

# The New Neurobiology of Addiction

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# Outline

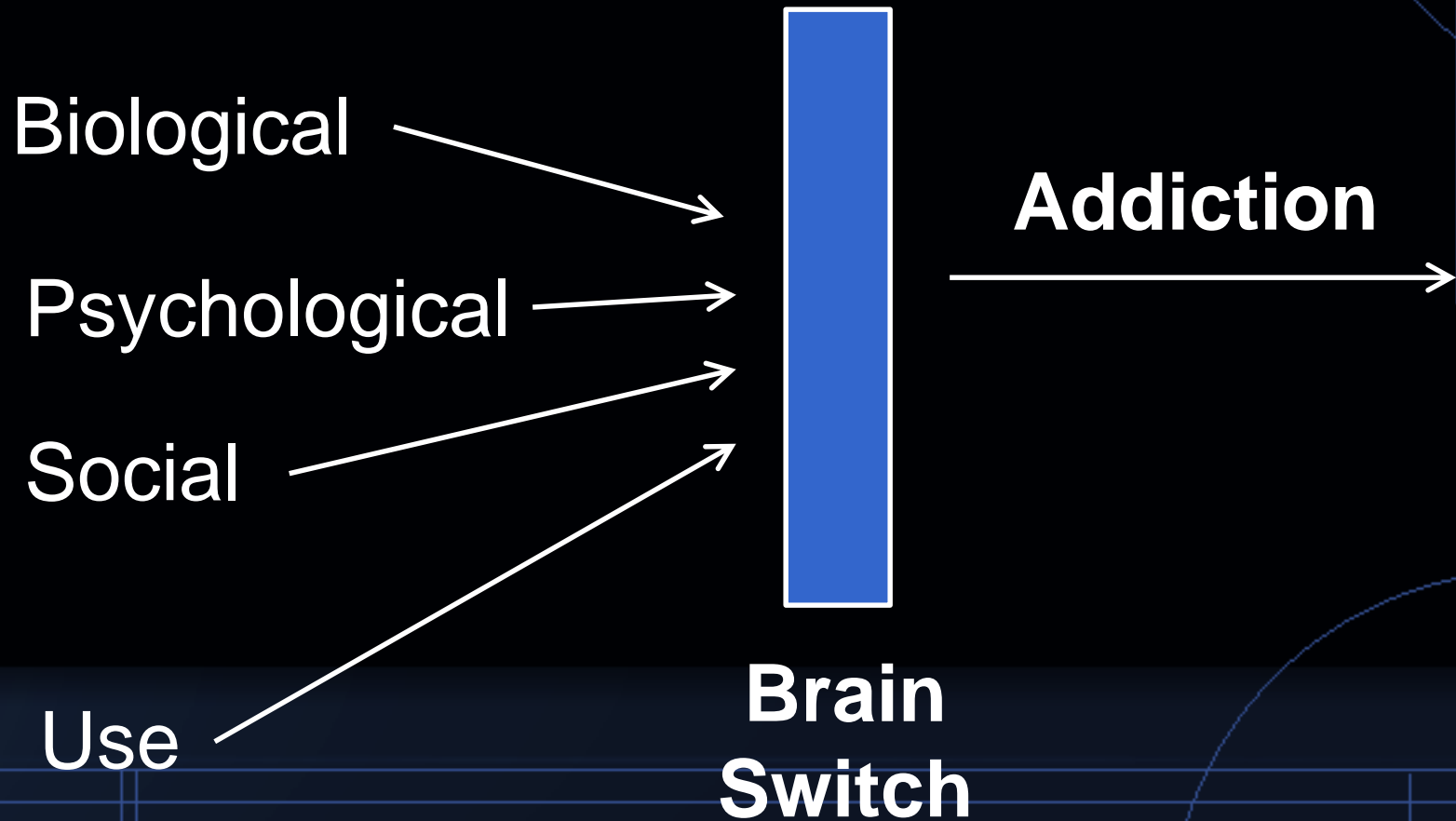
1. The Basic Model
2. Neurobiology of Addiction
3. New Neurobiological Concepts
4. Addiction Treatments
5. New Directions

<b>Drugs of Abuse</b>	<b>Endogenous Neurotransmitter</b>
Alcohol	GABA and Glutamate
Amphetamines and Cocaine	Dopamine
Benzos and GHB	GABA
Cannabis	Anandamide
Hallucinogens and MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
PCP and Ketamine	Glutamate

