



National American Indian & Alaska Native



ATTC

Addiction Technology Transfer Center Network  
Funded by Substance Abuse and Mental Health Services Administration



Native Center for  
Behavioral Health



**SAMHSA**  
Substance Abuse and Mental Health  
Services Administration

# Stimulants and their Effects on Brain Chemistry

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May 26, 2021

# **SAMHSA**

Substance Abuse and Mental Health  
Services Administration

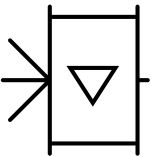
The Tribal Opioid Response Technical Assistance Center is supported by a grant from the Substance Abuse and Mental Health Services Administration (SAMHSA).

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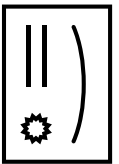


# Follow-up

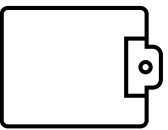
Following today's event, you will receive a follow up email, which will include:



Links to the presentation slides and recording, if applicable



Information about how to request and receive CEUs



Link to our evaluation survey (GPRA)

# Land Acknowledgement

We would like to take this time to acknowledge the land and pay respect to the Indigenous Nations whose homelands were forcibly taken over and inhabited. Past and present, we want to honor the land itself and the people who have stewarded it throughout the generations.

This calls us to commit to forever learn how to be better stewards of these lands through action, advocacy, support, and education.

We acknowledge the painful history of genocide and forced occupation of Native American territories, and we respect the many diverse indigenous people connected to this land on which we gather from time immemorial.

While injustices are still being committed against Indigenous people on Turtle Island, today we say thank you to those that stand with Indigenous peoples and acknowledge that land reparations must be made to allow healing for our Indigenous peoples and to mother earth, herself.

Dekibaota, Elleh Driscoll, Meskwaki and Winnebago Nations  
Ttakimaweakwe, Keely Driscoll, Meskwaki and Winnebago Nations  
Keokuk, Sean A. Bear, 1<sup>st</sup>. Meskwaki Nation

# Learning Objectives

Connect behaviors of people with substance use disorder to what is happening in the brain

