ASAM REVIEW COURSE 2024

Neurobiology of Addiction: Key Concepts and Models

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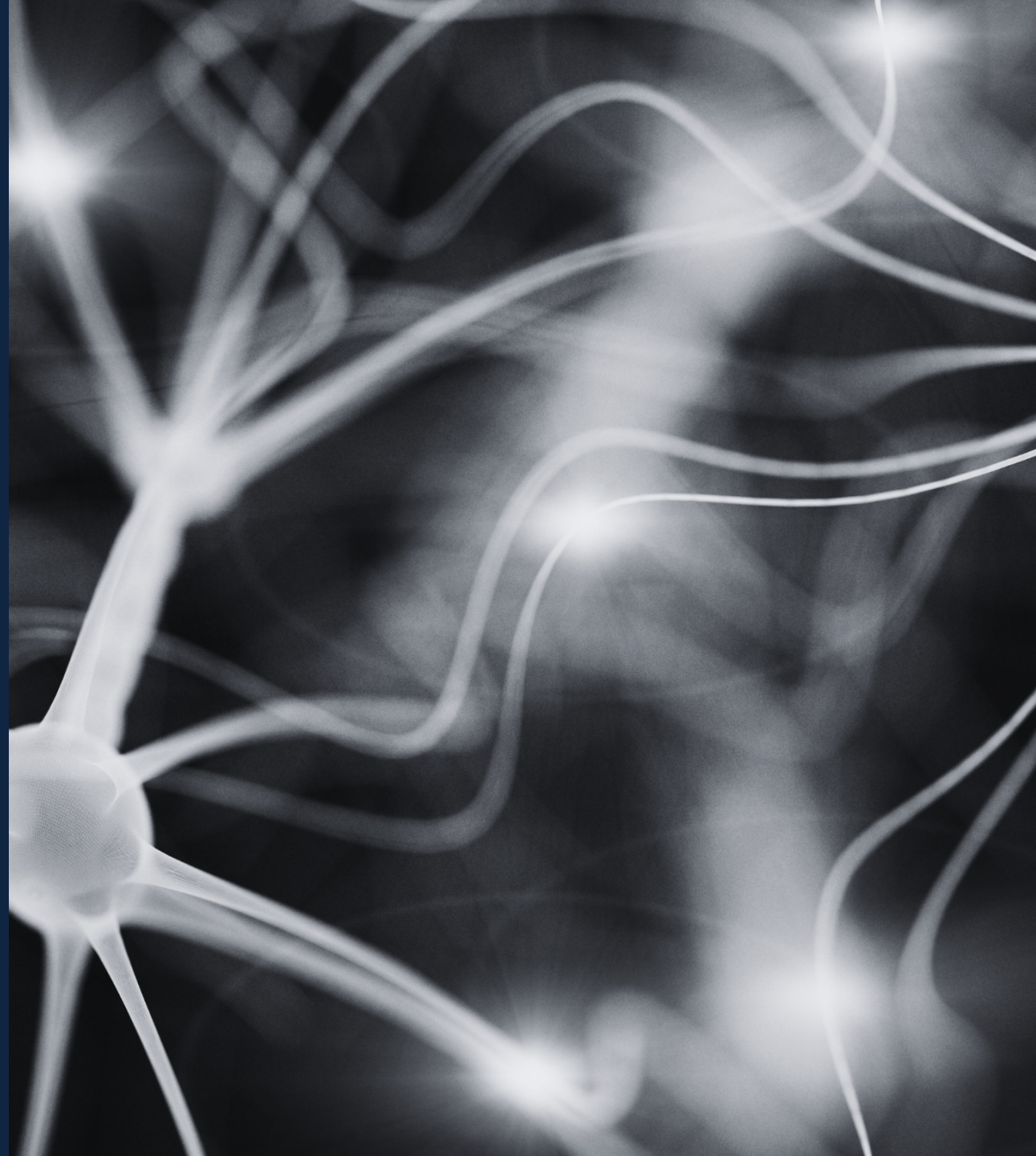

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Petros Levounis, MD, MA

- 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

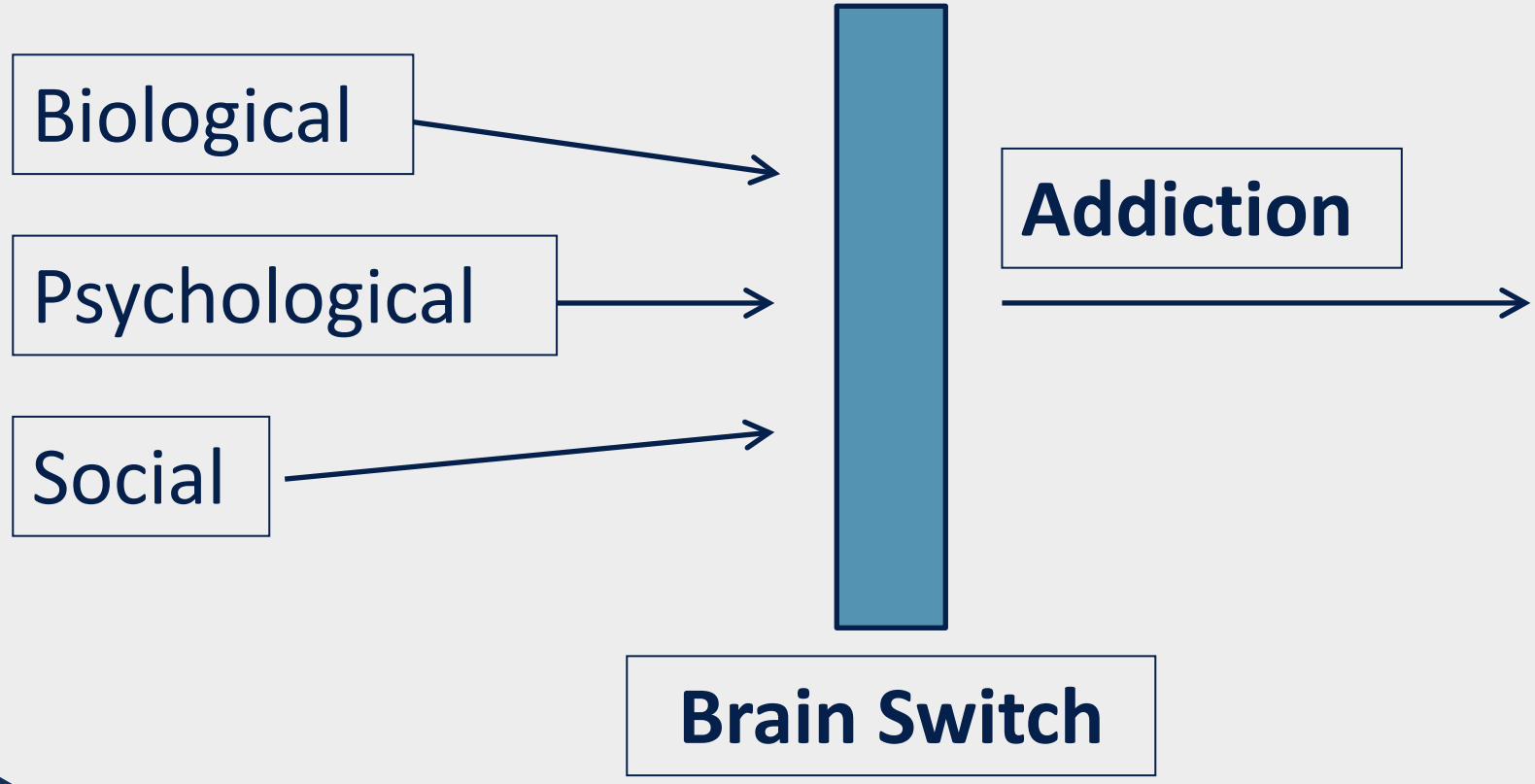
Neurotransmitters

Substance	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
Benzodiazepines & GHB	GABA
Cannabis	Anandamide
Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	Glutamate*

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

The Fundamental Model

Addiction: A Biopsychosocial Illness



Olsen and Levounis, Sober Siblings, 2008.

