - 40-60 mg/d: sufficient to block withdrawal symptoms
2. Buprenorphine and Buprenorphine/Naloxone
   - μ Receptor partial agonist
   - Kappa receptor partial antagonist
   - 12-16 mg/d
   - Combination ↓ risk of diversion
3. Naltrexone
   - Opioid antagonist
   - Oral or injectable
   - This extended-release injectable medication is the most recent drug, approved in October of 2010, for the treatment of opioid addiction.
4. Naloxone- Overdose Prevention-Training required for all practitioners who are prescribing opioids to patients

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Medications for Cravings

Naltrexone is the only FDA approved medication indicated to treat cravings in OUD

By blocking opioid receptors and inhibiting euphoric effects, Naltrexone stops the positive reinforcement associated with opioid use

And there are MAT for alcohol use disorders:

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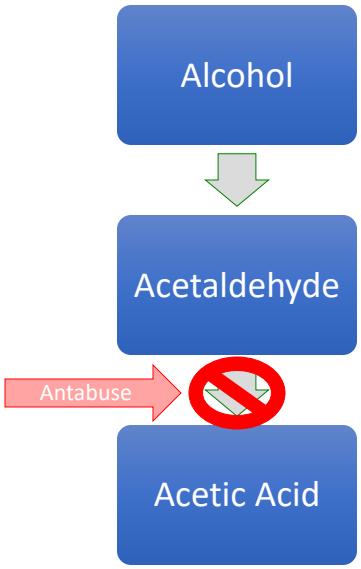
Antabuse (Disulfiram)

- **This medication is an alcohol abuse deterrent**
- **Prevents the second step in alcohol metabolism**
- **Therefore when you consume alcohol:**
  - **This causes a buildup of acetaldehyde**
  - **Flushing, nausea, and palpitation will occur**
  - **If these effects are ignored and drinking is continued, symptoms can build to fatal results!**



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Antabuse (Disulfiram)

Do not take

- Do not take the first dose of this medication for at least 12 hours after drinking alcohol

Avoid

- Avoid alcohol in sauces, foods, and medications
  - Read Labels

Avoid

- Avoid paint fumes, paint thinner, and shellac

Use

- Use caution with colognes, aftershave, and rubbing alcohol

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Antabuse (Disulfiram)

Black Box Warning

Disulfiram should never be administered to a patient when he is in a state of alcohol intoxication, or without his full knowledge. The physician should instruct relatives accordingly.

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Campral (Acamprosate)

- This medication is an anti-alcohol agent to be used in combination with a treatment program that includes social support
- Helps restore chemical balance by increasing GABA activity and decreasing glutamate activity this results in blocking pain and less cravings
- Reduces long term withdrawal symptoms such as insomnia, anxiety, restlessness, and uncomfortable moods
- Shown to help patients with severe dependence remain abstinent for several weeks to months

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Campral (Acamprosate)

- Does not produce a Disulfiram-like reaction
- Will not reduce or eliminate alcohol withdrawal symptoms
- Minor side effects including nausea, diarrhea, and dizziness may be due to alcohol abstinence not the medication
- Must report feeling of depression, anxiety, or any suicidal thoughts to your health care provider

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Vivitrol/ Revia (Naltrexone)

- Vivitrol- monthly injection
- ReVia- daily tablet
- This medication is a narcotic antagonist
- It does not decrease alcohol or opioid withdrawal symptoms
- Treats the cravings, NOT the addiction
- A person cannot have any opioids in system because sudden withdrawal symptoms will result
- Must be opioid free for 7 to 10 days before starting naltrexone

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Vivitrol/ ReVia (Naltrexone)

Black Box Warning

Hepatotoxicity: Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses. Naltrexone does not appear to be hepatotoxic at the recommended doses. Warn patients of the risk of hepatic injury and advise them to seek medical attention if they experience symptoms of acute hepatitis. Discontinue use of naltrexone in the event of symptoms and/or signs of acute hepatitis.

