The Science of Addiction

Opioid Use Disorder and the Medications Used to Treat It

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Opioid Response Network
STR-TA

Working with communities to address the opioid crisis.

- SAMHSA's State Targeted Response Technical Assistance (STR-TA) grant created the *Opioid Response Network* to assist STR grantees, individuals and other organizations by providing the resources and technical assistance they need locally to address the opioid crisis .
- Technical assistance is available to support the evidence-based prevention, treatment, and recovery of opioid use disorders.

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Disclosures

- I have no relevant financial disclosures

Learning Objectives

- Recognize the “Chronic Disease Model” of Addiction
- Explain how Adverse Childhood Experiences effect your risk of developing Substance Use Disorder
- Name the neurotransmitter implicated in addiction with drugs of abuse
- Name the 3 types of pharmacotherapy available for treating Opioid Use Disorder (OUD)
- Give at least one reason why pharmacotherapy is indicated for OUD

The Science of Addiction

Myths vs. Facts

Myths

- Drug Addiction is a voluntary behavior.
- More than anything else, drug addiction is a character flaw. Many people relapse, so treatment obviously doesn't work
- You have to want drug treatment for it to be effective.
- Treatment for addiction should be a one-shot deal.
- We should strive to find a “magic bullet” to treat all forms of drug abuse.
- The most important measure of treatment success is having a “clean” urine.

Reference: https://archives.drugabuse.gov/exploring-myths-about-drug-abuse

Myths vs. Facts

Facts

- Addiction is a treatable chronic disease. As with other chronic diseases such as diabetes and hypertension, treatment usually isn't a cure.
- Chemical changes within the brain mean most people with addictions can't stop using successfully without treatment, no matter how strong their "will power"
- As with other chronic disease, there is no one size fits all approach to treating addictions and people need access to a range of medication and behavioral treatments
- The goal of treatment is to help individuals manage their disease and regain control of their lives, while minimizing the harms of addiction.

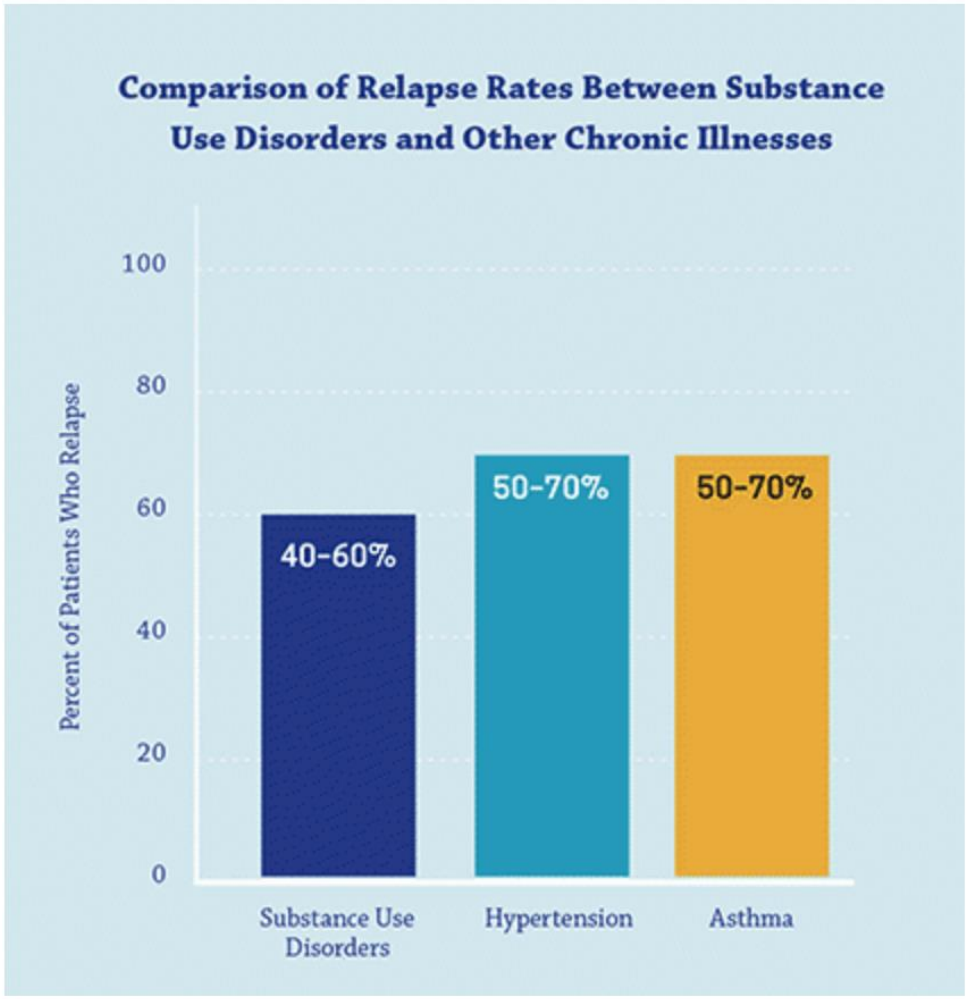
What is Addiction?

"Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases. "

Consensus Statement adopted by the ASAM (American Society of Addiction Medicine) Board of Directors September 15, 2019.

Relapse Rates of Chronic Diseases



JAMA, 284:1689-1695, 2000.

Vulnerability to Addiction

Chronic, dysfunctional upregulation of the stress response in children who are exposed to high ACE levels during early childhood already have disruption of normal brain chemistry and development.