Be familiar with current and developing treatment options

Describe the relationship between opioids, stimulants and overdose

Understand the connection between stimulants and psychosis



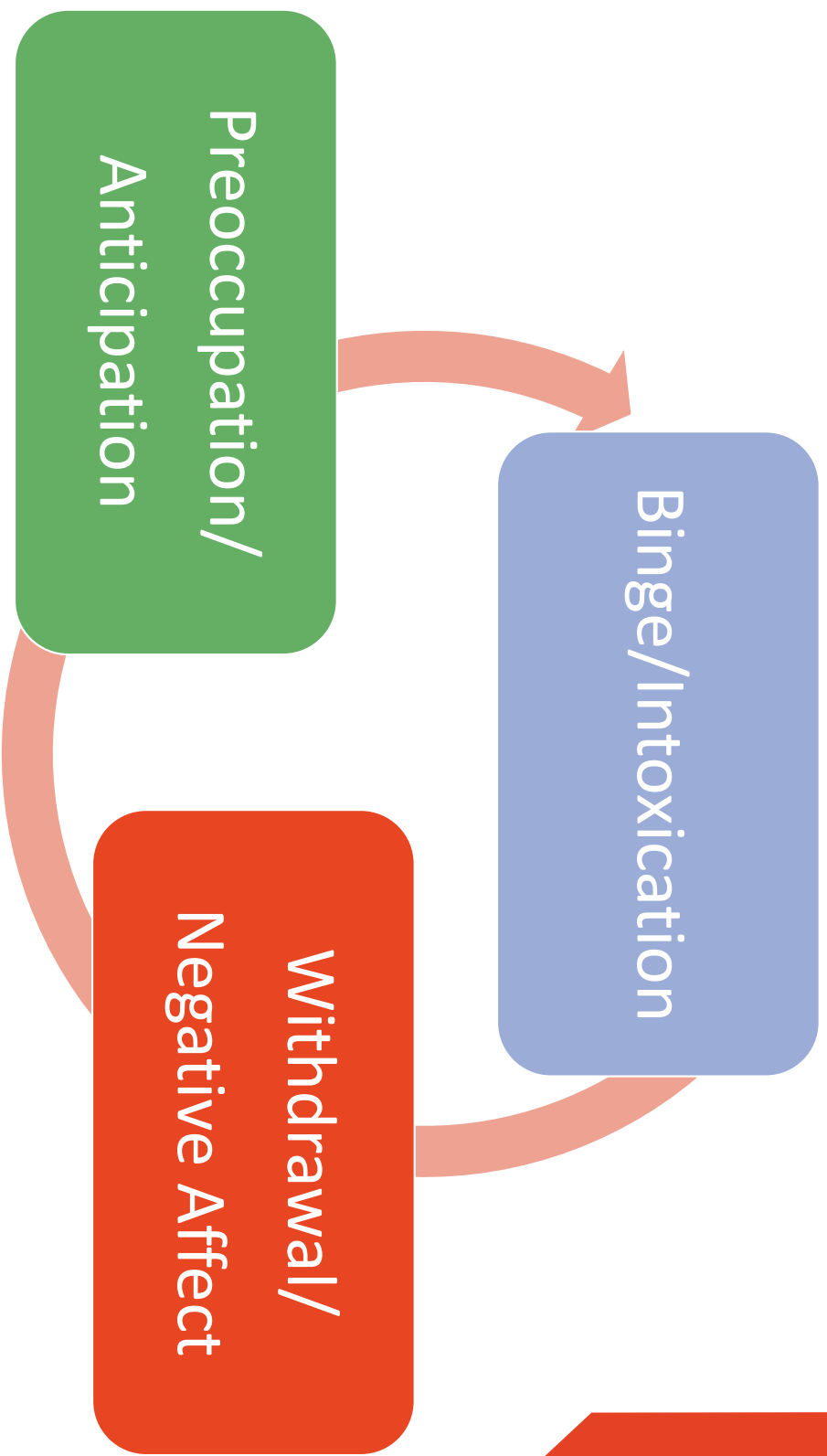
# People recover from addiction

Recovery includes:

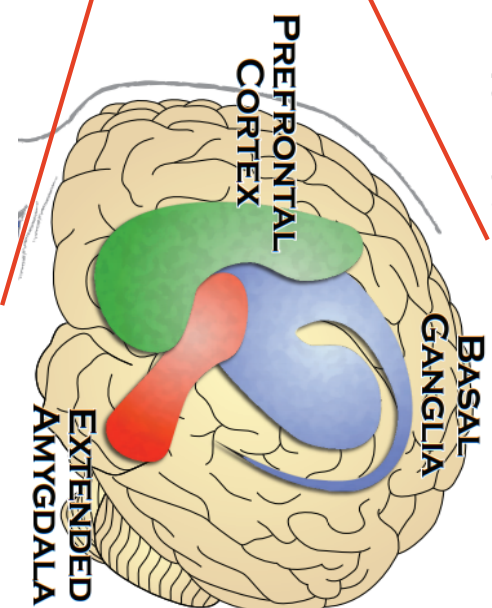
- Health
  - Home
  - Purpose
  - Community
- And
- Culture



# The Addiction Process



# Addiction and our brain

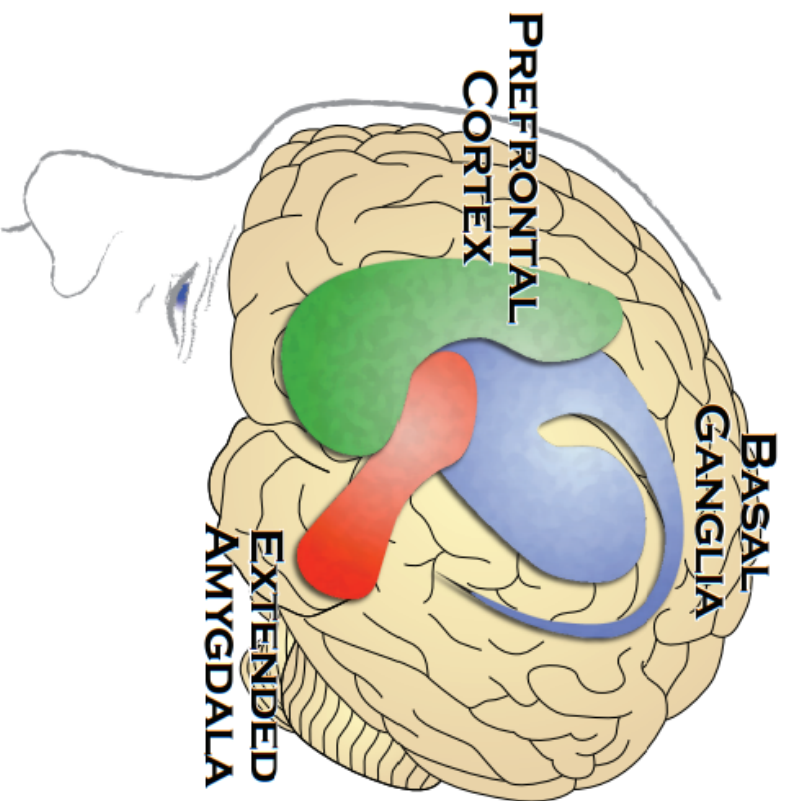


Addiction happens in the same three parts of the brain no matter what drug is used.

U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington, DC: HHS, November 2016.



