



ASAM REVIEW COURSE 2026

Neurobiology of Addiction: Key Concepts and Models

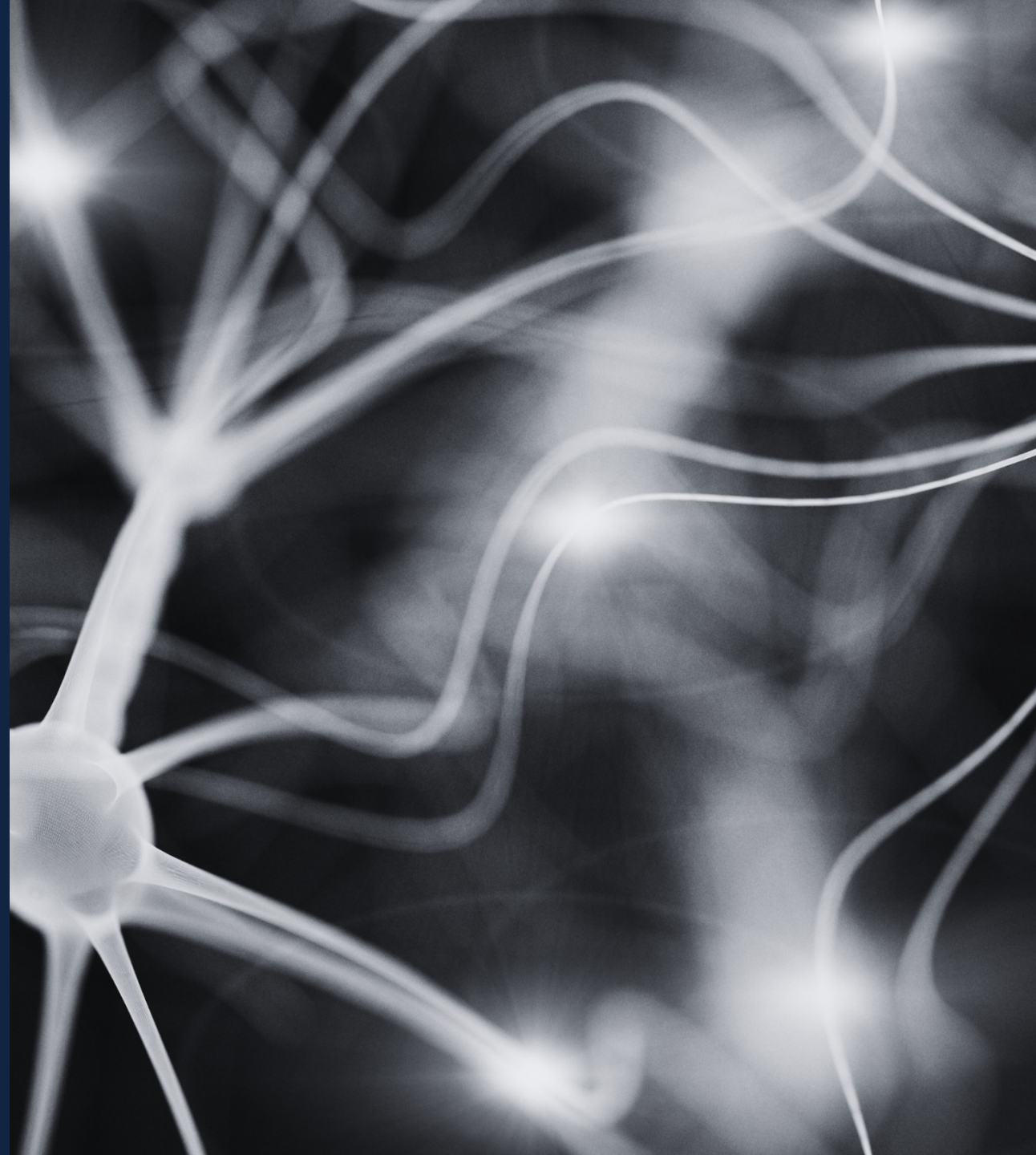
Petros Levounis, MD, MA

Professor and Chair, Department of Psychiatry, and Associate
Dean, Rutgers New Jersey Medical School

Chief of Service, University Hospital, Newark, New Jersey

Director, Northern New Jersey Medications for Addiction
Treatment Center of Excellence

Past President, American Psychiatric Association





Financial Disclosure

Petros Levounis, MD, MA

- No relevant disclosures

LEARNING OBJECTIVE

Identify key neurotransmitters, brain pathways, and brain structures implicated in addiction and addiction treatment.

