

ASAM REVIEW COURSE 2024

**Neurobiology of Addiction:
Key Concepts and Models**

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1

Financial Disclosure

Petros Levounis, MD, MA

- No relevant disclosures

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2

LEARNING OBJECTIVE

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

3

Outline

- 1 Neurotransmitters
- 2 The Fundamental Model
- 3 The New and Improved Model
- 4 Treatments

JULY 2024 REVIEW COURSE 2024

4

Neurotransmitters

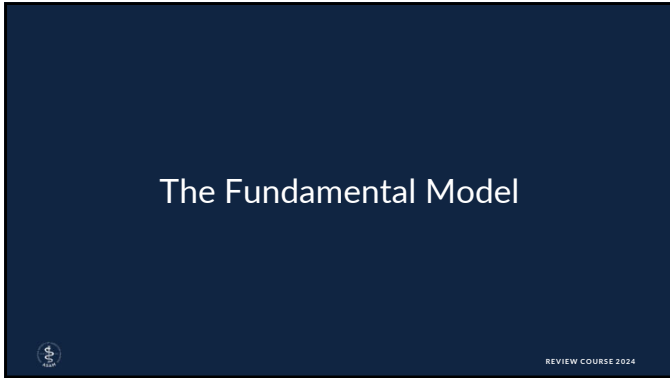
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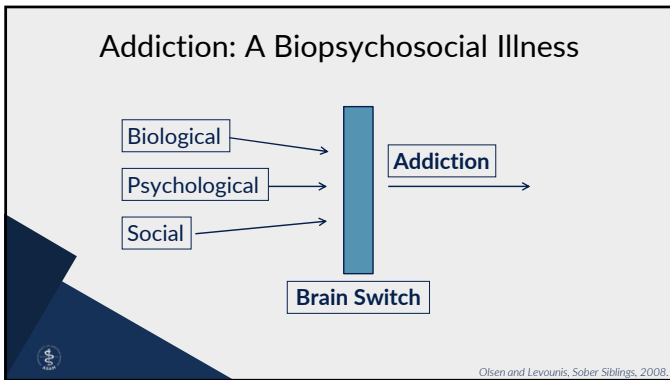
Substance	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
Benzodiazepines & GHB	GABA
Cannabis	Anandamide
Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	Glutamate*

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

6



7



8

A slide with a light gray background and a dark blue triangle in the bottom left corner. The title is "The Root Cause of the Disaster". It contains a text box with the following content:

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

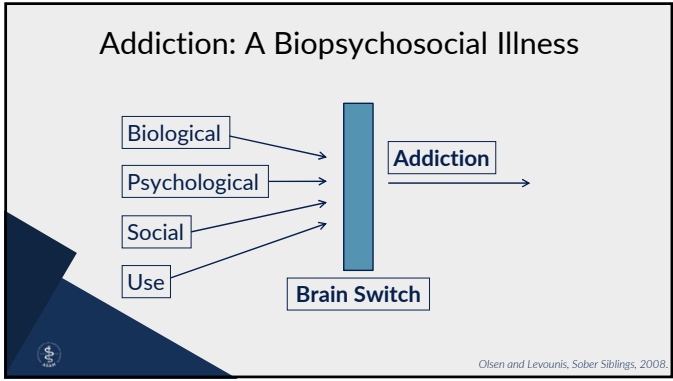
To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,746 hospitalized medical patients* who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably 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, Percodan in one, and buprenorphine 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
HASKINS, JACK, M.D.
Boston Collaborative Drug
Surveillance Program
Waltham, MA 02154 Boston University Medical Center

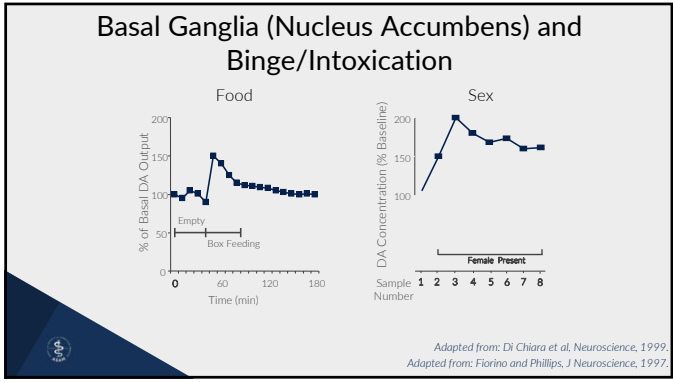
1. Jick H, Mattinen OS, Shapiro S, Lewis GP, Siskind Y, Stone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1976; 18:169-8.

