

# THE NEUROBIOLOGY OF ADDICTION

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Petros Levounis, MD, MA  
No Disclosures



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### Outline

1. Neurotransmitters
2. The Basic Model
3. The New and Improved Model
4. Treatments
5. Neurotransmitters
6. Conclusions



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# 1

## Neurotransmitters



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DRUG OF ABUSE	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.



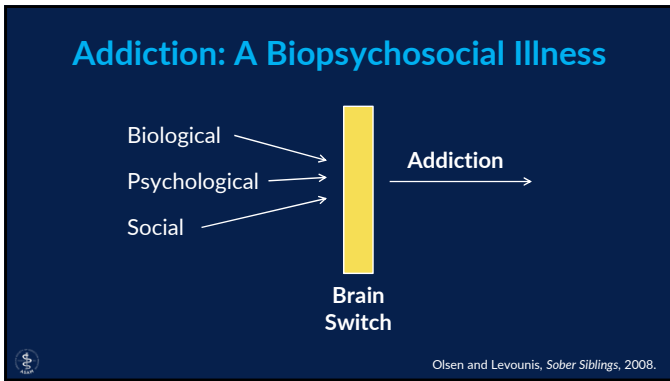
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## The Basic Model



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## The Root Cause of the Disaster

**ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS**

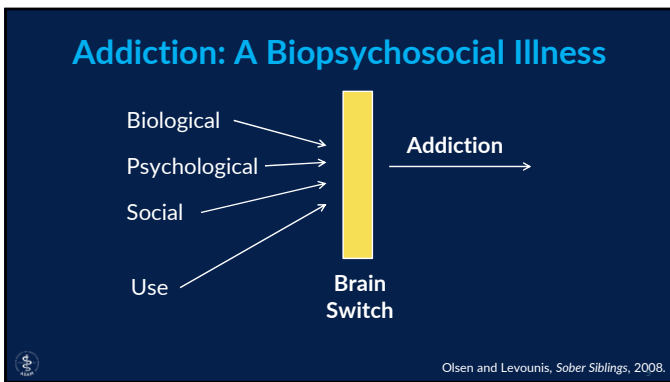
*To the Editor:* Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients<sup>1</sup> who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic prescription, there were only four cases 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 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 JACK, M.D.  
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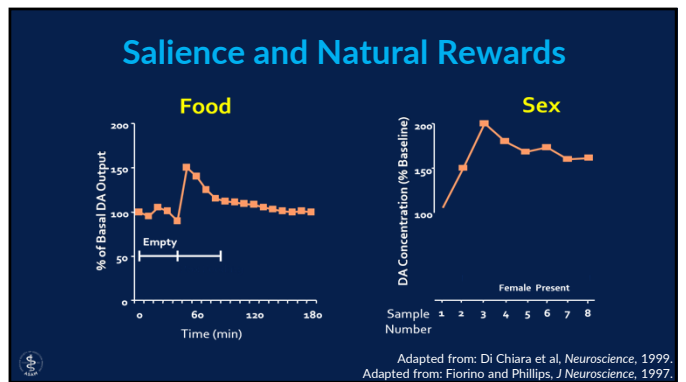
1. Jack H, Miettinen OS, Shapiro S, Lewis GP, Siskind V, Slovic D. Comprehensive drug surveillance. *JAMA*. 1970; 213:1455-60.
2. Miller RR, Jack H. Clinical effects of meperidine in hospitalized medical patients. *J Clin Pharmacol*. 1978; 18:180-8.

Porter and Jack, *N Engl J Med*, January 10, 1980.

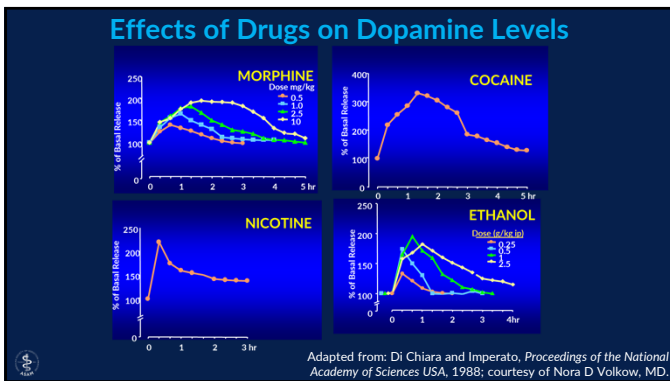
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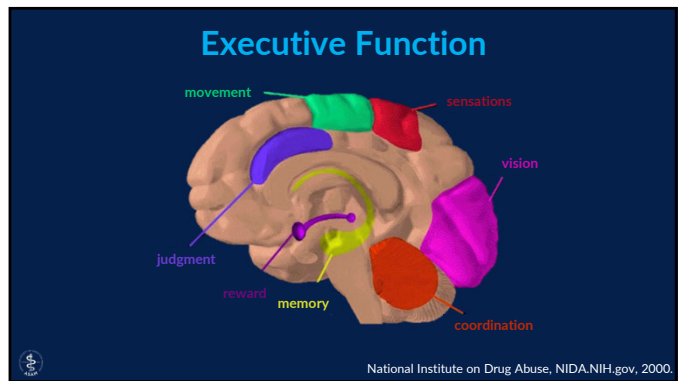
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# 3

## The New and Improved Model



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## Three Novel Areas

1. Motivational Circuitry
2. Antireward Pathways
3. Interoception



Levounis, *Journal of Medical Toxicology*, 2016.