There are genetic and environmental factors that also influence risk of developing addictions

ACEs & Substance Use Disorders

Compared to people with no ACES, if you have 4 or more ACEs, you are-

- 2x more likely to smoke cigarettes
- 7x more likely to have an alcohol use disorder
- 10x more likely to inject drugs
- 6x more likely to be depressed
- 12x more likely to have attempted suicide

https://www.cdc.gov/vitalsigns/aces/index.html

Is addiction a normal reaction to ACEs and other trauma?

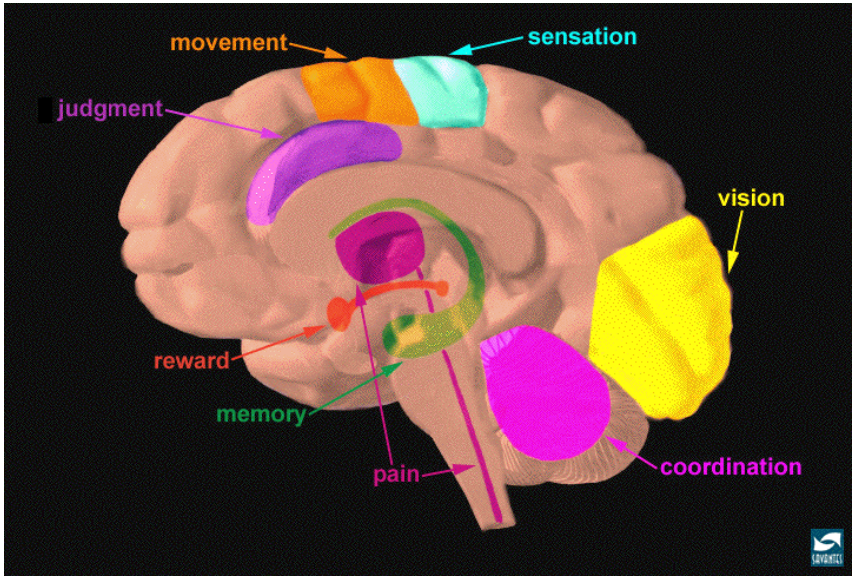
Addiction may be better understood as "ritualized compulsive comfort seeking behavior"

- Dr. Daniel Sumrok, Director of the Center for Addiction Sciences at the University of Tennessee Health Science Center
- Source: https://acestoohigh.com/2017/05/02/addiction-doc-says-stop-chasing-the-drug-focus-on-aces-people-can-recover/

"Ritualized compulsive comfort-seeking (what traditionalists call addiction) is a *normal* response to the adversity experienced in childhood, just like bleeding is a normal response to being stabbed."

"The solution to changing the illegal or unhealthy ritualized compulsive comfort-seeking behavior of opioid addiction is to address a person's adverse childhood experiences (ACEs) individually and in group therapy; treat people with respect; provide medication assistance in the form of buprenorphine, an opioid used to treat opioid addiction; and help them find a ritualized compulsive comfort-seeking behavior that won't kill them or put them in jail."

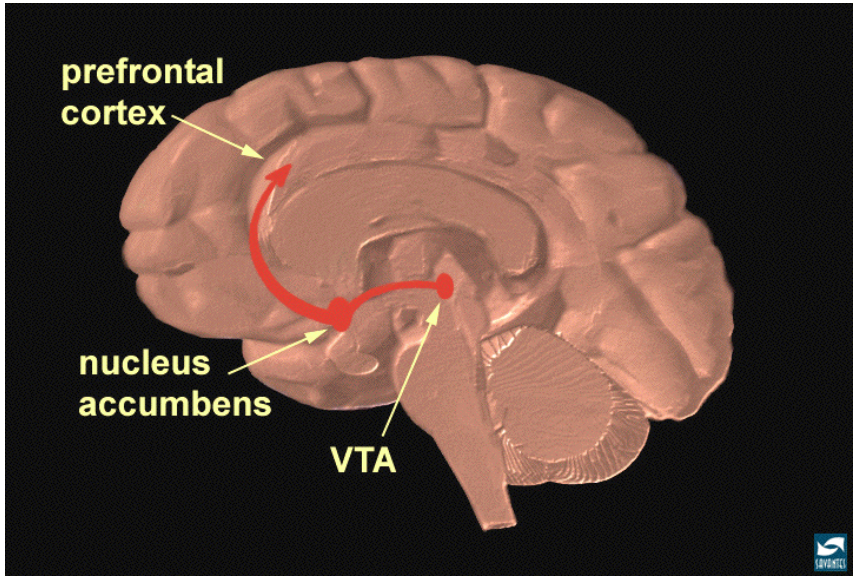
Neurobiology of Addiction: Brain Regions and Pathways



- Memory: Hippocampus (green)
- Coordination: Cerebellum (pink)
- Reward pathway (dark orange)
- Pain processing: Thalamus (magenta)