Outline



1

Neurotransmitters

2

The Fundamental
Model

3

The New and
Improved Model

4

Treatments

Neurotransmitters

Substance

Alcohol

Amphetamines & Cocaine

Benzodiazepines & GHB

Cannabis

Hallucinogens & MDMA

Nicotine

Opioids

Phencyclidine & Ketamine

Endogenous Neurotransmitter

GABA / Glutamate*

Dopamine

GABA

Anandamide

Serotonin

Acetylcholine

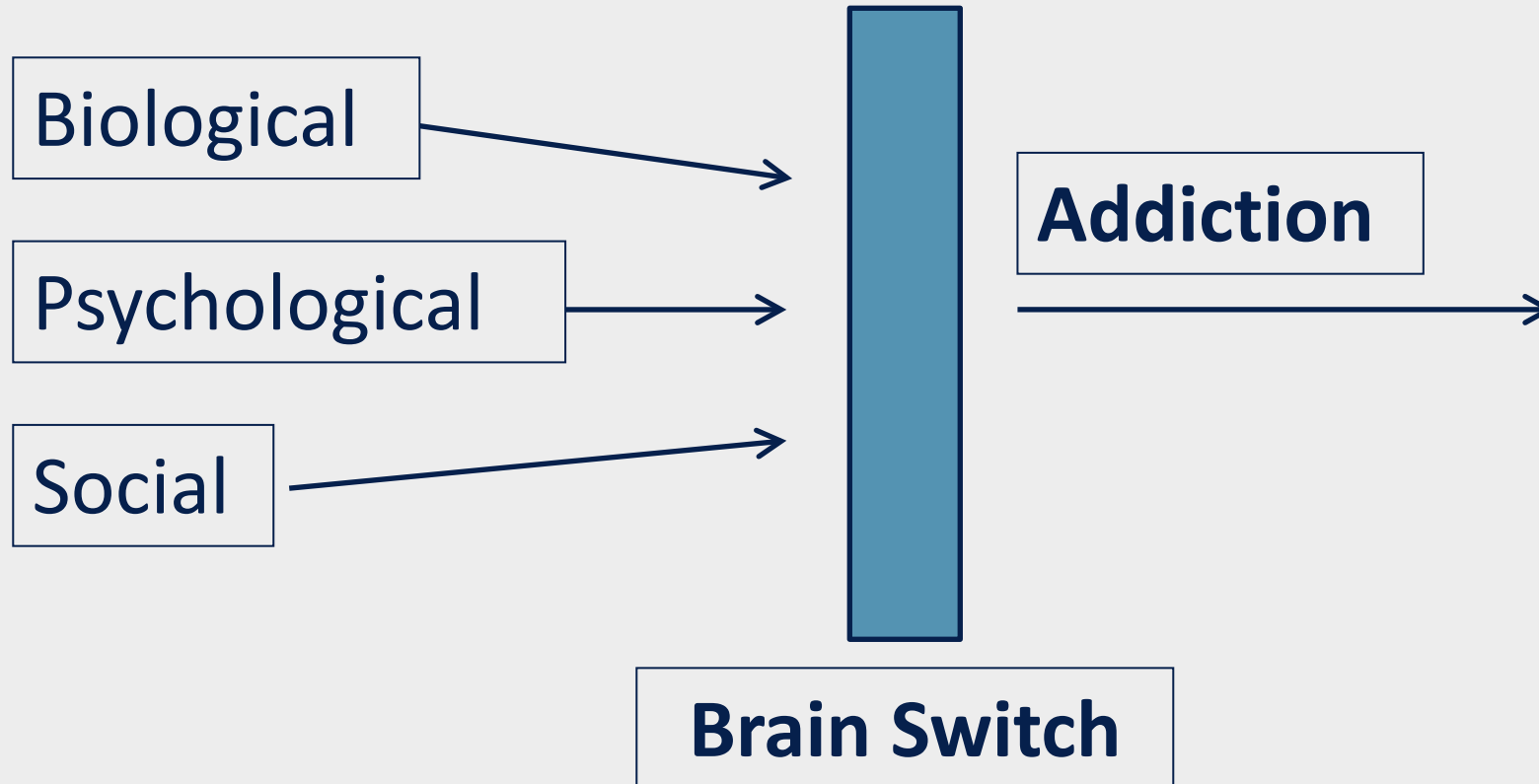
Endorphins

Glutamate*

*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

The Fundamental Model

Addiction: A Biopsychosocial Illness



The Root Cause of the Disaster

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients¹ who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,² Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

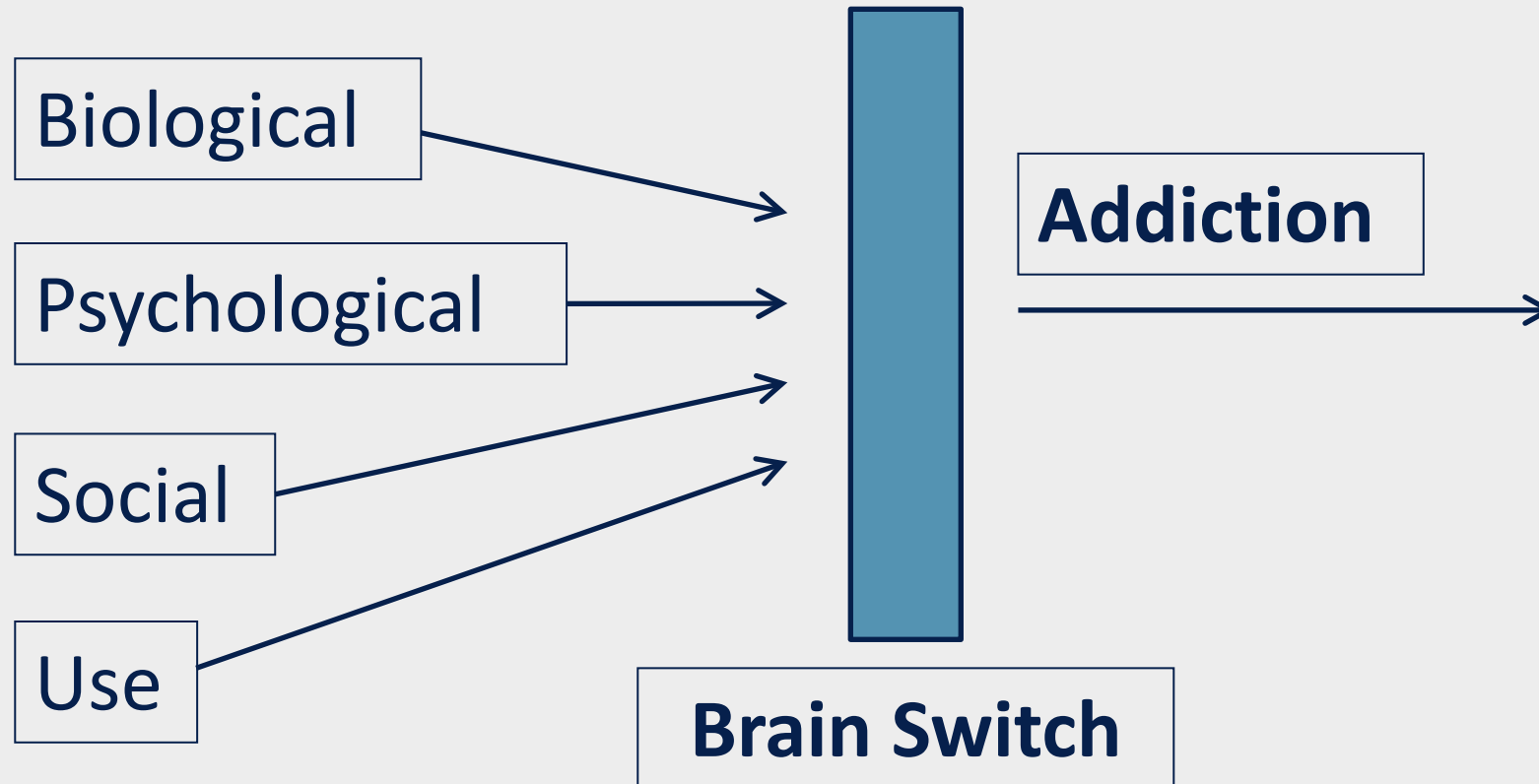
JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug
Surveillance Program