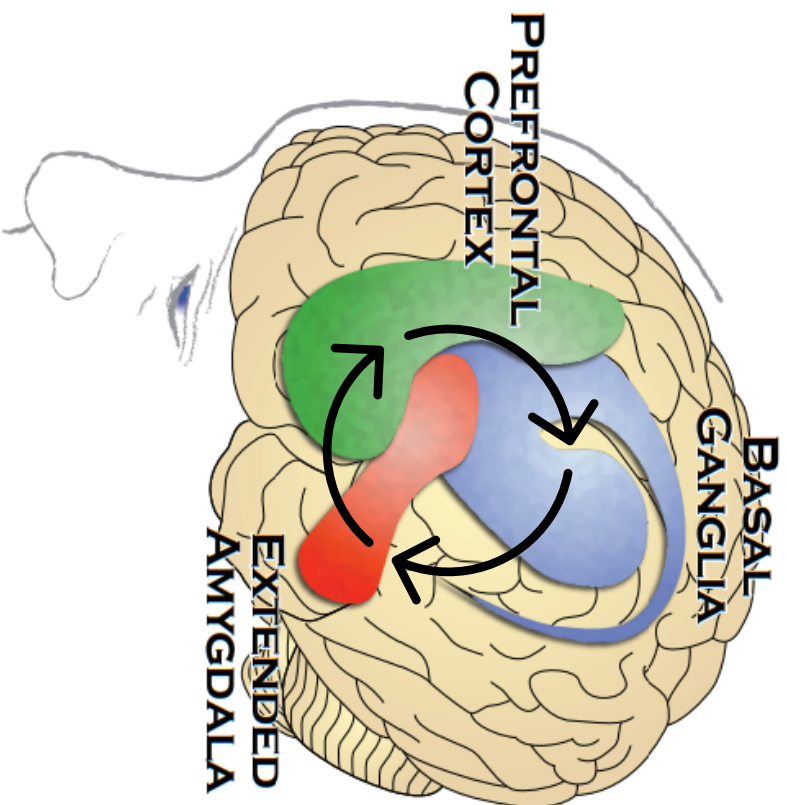
# The addiction process—structures of the brain



**These structures coordinate our experience of meaning, pleasure and decision making.**

**The function of these structures is impacted by trauma.**

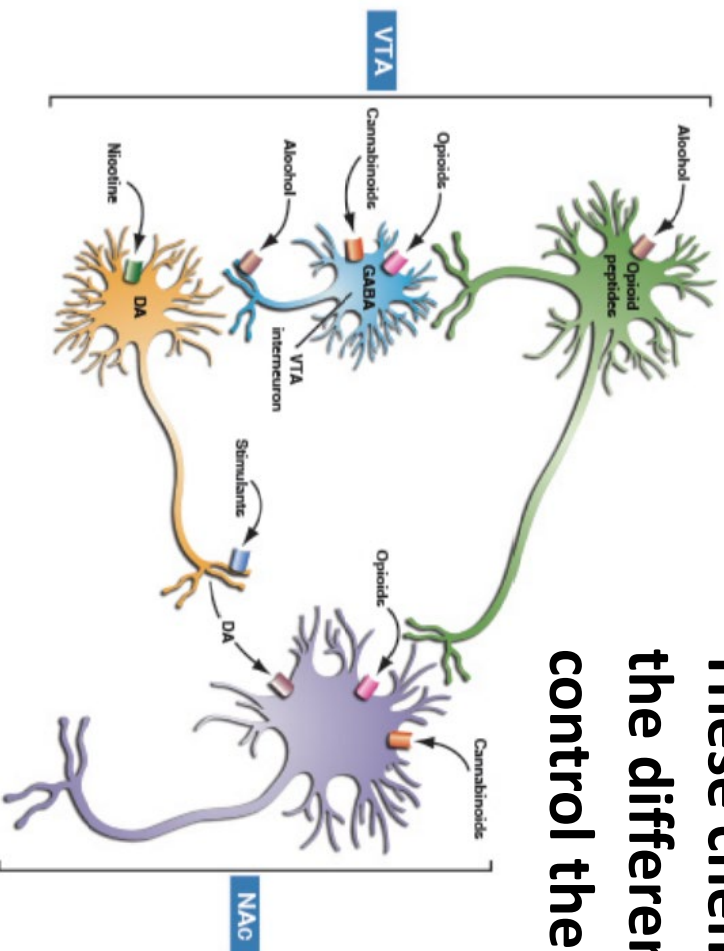
# The addiction process—structures of the brain and their functions



- Basal Ganglia
  - Binge/intoxication
  - Learning routine behaviors/forming habits/experiencing rewards
- Extended Amygdala
  - Withdrawal/negative affect
  - Regulates reactions to stress
- Prefrontal Cortex
  - Preoccupation/anticipation
  - Set priorities, organize tasks, regulate emotions and impulses