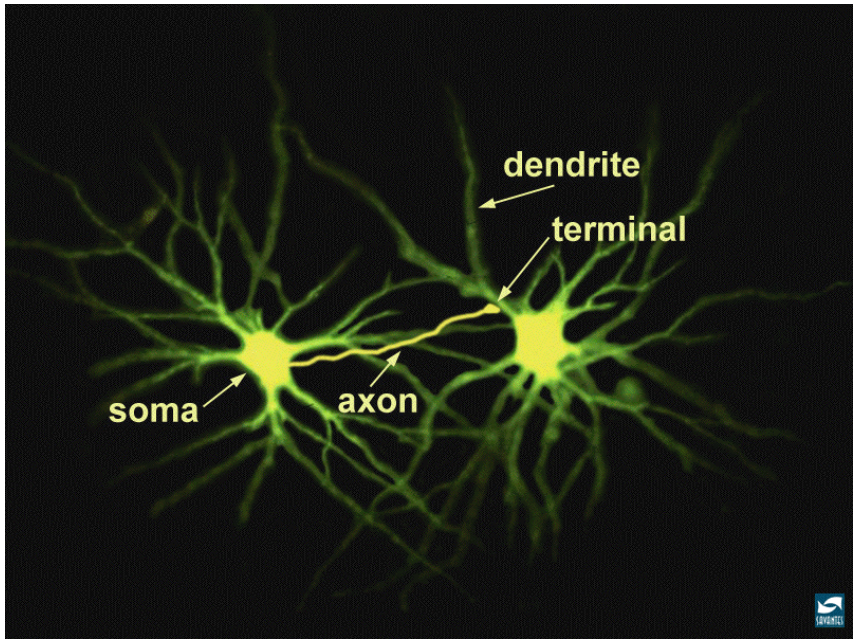
The Reward System

- Our brains are programed to respond to “natural” rewards
  - Food
  - Water
  - Sex
  - Nurturing
- These pleasurable feelings make us seek to repeat these activities and ensure our survival as a species



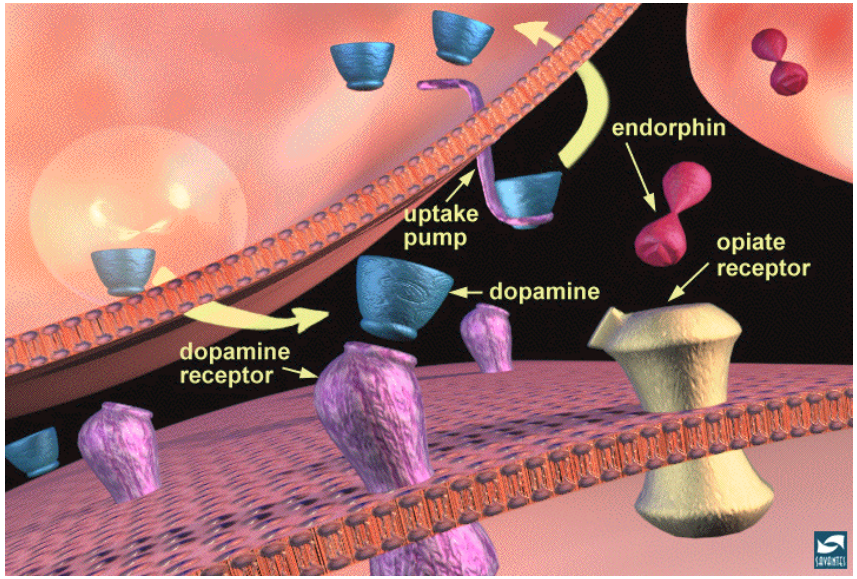
Signal Transmission

- Neurons (cells that send and receive signals)
- Electrical signals
- Neurotransmitters (chemicals that carry signals between these cells)
- Synapse (connection between two neurons)



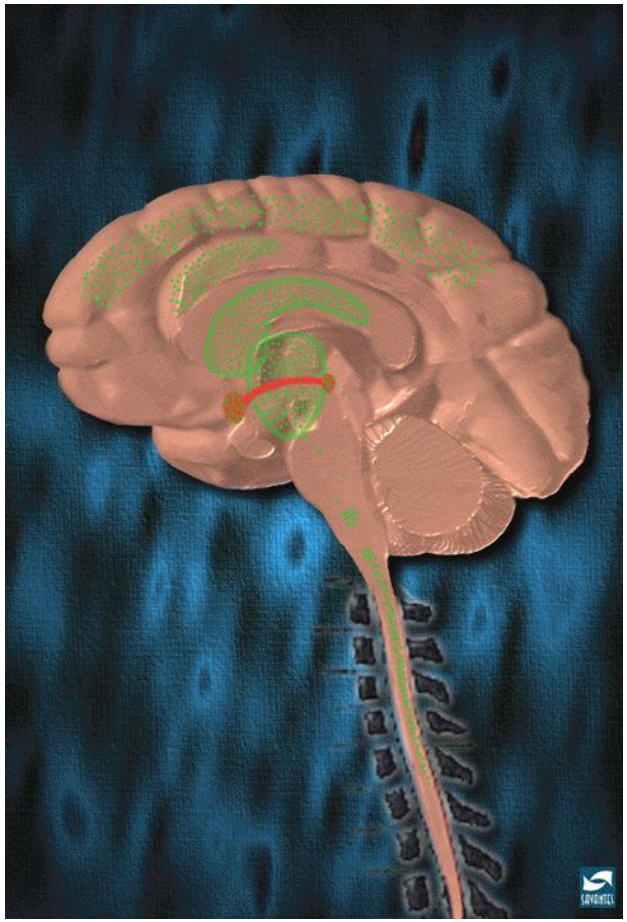
Synaptic Transmission

- Dopamine is released from the terminal and binds to post-synaptic receptor
- It falls off and is taken back into the terminal by uptake pumps
- Natural endorphins (neuromodulator) bind to opioid receptors, causing increased release of dopamine