Waltham, MA 02154

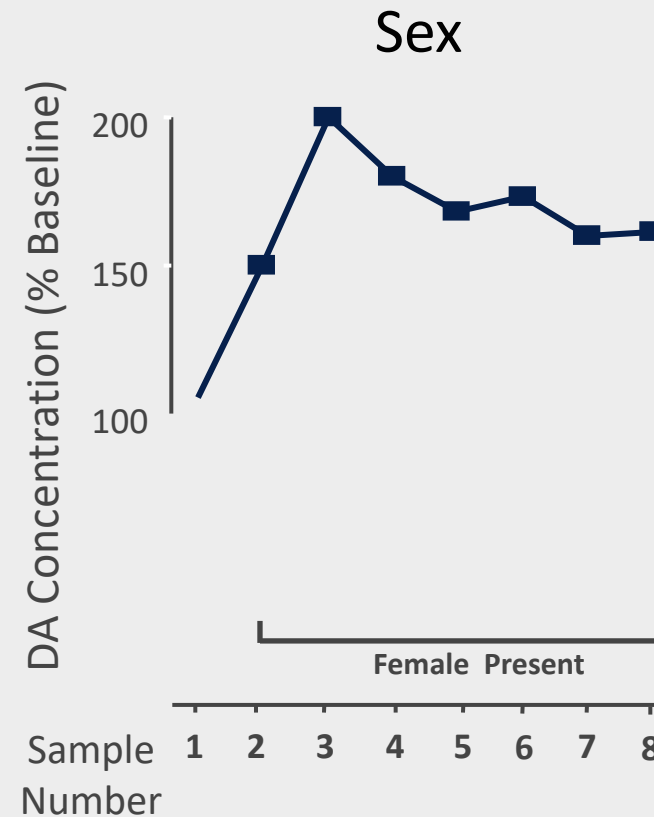
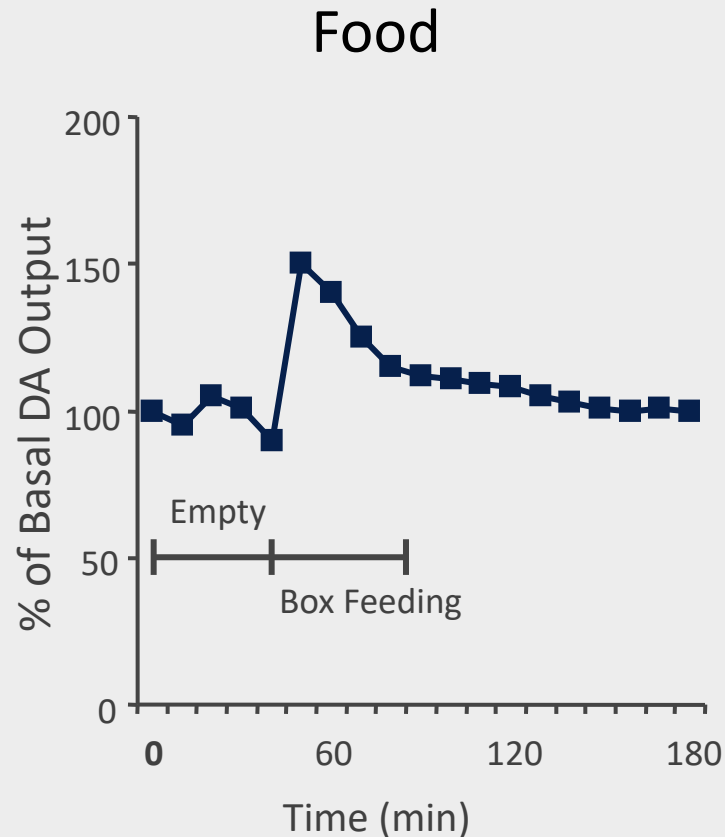
Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

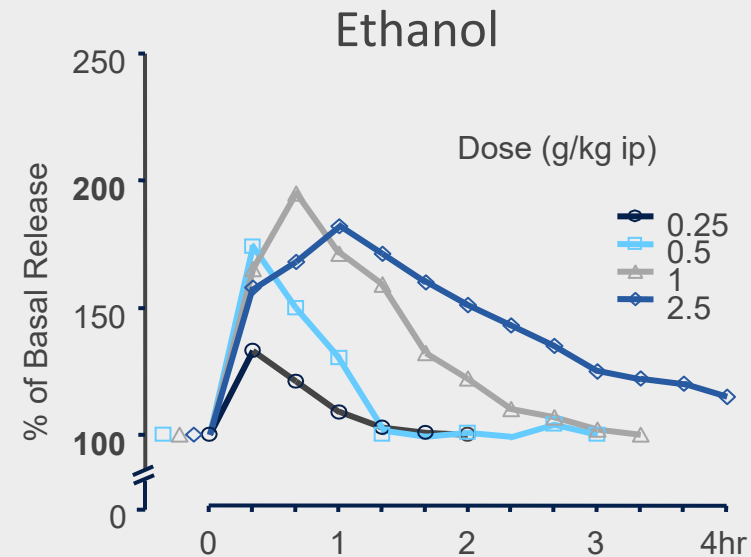
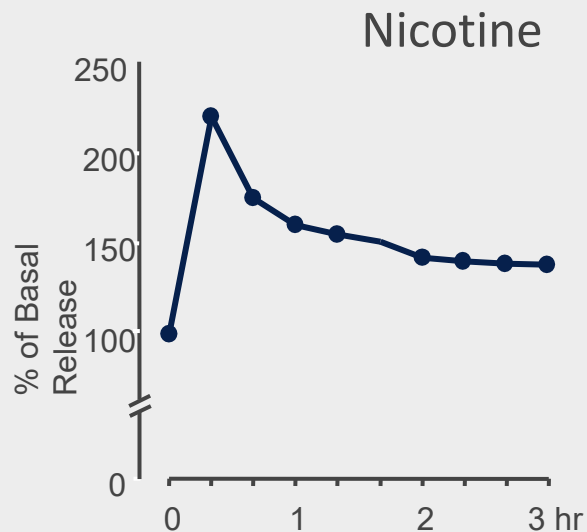
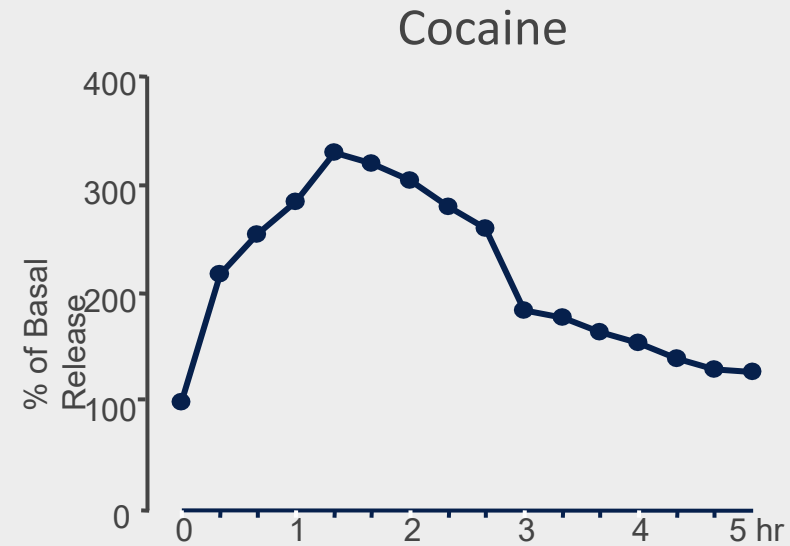
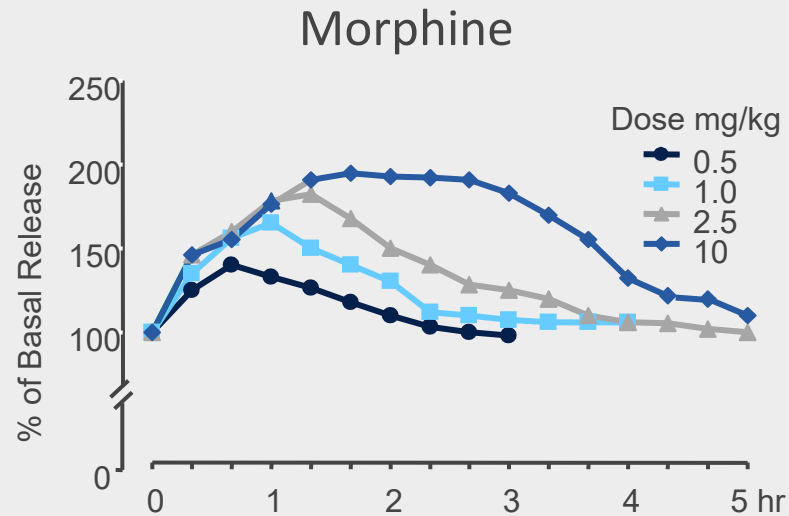
Addiction: A Biopsychosocial Illness