# The addiction process—brain chemistry

**These chemicals carry messages across the different parts of the brain and control their function**



Dopamine

Opioid peptides ✓

Norepinephrine

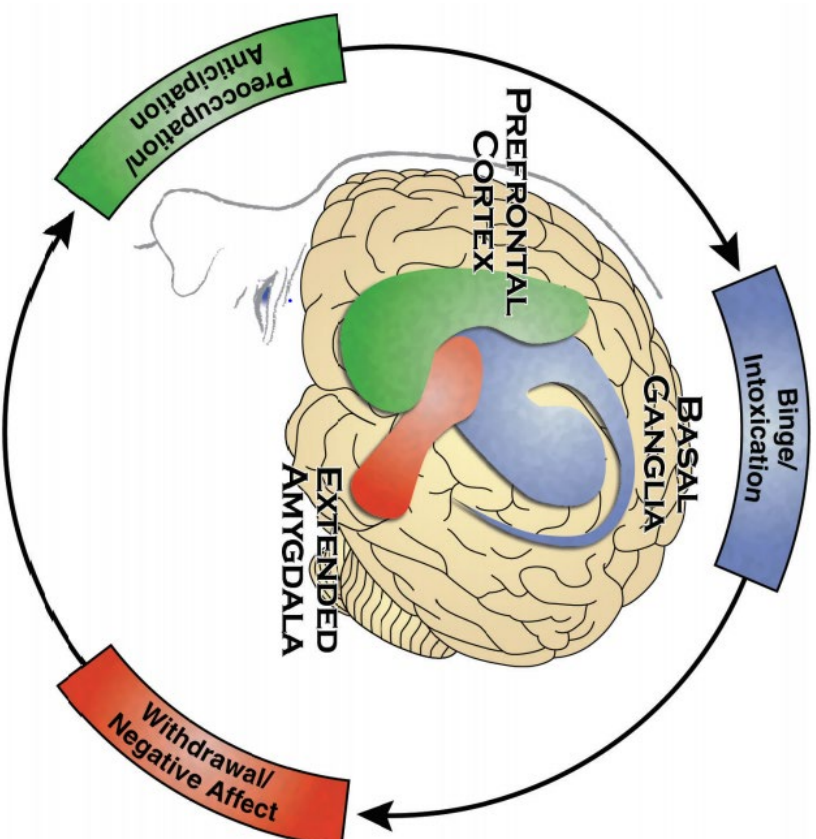
Corticotropin-releasing factor

Dynorphin

Glutamate

# The addiction process


- **Chemistry**  
Disturbing the chemistry or structure of these parts of the brain changes how they function.
- **Function**  
The altered function produces the behaviors we observe in people with addiction.
- **Structure**  
Exposure to drugs in adolescence may also alter the structure of the brain.





# Methamphetamine vs. Cocaine

## Methamphetamine versus Cocaine

 <b>Methamphetamine</b>	<b>Cocaine</b>
Stimulant	Stimulant and local anesthetic
Man-made	Plant-derived
Smoking produces a long-lasting high	Smoking produces a brief high
50% of the drug is removed from the body in 12 hours	50% of the drug is removed from the body in 1 hour
Increases dopamine release and blocks dopamine re-uptake	Blocks dopamine re-uptake
Limited medical use for ADHD, narcolepsy, and weight loss	Limited medical use as a local anesthetic in some surgical procedures



# Basal Ganglia: binge/intoxication

## Role of the basal ganglia in the brain

- experiencing rewards
- learning routine behaviors by paying attention
- forming habits

## Role of the basal ganglia in addiction

- “binge & intoxication” phase of addiction
- initially intense “pleasure” or escape from suffering provided by drugs hijacks the brains reward system
- people, places and things associated with drugs become triggers for drug use
- drug use becomes familiar and routine

# Binge/Intoxication

## What people experience

- People consume the intoxicating substance and experience its rewarding or pleasurable effects
- At first the pleasure is more intense than natural pleasure
- Later the ability to feel pleasure from anything is decreased
- People learn to associate pleasure or relief with drugs and look for cues related to drug use (people/places/things)

## What happens in the brain

- Dopamine release causes the experience of reward/pleasure
- Opioid peptide release also causes the experience of reward/pleasure
- Glutamine release
  - excites the neurons, telling the brain to “pay attention” and
  - remember the experience
  - laying the foundation for a habit.

# Binge/Intoxication: opioids vs. stimulants

## Opioids

- Directly replaces the function of naturally occurring opioid peptides
- Indirectly releases dopamine
- Creates feeling of peaceful relaxation and satisfaction
- Relieves emotional and physical pain

## Stimulants

- Directly releases dopamine and keeps it from being stored away again
- Indirectly released opioid peptides
- Creates feeling of energy, strength, confidence and capability
- Distracts for boredom and frustration
- Anger and possible psychosis
- Very prominent phase in stimulant use disorder

Both train the brain to think this is a rewarding activity and sets up triggers to do it again.