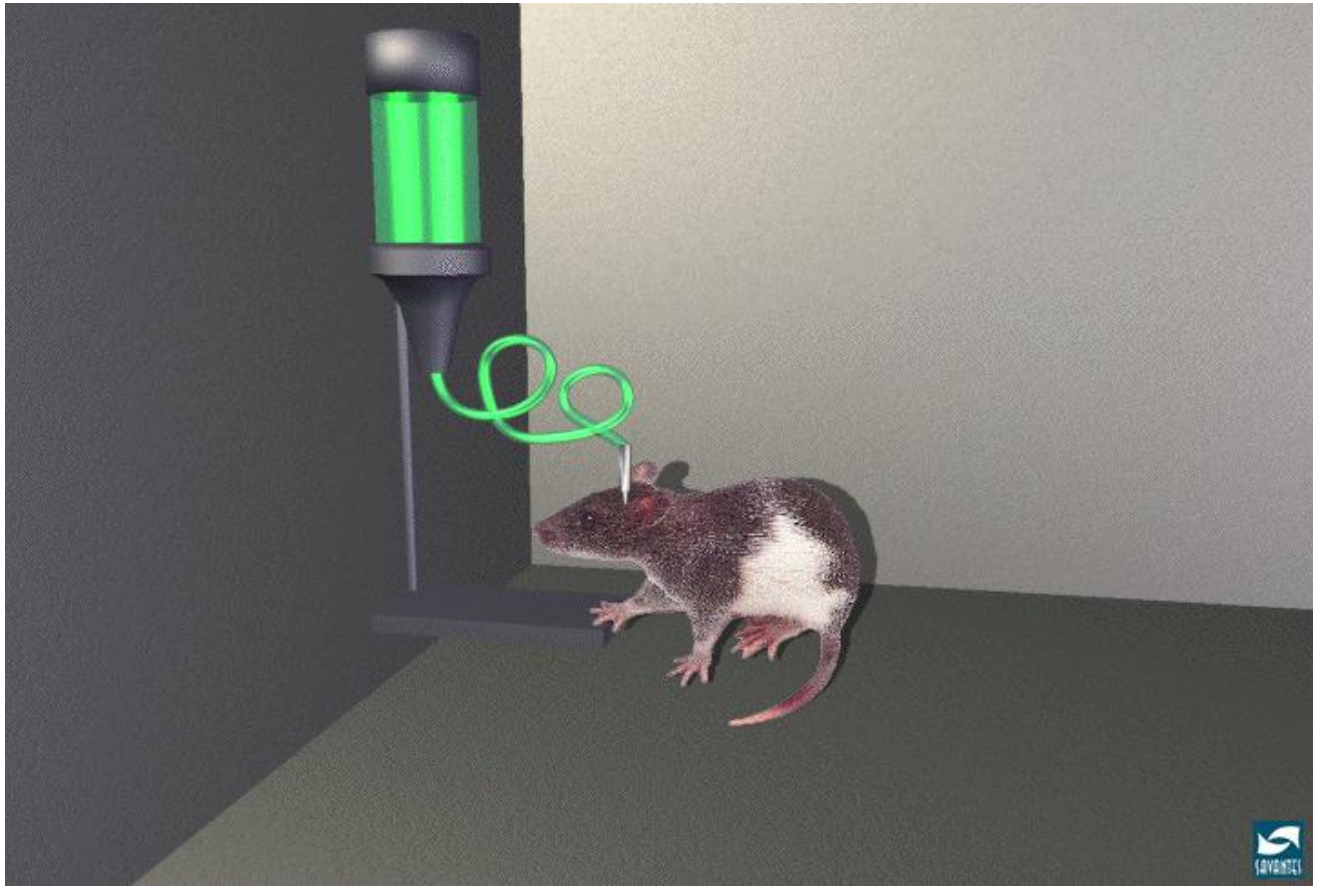


Opioids and the Reward System

- Licit and illicit opioids bind to opioid receptors throughout the CNS including
  - the VTA, NA, and cortex (reward pathway)
  - Thalamus, brainstem, and spinal cord (pain pathway)



This is your brain on drugs?