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

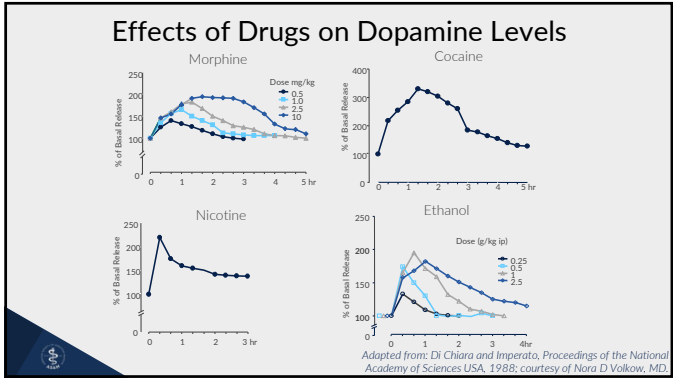
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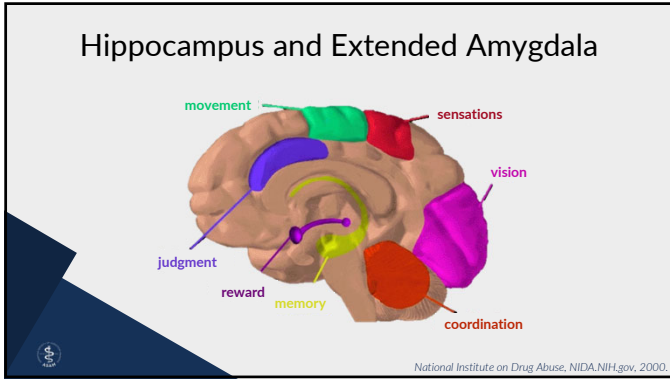
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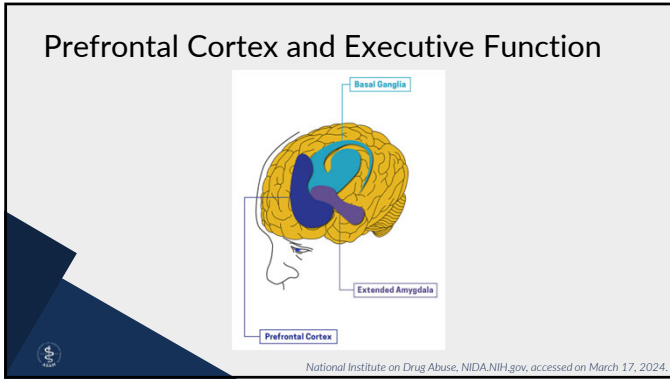
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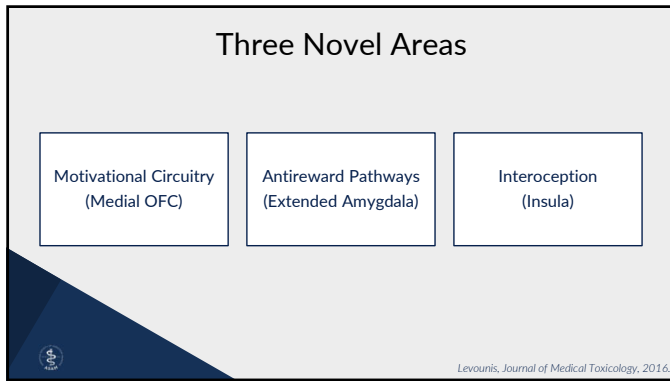
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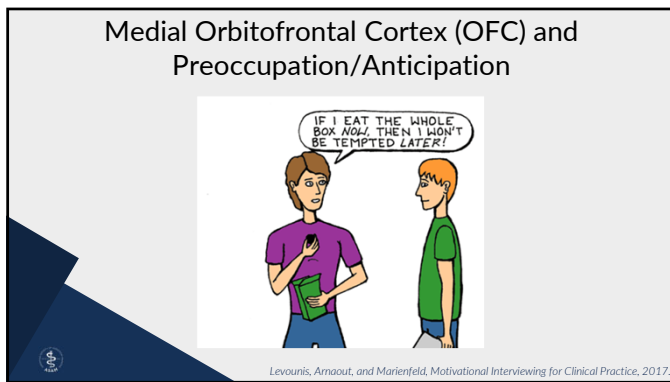
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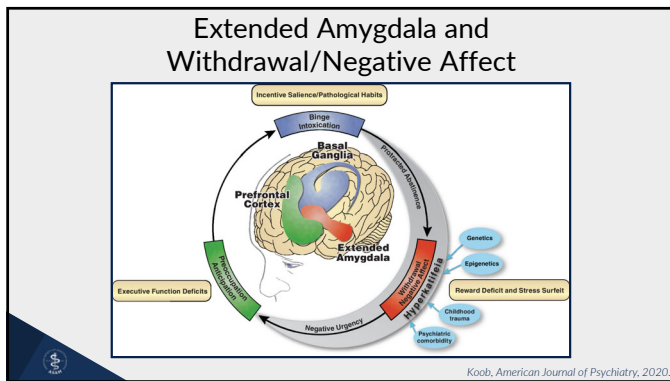
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16