# 1

# The Basic Model

# A Biopsychosocial Illness





**POLL**

# A Biopsychosocial Illness

- Biological
  - 40-60% of addiction is felt to be “heritable”
  - Both parents with alcoholism=7x increased risk
  - 30% of people with psychiatric disorders also have SUD

# A Biopsychosocial Illness

- Social / Environmental risk factors:
  - Low socioeconomic status
  - Poor parental support
  - Physical and psychological abuse
  - Drug availability (access)



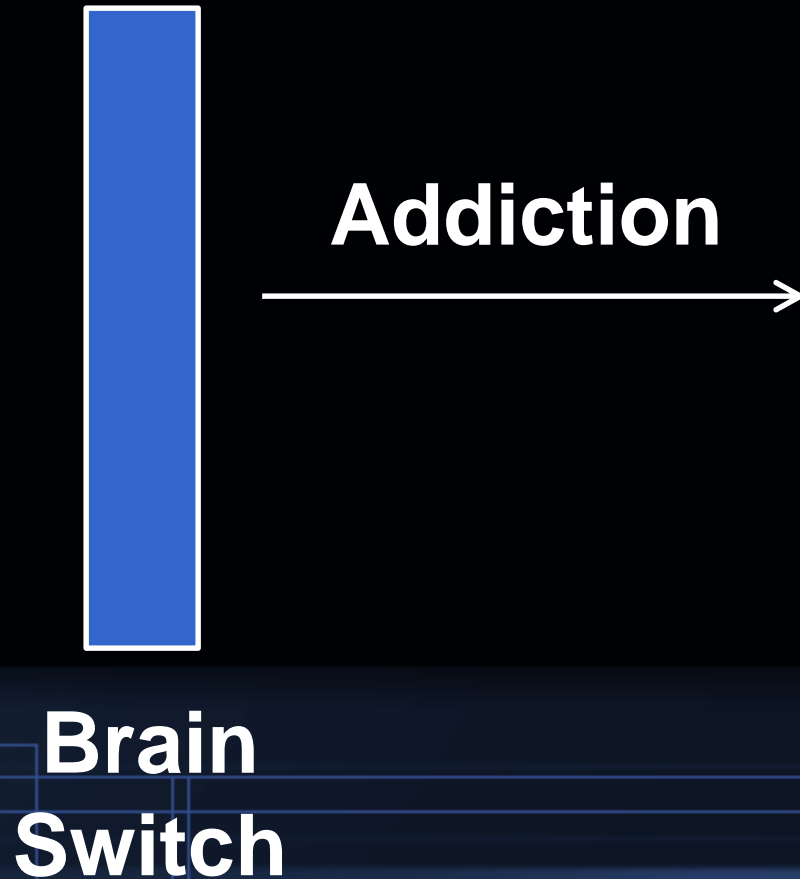
# A Biopsychosocial Illness

- Psychological
  - Self-medicate to numb or “treat” one’s own emotional or physical illness

# A Biopsychosocial Illness

- Use begets use

# A Biopsychosocial Illness



- Addiction is its own disease independent of the other factors
- BUT modifying the other factors (biopsychosocial) can help with relapse prevention
- Relapse “primer” include
  - Stress
  - Trigger (cues)
  - Exposure