# Binge/Intoxication: opioids vs. stimulants



## Opioids work for OUD

- Directly replaces the function of naturally occurring opioid peptides
- Indirectly releases dopamine
- Creates feeling of peaceful relaxation and satisfaction
- Relieves emotional and physical pain

## Stimulant use disorder

- Directly releases dopamine and/or keeps it from being stored away again
- Indirectly released opioid peptides
- Creates feeling of energy, strength, confidence and capability
- Distracts for boredom and frustration
- Anger and possible psychosis
- Very prominent phase in stimulant use disorder

# Extended Amygdala: ↪ withdrawal/negative affect

## Role of Extended Amygdala in the brain

- Regulates reactions to stress
- Links the feeling of reward to decision making

## Role of Extended Amygdala in addiction

- Withdrawal/negative affect phase of addiction
- Interrupts the connection between natural rewards and decision making

# Withdrawal/negative affect

## What people experience

- Without the substance people feel physically sick
- Their outlook becomes generally negative, sad or angry
- Things they used to enjoy seem boring or not worth the effort

## How the brain is changed

- The extended amygdala is very active creating feelings of stress, sadness, anger
  - Levels of corticotropin releasing factor, glutamate and dynorphin are high
- The reward system is less active making it hard to feel pleasure or enjoyment.
  - Brain makes less dopamine

# Withdrawal/negative affect opioids vs. stimulants

## Opioids

- Intense physical withdrawal (pain, sweating, twitching, diarrhea, vomiting)
- Intense sadness and hopelessness
- Desire to avoid this experience drives use (very prominent phase in opioid use disorder)
- With ongoing use withdrawal and negative affect start sooner and become more intense (tolerance)

## Stimulants

- The “Crash”
- Negative mood/sadness/not caring
- Inactivity/overwhelmed
- Irritable/angry (too much glutamate)
- Lack of motivation (less dopamine)

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# Prefrontal Cortex: Preoccupation/Anticipation

## Role of the prefrontal cortex in the brain

- “executive function”
- organize thoughts and activities,
- prioritize tasks,
- manage time,
- make decisions, and
- regulate one’s own actions, emotions, and impulses.

## Role of the prefrontal cortex in addiction

- Over-rides caution/duty/obligation
- Promotes acting on impulses
- The drive to act is increased so that impulses to repeat the experience is strong
- The ability to stop, think and make decisions is decreased

# Preoccupation / anticipation

## What people experience

- The person wants to experience the emotions and physical sensations produced by the drug again
- Looking forward to having the experience again distracts them from daily life and responsibilities
- Waiting for the next opportunity to use the drug is hard to bear

## How the brain is changed

- The prefrontal cortex becomes smaller
- More sensitive to stress signals from extended amygdala
- Links the relief of stress to the drug related cues completing the “habit loop” to the basal ganglia
- Prioritizes acting on cues and cravings over other decisions and actions.

# Preoccupation/anticipation opioids vs. stimulants

## Opioids

- Need to relieve physical symptoms in order to function (kind of an extension of the withdrawal/negative affect phase)
- Desire to escape miserable negative mood/hopelessness

## Stimulants

- Intense drive to use
- Desire to escape feelings of incompetence and worthlessness
- Rationalizing use stimulants to “function”
- Extremely sensitive to cues/triggers



# Preoccupation/anticipation opioids vs. stimulants



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- Intense drive to use
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## Differences: opioids vs. stimulants

- Binge/intoxication phase is very prominent
- MA stays in the body a long time
- MA directly releases dopamine and keeps it from being stored away in the cells
- MA indirectly releases opioid peptides
- Not enough dopamine anymore
- Glutamate causing irritability



## Differences: binge/intoxication

- Binge/intoxication phase is very prominent
- MA stays in the body a long time
- People with MA use disorder what to feel competent and confident
- Withdrawal/negative affect is more prominent in OUD.
- Opioid medications relieve these symptoms without needing to replace binge/intoxication.
- People with OUD want to avoid being sick



## Differences: the brain makes its own opioids

- Brain makes opioid peptides
- MA indirectly releases opioid peptides
- Opioid medications directly fulfill the role of naturally occurring opioid peptides but there is not naturally occurring stimulant peptide.
- Naltrexone and buprenorphine show promise for treatment of methamphetamine use disorder



## Differences: there's no dopamine pill


- MA directly releases dopamine and keeps it from being stored away in the cells
- Not enough dopamine anymore
- We can give people medications that help their brains start to make normal amounts of dopamine again
- Antidepressant and antipsychotic medications can help balance the dopamine
- This corrects the withdrawal/negative affect phase



# Differences: balancing impulses and caution

- Glutamate causing irritability
- Medications are being studied to help restore balance between urges/impulses and caution

# Stimulant medications

- Stimulant medications have been studied to see if they can treat stimulant use disorder.
  - They don't reliably help people keep from using drugs or help them function better.
  - Studies are still going on to see if a specific type or amount will work.
- 

# Other possible therapies

- **Transcranial Magnetic Stimulation**
  - TMS is a noninvasive method of stimulating the brain using magnetic pulses for therapeutic purposes. Researchers are studying this approach as a treatment for substance use disorders, but this work is in very early stages
- **Neurofeedback**
  - Neurofeedback is a type of biofeedback that uses real-time displays of brain activity—most commonly electroencephalography—to teach people how to regulate their own brain function.
- **Vaccines and antibodies**
  - Train the immune system to block MA from reaching the brain

[What treatments are under development for methamphetamine use and addiction? | National Institute on Drug Abuse \(NIDA\)](#)



# Stimulants and Psychosocial Treatment

## Contingency Management

Giving patients tangible rewards to reinforce positive behaviors such as abstinence

Voucher based reinforcement: vouchers are given for negative urine toxicology tests.

