

Addiction: A Disease of the Brain

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Teaching Points

1. Addiction is a disease which has a specific neurophysiology, course, and set of treatments.
2. A key neurotransmitter in addiction is dopamine.
3. Risk factors for addiction include inherited factors, but also social and environmental factors.
4. Many factors can lead to relapse, including psychiatric problems, social problems, protracted abstinence, and conditioned responses.

Outline

- I. What is Abuse/Dependence?
- II. General Principles
 - A. Neurophysiology of Dependence
 - B. Agent/Host/Environmental Factors
 - C. Definitions
- III. Examples
- IV. Factors Leading to Relapse
 - A. Psychiatric Problems
 - B. Social Problems
 - C. Protracted Abstinence
 - D.. Conditioned Responses
- V. Neuroanatomy
- VI. Discussion

Pre-Lecture Exam

Question 1

1. Which of the following is necessary in order to be addicted to a drug?
 - a. Daily use
 - b. Tolerance
 - c. Physiologic Dependence
 - d. Withdrawal
 - e. None of the Above

Question 2

2. Which of the following drugs increase dopamine levels?
- a. Morphine
 - b. Nicotine
 - c. Cocaine
 - d. Amphetamines
 - e. All of the above

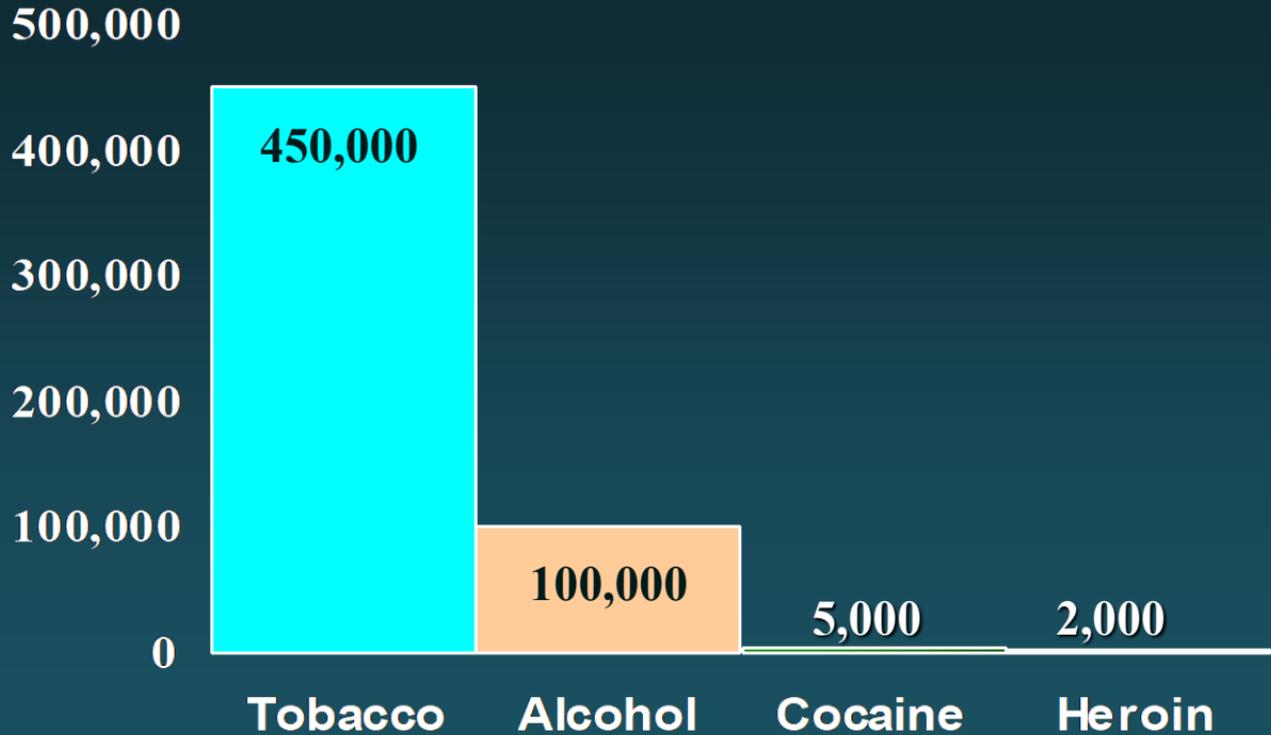
Question 3

3. Which of the following can be factors in relapse?
- a. Depression
 - b. Family Problems
 - c. Changes in Gene Transcription
 - d. Environmental Cues
 - e. All of the above

Question 4

4. Having tried these drugs, which one is most likely to lead to dependence?
- a. Tobacco
 - b. Cocaine
 - c. Alcohol
 - d. Heroin

Annual Deaths USA



Is Addiction a Disease?