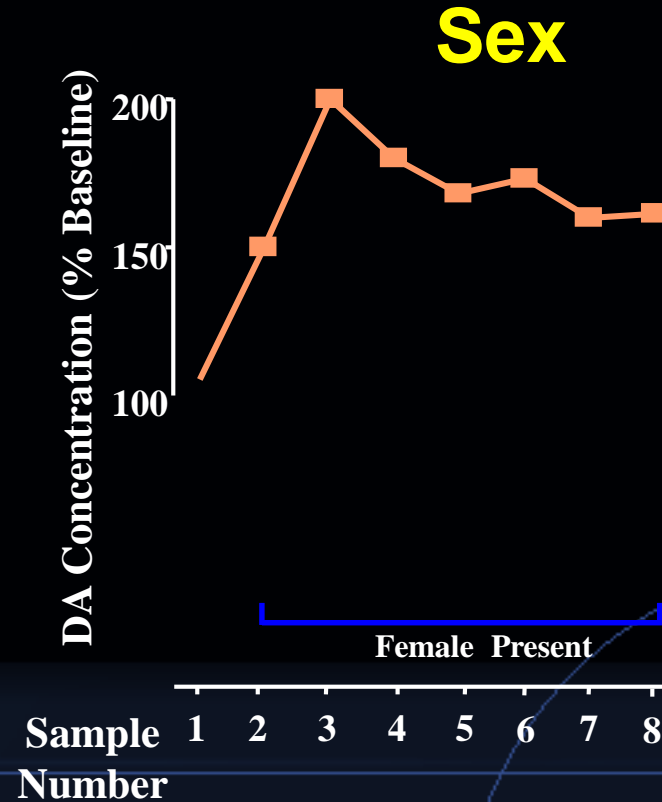
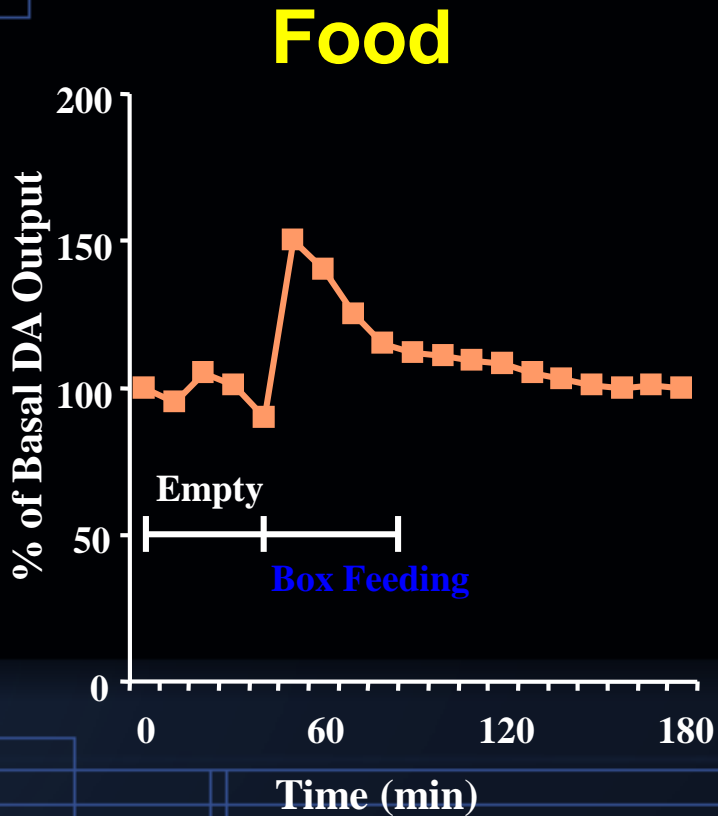
# 2