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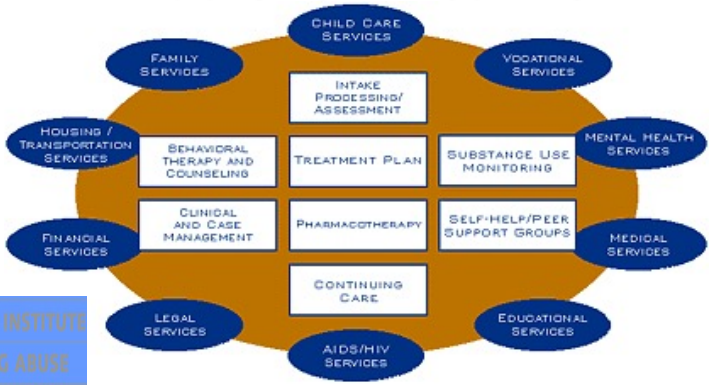
Components of Comprehensive Drug Addiction Treatment



NIDA NATIONAL INSTITUTE ON DRUG ABUSE

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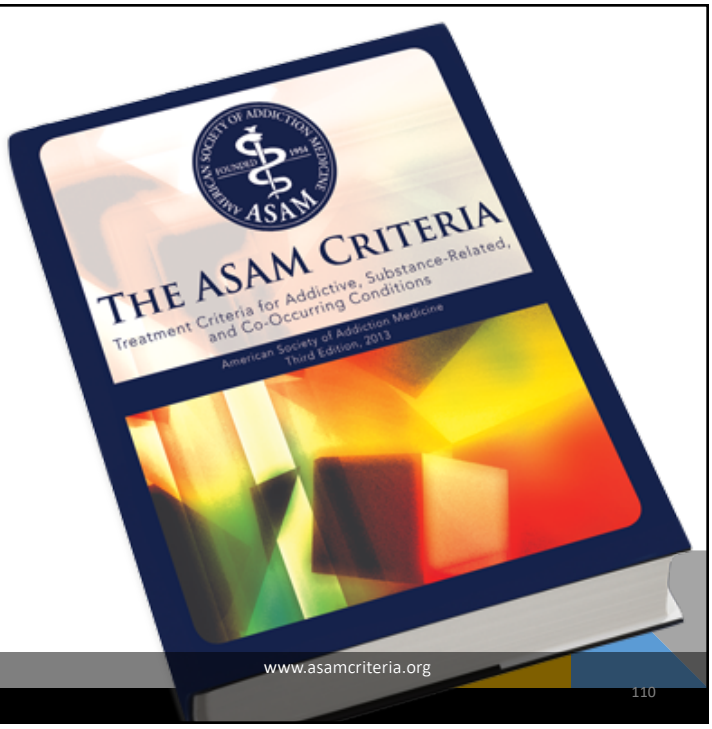
American Society of Addiction Medicine Patient Placement Criteria

- Decision making criteria
- SUDS for healthcare
- Practitioners



www.asamcriteria.org

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ASAM Criteria Levels of Care

- **Level 0.5: Early Intervention Services -** Individuals with problems or risk factors related to substance use, but for whom an immediate Substance - Related Disorder cannot be confirmed
-
- **Opioid Maintenance Therapy (OMT) -** Criteria for Level I Outpatient OMT, but OMT in all levels → **Opioid Treatment Program** (OTP) with **Opioid Treatment Services** (OTS) = antagonist meds (naltrexone) and Office-Based Opioid Treatment (OBOT) - buprenorphine
- (*The ASAM Criteria*, 2013, pp.179,290)

