



TNX-1300

Cocaine Intoxication

NASDAQ: TNXP

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TNX-1300*: Cocaine Intoxication

Cocaine Esterase (CocE)

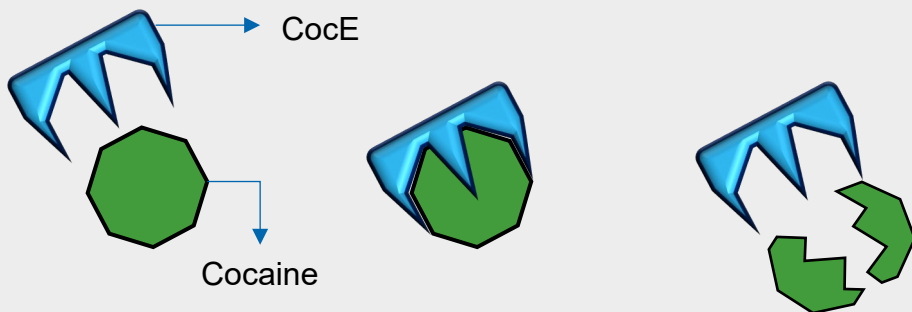
PROFILE

Cocaine is the main cause for drug-related ED visits¹

CocE is a recombinant protein that degrades cocaine in the bloodstream

- Rapidly reverses physiologic effects of cocaine
- Drops plasma exposure by 90% in 2 minutes

Differentiators: Rapidly metabolizes cocaine in the bloodstream; no other product currently on the market for this indication



Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Cocaine Intoxication

Status: Phase 2 'CATALYST' study ongoing

Next Steps: Expected to enroll approximately 60 emergency department patients at sites in the US

FDA Breakthrough Therapy Designation

Awarded Cooperative Agreement Grant from National Institute on Drug Abuse (NIDA)

*TNX-1300 has not been approved for any indication.

¹Havakuk et al., 2017. *J Am Coll Cardiol.* 70:101-113

ED = emergency department.

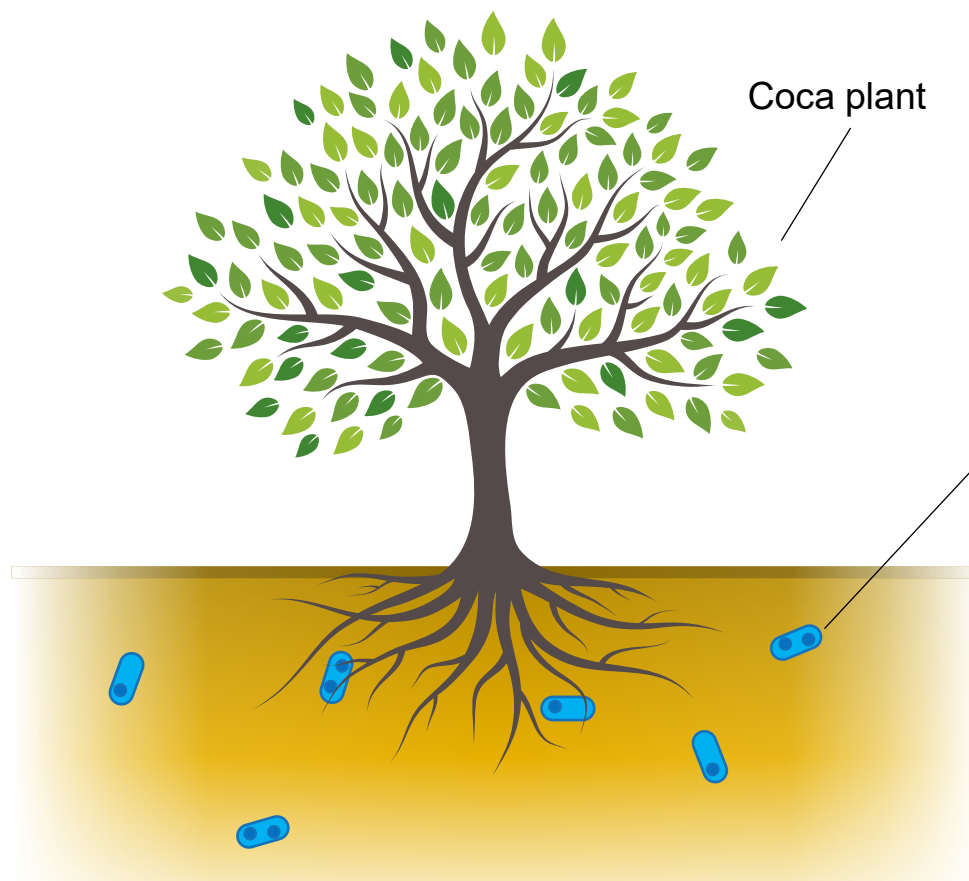




About the Phase 2 CATALYST Study

- Single-blind, open-label, placebo-controlled, randomized study comparing the efficacy and safety of a single 200 mg dose of TNX-1300 to placebo injection plus standard of care alone
- Conducted in the emergency departments of 6 academic medical centers in the US
- Approximately 60 subjects presenting with cocaine intoxication.
- During the treatment period, subjects randomized to receive TNX-1300 will receive a single *i.v.* injection of TNX-1300 administered over two minutes or less
- Subjects randomized to receive standard of care alone will receive a single *i.v.* saline injection over two minutes or less
 - For both study arms, signs and symptoms of cocaine intoxication will be assessed at pre-determined time points after treatment
- Primary endpoint is ***reduction of systolic blood pressure associated with acute cocaine intoxication*** identified at study baseline comparing TNX-1300 to placebo with standard of care after 60 minutes
 - Secondary endpoints will include reduction of circulating cocaine and levels of its metabolites at multiple post-baseline timepoints

About TNX-1300



Cocaine is derived from the coca plant¹

Produced through rDNA technology in non-disease-producing strain of *E. coli*

- Cocaine esterase (CocE) was identified in bacteria (*Rhodococcus*) that use cocaine as its sole source of carbon and nitrogen and that grow in soil surrounding coca plants²
- The gene encoding CocE was identified, and the protein was extensively characterized²⁻⁴
- Wild-type CocE is unstable at body temperature, so targeted mutations were introduced in the CocE gene and resulted in the *T172R/G173Q Double-Mutant CocE*, which is active for approximately 6 hours at body temperature⁵

¹Narasimhan D, et al. *Future Med Chem.* 2012;4(2):137-150.

²Bresler MM, et al *Appl Environ Microbiol.* 2000;66(3):904-908.

³Larsen NA, et al. *Nat Struct Biol.* 2002;9(1):17-21.