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 patients[1] 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.

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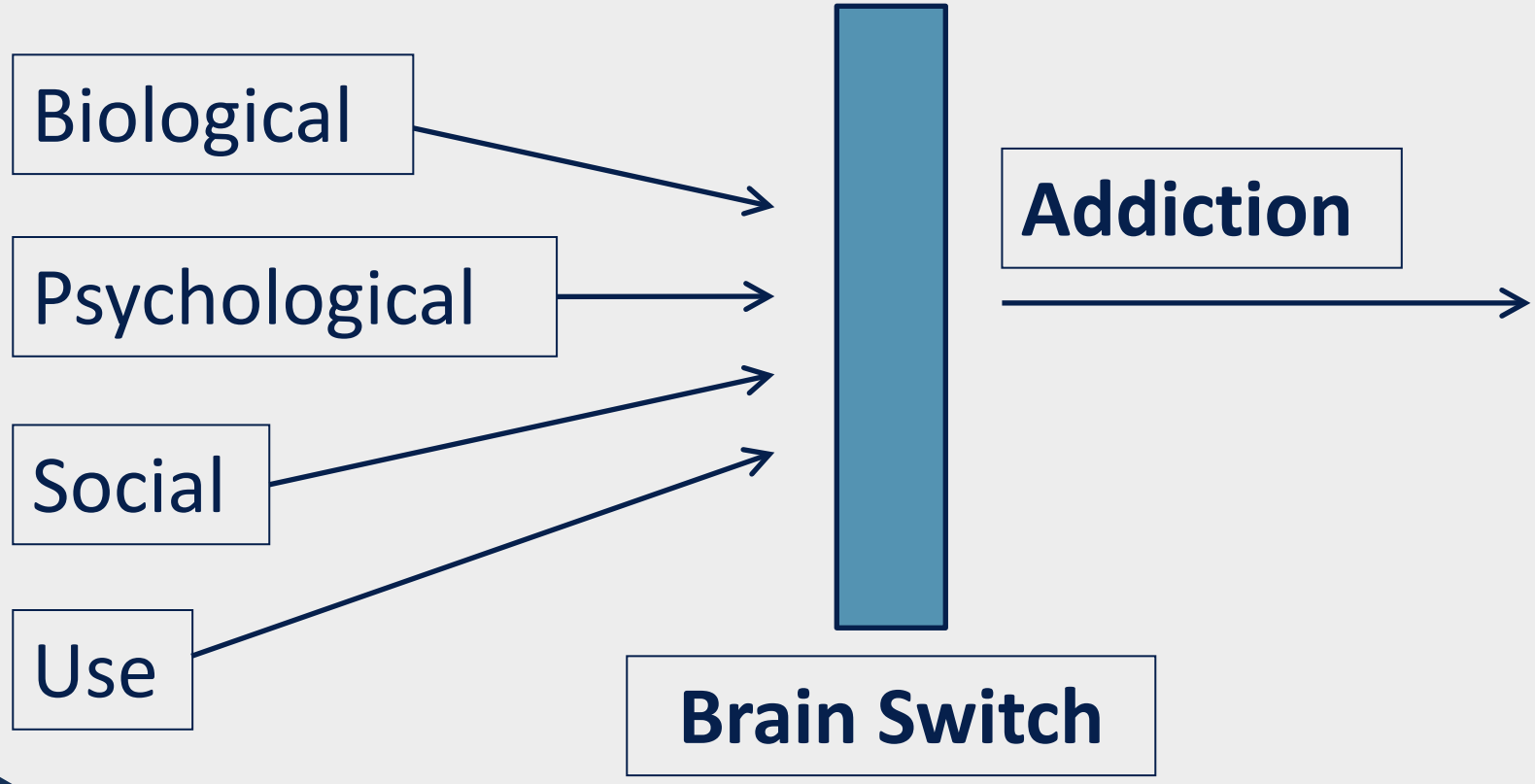
1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

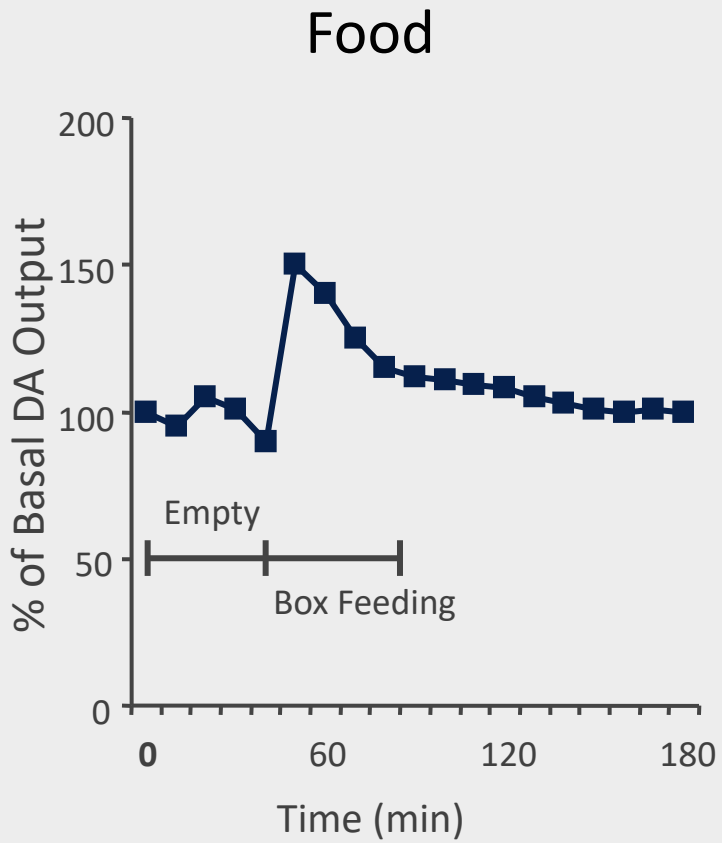
Porter and Jick, N Engl J Med, January 10, 1980.

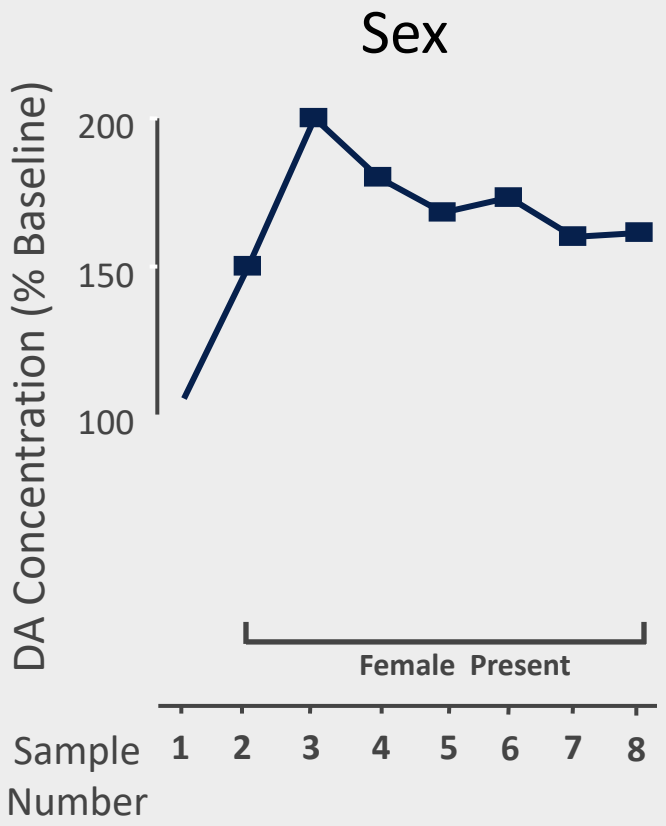
Addiction: A Biopsychosocial Illness



Olsen and Levounis, Sober Siblings, 2008.