- Volitional aspects at start
- Involuntary behavior in dependent state
- Chronic disease: relapses and remissions
- No cures, stable long term remission with risk of relapse

What is Addiction/Dependence?

- Drug use “out of control”
- NOT necessarily
 - Daily use
 - Tolerance
 - Physiol. Dependence
 - Withdrawal

Use → **Abuse** → **Addiction**

Use

Use → **Abuse**

Use → **Abuse** → **Addiction**

Use

Which drug has the highest rate of addiction among those who try it?

1. Heroin
2. Cocaine
3. Nicotine
4. Alcohol
5. Marijuana

Risk of Addiction

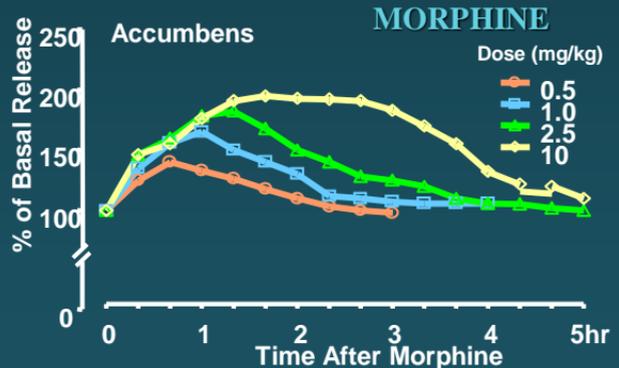
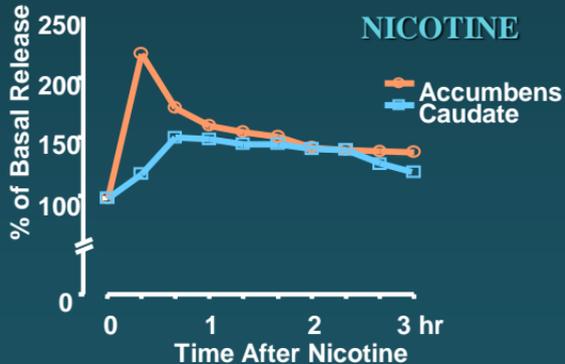
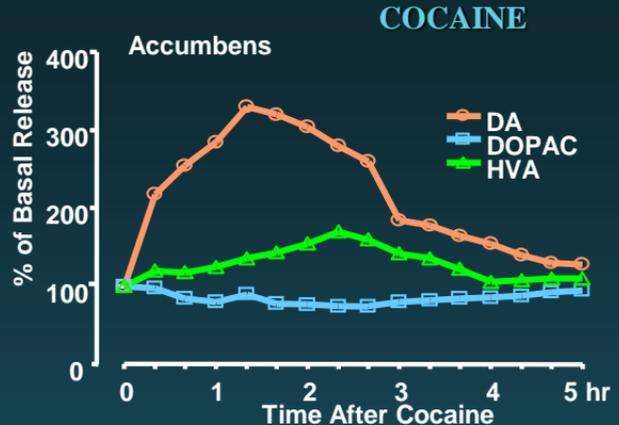
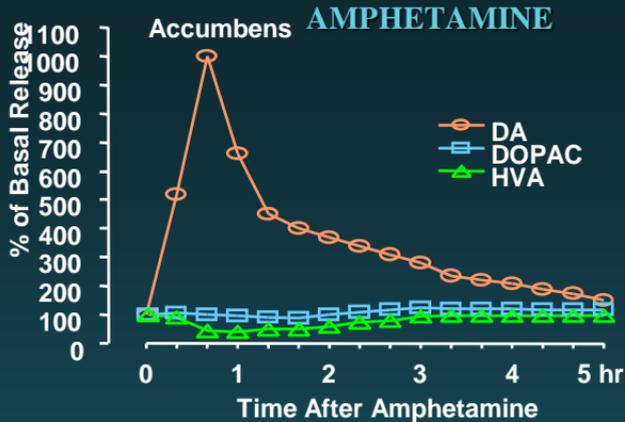
	<i>Ever used</i>	<i>Dependence</i>	<i>Risk</i>
Tobacco	75.6%	24.1%	31.9%
Cocaine	16.2	2.7	16.7
Heroin	1.5	0.4	23.1
Alcohol	91.5	14.1	15.4
Cannabis	46.3	4.2	9.1

Anthony et al, 1994.