Basal Ganglia (Nucleus Accumbens) and Binge/Intoxication

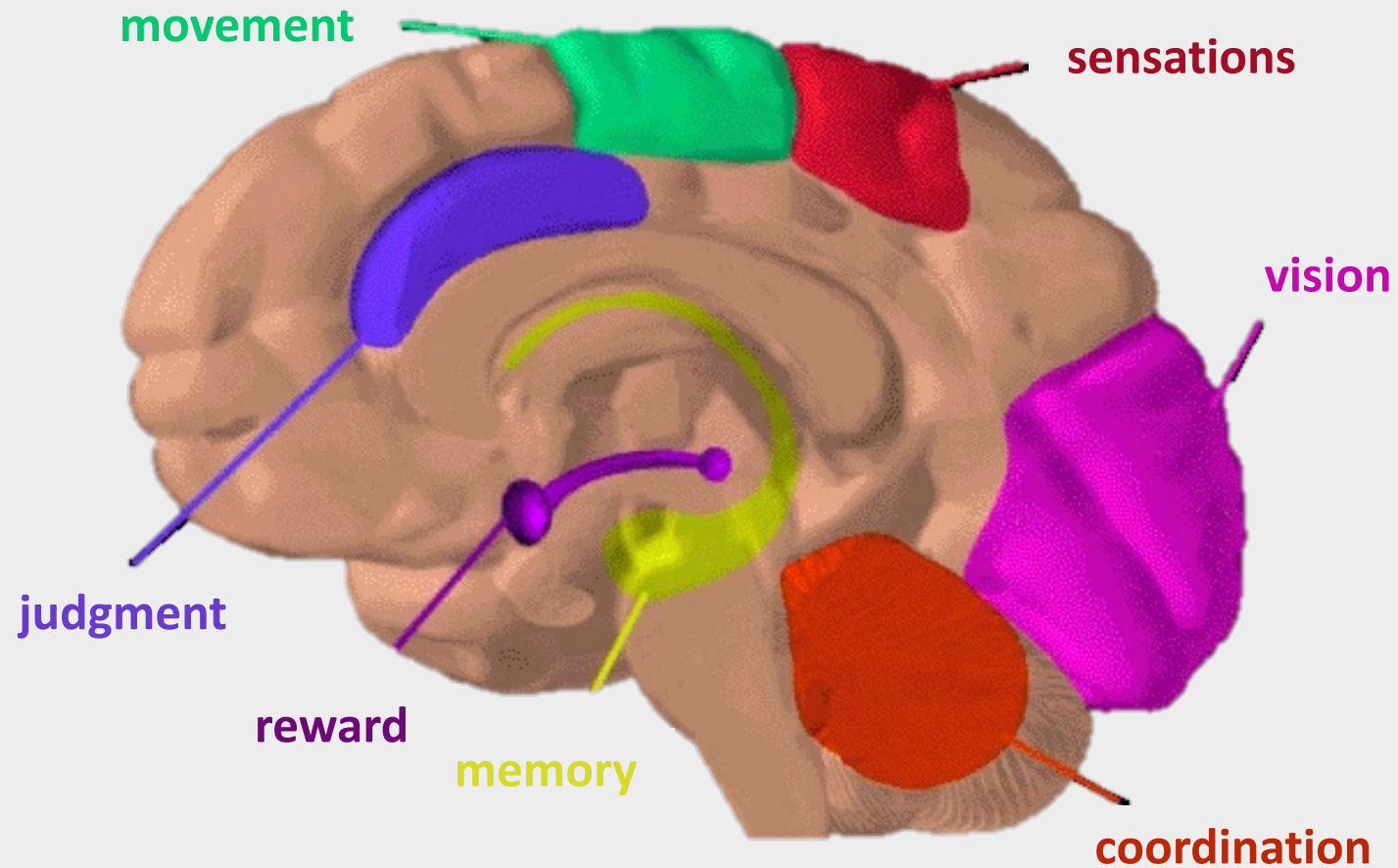


Effects of Drugs on Dopamine Levels

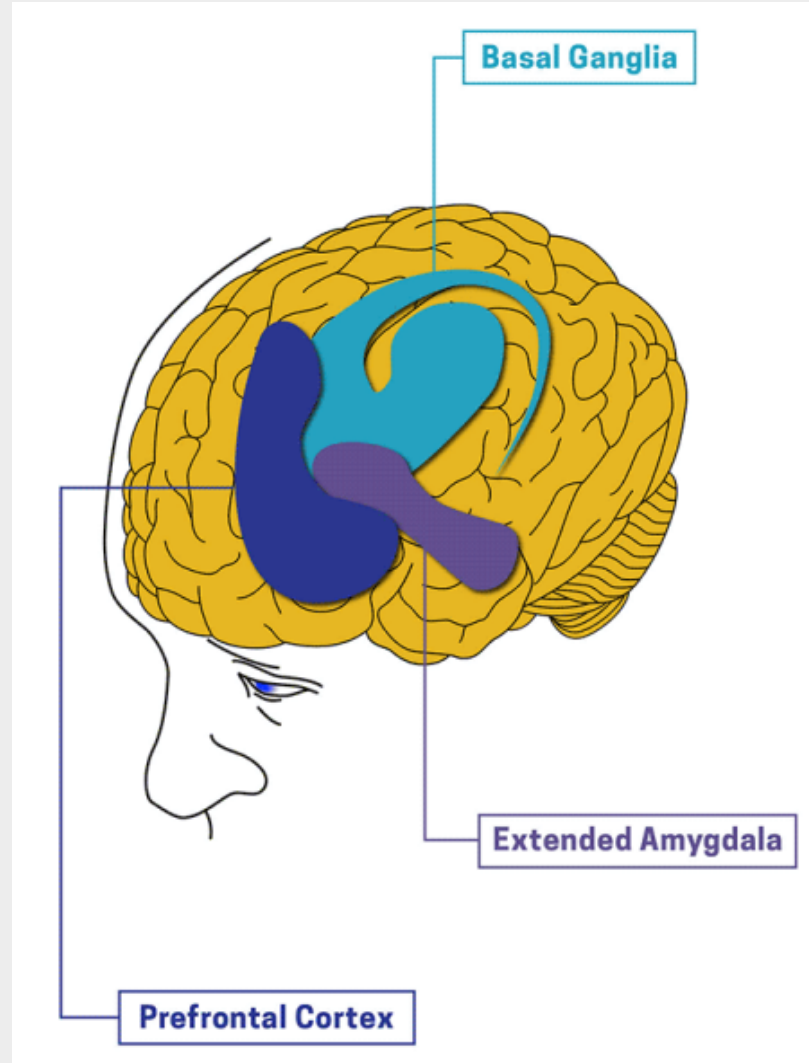


Adapted from: Di Chiara and Imperato, *Proceedings of the National Academy of Sciences USA*, 1988;
courtesy of Nora D Volkow, MD

Hippocampus and Extended Amygdala



Prefrontal Cortex and Executive Function



National Institute on Drug Abuse, NIDA.NIH.gov, accessed on May 1, 2026