Basal Ganglia (Nucleus Accumbens) and Binge/Intoxication

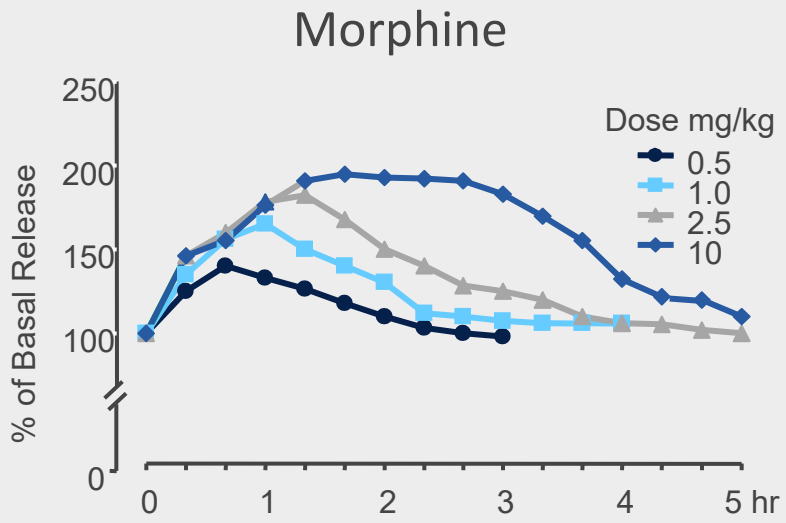


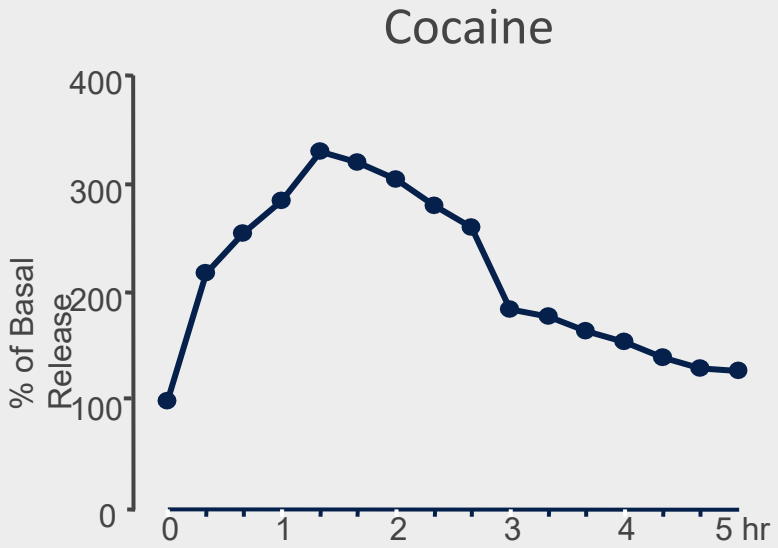


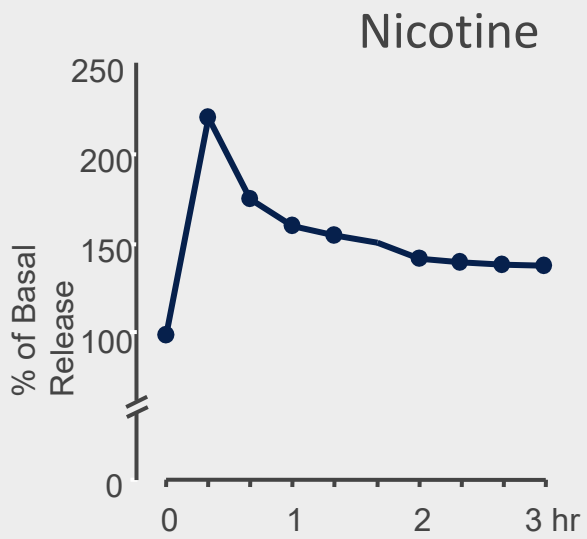
Adapted from: Di Chiara et al, Neuroscience, 1999.

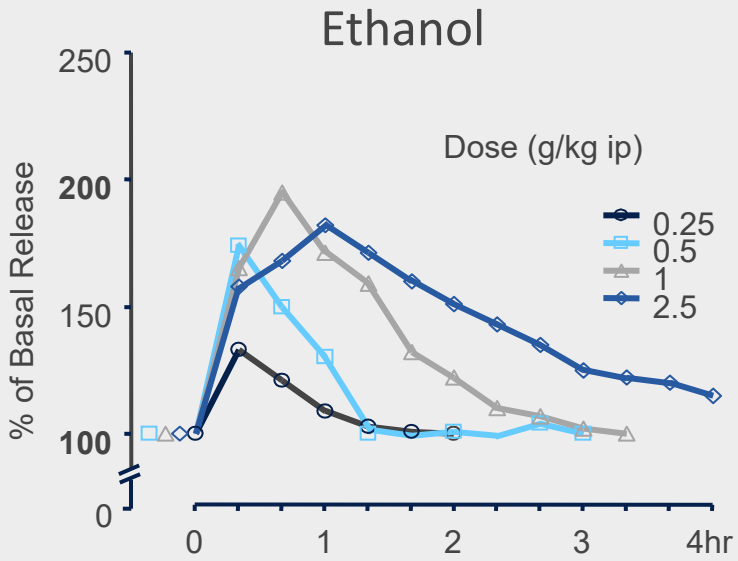
Adapted from: Fiorino and Phillips, J Neuroscience, 1997.