# Neurobiology of Addiction



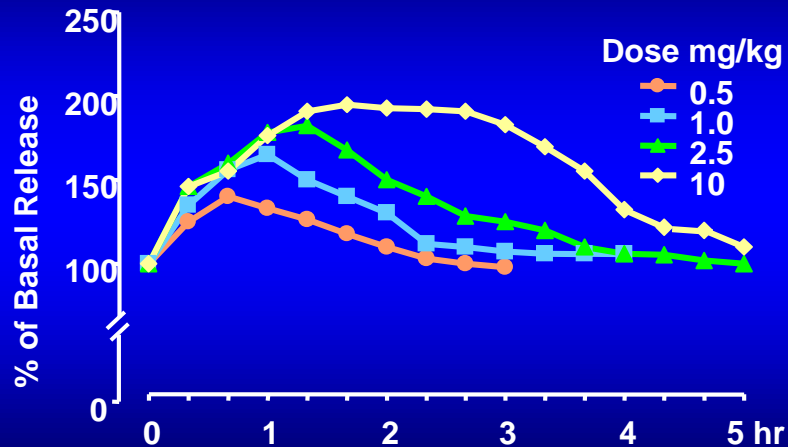
**POLL**

# Natural Rewards

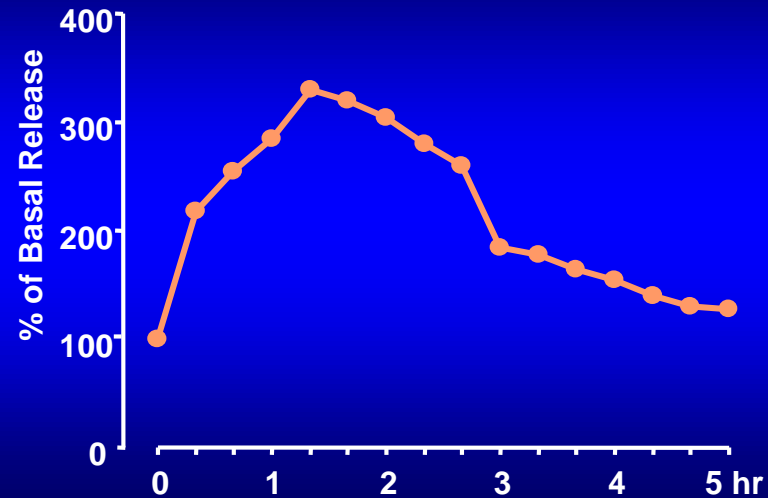


# Effects of Drugs on Dopamine Levels

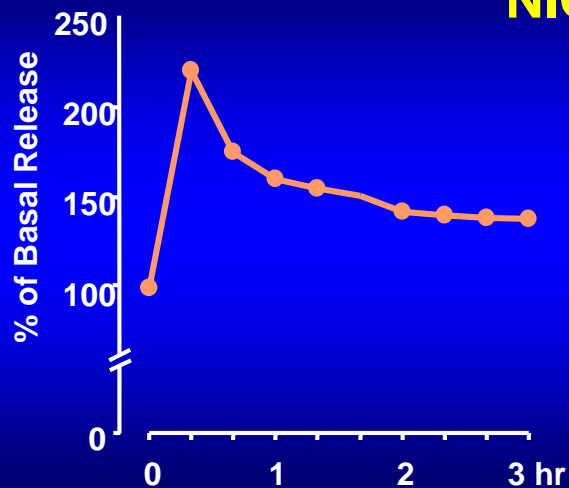