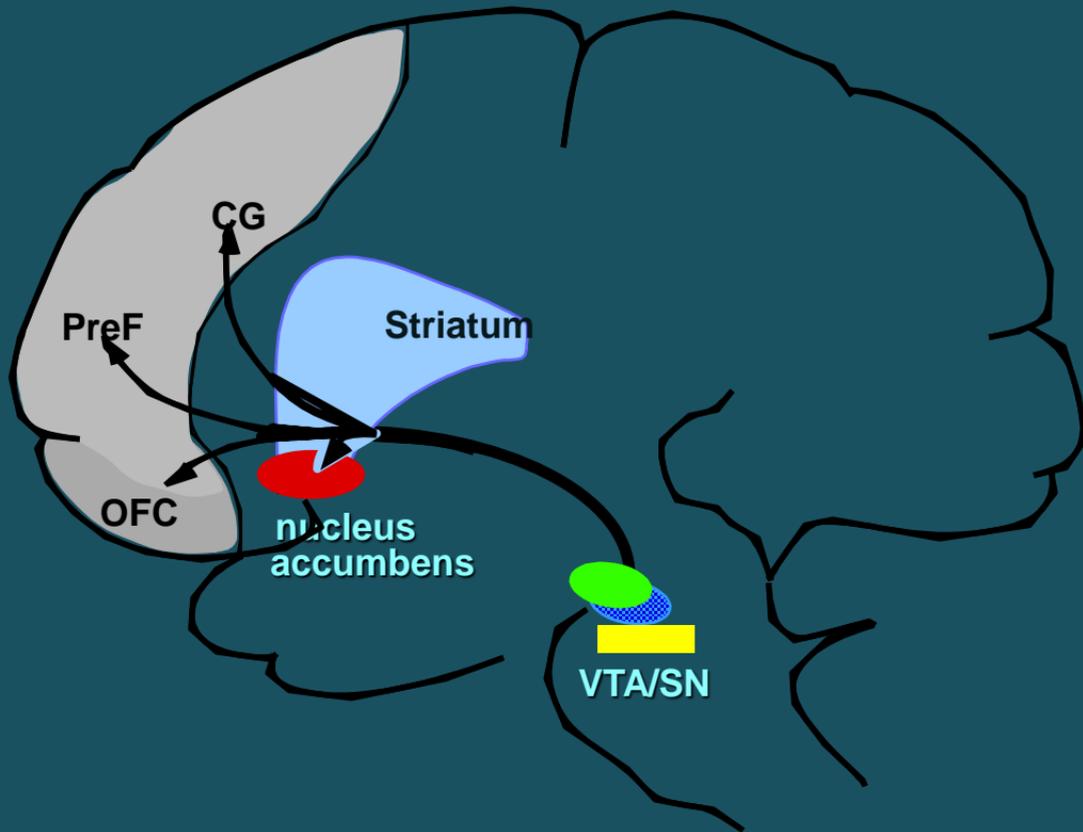
DA increased in Nucleus Accumbens

- **Nicotine**
- **Alcohol**
- **Opiates**
- **Cocaine**

Effects of Drugs on Dopamine Levels



BRAIN DOPAMINE SYSTEM



Result of interacting variables

Agent (Drug)



Host



Environment



Outcomes:

No use

Use

Abuse

Addiction

Agent

- **Availability**
- **Dose**
- **Price, Purity**
- **Gateway hypothesis vs. Random cigarettes/marijuana most available**
- **Crack as gateway drug in certain areas**

Host

- **Individual vulnerability**
 - Heredity**
- **Rapidity of tolerance**
- **Metabolism (nicotine, alcohol)**
- **Amount of reward**
- **Psychiatric Disorders,**
“self medication”

Inherited Factors

Initial Drug Exposure

- **Dose - Plasma level**
- **Absorption**
- **Disposition**
- **Flushing Response**
- **Perception of Pleasant Effect**
- **Rapidity of Tolerance Development**

Environment

- **Role models**
- **Other reinforcers**
- **Stress**
- **Boredom**
- **Peer pressure**

Tolerance

Innate

Acquired

Pharmacokinetic

Pharmacodynamic

Behavioral Tolerance

Conditioned Tolerance

Cross Tolerance

**Useful in choosing detox
Medications**

heroin-methadone

alcohol-oxazepam

Dependence

Withdrawal Syndrome

(normal reactions, not necessarily
a sign of addiction)