Effects of Drugs on Dopamine Levels



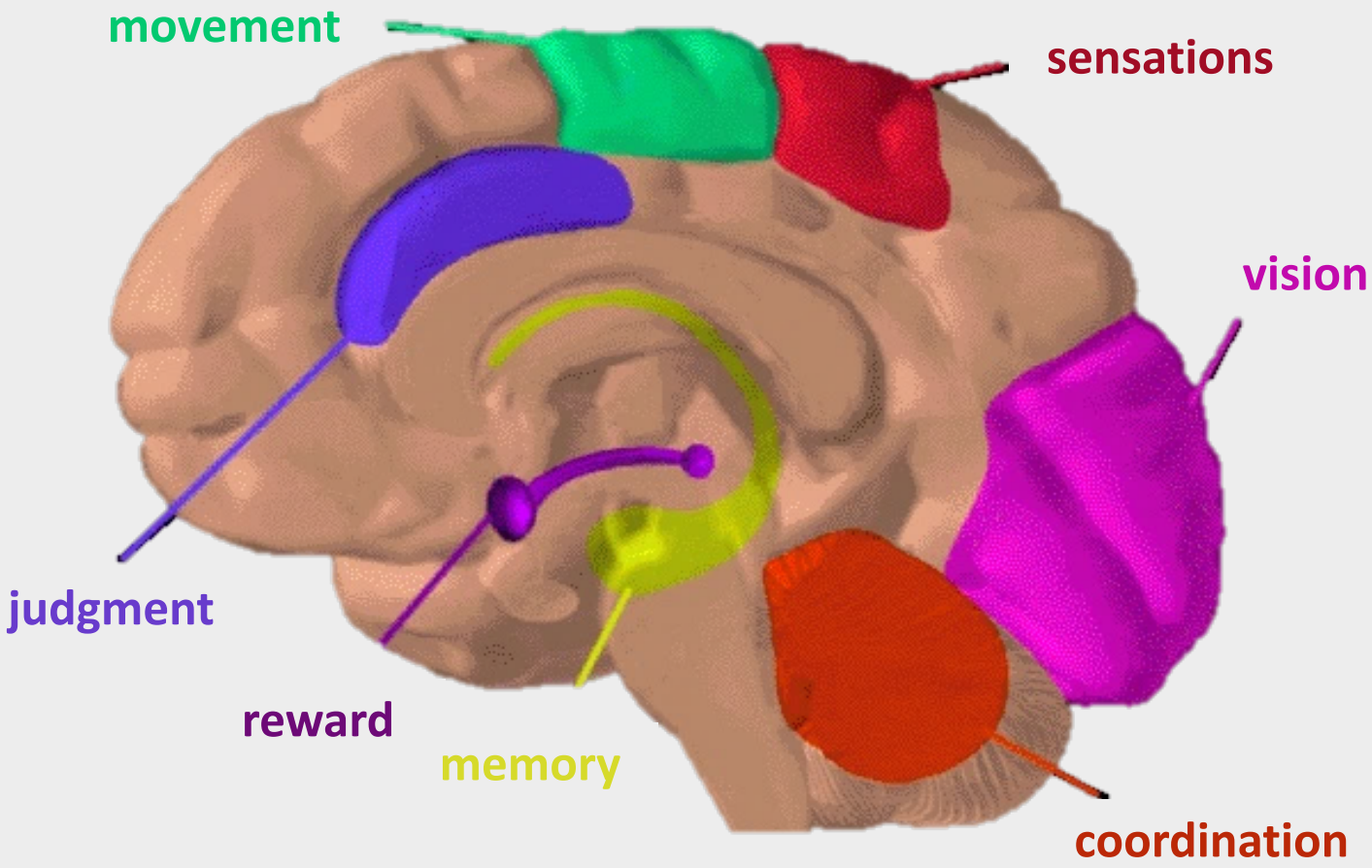






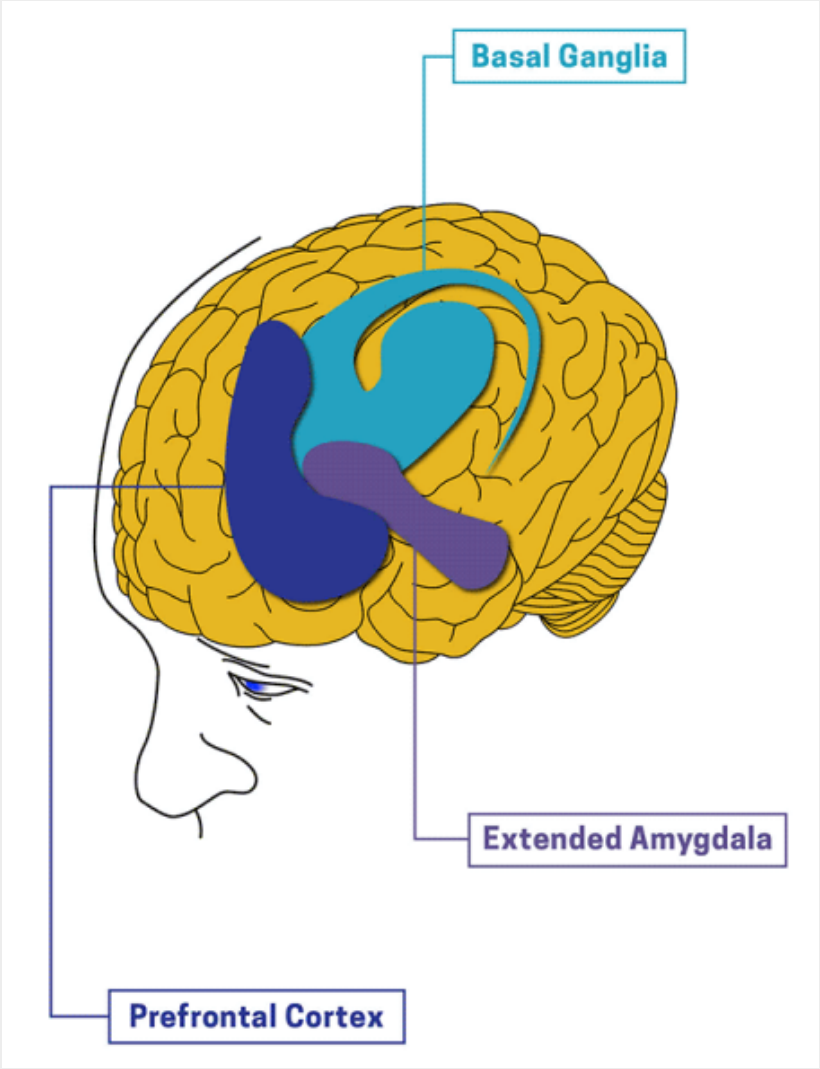
Adapted from: Di Chiara and Imperato, Proceedings of the National Academy of Sciences USA, 1988; courtesy of Nora D Volkow, MD.

Hippocampus and Extended Amygdala



National Institute on Drug Abuse, NIDA.NIH.gov, 2000.

Prefrontal Cortex and Executive Function



National Institute on Drug Abuse, NIDA.NIH.gov, accessed on March 17, 2024.

The New and Improved Model

Three Novel Areas

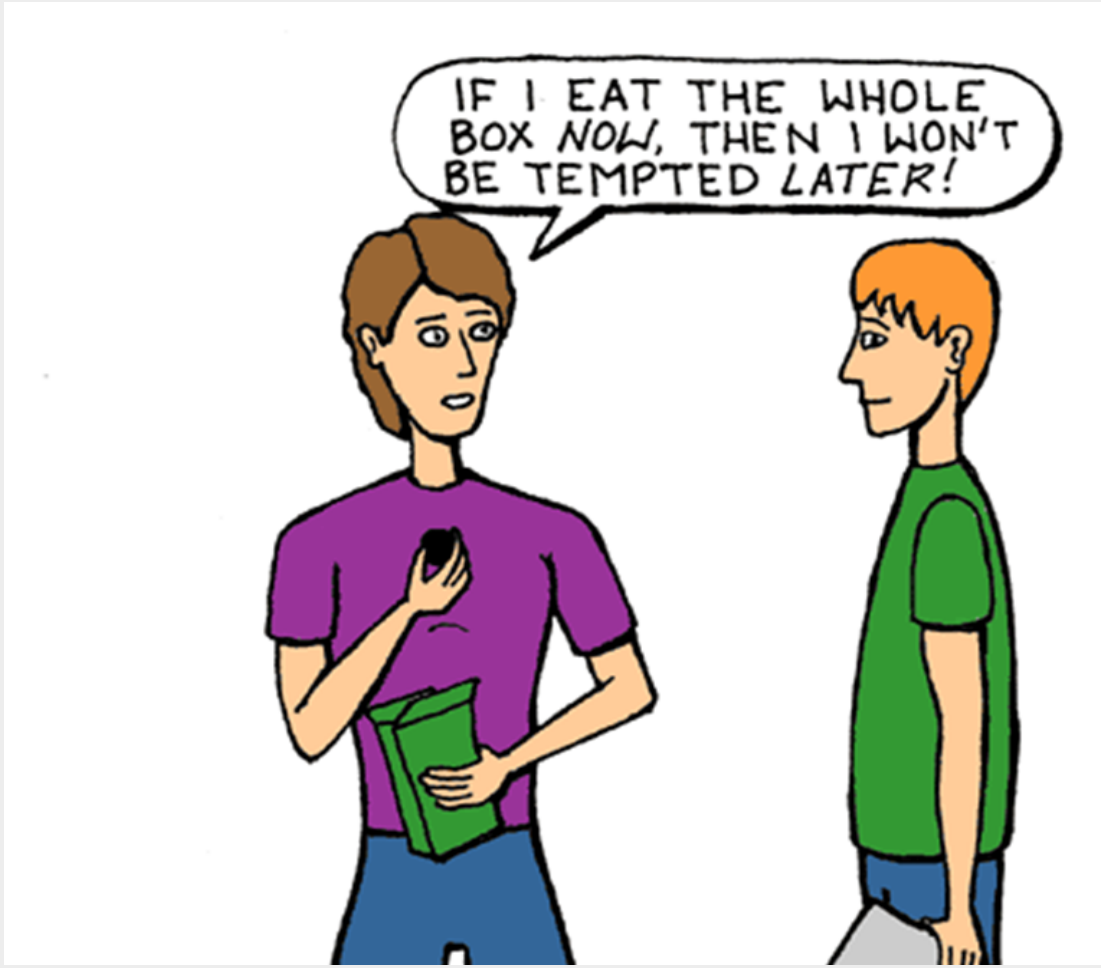
Motivational Circuitry
(Medial OFC)