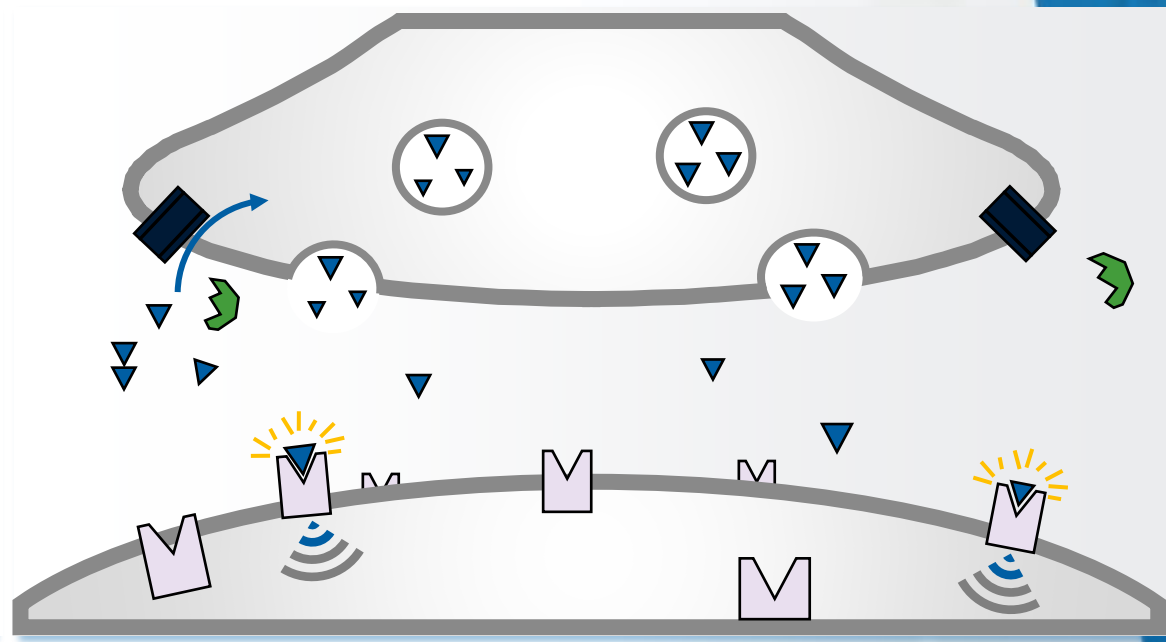
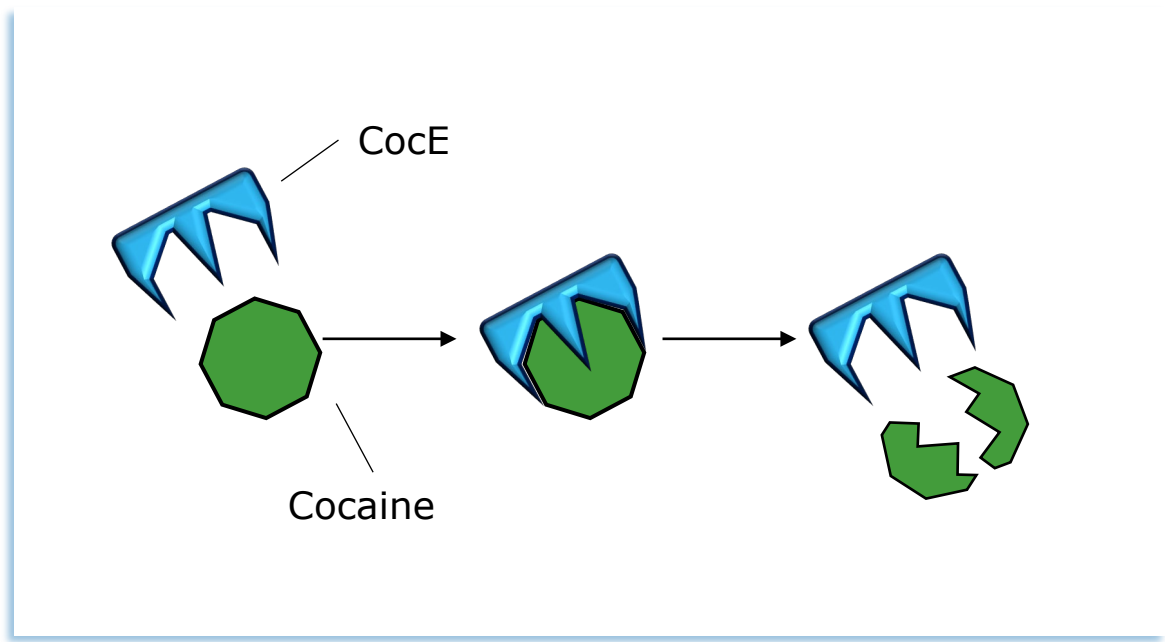
⁴Turner JM, et al. *Biochemistry.* 2002;41(41):12297-12307.

⁵Gao D, et al. *Mol Pharmacol.* 2009;75(2):318-323.





TNX-1300 Is a Fast-acting Cocaine Antidote



- CocE cleaves chemical bonds in cocaine and disintegrates it 800 times faster than the rate that naturally occurs in the human body¹

- CocE products are inactive, unable to affect dopamine transporters²
- Cocaine levels after TNX-1300 administration are not toxic²

¹Narasimhan D, et al. *Future Med Chem.* 2012;4(2):137-150.
²Brim RL, et al. *Mol Pharmacol.* 2011;80(6):1119-1127.

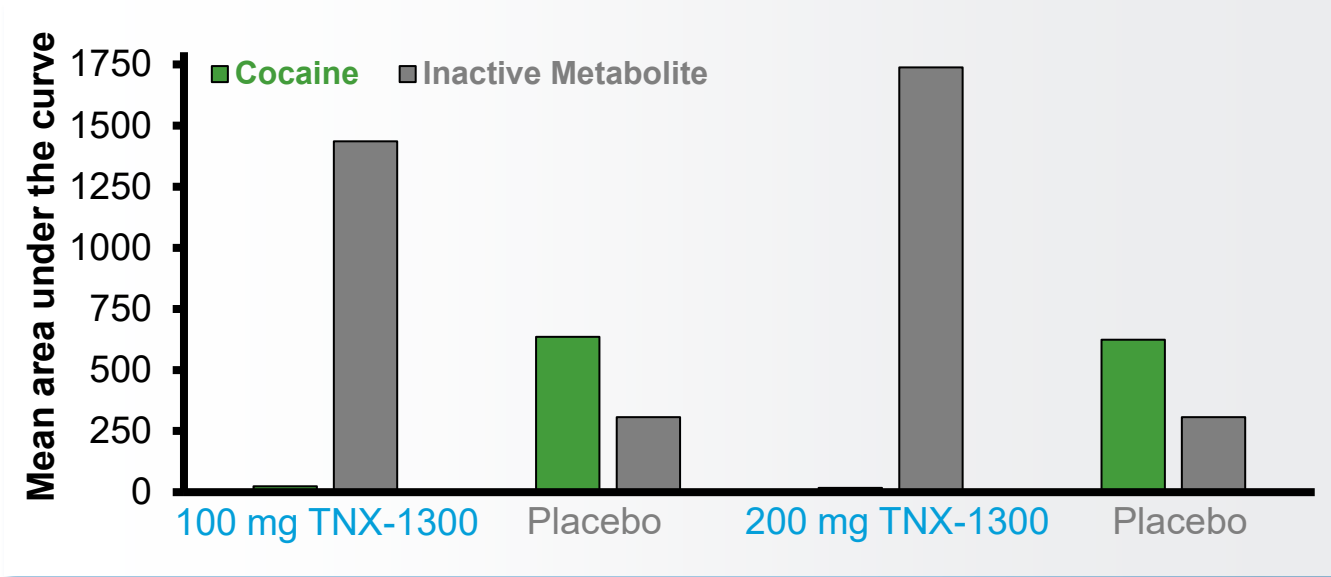


TNX-1300 for the Treatment of Cocaine Intoxication

Phase 2 study completed by Rickett Benckiser (TNX-1300 was formerly RBP-8000)



+ 100 mg TNX-1300
OR
+ 200 mg TNX-1300



- Rapidly reversed the physiologic effects of cocaine; cocaine plasma exposures dropped by 90% within two minutes