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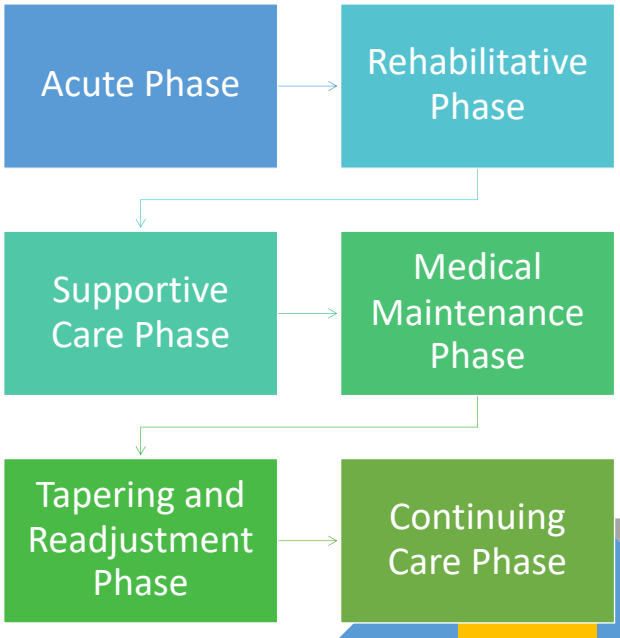
Level 1 OMT 6 Phases



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OMT - Acute Phase

- Initial phase of treatment that begins when the patient is admitted to the OTP program
- Can last days to months (max 180 days)
- The goals are to eliminate withdrawal symptoms and opioid craving, abstain from illicit opioid use, and comply with treatment medications regimens (confirmed by drug tests)
- Patient comes in daily for in-person dosing
- Treatment includes mental health assessments and developing a treatment plan going forward

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OMT – Rehabilitative Phase

- Patient is stabilized on their established dosage for at least 24 hours before moving to this phase – adjustments may still occur
- Take-home medications are available as opposed to daily in-person dosing
- With consistent negative drug test results, the frequency of drug screenings will decrease
- To create a well-rounded recovery, patients are encouraged to put effort towards employment, education, volunteer work, resolving legal problems, developing coping skills for relapse triggers, and connecting with community support groups

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OMT – Supportive-Care Phase

- Patients in this phase are no longer participating in illicit drug use or criminal activities
- More take-home medications and fewer drug screenings
- Counseling is continued

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OMT – Medical Maintenance Phase

- Patients receive up to 30 days of take-home medications and further reductions in treatment visits
- If a patient does not pass a drug screen or diverts medication, they are moved back to a previous, appropriate phase of treatment
- At this phase, patients have a stable environment and income, no legal involvement for at least 3 years, and have no current parole or probation status
- Continuation of random drug testing, callbacks of medication, and monitoring for relapse risks

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OMT – Continuing Care Phase

- Medical follow-up by a primary care physician, occasional check-ins with an OTP counselor, and participation in recovery groups
- Appointments with the OTP should be scheduled for every 1–3 months
- Some patients might need referral to a non-MAT outpatient program

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ASAM Criteria Levels of Care

- **Level I and II Services**
  - **Level I Outpatient Treatment**
  - **Level II.1 Intensive Outpatient Treatment**
- **Level II.5 Partial Hospitalization**

- (*The ASAM Criteria*, 2013, pp.132-134)

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ASAM Criteria Levels of Care

- **Level III.1 Clinically-Managed, Low Intensity Residential Treatment (Adult Level only**
- **Level III.3 Clinically-Managed, Medium Intensity Residential Treatment (Adult Level only)**
- (*The ASAM Criteria*, 2013, pp.133-141)

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ASAM Criteria Levels of Care

- **Level III.5 Clinically-Managed, Medium/High Intensity Residential Treatment**
- **Level III.7 Medically-Monitored Intensive Inpatient Treatment**
- (*The ASAM Criteria*, 2013, pp.133-141)