17




18

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.

19

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.

20

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.

21

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.

22

Human Nature

People avoid risks to ensure gains.	People take risks to avoid definite losses.	Psychology trumps probability.
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23

The Ultimate Gatekeeper: Insula

sensual touch

thirst temperature

INTEROCEPTION

PAIN hunger

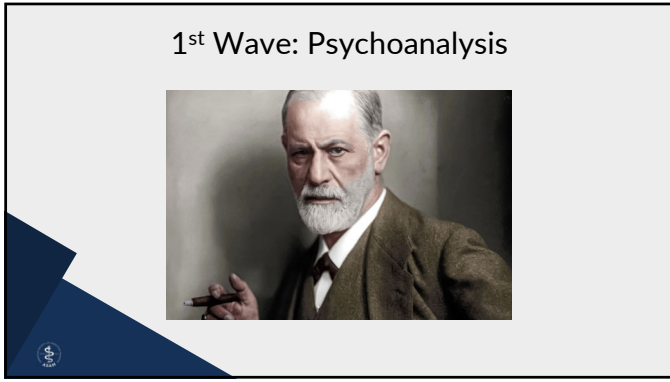
itch breathlessness

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

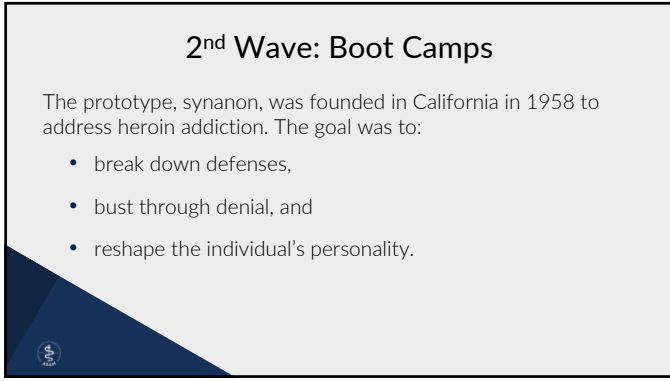
24



25



26



27

3rd Wave: Current Treatments

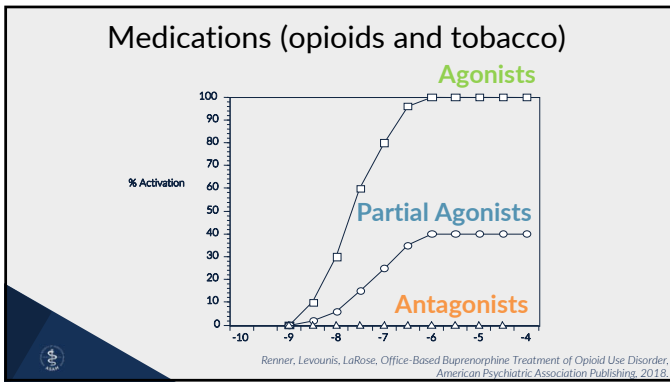
Medications

Mutual Help

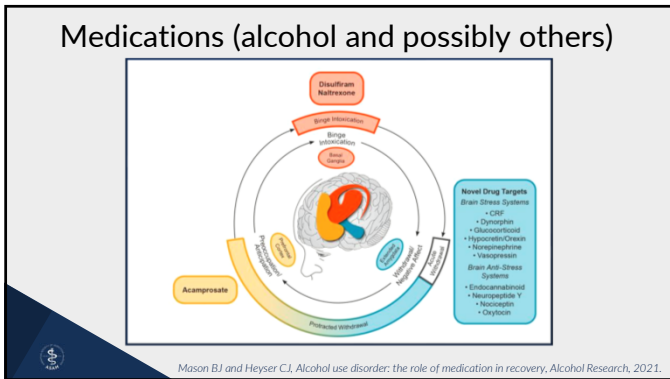
Psychotherapy and Counseling



28



29



30

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.
Fazio L, Galanter M, Dermatis H, Levounis P. Evaluation of medical student attitudes toward Alcoholics Anonymous. *Substance Abuse*, 2003.