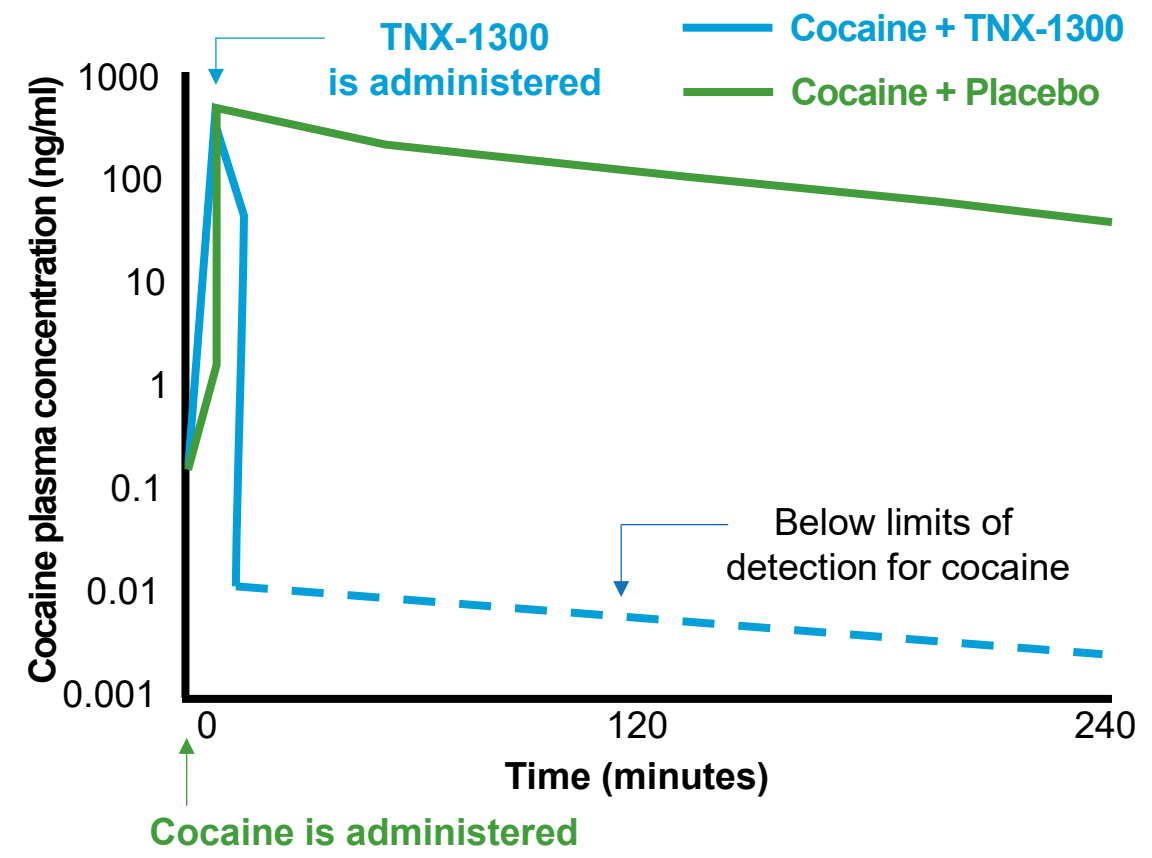
Well-tolerated & Most Common

- Dry mouth
- Nausea
- Headache, dizziness
- Hyperhidrosis, dermatitis

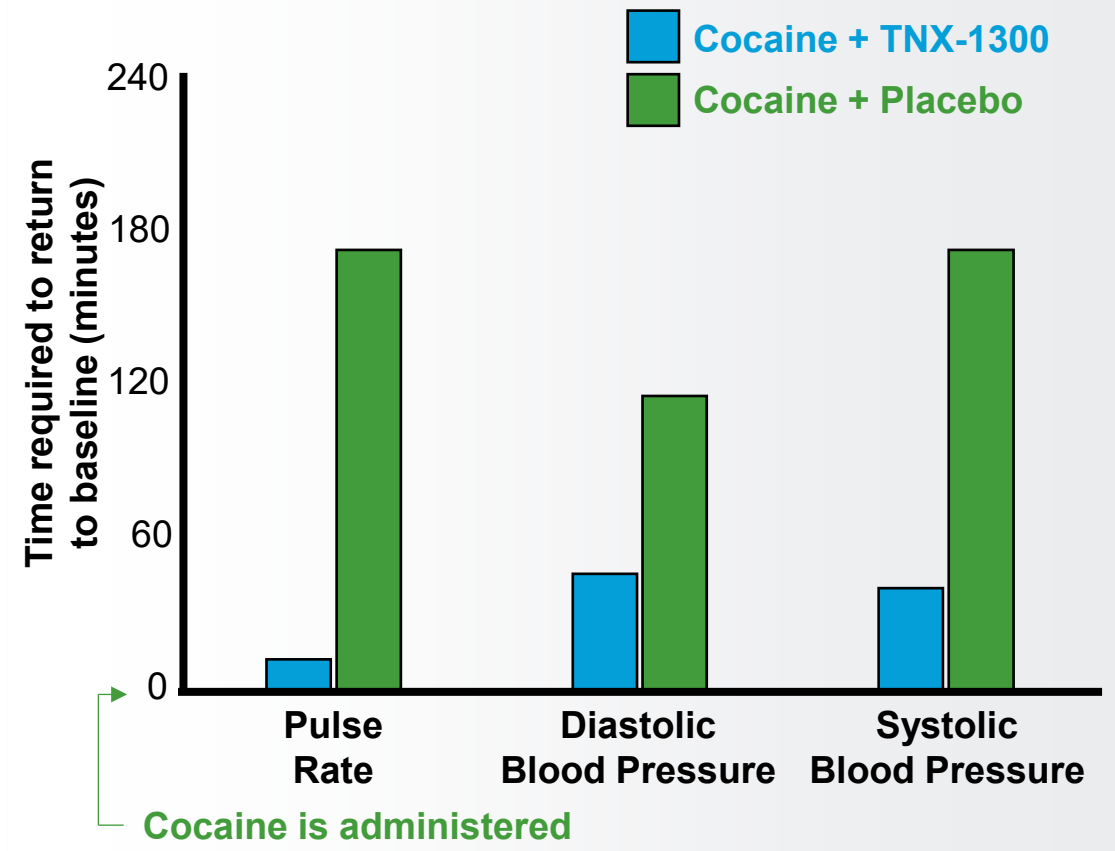


TNX-1300 Accelerates Recovery From Cocaine Intoxication in Humans

TNX-1300 cleaves cocaine in humans and removes it from the blood circulation¹ (N=29)



TNX-1300 accelerates recovery from cocaine intoxication without inducing serious side effects¹



Note: Figures are for illustrative purposes

Nasser AF, et al. *J Addict Dis.* 2014;33(4):289-302.



The Prevalence of Cocaine Usage and Overdose (US)

Cocaine Usage in the U.S.

- Over 5 million Americans reported current cocaine use in 2020, which is almost 2% of the population¹
- About 2 million surveyed in 2020 reported cocaine use in the past month¹
- In 2021, >24,900 individuals in the U.S. died from drug overdose deaths involving cocaine²

Prevalence of Cocaine Overdose

Based on Drug Abuse Warning Network (DAWN) last compiled in 2011^{3,4}

505,224 emergency department visits for cocaine (2011)^{3,4}

- ➔ **270,677 (53%) treated and released** Less likely to be treated aggressively
- ➔ **167,570 (33%) were admitted to the same hospital** More likely to be treated
- ➔ **60,609 (14%) visits involving drug detox services** Treated to reverse toxicity

¹Substance Abuse and Mental Health Services Administration. (2021). Results from the 2020 National Survey on Drug Use and Health: Detailed Tables: Prevalence Estimates, Standard Errors, and Sample Sizes.
²Centers for Disease Control and Prevention (CDC) - <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