The New and Improved Model

Three Novel Areas

Motivational Circuitry
(Medial OFC)

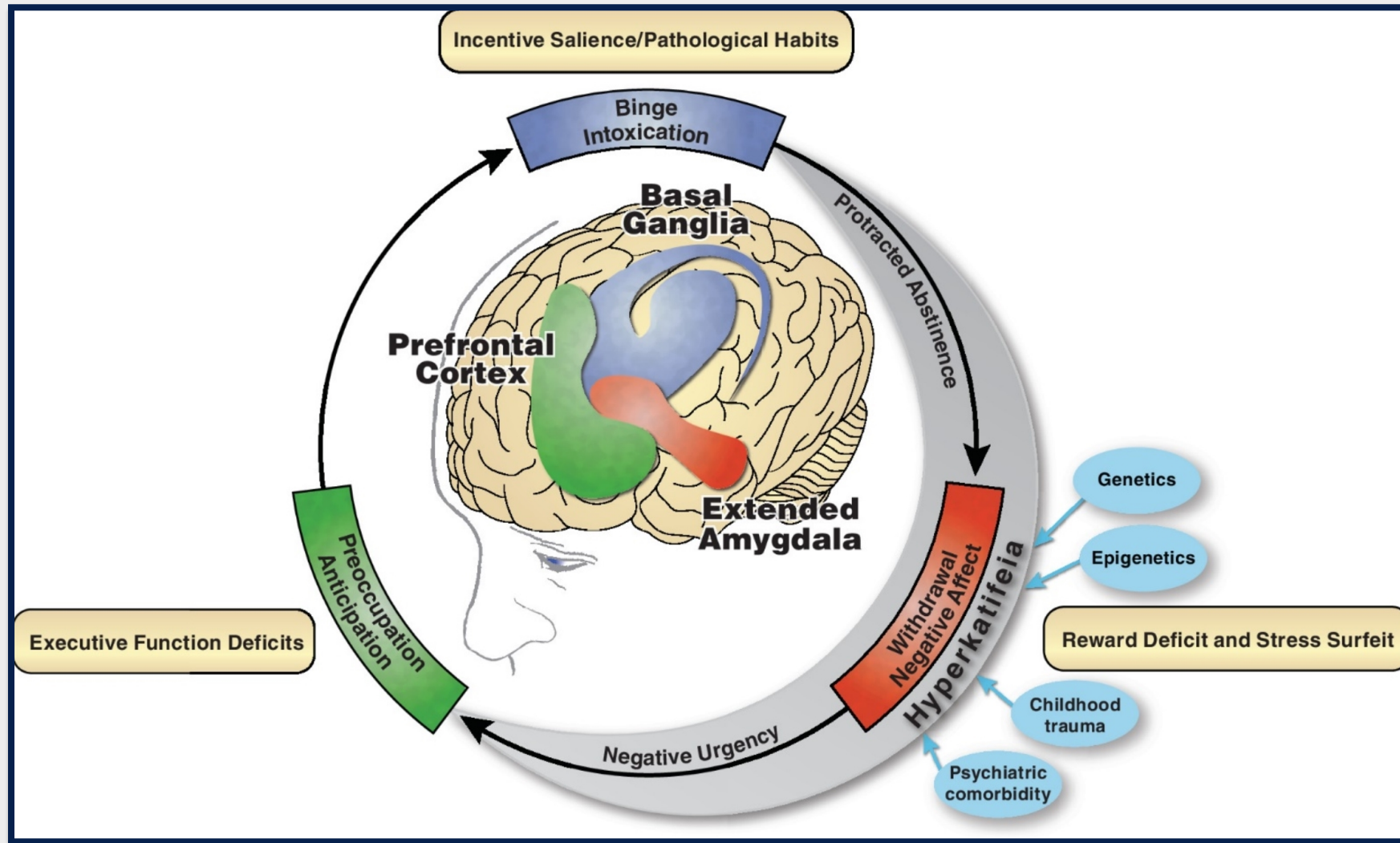
Antireward Pathways
(Extended Amygdala)

Interoception
(Insula)

Medial Orbitofrontal Cortex (OFC) and Preoccupation/Anticipation



Extended Amygdala and Withdrawal/Negative Affect



Reward Systems

Game #1

- A. A sure gain of \$250
- B. 25% chance to gain \$1,000, 75%
 chance to gain nothing.