Antireward Pathways
(Extended Amygdala)

Interoception
(Insula)

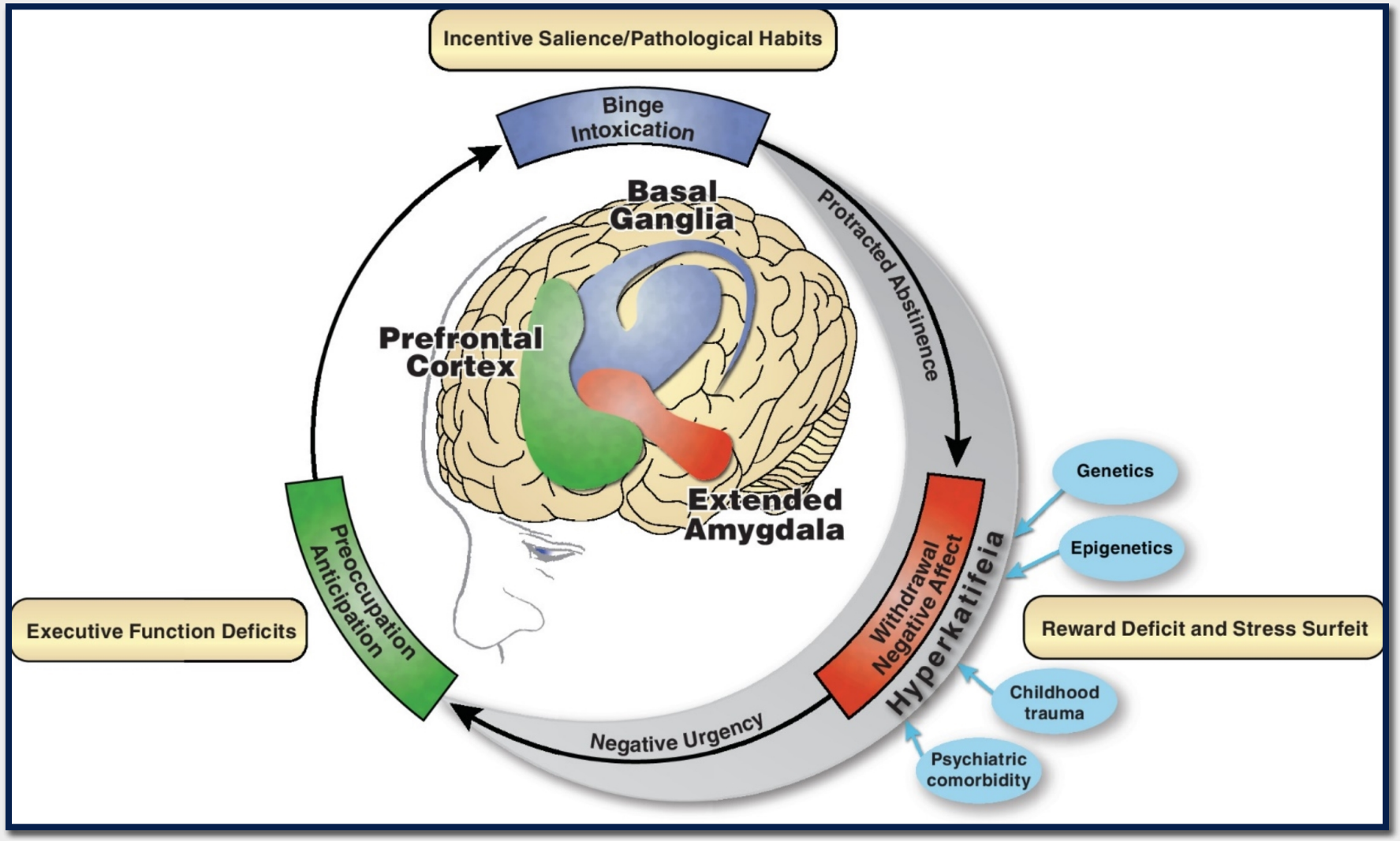
Levounis, Journal of Medical Toxicology, 2016.

Medial Orbitofrontal Cortex (OFC) and Preoccupation/Anticipation



Levounis, Arnaout, and Marienfeld, Motivational Interviewing for Clinical Practice, 2017.

Extended Amygdala and Withdrawal/Negative Affect



Koob, American Journal of Psychiatry, 2020.

Reward Systems

Game #1

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

Adapted from: Tversky and Kahneman, Science, 1981.

Reward Systems

Game #1

A. A sure gain of $250 **84%**

B. 25% chance to gain $1,000, 75%
chance to gain nothing **16%**

Adapted from: Tversky and Kahneman, Science, 1981.

Anti-Reward Systems

Game #2

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

Adapted from: Tversky and Kahneman, Science, 1981.

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%**

Adapted from: Tversky and Kahneman, Science, 1981.

Human Nature

People avoid risks to ensure gains.

People take risks to avoid definite losses.