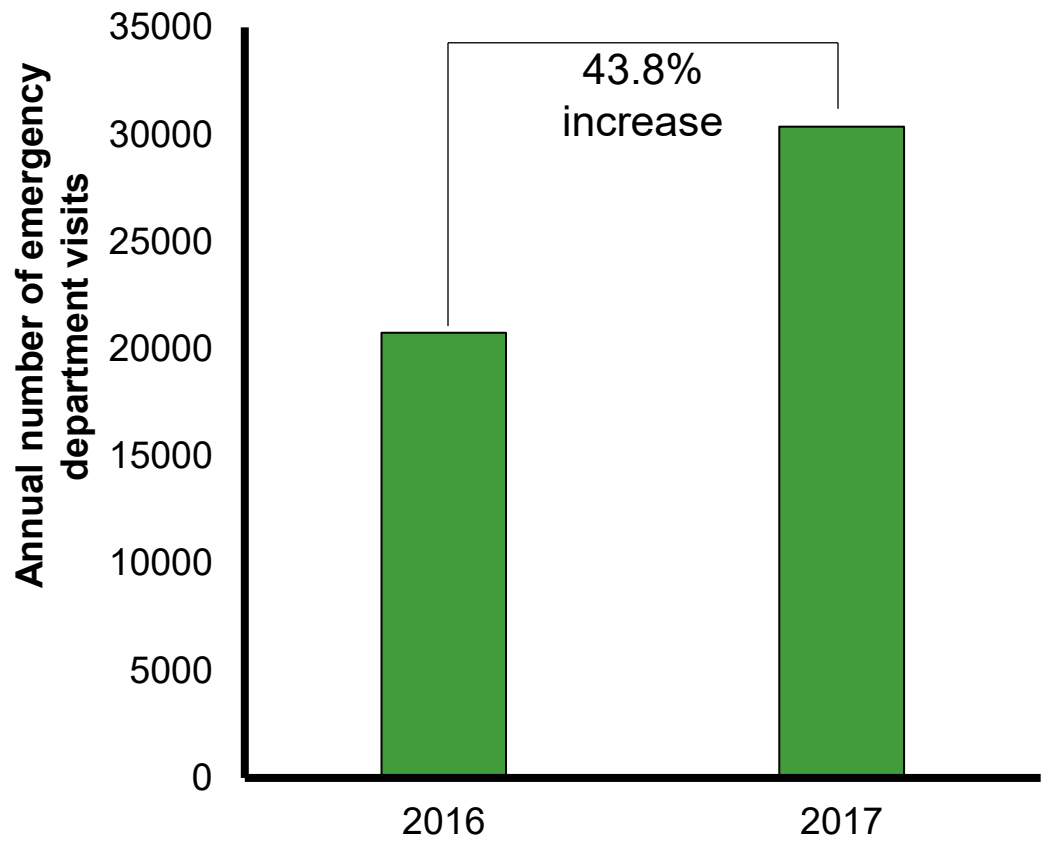
³Substance Mental Health Services Administration, Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.
⁴ Drug Abuse Warning Network, 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits. Rockville, MD: Center for Behavioral Health Statistics and Quality, SAMHSA, 2013.



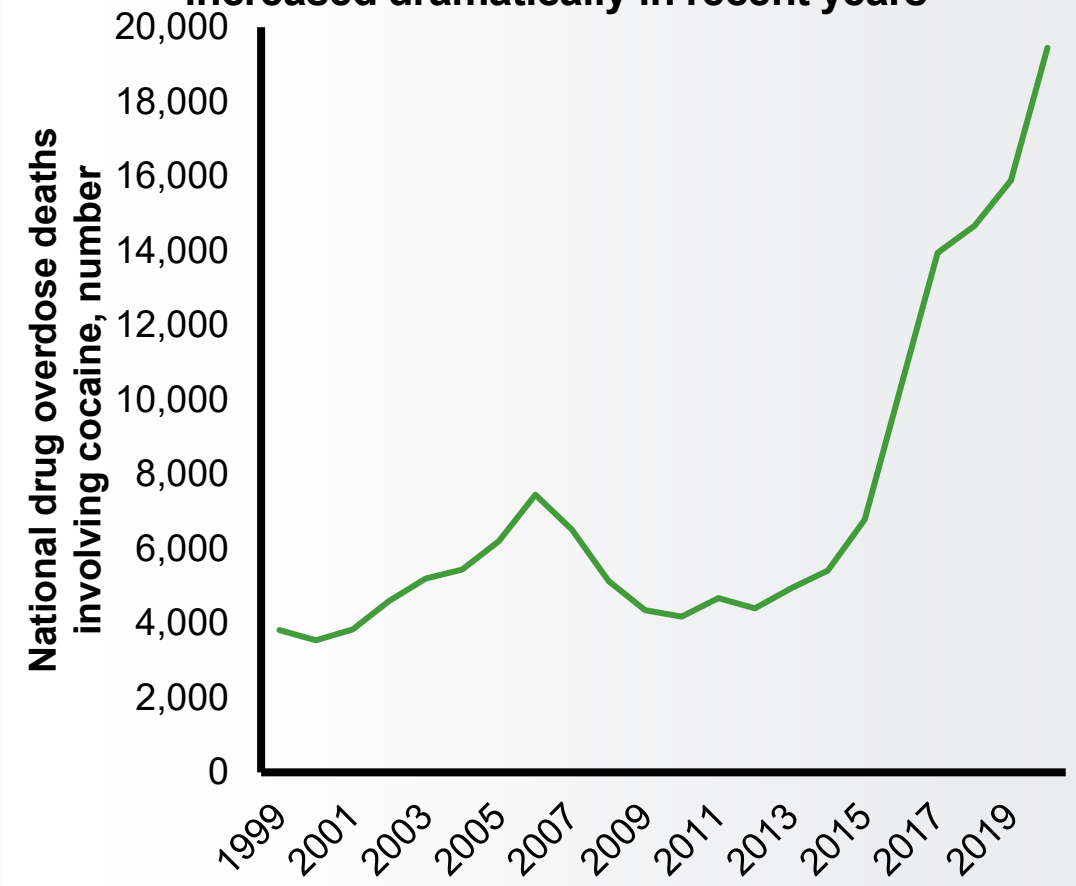


Cocaine Intoxication Is a Growing Problem in the US

From 2016 to 2017, emergency department visits due to unintentional nonfatal overdoses of cocaine increased by almost 50%¹



Drug overdose deaths involving cocaine have increased dramatically in recent years²



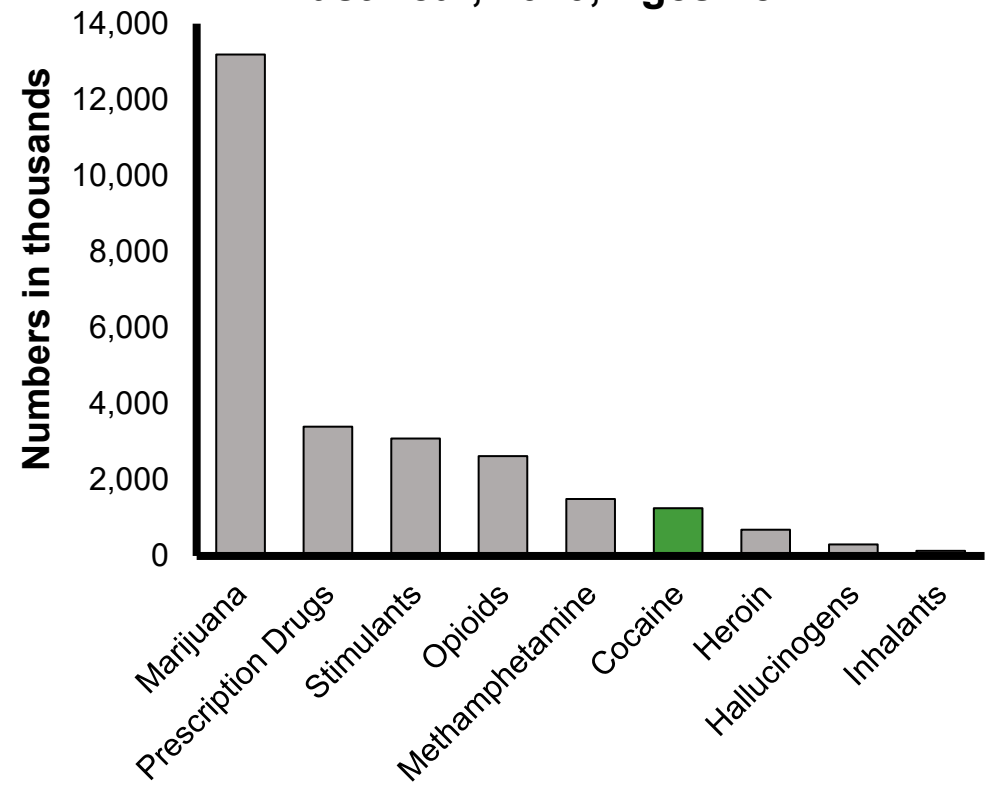
¹Vivolo-Kantor AM, et al. *MMWR Morb Mortal Wkly Rep.* 2020;69(13):371-376.