Reward Systems

Game #1

- | | |
|--|-----|
| A. A sure gain of \$250 | 84% |
| B. 25% chance to gain \$1,000,
75% chance to gain nothing | 16% |



Anti-Reward Systems

Game #2

- A. A sure loss of \$750
- B. 25% chance to lose nothing, 75% chance to lose \$1,000.



Anti-Reward Systems

Game #2

- | | |
|---|-----|
| A. A sure loss of \$750 | 13% |
| B. 25% chance to lose nothing,
75% chance to lose \$1,000. | 87% |



Human Nature

People avoid risks to ensure gains.

People take risks to avoid definite losses.

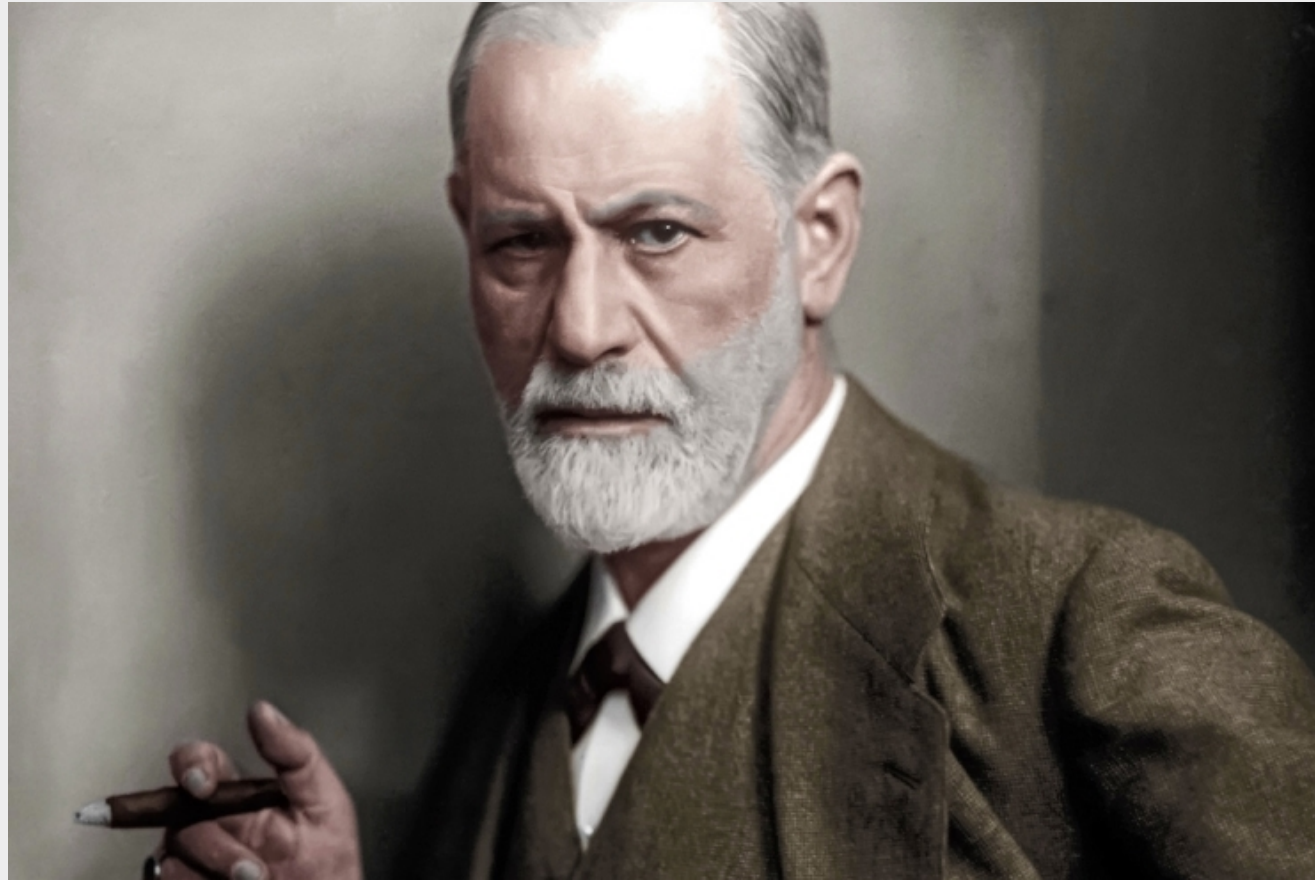
Psychology trumps probability.

The Ultimate Gatekeeper: Insula



Treatments

1st Wave: Psychoanalysis



2nd Wave: Boot Camps

The prototype, Synanon, was founded in California in 1958 to address heroin addiction. The goal was to:

- break down defenses,
- bust through denial, and
- reshape the individual's personality.