## MORPHINE



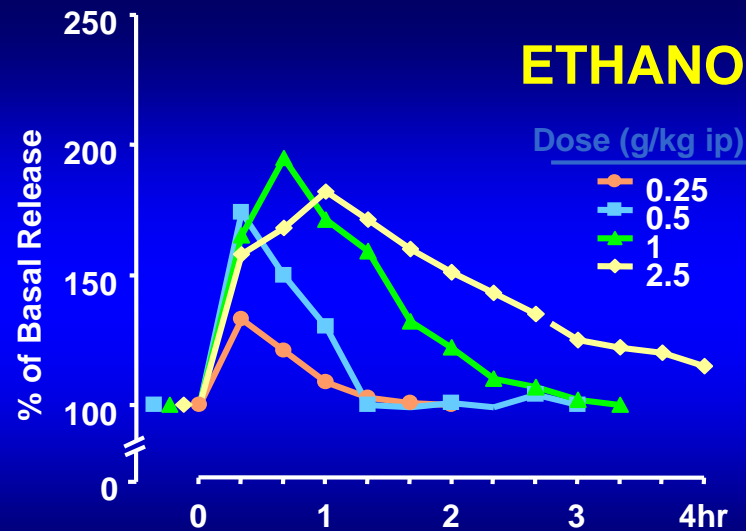
## COCAINE



## NICOTINE



## ETHANOL



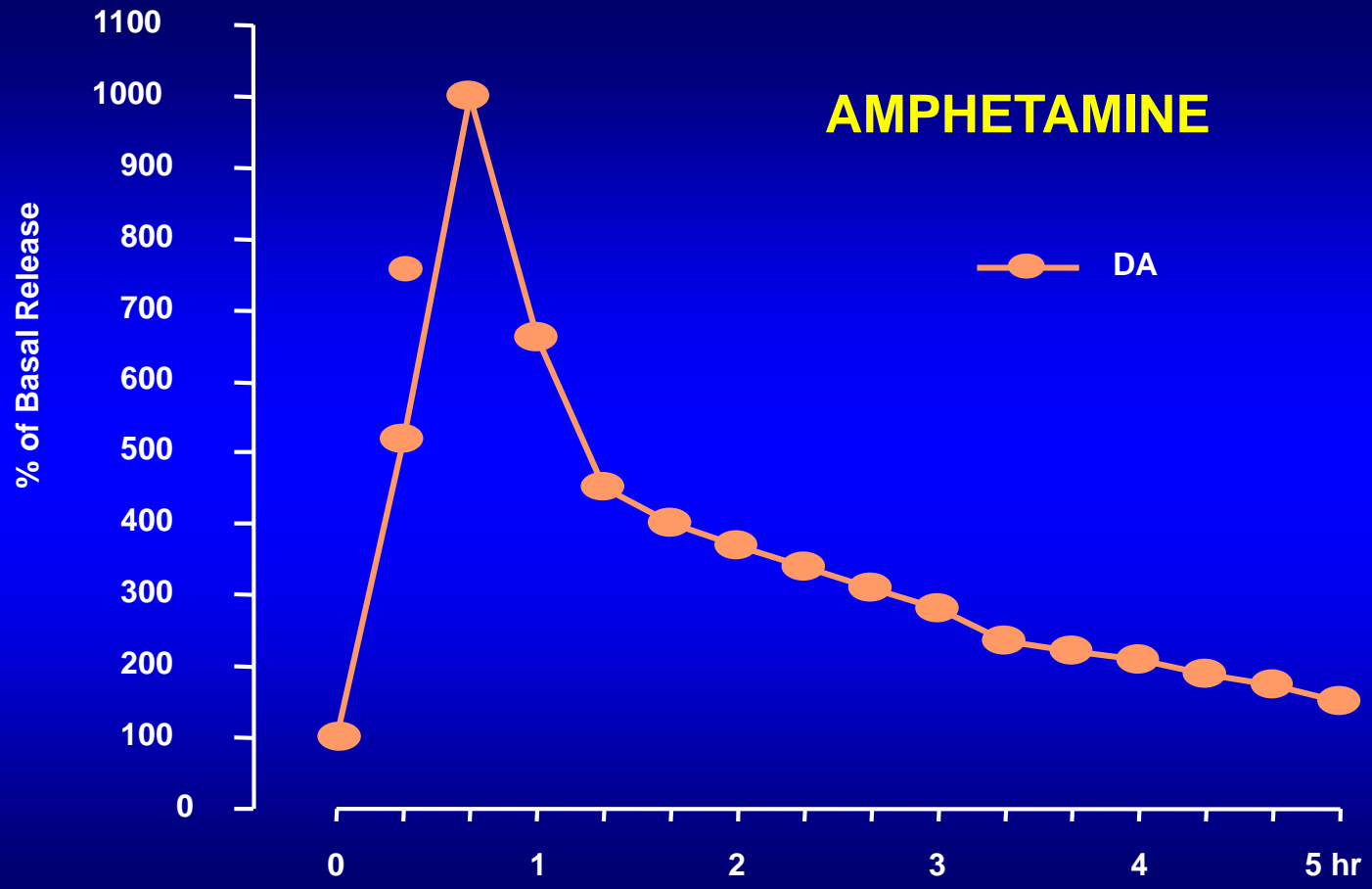
# Effects of Drugs on Dopamine Levels

Most 200-300% above baseline

“High jacking of pleasure /  
reward in nucleus accumbens”