²Overdose Death Rates. National Institute on Drug Abuse. January 20, 2022. Accessed May 11, 2022. <https://nida.nih.gov/drug-topics/trends-statistics/overdose-death-rates>

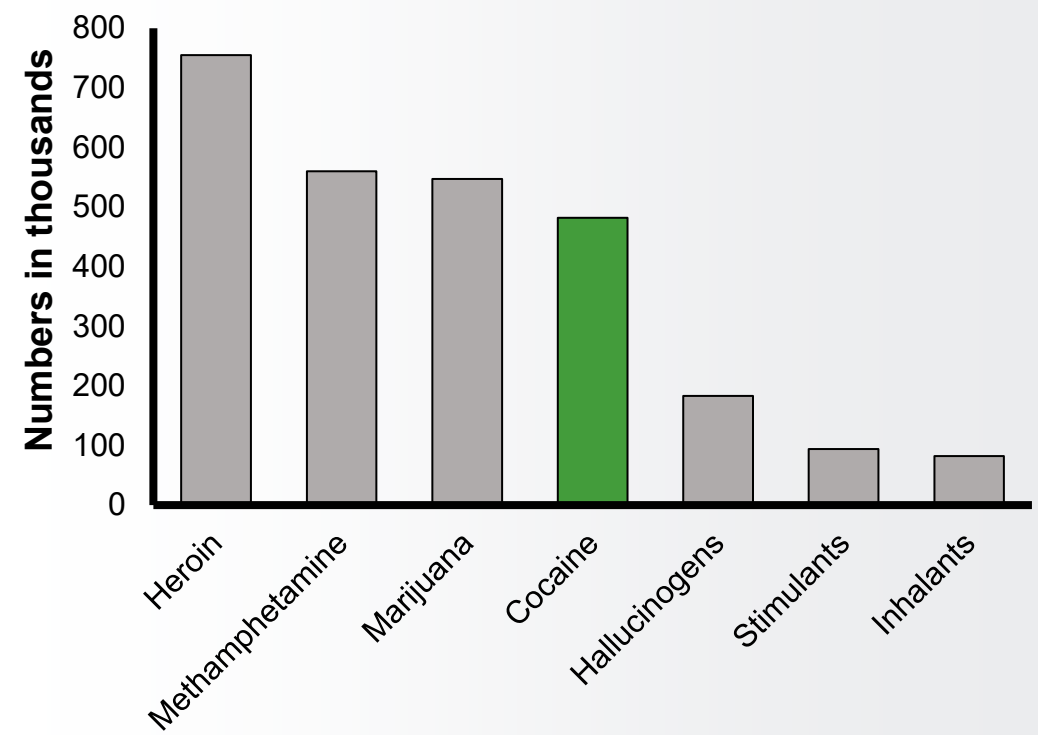


Many Adults Who Use Cocaine Receive Treatment

Substance Use Disorder for Illicit Drugs in Past Year, 2020, Ages 18+



Illicit Drugs for Which Last or Current Treatment Was Received in Past Year, 2020, Ages 18+

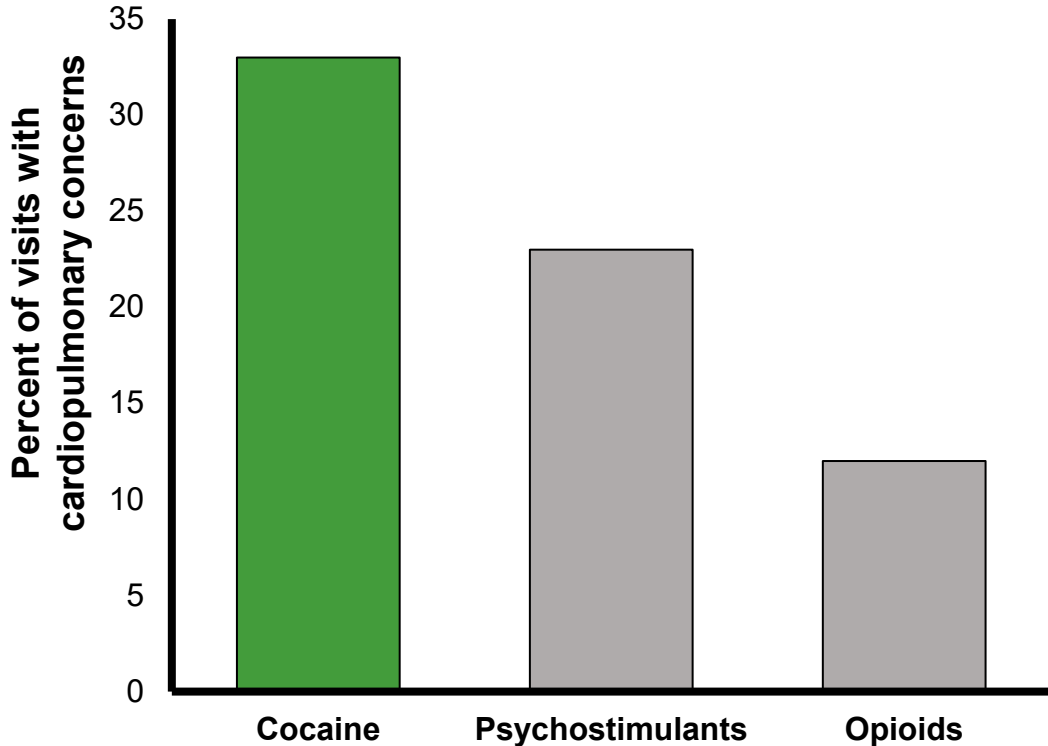


Substance Abuse and Mental Health Services Administration. (2021). Results from the 2020 National Survey on Drug Use and Health: Detailed Tables: Prevalence Estimates, Standard Errors, and Sample Sizes.

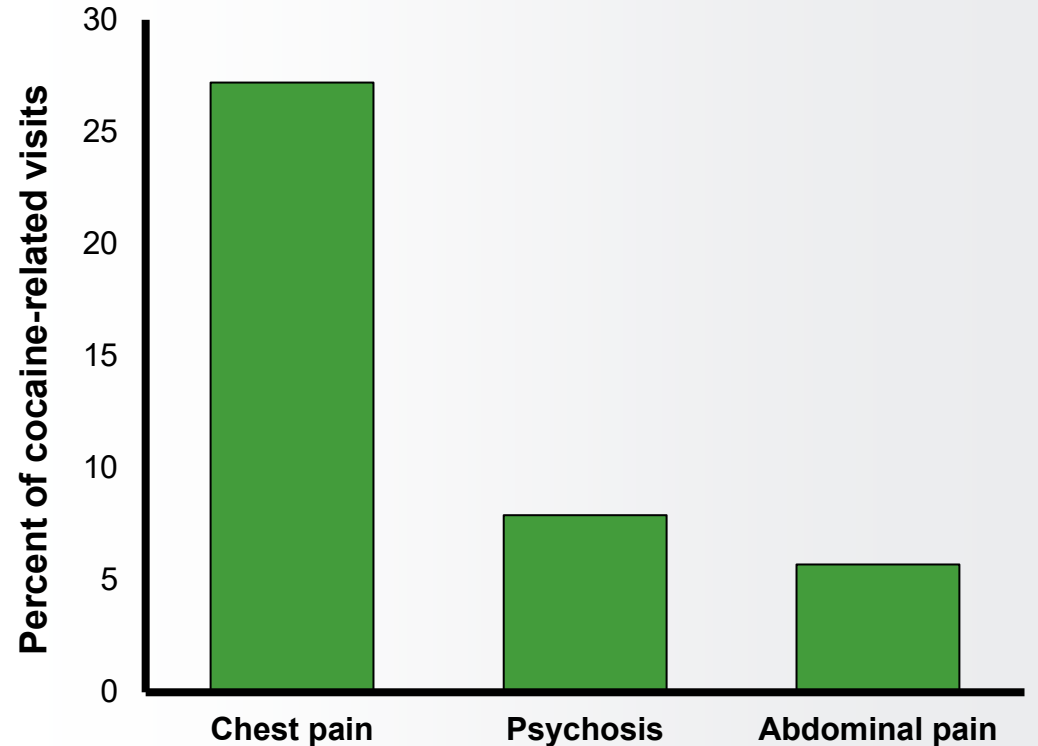
Cocaine Intoxication Presents Often with Cardiopulmonary Concerns in the Emergency Department