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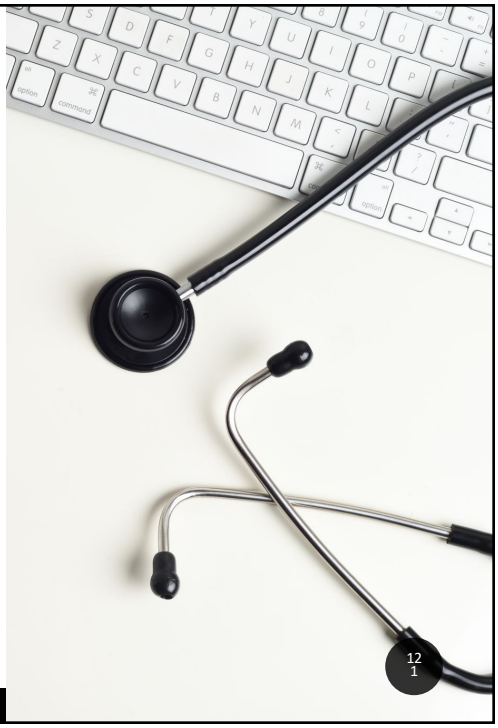
ASAM Criteria Levels of Care

- **Level IV Medically-Managed Intensive Inpatient Treatment**

- (*The ASAM Criteria*, 2013, pp.133-141)



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Recovery Mechanisms Can Reverse the Depletion-A Day At A Time

- **FIND AND GO TO A MEETING;**
- **WORK THE STEPS OR SIMILAR SPIRITUAL PROGRAM;**
- **REPEAT DAILY**
- **If a person follows the Fabulous Five Essentials of Recovery, the dynorphins begin to be restored and as long as the process is in place-relapse and cravings are avoided. Stop the process, the dynorphins are depleted and relapse and cravings return.**

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Recovery Mechanisms Can Reverse the Depletion-A Day At A Time

- To recover from this biological hijacking of the drugs of choice, the brain must reestablish a human dynorphin experience, thus the beginning the recovery process.
- To establish the recovery process (Dynorphin re-establishment), human relationships are essential;
- The Fabulous Five elements of establishing these human recovery relationships are;
- DO NOT DRINK OR USE;
- FIND AND CALL A SPONSOR;

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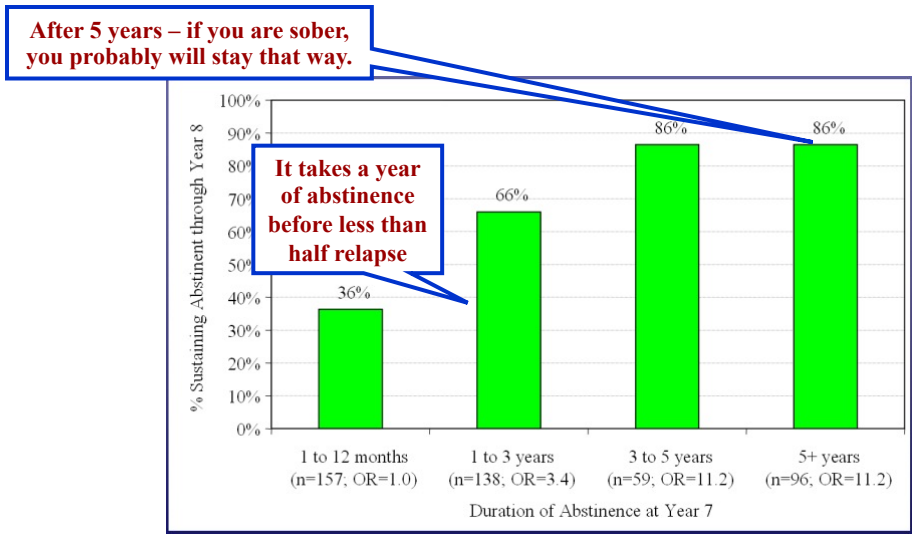
Extended Abstinence is Predictive of Sustained Recovery



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Thank You For Your Time

Any Questions?

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Thank You For Your Time

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