Value of voucher increases with the number of consecutive negative tests.

Prize incentives: participant draws for a prize when a goal is met (attends counseling, negative toxicology, etc.).

Number of draws increases with each consecutive success.

## Matrix Model

The Matrix Model provides a framework for engaging stimulant users in treatment and helping them achieve abstinence.

Patients learn about issues critical to addiction and relapse, receive direction and support from a trained therapist, and become familiar with self-help programs. Patients are monitored for drug use through urine testing.

The therapist functions simultaneously as teacher and coach, fostering a positive, encouraging relationship with the patient and using that relationship to reinforce positive behavior change.

[Matrix Model | RCORPTA \(rcorp-ta.org\)](https://www.rcorp-ta.org)

[Treatment for Individuals Who Use Stimulants \(TRUST\) | RCORPTA \(rcorp-ta.org\)](https://www.trust1.org)

# Stimulants and Psychosocial Treatment

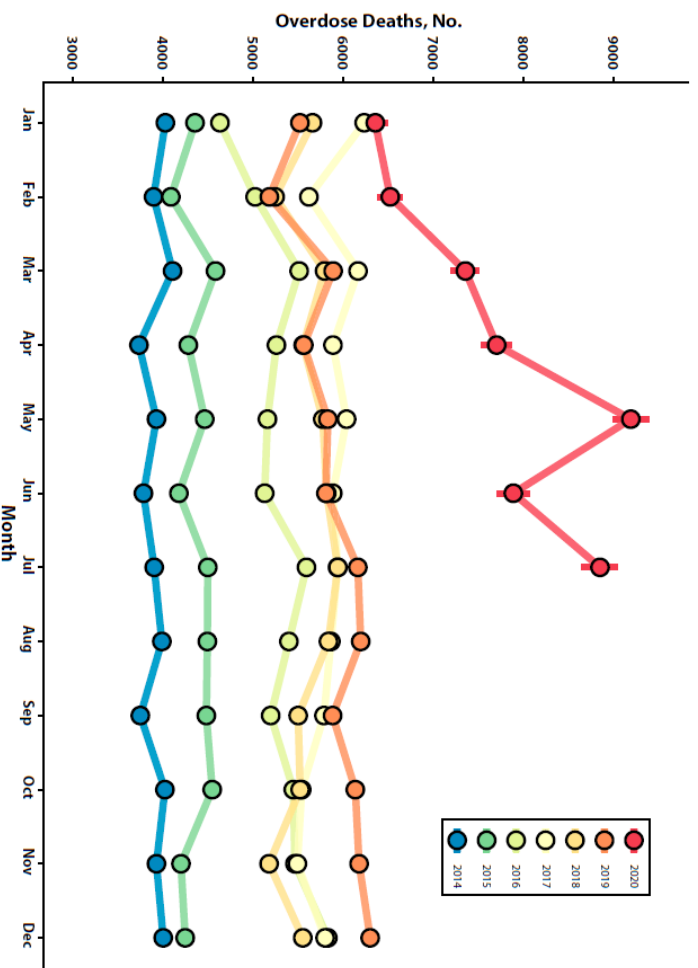
## Cognitive Behavioral Therapy

- helps patients recognize, avoid, and cope with the situations in which they are most likely to use drugs

## 12-step facilitation

- Twelve-step facilitation therapy is an active engagement strategy designed to increase the likelihood a person with SUD becoming affiliated with and actively involved in 12-step self-help groups, thereby promoting abstinence.