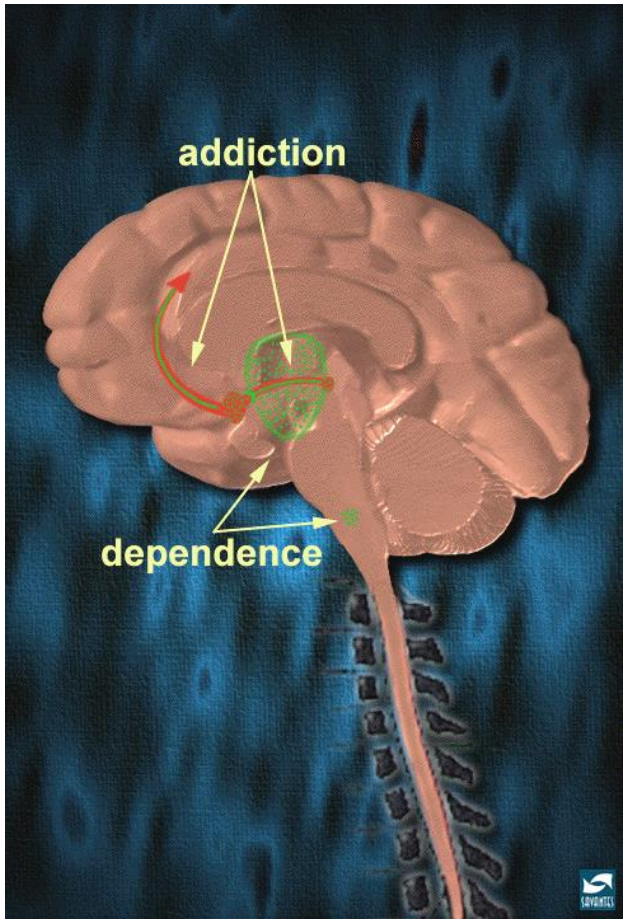


Tolerance and Dependence v. Addiction

- As your brain adjusts to repeated use of opioids it takes more drug to get the same effect (dopamine release/pain relief). This is NOT addiction.
- Your brain chemistry adjusts so that it only functions in a near normal way when the drug is present, and you become ill when the level of drug drops. This is also NOT addiction.

What is Addiction?

- Addiction is essentially a disease of the reward pathway in the brain, in the same way that childhood diabetes is a disease of the pancreatic islet cells
- This manifests as compulsive use of a substance in spite of negative effects associated with use.

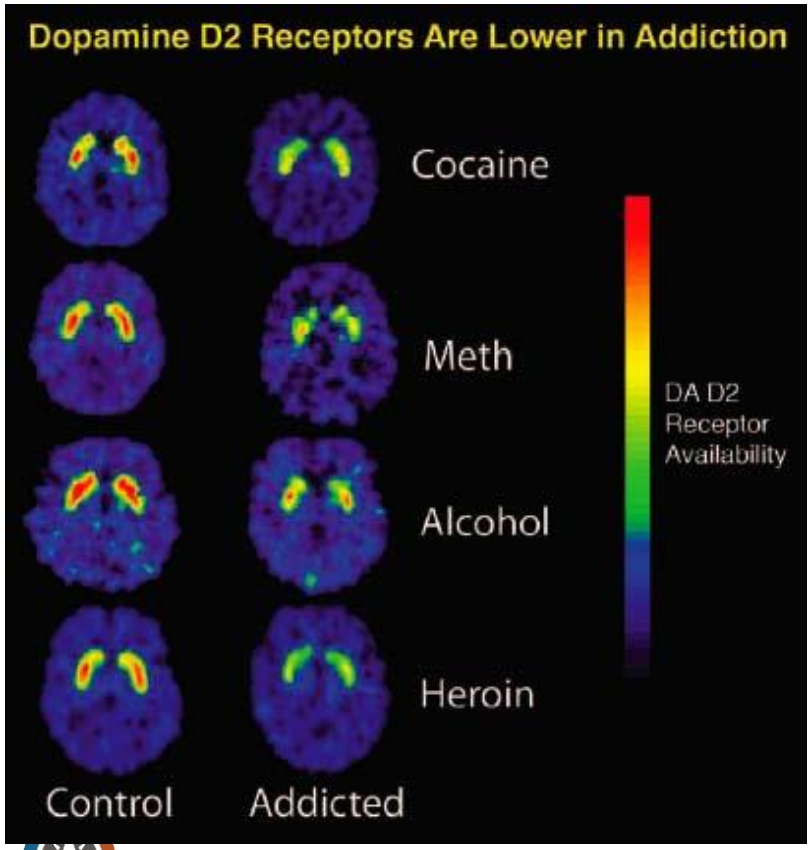


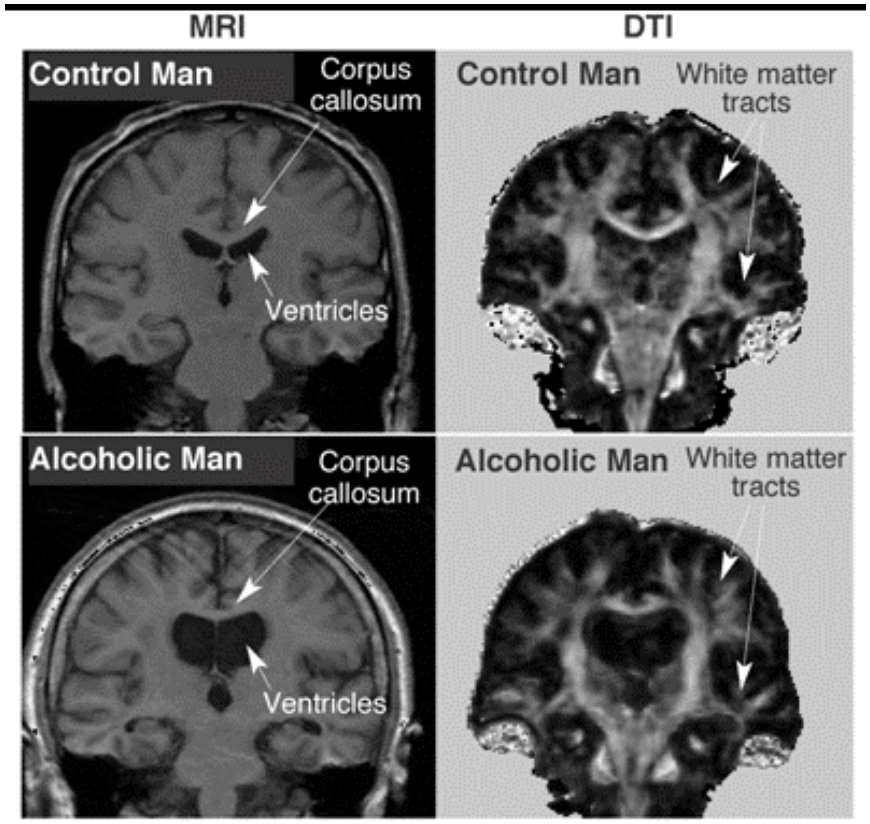
Effects on the Brain

Regular use of opioids rewire the brain's messaging systems and can impact:

- Enjoyment of regular activities
- Experience of pain and suffering
- Memory
- Rational decision-making
- Self-regulation

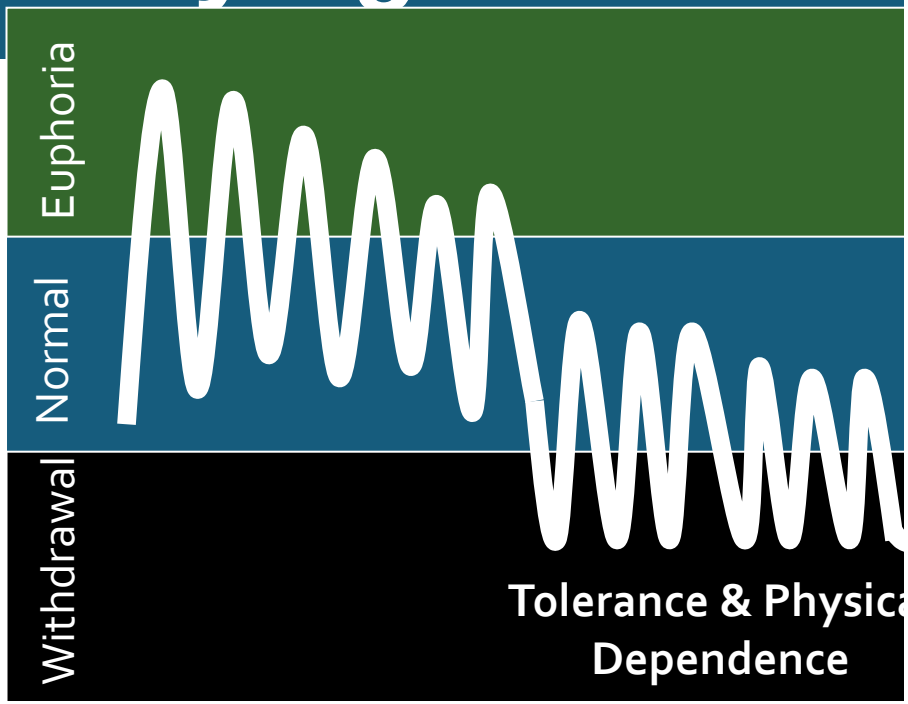
Brain Studies





Slide courtesy of Jennifer Riha, BASc, MAC

Staying well



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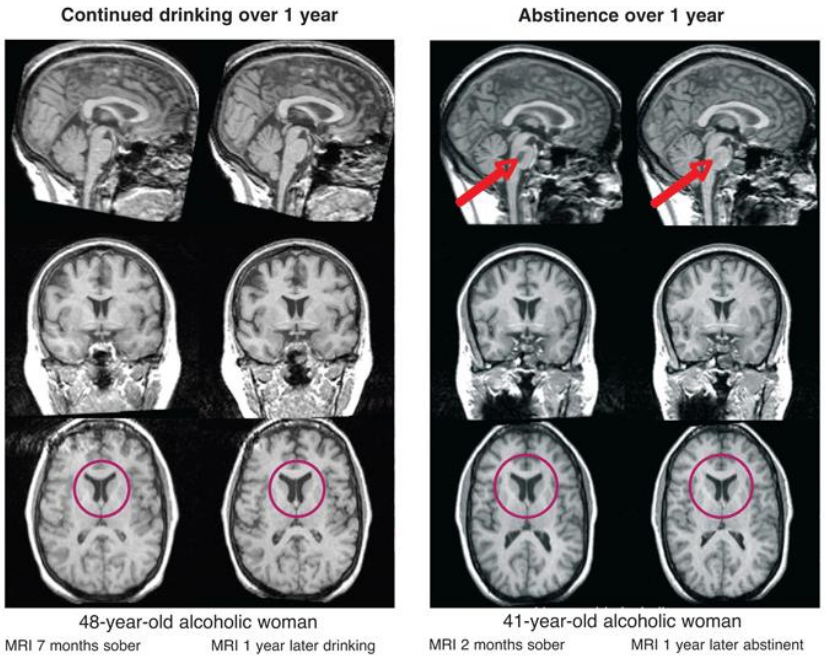
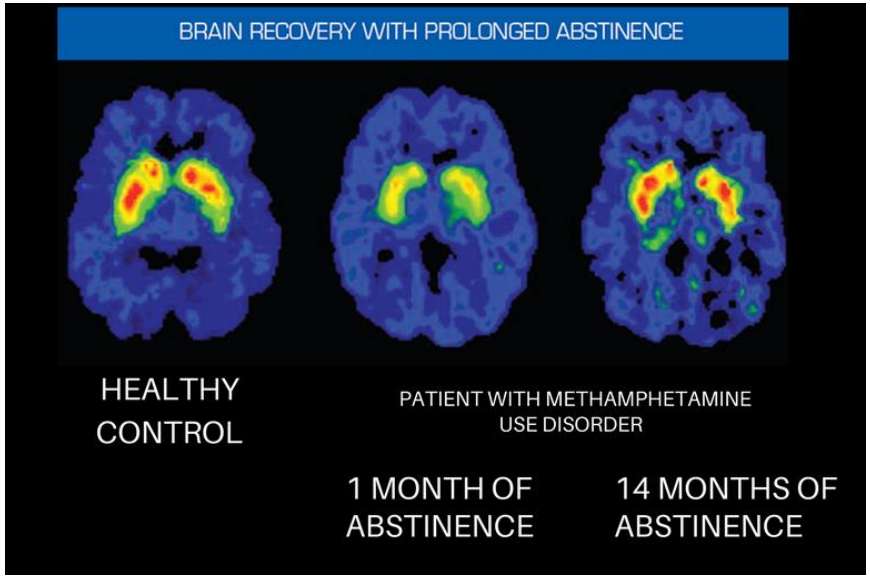
The Science of Recovery