Tolerance/Withdrawal

- **Neither necessary nor sufficient**
- **Patients with tolerance/withdrawal
---no addiction**
- **Patients with addiction--- no
tolerance/withdrawal**

Sensitization

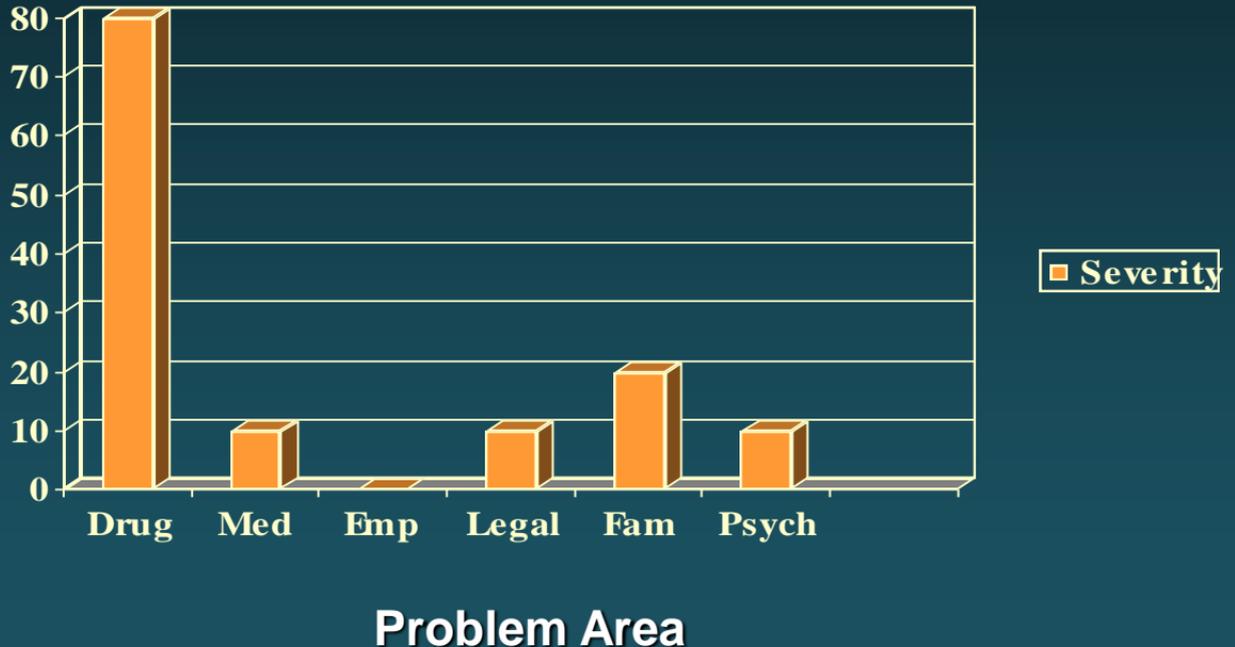
Reverse of tolerance

Stimulants - increased effect with
repeated, spaced dosing

Compulsion

- **An irresistible impulse to act, regardless of the rationality of the motivation**
- **A strong irrational impulse to carry out a given act**