# Drug Overdose Deaths during COVID-19



**FIGURE 1** Monthly Overdose Deaths From January 2014 to July 2020: United States

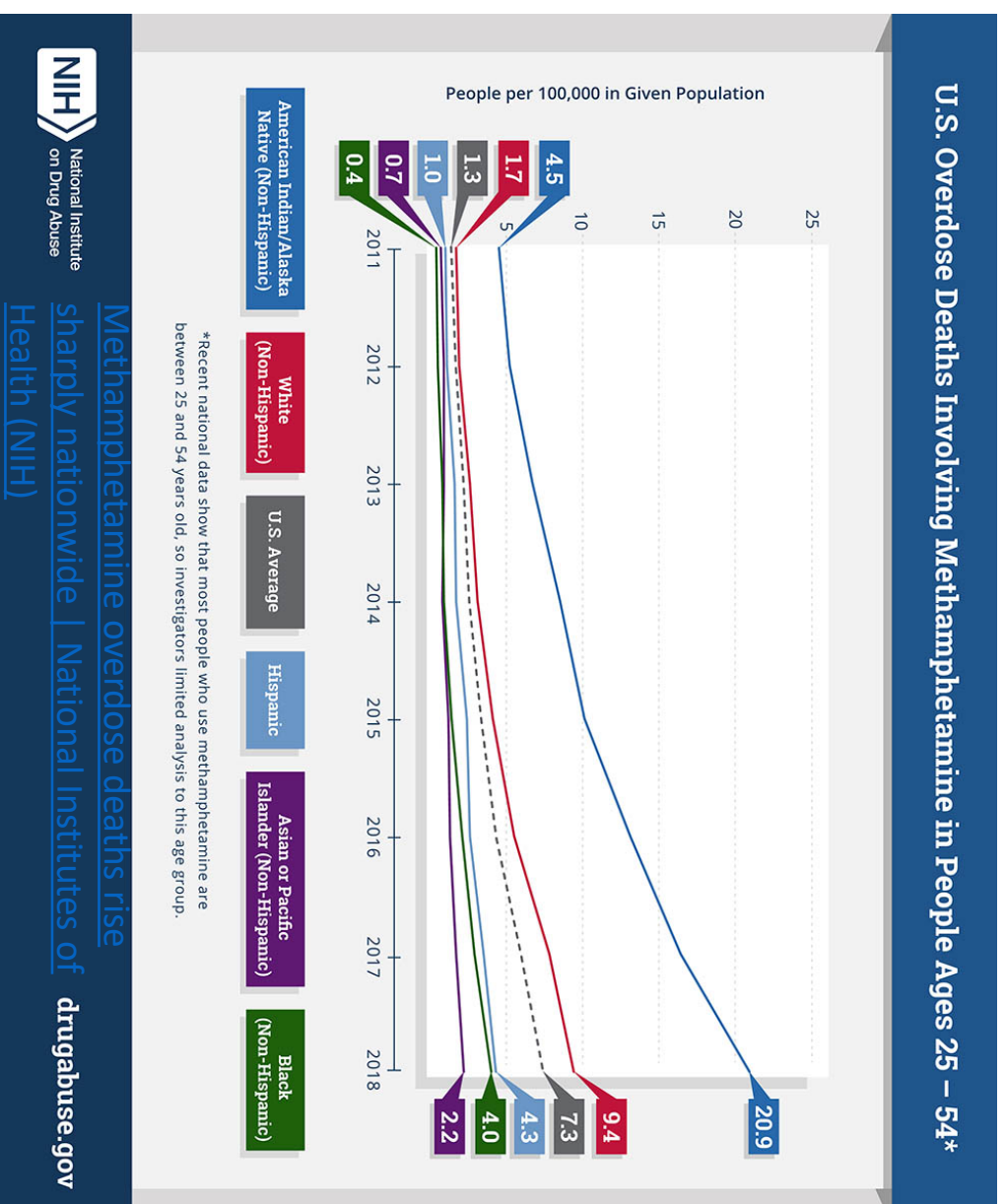
Note: Overdose deaths in the United States are shown by month, from January 2014 to July 2020. For values in 2020, 95% prediction intervals are shown, recovered using the algorithm described in this analysis. This figure reveals that May 2020 was the deadliest month for overdose death in the United States in recent history, elevated above May 2019 by about 60%.

- May 2020 was the deadliest month ever recorded
- A 57.7% increase over May 2019

Joseph Friedman and Samir Akre. 0: COVID-19 and the Drug Overdose Crisis: Uncovering the Deadliest Months in the United States, January–July 2020 American Journal of Public Health 0, e1\_e8, <https://doi.org/10.2105/AJPH.2021.306256>