Slide courtesy of Jennifer Riha, BASc, MAC

Cravings and Relapse

Post Acute Withdrawal Syndrome (PAWS)

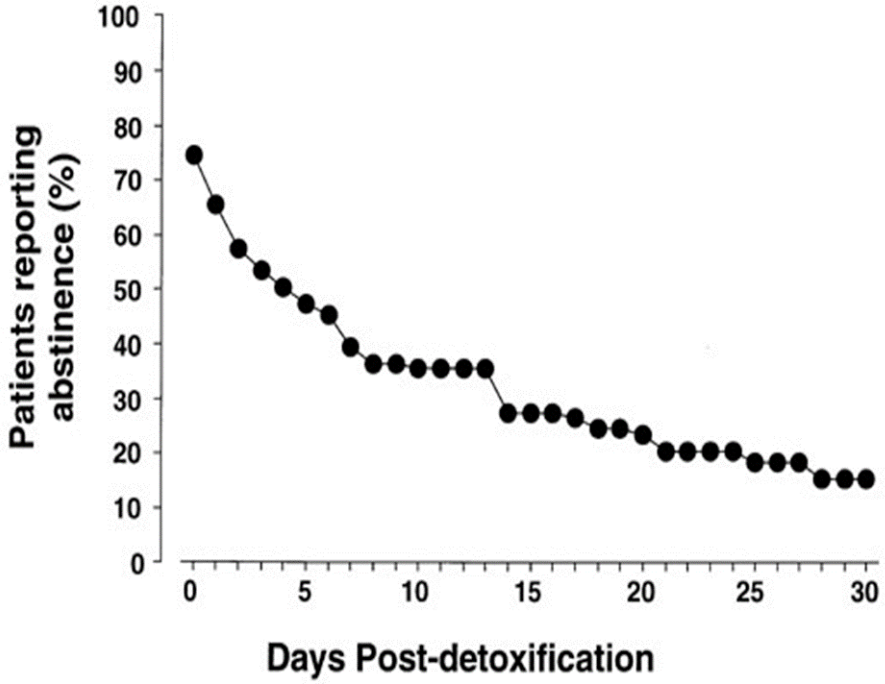
- Happens after detoxification has ended
- Can persist for many months after detox
- Is a result of the brain's decreased ability to function
- Associated with a very high risk of relapse
- Associated with a very high risk of death from overdose due to decreased physical tolerance
- Can last for years with opioid use disorder

PAWS Symptoms

- Low energy
- Low concentration/ poor attention span
- Poor memory
- Poor sleep
- Poor appetite
- Anxiety
- Depression
- High irritability
- Anger
- Feeling "restless"