31



32

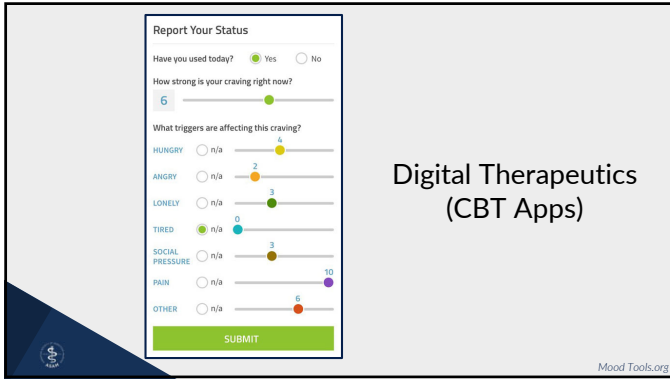
4th Wave: Mindfulness

“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

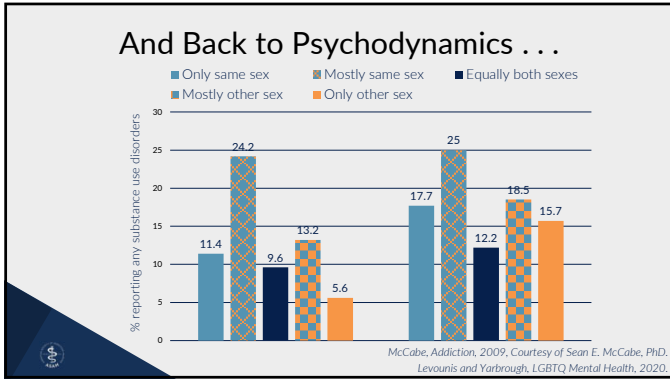
Frankl, *Man's Search for Meaning*, 1959.
Zerbo, Schlechter, Desai, and Levounis, *Becoming Mindful*, 2017.

33



Digital Therapeutics (CBT Apps)

34



And Back to Psychodynamics . . .

35



Neurotransmitters

36

Substance	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
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*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

37

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!	

38


Knowledge Check

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39

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



40

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



41

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?

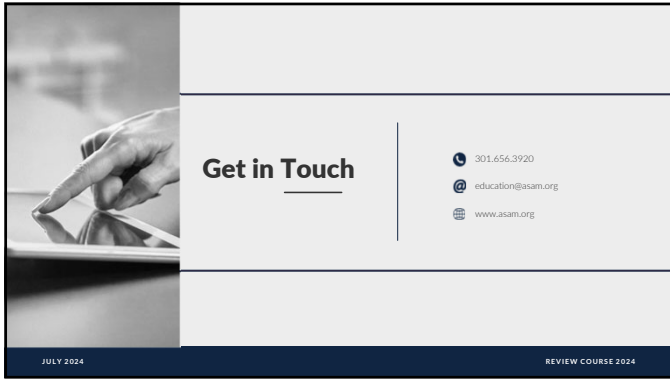
- A. Medial Orbito-Frontal Cortex (OFC)
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42



43



44