Cardiopulmonary concerns are common in emergency department visits related to cocaine use



Chest pain is the primary emergency department complaint in visits related to cocaine use

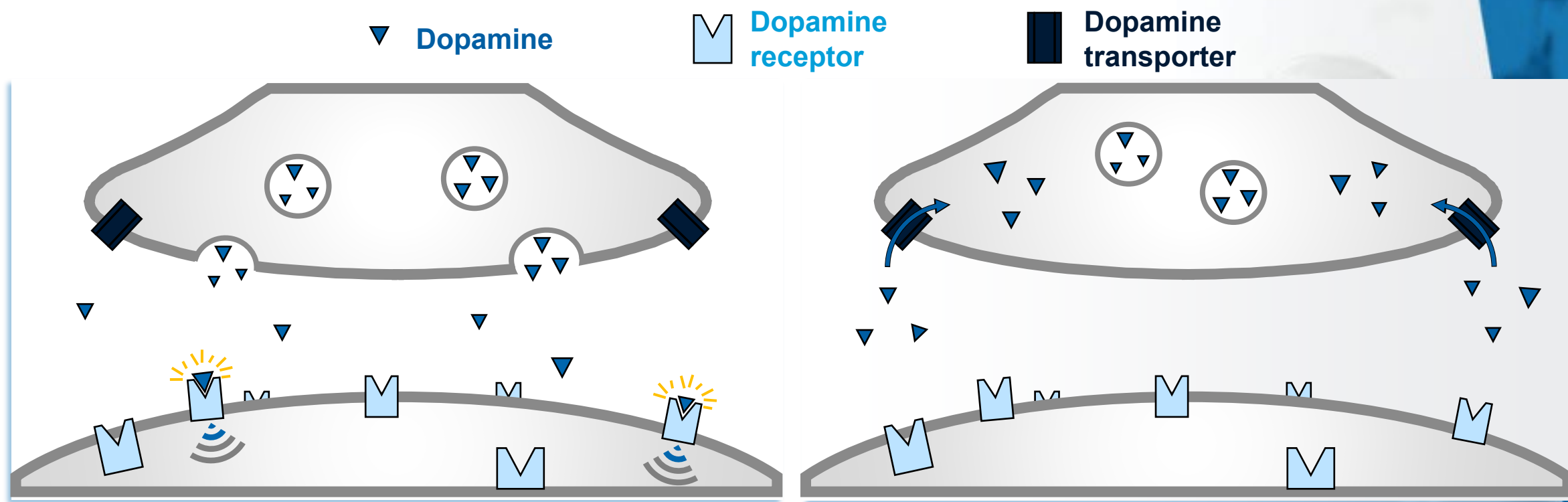


Diagnostic testing, specifically cardiovascular, is high in cocaine-related emergency room visits

Suen LW, et al. *BMC Emerg Med.* 2022;22(1):19.



Dopamine Mechanism of Action (MOA)



When **dopamine** is released into the synapse, it stimulates **dopamine receptors**

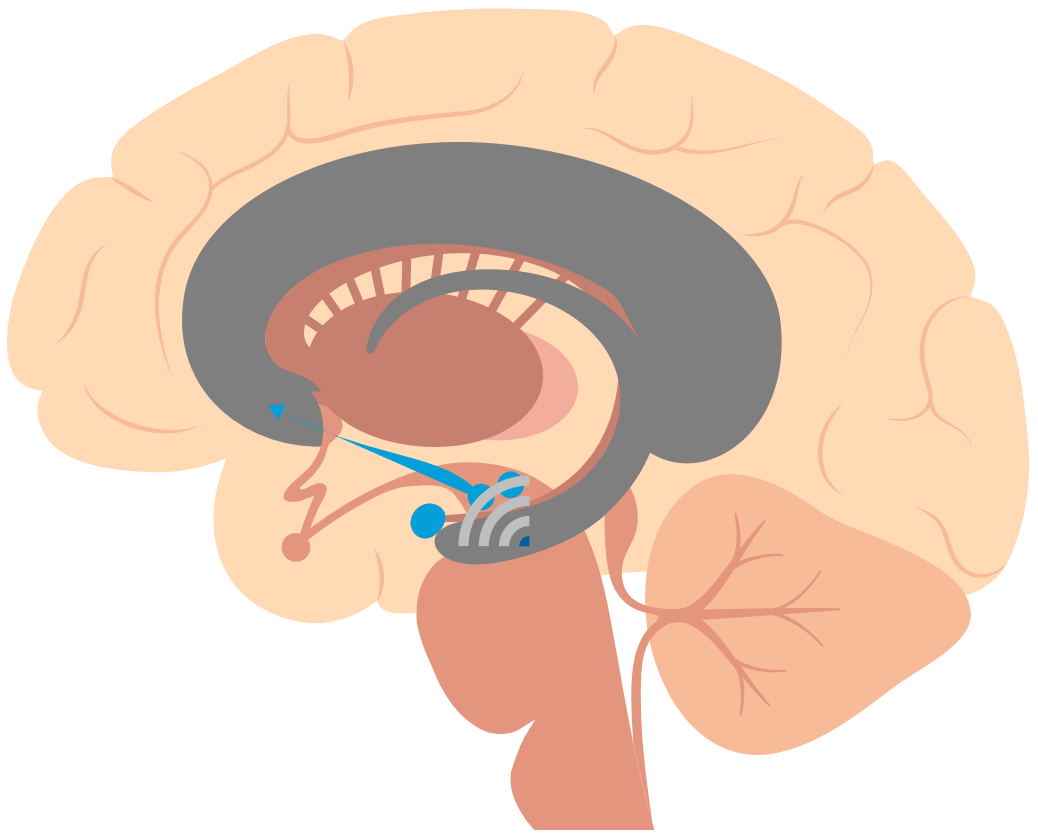
Subsequently, **dopamine** is removed from the synapse and recycled by **dopamine transporters**

¹Benowitz NL. *Pharmacol Toxicology*. 1993;72(1):3-12.
²Stahl SM. 5th ed. New York, NY: Cambridge University Press; 2021.