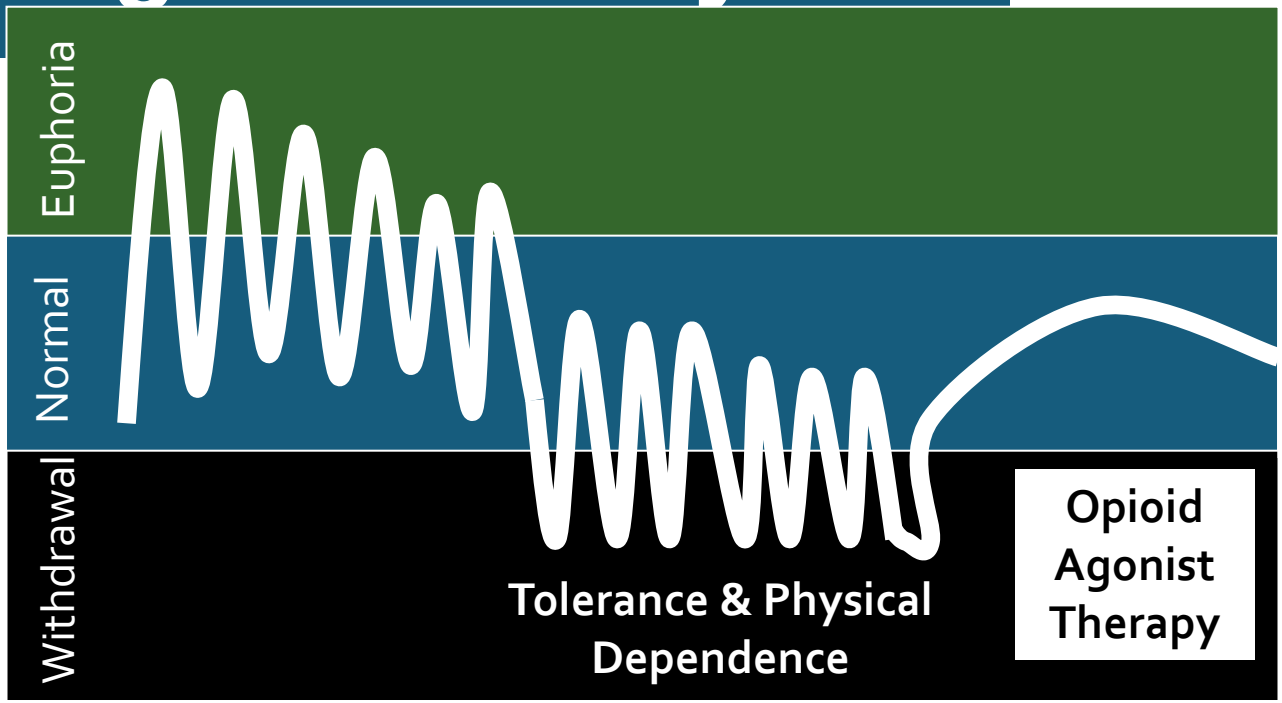
This is why Detox doesn't work-

- High risk of relapse (59-90%)
- Decreased tolerance increases the risk of overdose in the post-detox period



Pharmacotherapy for OUD (Opioid Use Disorder)

No longer in the cycle



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Non MAT Opioids: full agonist heroin, oxycodone, Percocet, etc

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Activates receptor, prevents binding
Risk of sedation
Only at special clinics

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Naloxone (Narcan), Naltrexone (Vivitrol):
Full antagonist, high affinity

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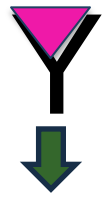

Methadone: full agonist
Activates receptor, prevents binding, risk of sedation

Buprenorphine (Suboxone, Subutex):
partial agonist
High affinity, ceiling effect
Risk of precipitated withdrawal
Any prescriber with X waiver

Naloxone (Narcan), Naltrexone (Vivitrol):
Full antagonist, high affinity

Pharmacotherapy for OUD

There are two classes:

- **Agonists** bind to and (partially) activate mu opioid receptors
  - Minimize withdrawal symptoms
  - Provide stabilization of the dopamine axis
- **Antagonists** bind to and block opioid receptors, preventing activation of the receptor

Understanding the Medications Used to Treat Addiction

- Full agonist – methadone
- Partial agonist – buprenorphine products w/ or w/o naloxone
  - Buccal and transdermal products (approved for treatment of pain only)
  - Sublingual tablet/strip, XR injectable, subdermal implant (approved for treatment of addiction only; DATA Waiver 2000)
- Antagonists – naltrexone
  - Oral (daily)
  - Injectable (monthly)

Life expectancy with IV heroin use

- Without pharmacotherapy, individuals who use IV heroin have a life expectancy of approximately 20 years from onset of disease.
- Treatment with MAT increased life expectancy by almost 8 years.
- Suicide remains a significant cause of death in both treated and untreated groups (16x more likely than in matched individual without OUD), so adding effective mental health treatment to pharmacotherapy has the potential to further increase average life expectancy.
- https://doi.org/10.1016/j.drugalcdep.2015.05.033.
- https://archives.drugabuse.gov/news-events/nida-notes/2008/06/reduced-longevity-among-male-heroin-abusers-1962-1997

Methadone: Full Agonist

- Methadone has a treatment has a success rate of 60–90%.
- It can only legally be prescribed for management of addiction through a licensed OTP.
- Individuals in treatment are physically dependent on methadone and will experience withdrawal if medication is stopped, but have decreased behaviors of addiction
- Methadone can cause respiratory suppression, heart arrhythmias, constipation and all of the other typical opioid side effects, but is significantly safer than untreated OUD

Buprenorphine: (Partial) Agonist

- Treatment can be provided in regular medical practices
- It can only legally be prescribed for management of addiction by a clinician who has a DATA 2000 waiver.
- Individuals in treatment will still have dependence and withdrawal if medication is stopped.
- While bup can cause constipation and other common opioid side effects they are typically much less severe, and there is an effective ceiling on respiratory suppression which makes it very difficult to abuse or OD on this.

Naltrexone: Full Antagonist

- Naltrexone is a long acting Opioid Blocker
- Not as good at reducing cravings/maintaining people in treatment, although it works well in selected populations
- Is an option for individuals who cannot take opioid replacement therapy (physicians/pilots/etc.)
- Is not recommended for pregnant women, women who may become pregnant, and individuals who may require significant pain management.
- Must be abstinent from all opioids for at least 7-10 days before starting.

Naloxone (Narcan)

- Naloxone is a fast-acting opioid agonist (blocker)
- Naloxone can reverse overdoses caused by opiates/opioids
- Naloxone wears off quickly
  - Half life is 30-90 minutes
  - Think Epi-Pen or Glucagon injection

Medication-Assisted Recovery

- A combination of pharmacotherapy and behavioral therapies is the most effective intervention to treat opioid use disorder.
- The goal of treatment in ALL chronic diseases is to minimize the suffering and health complications that occur secondary to the disease, not to set a specific time frame for how long and with what you will treat an individual.
- The need for individual medications and behavioral therapies may fluctuate over time. This is the same pattern we see in all chronic diseases.

Questions?

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