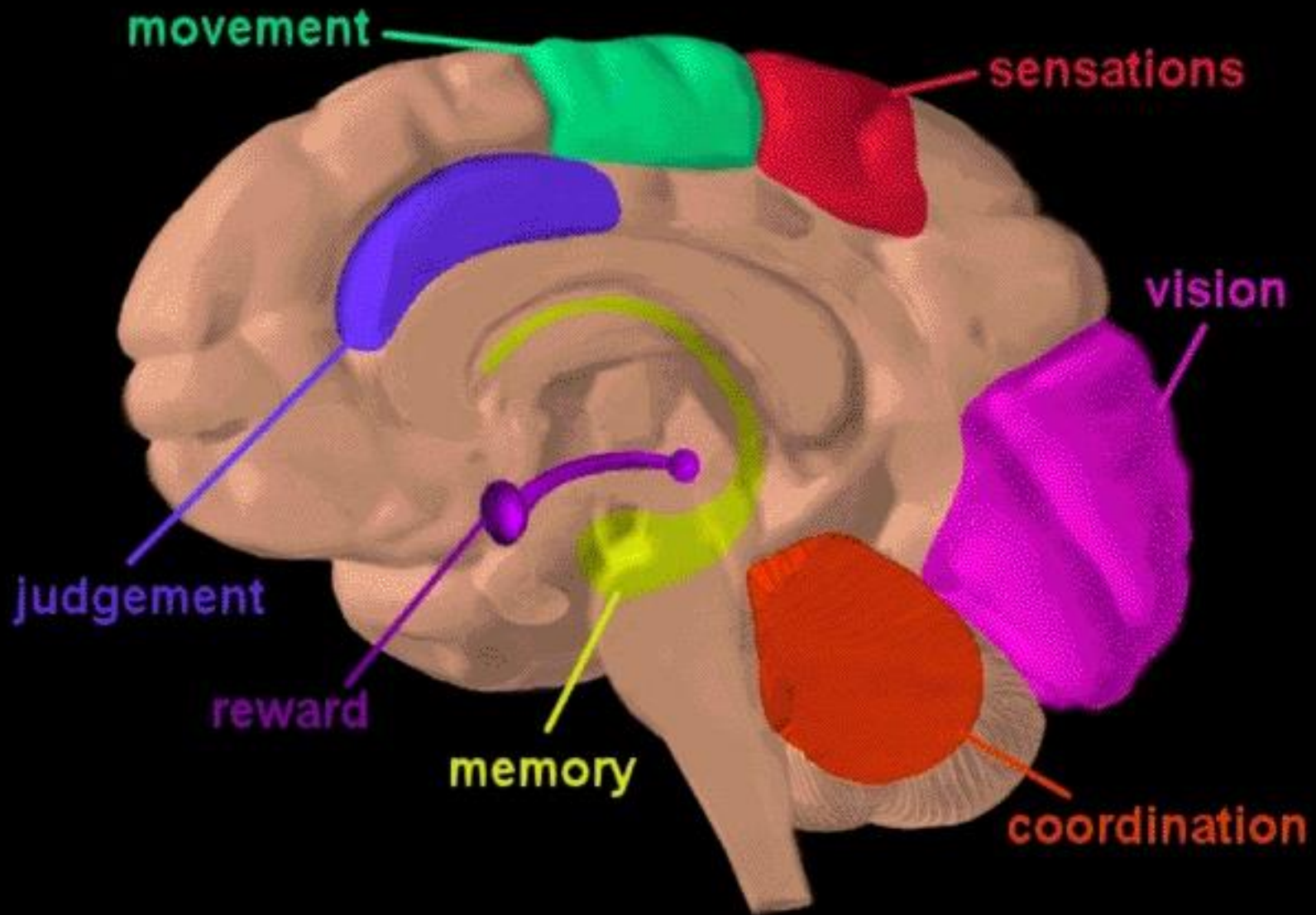
# Effects of Amphetamines on Dopamine Levels



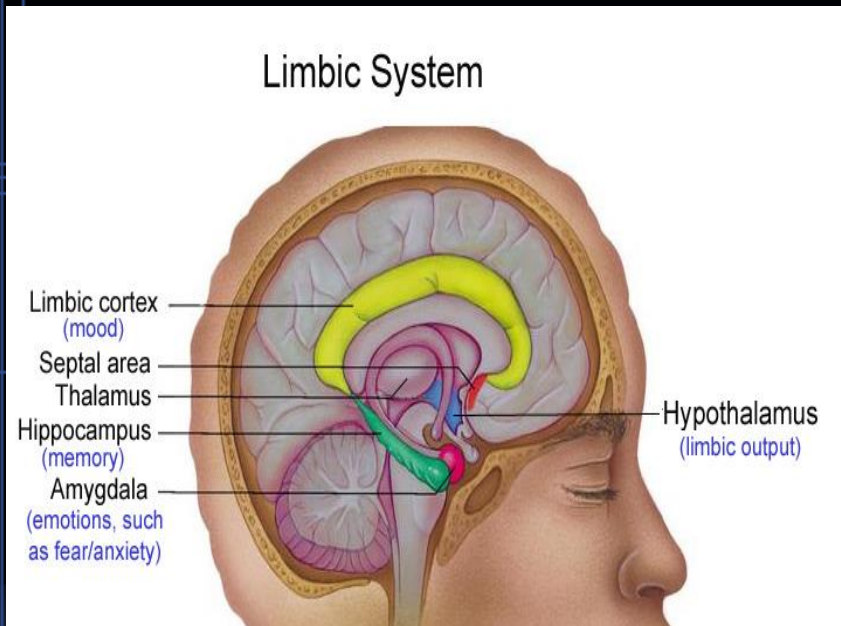
**Amphetamines >>> 1000%**

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

# Pleasure-Reward Pathways



# Limbic System



- Nucleus accumbens- reward center
  - Hippocampus- memory center
  - Amygdala- emotional center
- \* Primitive brain
- \* Frontal lobe not well connected until after age 22

“Sex is absurd from a strictly frontal lobe standpoint.”