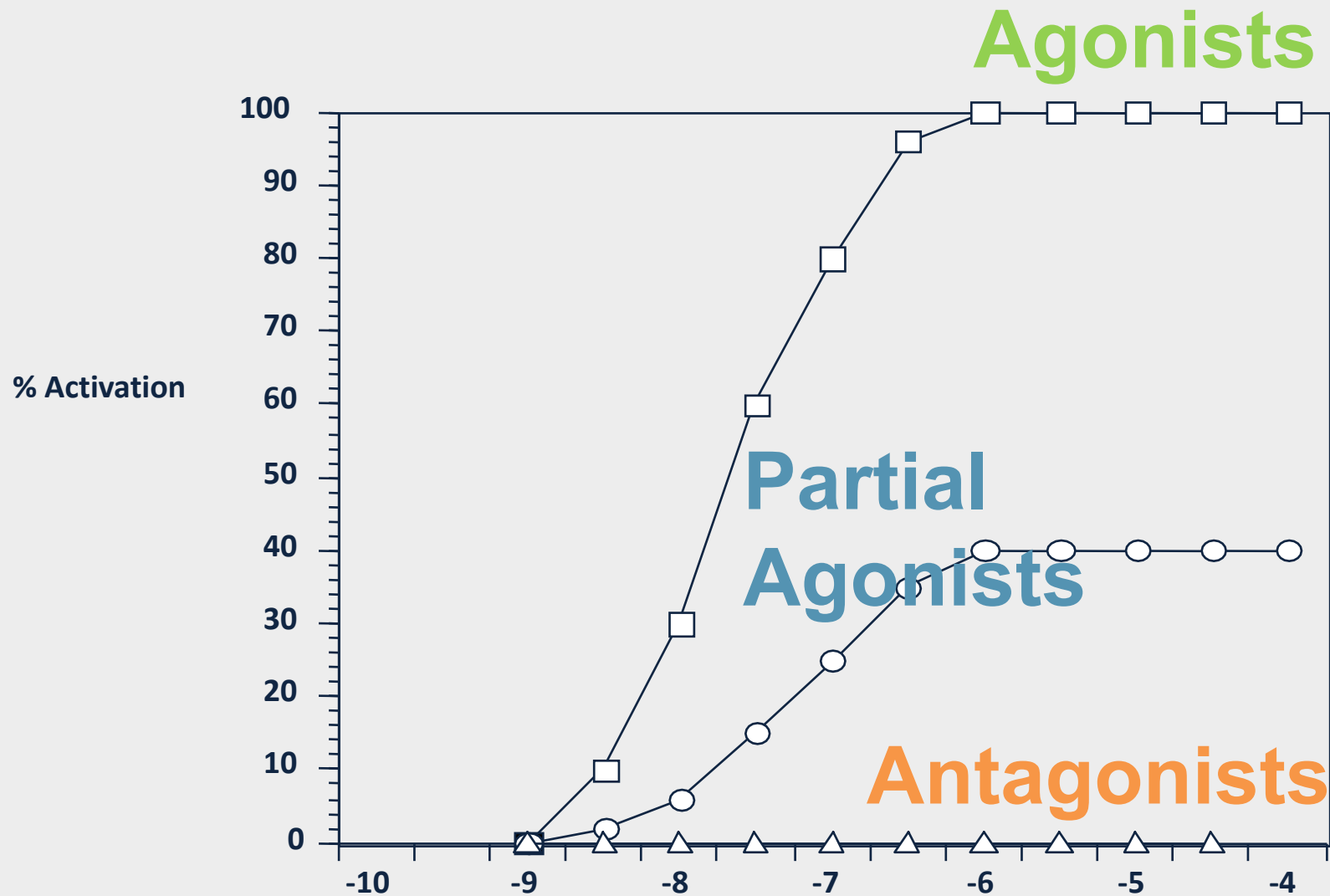
3rd Wave: Current Treatments

Medications

Mutual Help

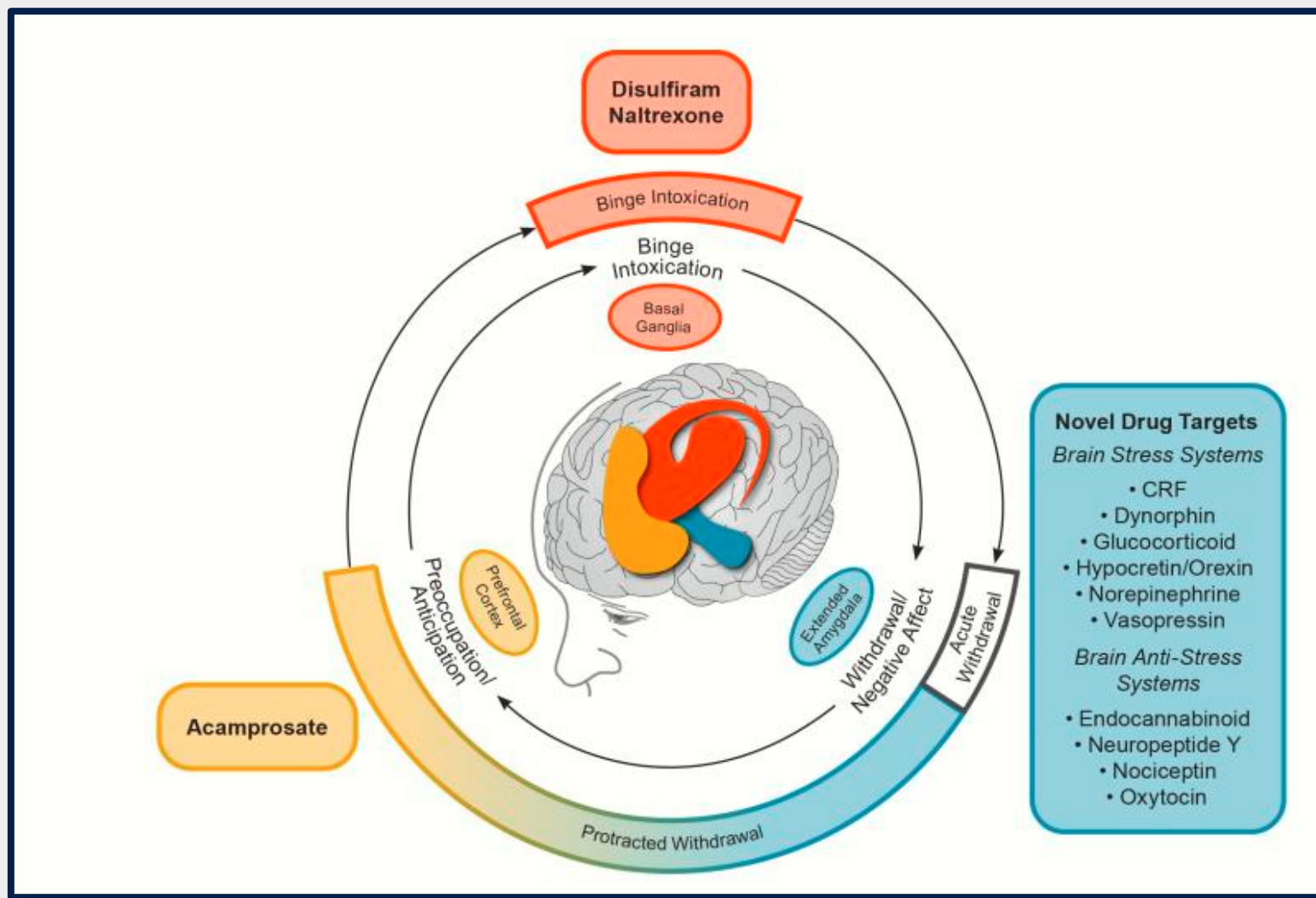
Psychotherapy and
Counseling

Medications (opioids and tobacco)



Renner JA, Chen C, Suzuki J, and Levounis P, *Buprenorphine Treatment of Opioid Use Disorder, 3rd Edition*, American Psychiatric Association Publishing, 2026, in press

Medications (alcohol and possibly others)



Mason BJ and Heyser CJ, Alcohol use disorder: the role of medication in recovery, *Alcohol Research*, 2021; DeVido J, Marienfeld C, Kranzler HR, and Levounis, P, *Clinical Manual of Addiction Psychopharmacology*, 3rd Edition, American Psychiatric Association Publishing, 2026