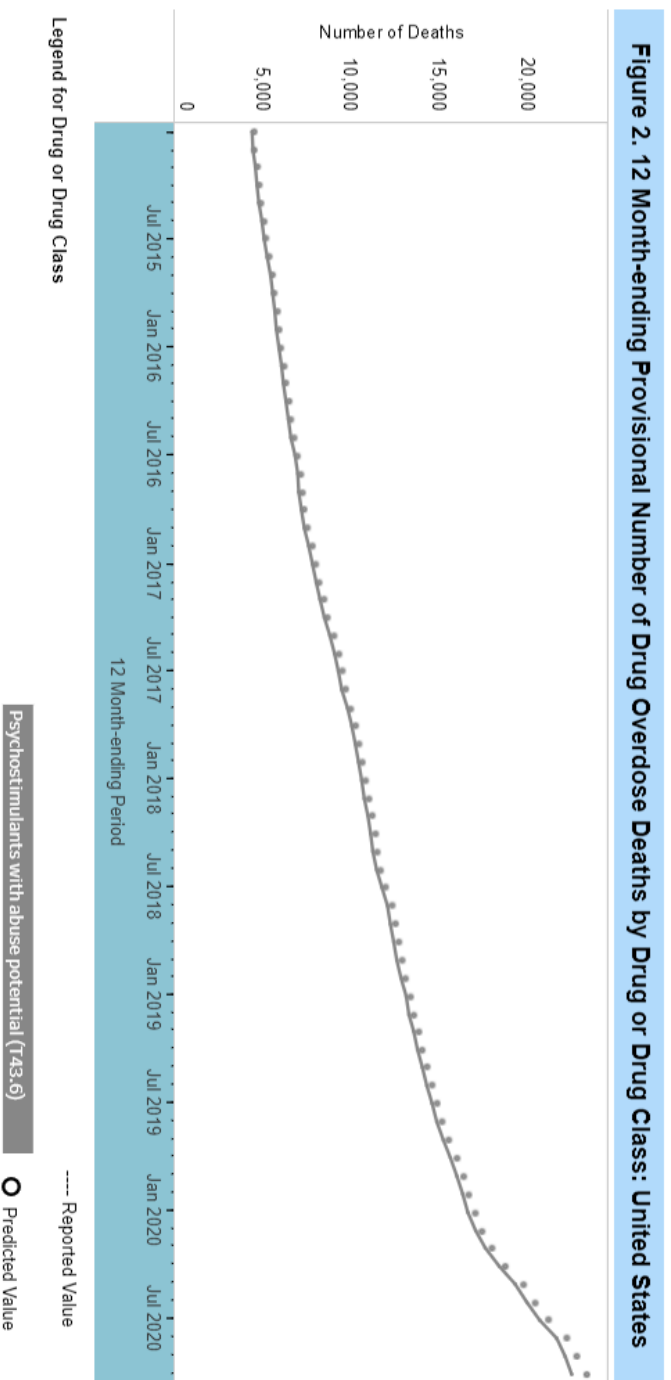
# Methamphetamine Overdose

- Deaths involving MA more than quadrupled between 2011 and 2018 for non-Hispanic American Indians and Alaska Natives ages 25-54.
- In 2011 the rate of deaths for non-Hispanic AI/AN was already more than 3 times higher than the U.S. average



# Recent Increases in Overdose due to Methamphetamine (MA)


- Overdose due to stimulants increased 39% from June 2019 to June 2020



# Stimulants and overdose

- More people who use opioids are also using stimulants
- Fentanyl is increasingly found in other drugs causing opioid overdose among people who are not looking to use opioids
- 63% of all stimulant deaths in 2019 involved an opioid
- Anyone who uses drugs should have access to naloxone the antidote to opioid poisoning

# Methamphetamine and Mental Health


- Binge/Intoxication
    - Irritability, anger, psychosis
  - Withdrawal/negative affect
    - Sadness, anxiety, psychosis
  - Anticipation/preoccupation
    - Agitation, psychosis
  - Having depression or anxiety increases the risk of developing SUD
  - SUD can also cause depression or anxiety
  - Severe depression can cause psychosis
- 

# Methamphetamine and Psychosis

- Psychosis is losing touch with reality
- Hallucinations
  - hearing and feeling things that aren't there
- Ideas of reference
  - thinking things on television or radio are about you
- Paranoia
  - being convinced that people and their actions are intended to harm you
- Repetitive movement
- Potential to become violent



# Methamphetamine and Psychosis Risk

- 40% of people who use stimulants experience psychosis
  - Most are better within a week of stopping use
    - supportive, psychosocial treatment helps
  - Symptoms lasting more than a month or that come back without stimulant use
    - may be a separate psychotic disorder and need psychiatric evaluation
  - Risk of psychosis in increased with
    - large amounts/doses of methamphetamine
    - very frequent use
    - longer use of methamphetamine
    - Beginning MA at an early age
- 

# Treatment of MA associated psychosis

- Most psychosis will resolve without medication
  - Keep them safe and hydrated
- Antipsychotic medications
  - work for MA induced psychosis
- Benzodiazepines
  - can help people calm down but
  - don't directly treat the psychosis
  - Examples: Ativan®/lorazepam, Klonopin®/clonazepam



# MA Psychosis in the Community

- Family and friends may be frightened by behavior
- Law enforcement
  - not well equipped or trained for mental health crisis
  - Involvement may make situation worse
- Emergency department
  - may be far away
  - often makes agitation worse
  - not always prepared for psychiatric emergencies



# Wellness focused community response strategies for MA use

- Create a trauma-informed sobering site with integrated harm reduction services for individuals who are under the influence of MA.
- Serve as an alternative transport site for those with non-emergency needs and provide on-site medication services such as antipsychotics or sedatives if an individual presents with acute psychosis or agitation.
- Relieve pressure on Psychiatric Emergency Services (PES) and hospital emergency departments provide integrated services and staff trained to engage the population.
- Result in increased connection to services, improved health outcomes, reduced harms of use, and decreased impacts on the general public and the city's system of services.



## Summary

- The addiction process is the same for all substances
- Trauma impacts the same parts of the brain where addiction happens
- There are not yet medications that can treat MA use disorder but psychosocial treatments work
- People who use MA need naloxone
- Psychosis is common and responds to treatment
- A safe quiet place in the community can help people cope with psychosis