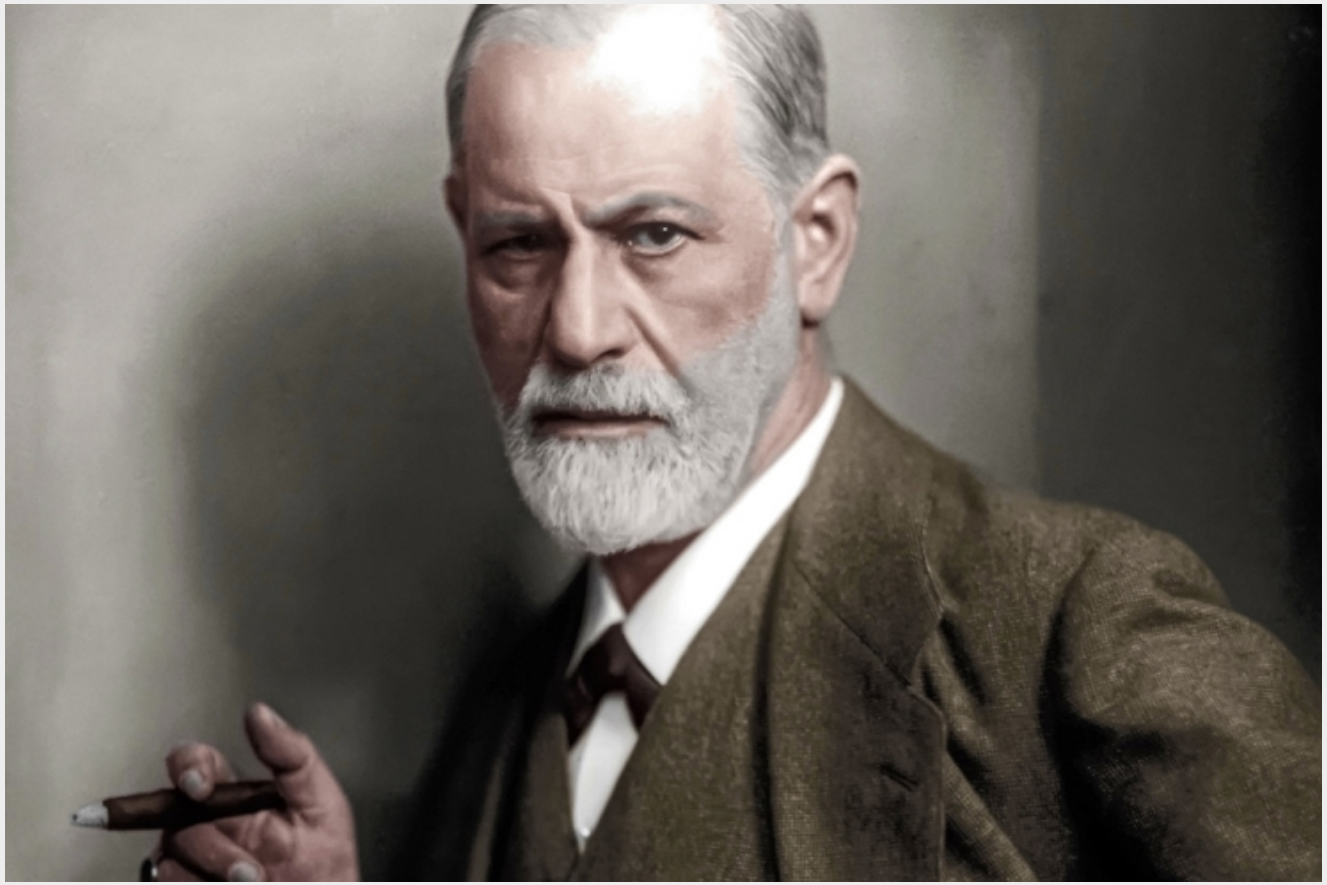
Psychology trumps probability.

The Ultimate Gatekeeper: Insula

Zerbo, Schlechter, Desai, and Levounis, Becoming Mindful, 2017.

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.