- Dr. Petros Levounis

# 3

## New Neurobiological Concepts

# Three Novel Areas

- ✓ Motivational Circuitry
- ✓ Anti-reward Pathways
- ✓ Interoception

# Motivation: The Stinking Thinking Part

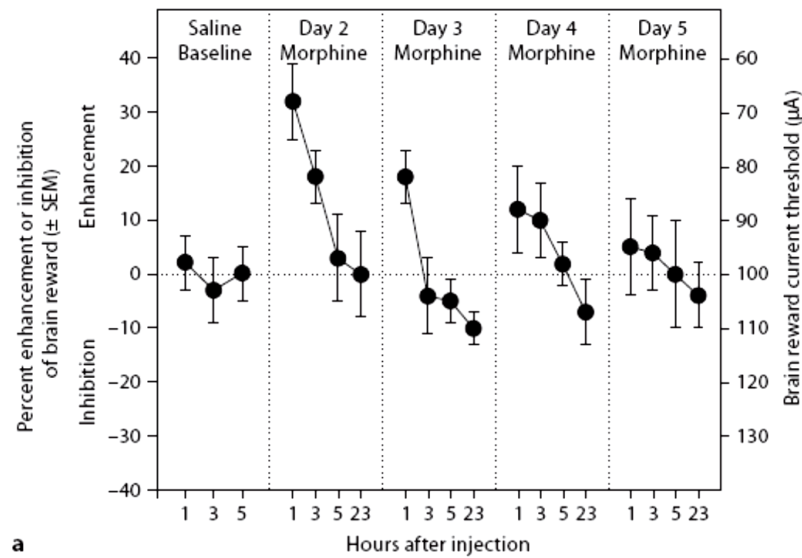


# Reward System

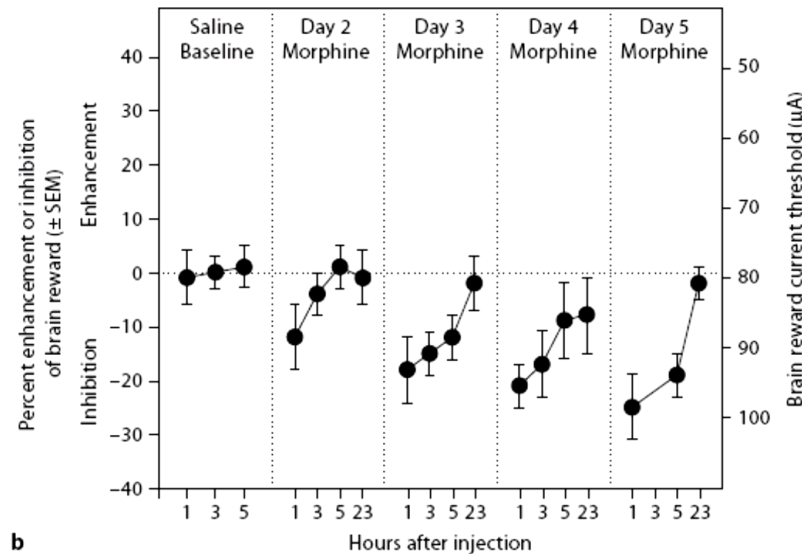
- Activation of dopaminergic pathway
- Emotion over logic
- Over time there is less dopamine uptake in the nucleus accumbens and the “reward” is less “rewarding”
- Poor inhibitory control and poor executive functioning mediated by prefrontal cortex (PFC)
- Actions become stereotyped: drug seeking and drug taking become repetitive and ritualistic



# Reward and Anti-reward Systems



a



b



**POLL**

# Anti-Reward (Habenula)

- Activated when expected results do not materialize
- Activity increased with repetitive drug exposure causing negative mood with drug withdrawal
- Using to not get sick rather than using to get high