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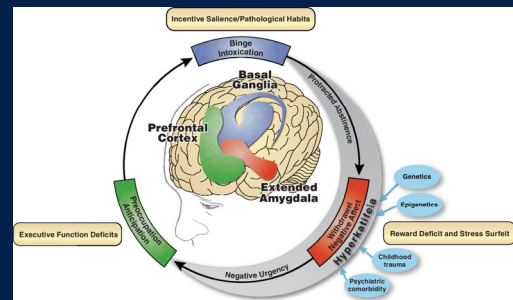
## Preoccupation - Anticipation



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

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## From Reward to Relief



Koob, *American Journal of Psychiatry*, 2020.

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## 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.

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## 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.

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## Antireward 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.

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## Antireward 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.

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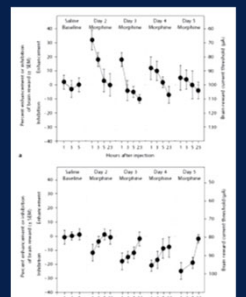
## Human Nature

1. People avoid risks to ensure gains.
2. People take risks to avoid definite losses.
3. Psychology trumps probability.

Ascher and Levounis, The Behavioral Addictions, 2015.

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## Withdrawal - Negative Affect



Gardner, Chronic Pain and Addiction, 2011.

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INTEROCEPTION

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

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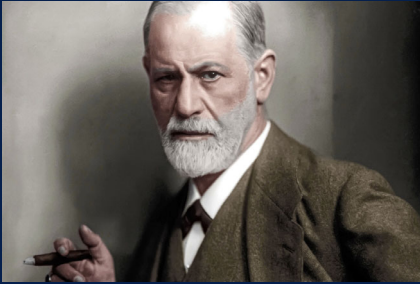
# 4

## Treatments

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

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## 1st Wave: Psychoanalysis



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## 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 addict's personality.

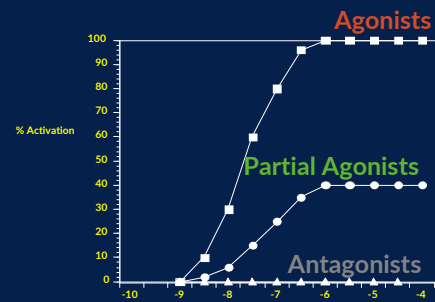
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## 3rd Wave: Current Treatments

1. Medications
2. Mutual Help
3. Psychotherapy and Counseling

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## Medications



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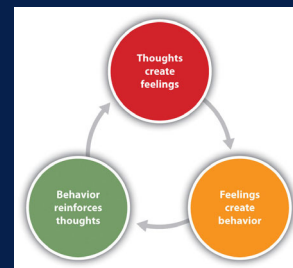
## Mutual Help

Medical Staff	Patients	What Medical Staff Think Patients Think
1. Housing	1. Inner peace	1. Housing
2. Gov't Services	2. God	2. Outpatient Treat.
3. Medical Services	3. Medical Services	3. Medical Services
4. Outpatient Treat.	4. AA	4. Job
5. Job	5. Housing	5. Trusting People
6. Community	6. Spirituality	6. AA
7. Trusting People	7. Outpatient Treat.	7. Inner Peace
8. Inner peace	8. Community	8. Community
9. God	9. Gov't Services	9. Gov't Services
10. Spirituality	10. Trusting People	10. Spirituality
11. AA	11. Job	11. God

Goldfarb, Am J Drug Alcohol Abuse, 1996.

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## Cognitive Behavioral Therapy & Motivational Interviewing



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

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## 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."

Viktor E. Frankl

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

## The CBT Apps

Client 9 6:00 PM  
Discard Entry Save

Title  
Made a mistake

Emotions Distress  
• Angry 8  
• Ashamed  
• Sad

Situation  
I made a mistake at work today and others had to come help me fix it.

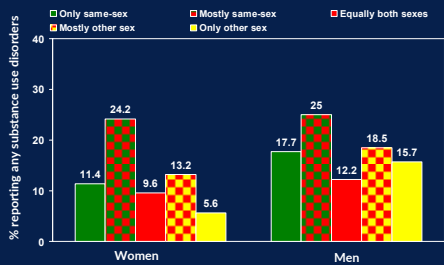
Negative Thoughts  
I was angry at myself for making such a simple mistake. I felt helpless that I could not fix the problem myself and useless when I had to ask others for help.

MoodTools.org

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## And Back to Psychodynamics...



McCabe, *Addiction*, 2009, Courtesy of Sean E. McCabe, PhD.  
Levounis and Yarbrough, *Pocket Guide to LGBTQ Mental Health*, 2020.

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# 5

## Neurotransmitters

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DRUG OF ABUSE	ENDOGENOUS NEUROTRANSMITTER
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# 6

## Conclusions

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1. Addiction is the war between the hijacked salience and reward pathways of the basal ganglia and the executive function of the prefrontal cortex.
2. Motivational circuitry, the anti-reward pathways, and interoception complete the 2021 model of addiction.
3. Pharmacological Treatments: agonists, antagonists, and partial agonists.
4. Psychosocial Treatments: mutual help, CBT, Motivational Interviewing, and mindfulness.
5. Know your neurotransmitters!

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Thank you

NJMS.Rutgers.edu/Psychiatry

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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 munching on brie and crackers at the café by the Seine? And that waiter? Jacques... Mon Dieu." Anna has been sober for several years but all of the sudden feels an intense craving for alcohol. What part of Anna's brain, most likely, 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

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Robert has been addicted to Candy Crush Saga since high school. He must also study for a neurobiology exam 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, most likely, got activated by Lollipop Meadow, just now?

- A. Medial Orbito-Frontal Cortex (OFC)
- B. Lateral Orbito-Frontal Cortex (OFC)
- C. Hippocampus and Extended Amygdala
- D. Insula

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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

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