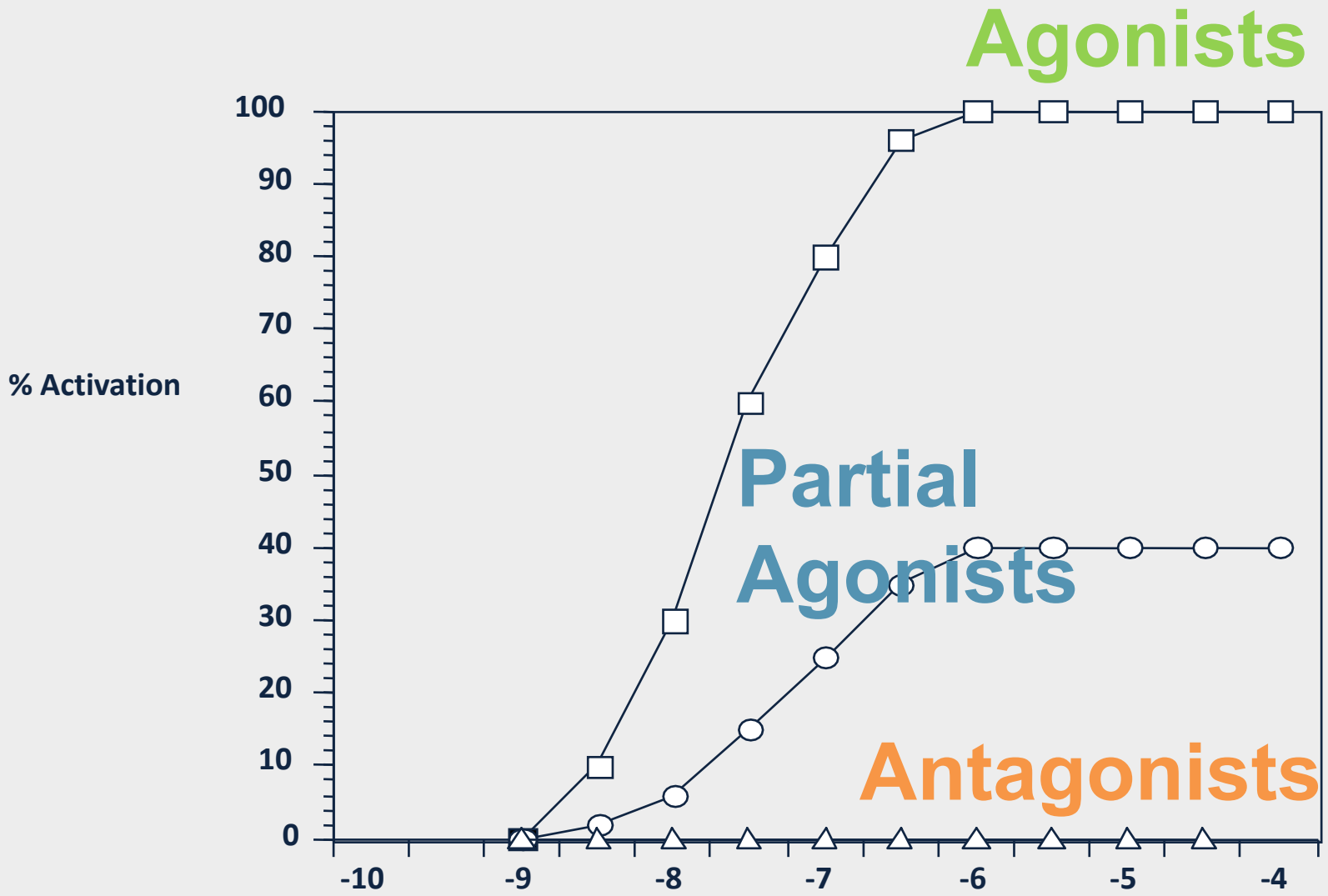
3rd Wave: Current Treatments

Medications

Mutual Help

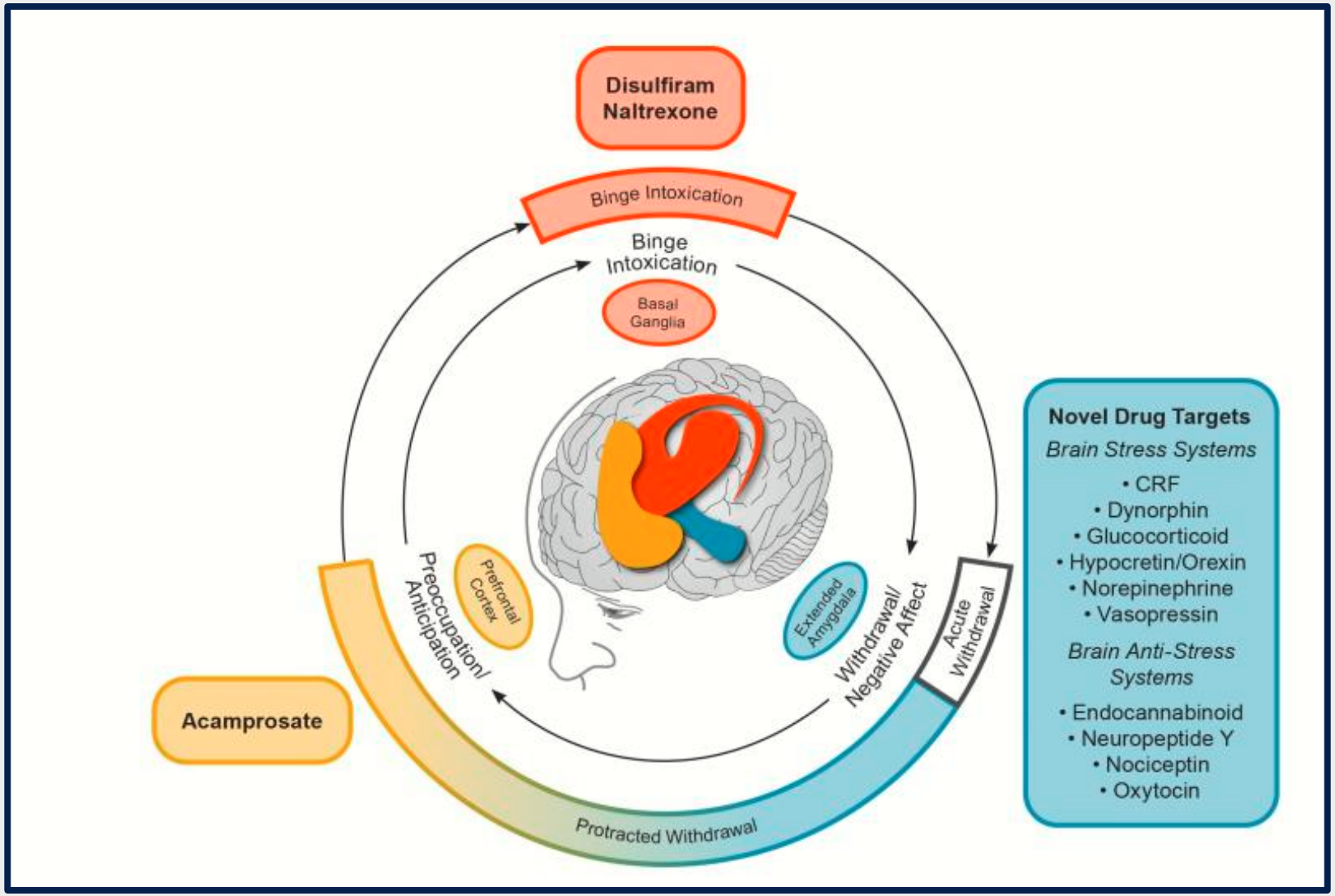
Psychotherapy and Counseling

Medications (opioids and tobacco)



Renner, Levounis, LaRose, Office-Based Buprenorphine Treatment of Opioid Use Disorder, American Psychiatric Association Publishing, 2018.

Medications (alcohol and possibly others)



Mason BJ and Heyser CJ, Alcohol use disorder: the role of medication in recovery, Alcohol Research, 2021.

Mutual Help

MEDICAL STUDENTS	PATIENTS	WHAT MEDICAL STUD. 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

Levounis, Zerbo, and Aggarwal, Pocket Guide to Addiction Assessment and Treatment, 2016.

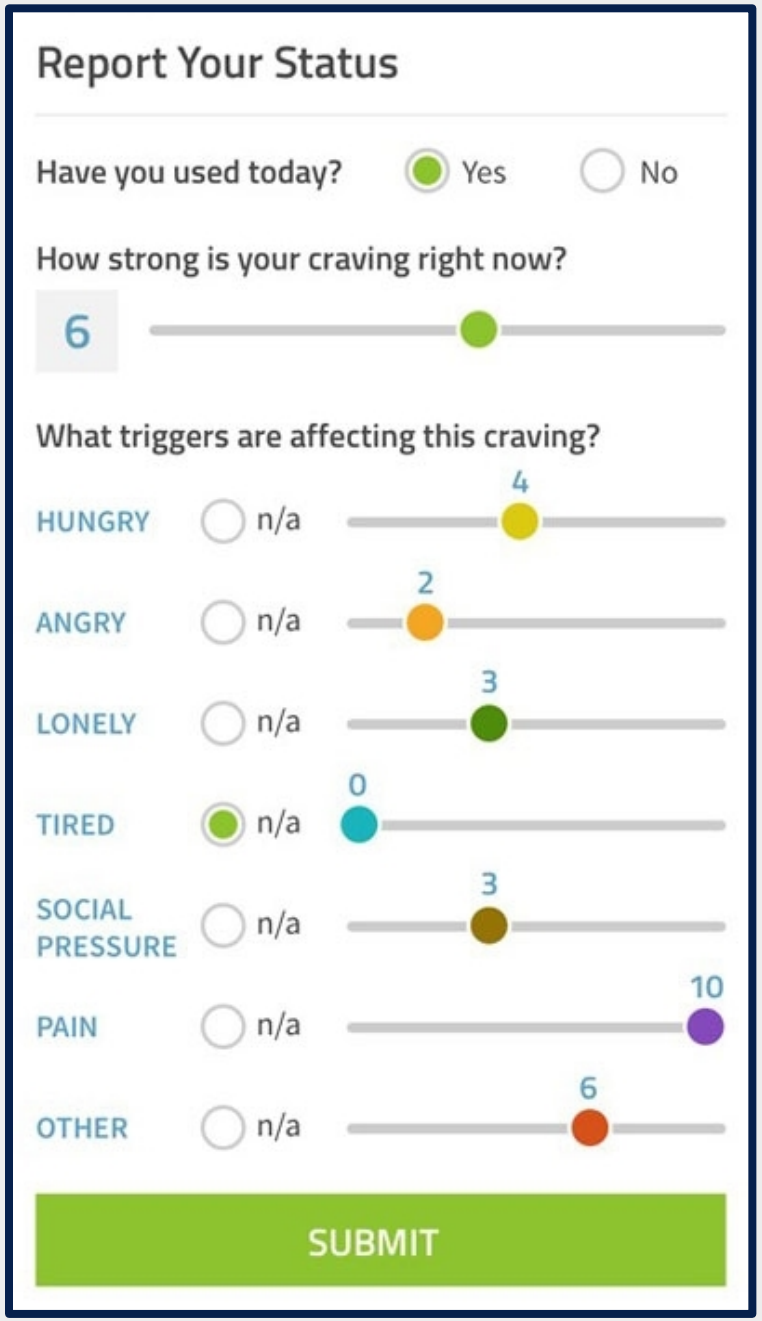
4th Wave: Mindfulness

"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.