*sensual touch*

thirst

temperature

INTEROCEPTION

PAIN

*hunger*

itch

breathlessness

# Interoception

- Insula takes sensations and makes sense of them
- Insula gives the person the “permission” to feel cravings

\* Insula stroke will take away cigarette cravings. Cravings still actually “there” but no longer have meaning

# Human Nature

1. People avoid risks to ensure gains  
(motivation reward)
2. People take risks to avoid definite loss  
(anti-reward)
3. Psychology trumps probability  
(interoception)

# 4

# Addiction Treatments

# The Current Approach

- ✓ Medications
- ✓ Motivational Interviewing
- ✓ Mutual Help (12-step)



# Two Main Strategies

- Agonists
  - Nicotine replacement therapies
  - Methadone for opioids
- Antagonists
  - Naltrexone for opioids



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# The New Strategy

- Partial Agonists
  - Varenicline for tobacco
  - Buprenorphine for opioids

# Motivational Interviewing

- Encourages internally driven change through a collaborative effect that elicits the patient's own recovery-oriented thoughts and feelings
- Promotes and supports the patient's sense of autonomy
- “Rolls with the resistance” toward treatment engagement

# Mutual Help (12-step)

- Provide patients with the chance to learn information about addiction, recovery and relapse
- Reduces the stigma associated with addiction and the humiliation of having lost control over own behavior
- Patients gain support, encouragement, feedback and confrontation from peers who understand
  - How SUD patients think, feel, and act including manipulation, schemes and diversions used to rationalize

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# New Directions

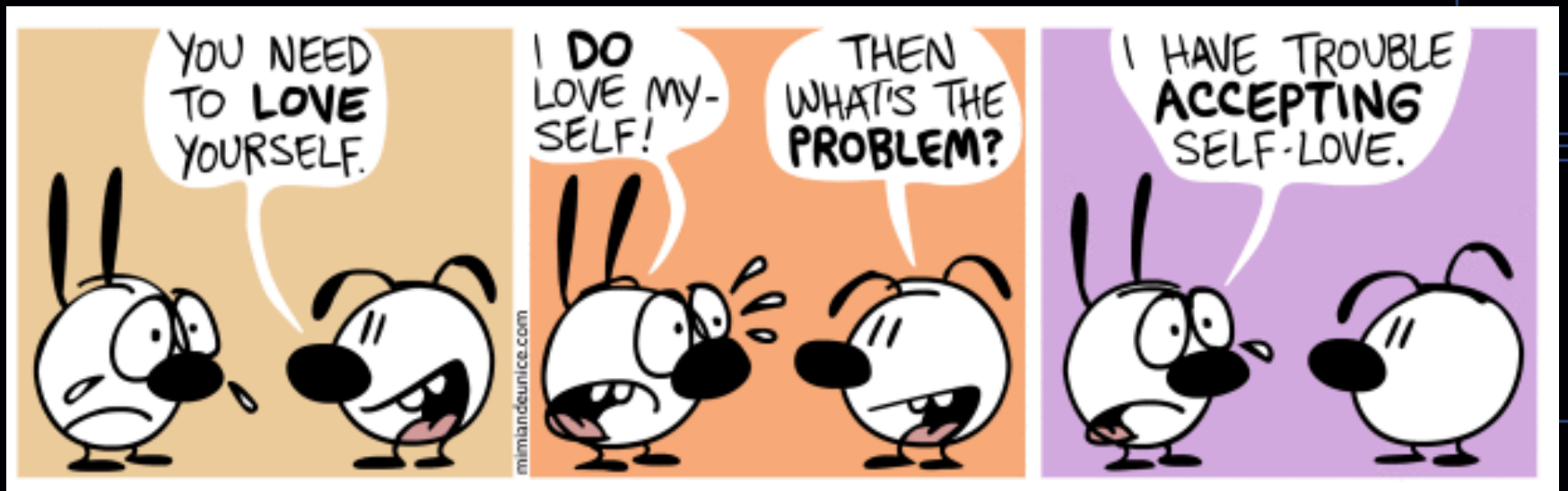
# 4<sup>th</sup> Wave: Mindfulness

“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

**“Trick” the insula to  
not give meaning to  
cravings/triggers**





What's the guy with guitar doing here?

Well, we don't just believe in using Western medicine, so he's giving you Country and Western medicine