Activation of the Reward Pathway

■ Dopamine



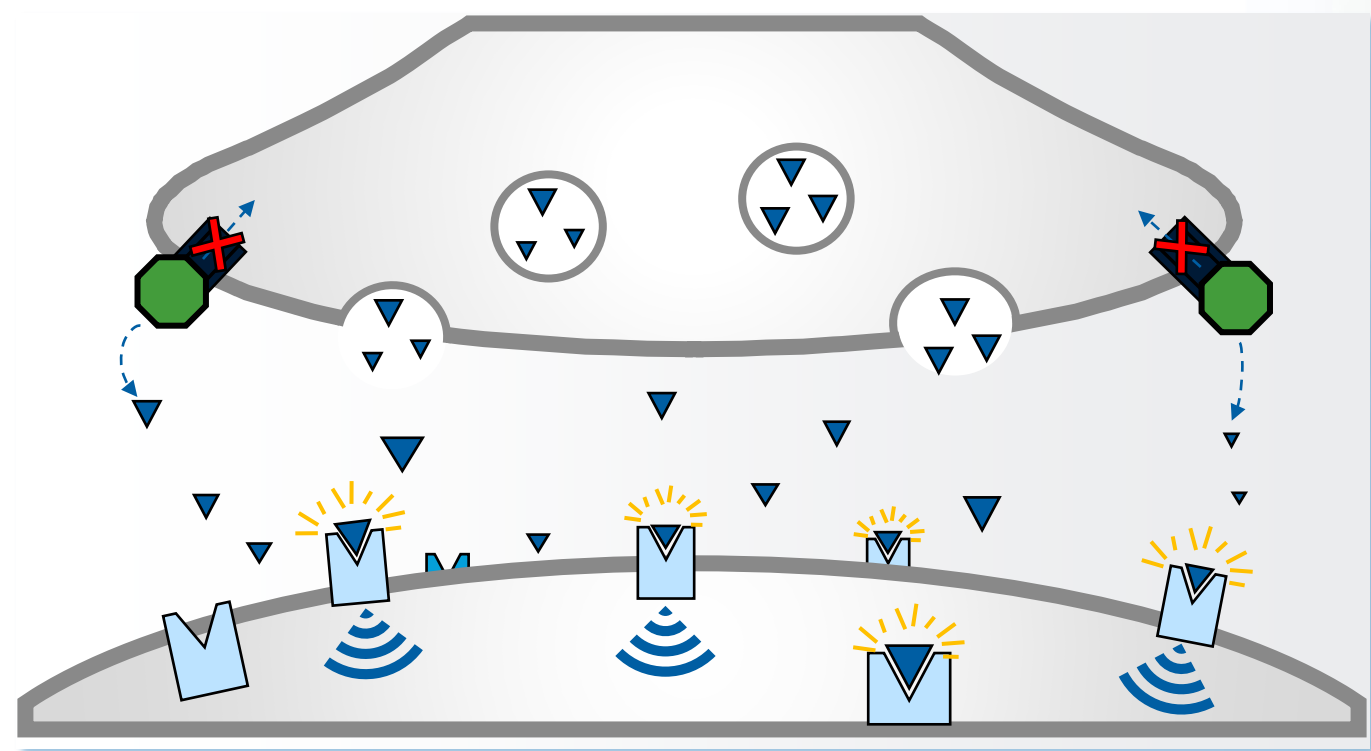
+ Dopamine



Dopamine mesolimbic pathway activation triggers feelings of reward



Cocaine Mechanism of Action (MOA)



Cocaine blocks **dopamine transporters**, leading to an accumulation of **dopamine** in the synapse and excessive stimulation of **dopamine receptors**^{1,2}

¹Roque Bravo R, et al. *Toxins (Basel)*. 2022;14(4):278.
²Stahl SM. 5th ed. New York, NY: Cambridge University Press; 2021.