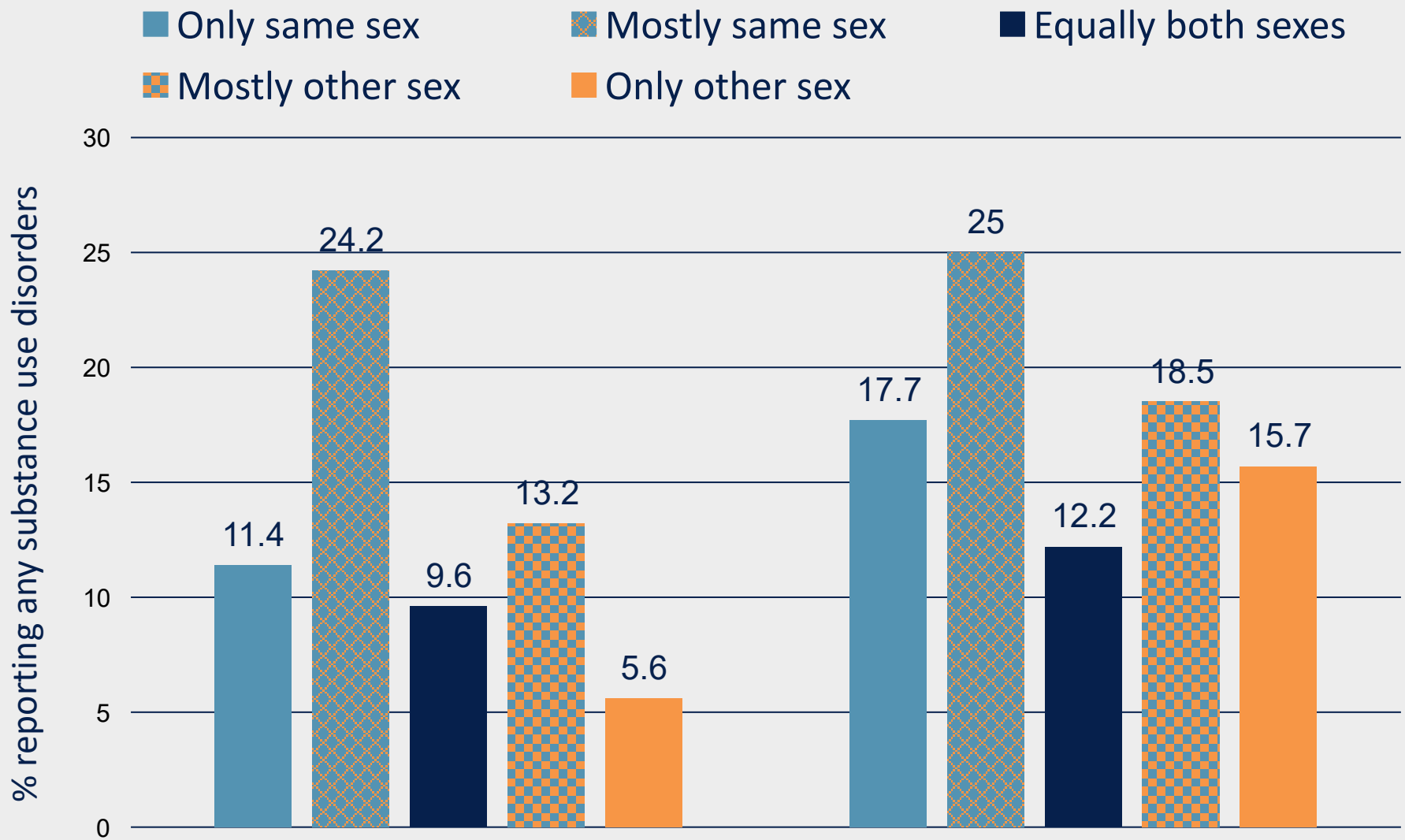
Zerbo, Schlechter, Desai, and Levounis, Becoming Mindful, 2017.



Digital Therapeutics (CBT Apps)

Mood Tools.org

And Back to Psychodynamics . . .



McCabe, Addiction, 2009, Courtesy of Sean E. McCabe, PhD.

Levounis and Yarbrough, LGBTQ Mental Health, 2020.

Neurotransmitters

Substance	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
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Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	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 2024 model of addiction.

Pharmacological Treatments:

agonists, antagonists, and partial agonists.

Psychosocial Treatments:

mutual help, CBT, motivational interviewing, and mindfulness.

Know your neurotransmitters!

Knowledge Check

At her 10th college reunion, Anna bumps into Marie, her old roommate from their junior year abroad. “Anna!” Marie exclaims. “Do you remember sipping wine and snacking on brie and crackers at the café by the Seine? And that waiter? Jacques… Mon Dieu!” Anna has not had any alcohol for several years but suddenly feels an intense craving for alcohol. What part of Anna’s brain got activated by Jacques, the hot waiter, just now?

A. Medial Orbito-Frontal Cortex (OFC)

B. Lateral Orbito-Frontal Cortex (OFC)

C. Hippocampus and Extended Amygdala

D. Insula

Robert has been addicted to Candy Crush Saga since high school. He must also study for the ABPM boards on Friday. It's now 10 pm on Thursday evening, and he hasn't started looking at the lectures. "Hmmm…," he thinks to himself. "If I get some Swedish fish to grab some candies, I can reach Lollipop Meadow by midnight, which will give me such a sense of accomplishment that I will have a clear head tomorrow to tackle any question. Perfect plan, to Lollipop Meadow it is!" What part of Robert's brain was activated by Lollipop Meadow?

A. Medial Orbito-Frontal Cortex (OFC)

B. Lateral Orbito-Frontal Cortex (OFC)

C. Hippocampus and Extended Amygdala

D. Insula

Which part of the brain is responsible for integrating, giving meaning, and helping people understand sensations such as hot, cold, hungry, full, and thirsty—along with cravings for a drug such as tobacco?

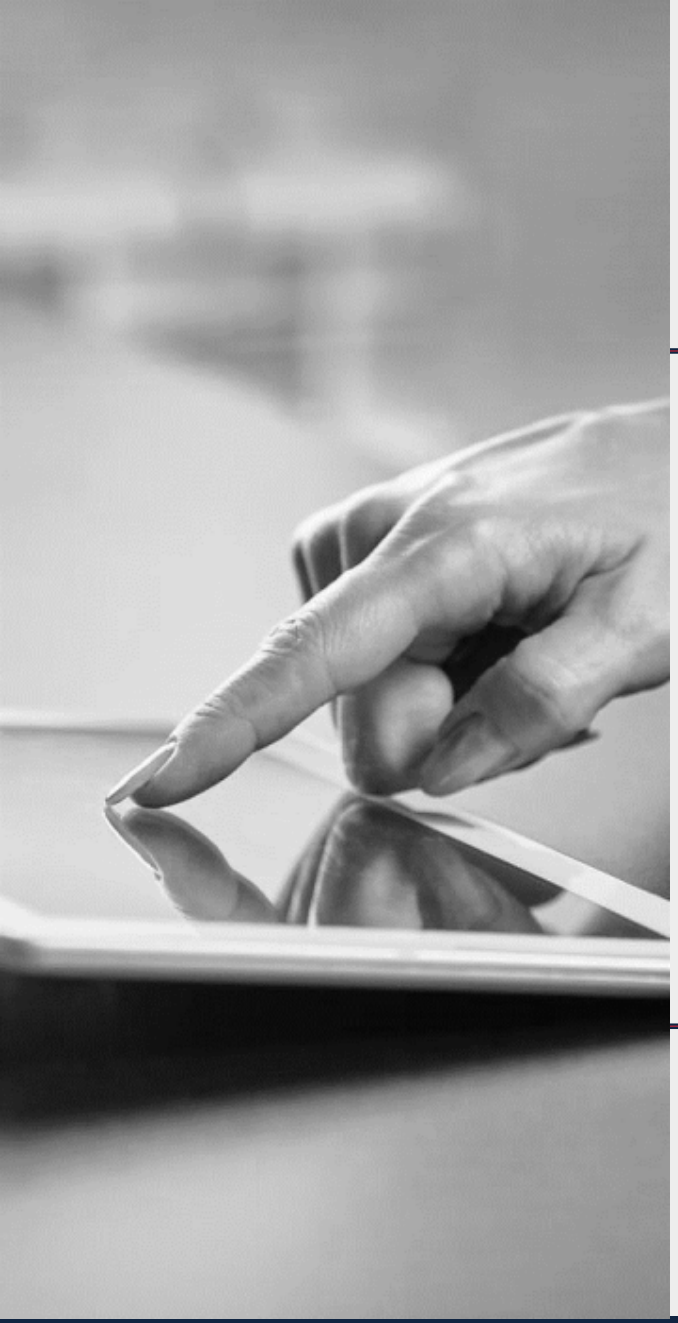
A. Medial Orbito-Frontal Cortex (OFC)

B. Lateral Orbito-Frontal Cortex (OFC)

C. Hippocampus and Extended Amygdala

D. Insula

Thank You



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