Mutual Help

MEDICAL STUDENTS	PATIENTS	WHAT MED STUDENTS THINK PATIENTS THINK
1. Housing	1. Inner Peace	1. Housing
2. Government	2. God	2. Outpatient Treatment
3. Medical Services	3. Medical Services	3. Medical Services
4. Outpatient Treatment	4. AA	4. Job
5. Job	5. Housing	5. Trusting People
6. Community	6. Spirituality	6. AA
7. Trusting People	7. Outpatient Treatment	7. Inner Peace
8. Inner Peace	8. Community	8. Community
9. God	9. Government	9. Government
10. Spirituality	10. Trusting People	10. Spirituality
11. AA	11. Job	11. God

Goldfarb LM, Medical student & patient attitudes toward religion and spirituality in the recovery process, American Journal of Drug & Alcohol Abuse, 1996; Fazzio L, Galanter M, Dermatis H, Levounis P, Evaluation of medical student attitudes toward Alcoholics Anonymous, Substance Abuse, 2003

Cognitive Behavioral Therapy & Motivational Interviewing



4th Wave: Mindfulness

“Between stimulus and response there is a space. In that space is our power to choose our response. In our response lie our growth and our freedom.”

Victor E. Frankl



*Frankl, Man's Search for Meaning, 1959;
Zerbo, Schlechter, Desai, and Levounis, Becoming Mindful, 2017*

Report Your Status

Have you used today? ☒ Yes ☐ No

How strong is your craving right now?

6

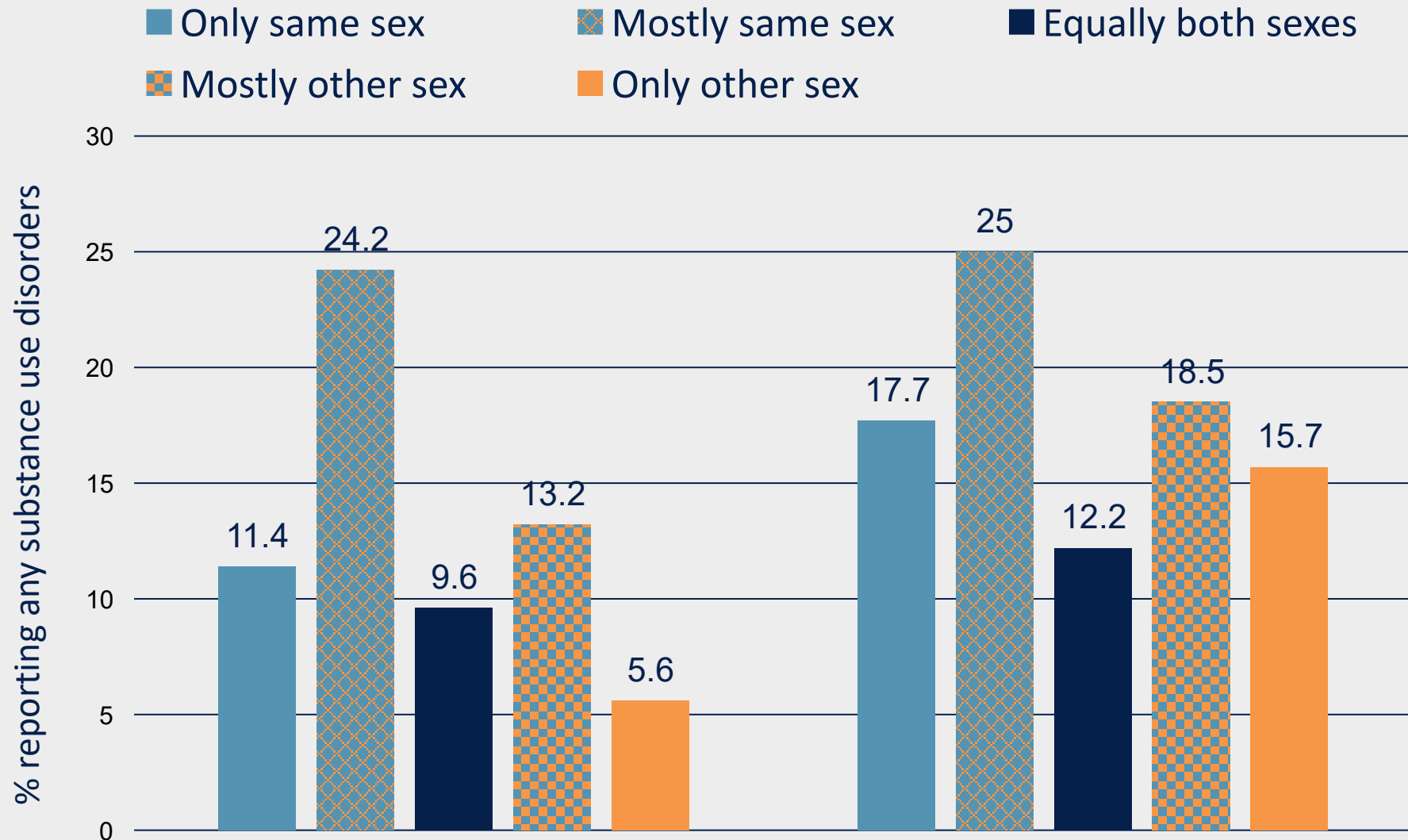
What triggers are affecting this craving?

HUNGRY	☐ n/a	4
ANGRY	☐ n/a	2
LONELY	☐ n/a	3
TIRED	☒ n/a	0
SOCIAL PRESSURE	☐ n/a	3
PAIN	☐ n/a	10
OTHER	☐ n/a	6

SUBMIT

Digital Therapeutics (CBT Apps)

And Back to Psychodynamics . . .



McCabe, *Addiction*, 2009; courtesy of Sean E. McCabe, PhD;

Levounis and Yarbrough, *LGBTQ+ Mental Health*, 2020

Neurotransmitters

Substance

Alcohol

Amphetamines & Cocaine

Benzodiazepines & GHB

Cannabis

Hallucinogens & MDMA

Nicotine

Opioids

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Endogenous Neurotransmitter

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Dopamine

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Anandamide

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Acetylcholine

Endorphins

Glutamate*

*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

In Summary

Addiction is the war between the hijacked pleasure and reward pathways of the basal ganglia and the executive function of the prefrontal cortex.

Motivational circuitry, the anti-reward pathways, and interoception complete the 2026 model of addiction.

Pharmacological Treatments:
agonists, antagonists, and partial agonists.

Psychosocial Treatments:
mutual help, CBT, motivational interviewing, and mindfulness.

Know your neurotransmitters!

Thank You





Get in Touch



301.656.3920



education@asam.org



www.asam.org