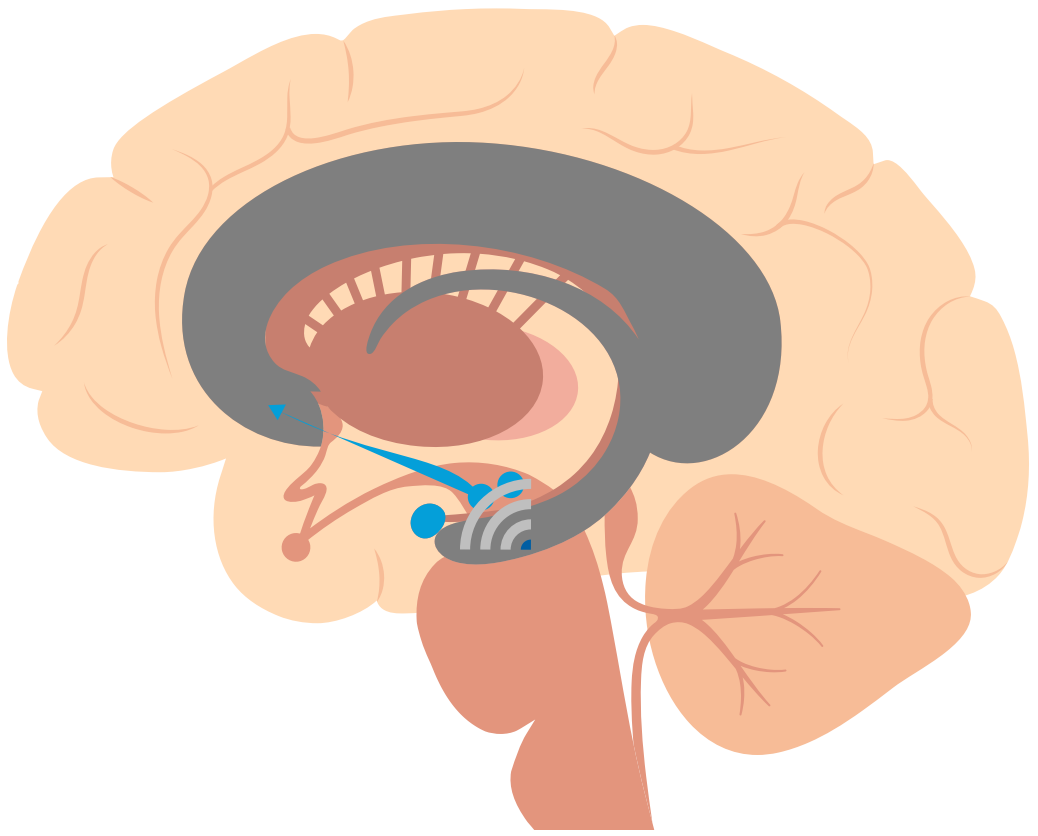


Cocaine's Effect on the Mesolimbic Pathway

— Dopamine

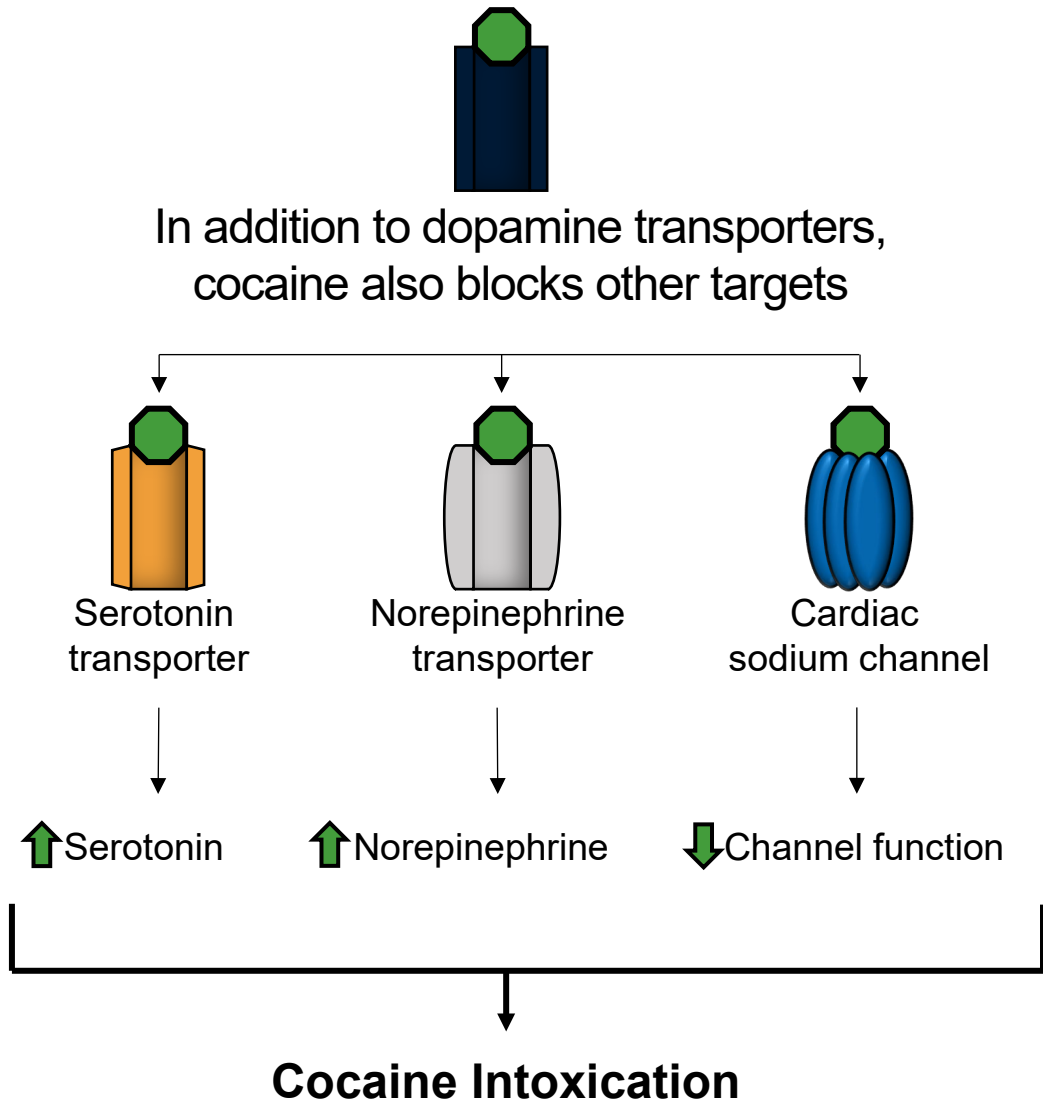
+ Cocaine

↑ Dopamine



Increased activation of the dopamine mesolimbic pathway contributes to the addictive capacity of cocaine

Cocaine Intoxication is the Result of Cocaine's Activity at Multiple Targets



The effects of cocaine intoxication include:



Seizures
Stroke



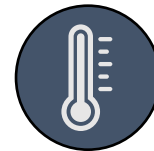
Arrhythmia
Tachycardia



Hypertension



Tremors
Multiorgan failure



Hyperthermia



Pharmacotherapies for Cocaine Intoxication Have Not Been Effective

Cocaine

Opiates

MOA of Toxicity Complex; mediated by multiple targets with distinct biological functions^{1,2}

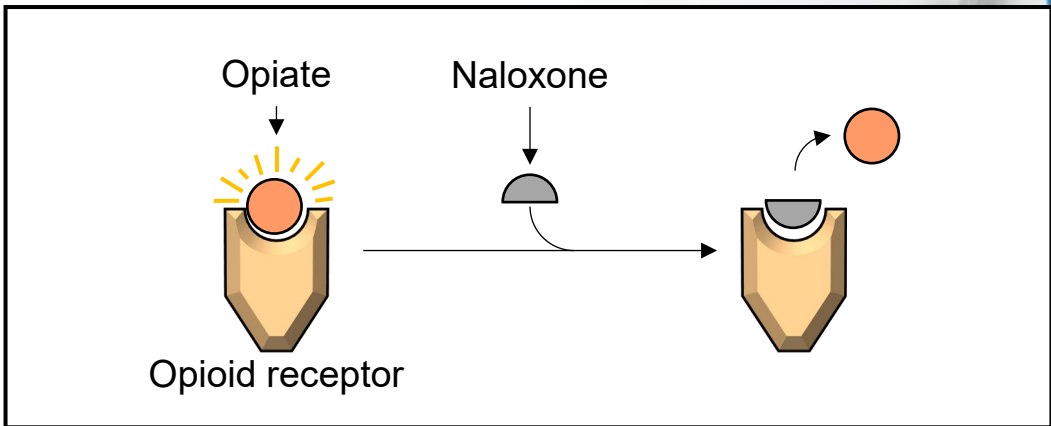
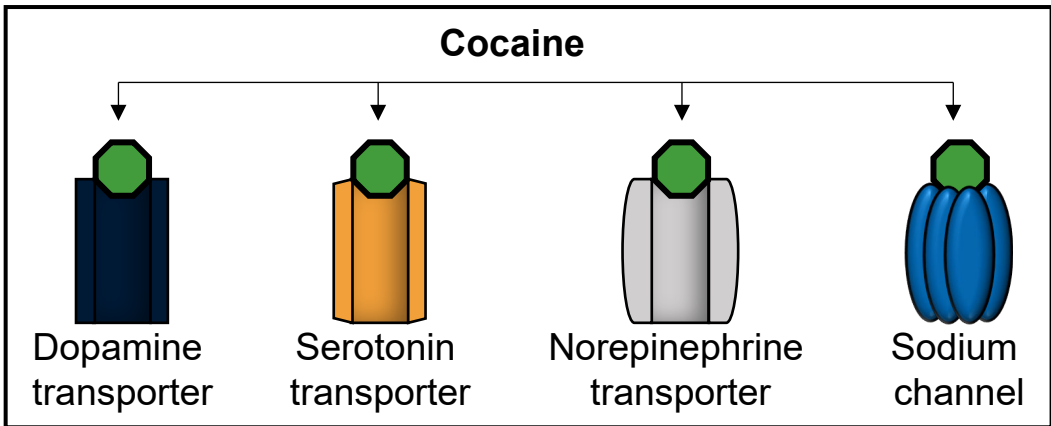
Simple; mediated by opioid receptors⁴

Pharmacology Antagonist³

Agonists³

Pharmacotherapy No FDA-approved medication exists^{1,2}

Naloxone^{4,5}



Unlike treatment for opiate intoxication, treatments have not been effective for cocaine

¹Brim RL, et al. *Mol Pharmacol.* 2011;80(6):1119-1127.
²Roque Bravo R, et al. *Toxins (Basel).* 2022;14(4):278.
³Stahl SM. 5th ed. New York, NY: Cambridge University Press; 2021.
⁴Kang Y, et al. *Sci Rep.* 2022;12(1):6429.
⁵Rzasa Lynn R, Galinkin JL. *Ther Adv Drug Saf.* 2018;9(1):63-88.



Treatment for Cocaine Intoxication

Current Standard of Care¹

- Patients present with acute agitation, hyperthermia, tachycardia, arrhythmias, and hypertension
- Patients have potential life-threatening sequelae of myocardial infarction, cerebrovascular accident, rhabdomyolysis, respiratory failure, and seizures
- Patients are currently managed only by supportive care for the adverse effects of cocaine intoxication on the cardiovascular and central nervous systems

Potential Benefit of TNX-1300

- By reversing the cause of cocaine intoxication (rather than treating the symptoms), TNX-1300 may offer significant advantages to the current standard of care for cocaine intoxication
 - Reduces circulating cocaine rapidly
 - Reduces significantly the time and resources required for other detox services
 - Reduces the risk of morbidity and mortality



Summary of TNX-1300

Key Features

- Full rights to the IP and to develop and commercialize TNX-1300 worldwide
- An inventory of investigational drug product
- Clinical trial results from previous Phase 2 study in which TNX-1300 at 100 mg or 200 mg IV doses was well tolerated and interrupted cocaine effects after cocaine 50 mg IV challenge

Development Plan

- Drug substance manufactured under-Good Manufacturing Practice (GMP)
- Completed non-clinical studies in reproductive toxicology
- Conduct a single blind, Phase 2 study in Emergency Room cocaine intoxication

Exclusivity

- Expected patent protection through 2029
- As a biologic and new molecular entity, TNX-1300 is eligible for 12 years of U.S. market exclusivity upon approval by the FDA

Unmet need

- No approved medicine to treat cocaine intoxication

A blue background featuring a large, semi-transparent molecular structure graphic. The structure consists of several interconnected spheres of varying sizes, representing atoms, connected by thin lines representing chemical bonds. The spheres have a metallic, reflective appearance.

THANK YOU