ASI Problem Severity Profile of a Cocaine Dependent Physician



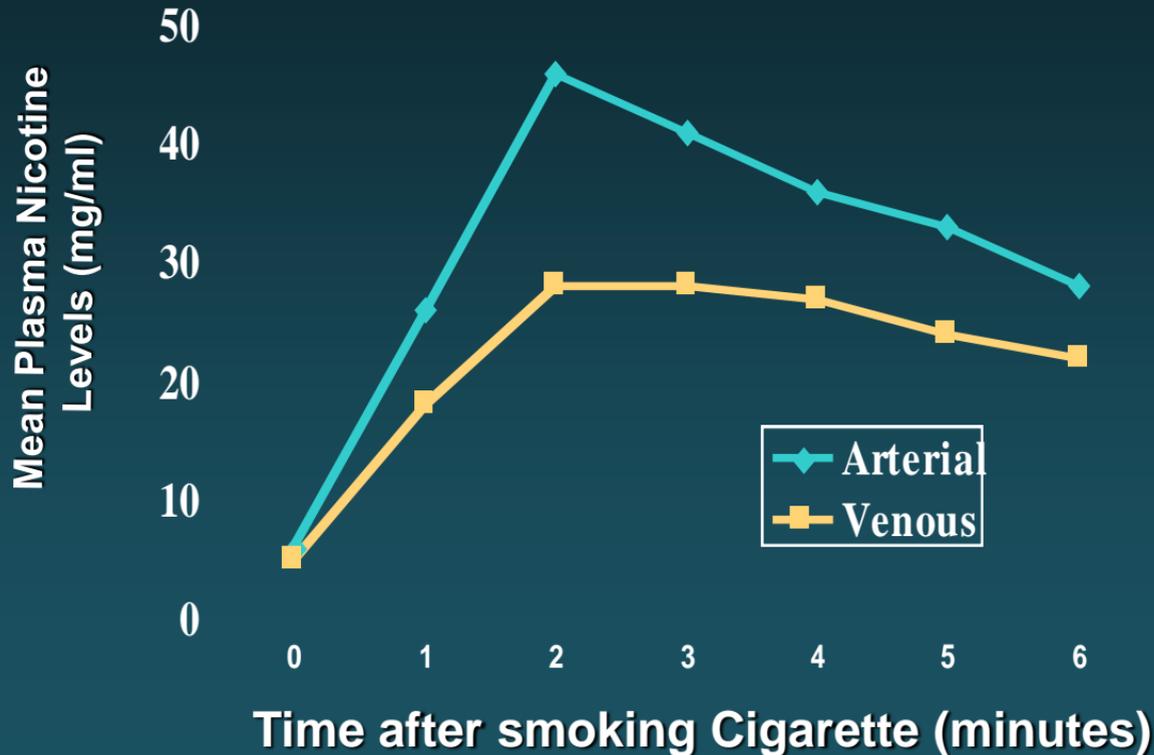
ASI Problem Severity Profile of a Cocaine Dependent Teen Mother



“Pure” addicts are rare

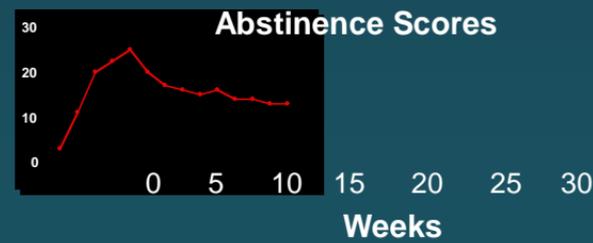
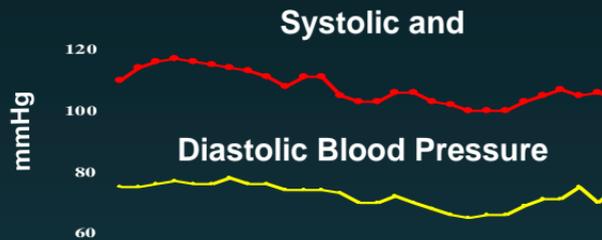
- most have additional problems
- treatment depends on additional problems
- high treatment success rate for “pure” addicts

Plasma Nicotine Levels



Factors Leading to Relapse

- **Psychiatric problems**
 - Depression
 - Anxiety
- **Social Problems**
 - Unemployment
 - Family problems
 - Peer influence
- **Protracted Abstinence**
- **Conditioned Responses**



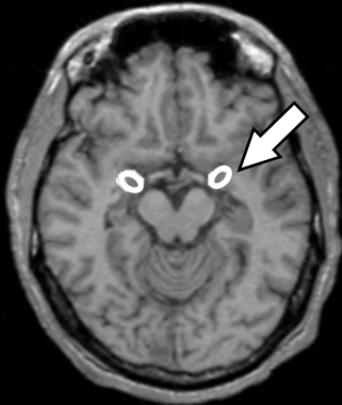
Conditioned Responses

- Thousands of pairings of environmental cues with drug effects
- Cellular level: changes in gene transcription
- Persist long after last use of drug

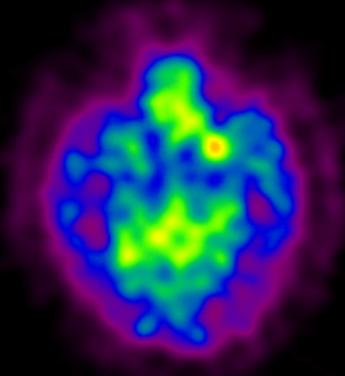
Cue induced craving

- 25 years after last dose of nicotine
- Not just recall of feeling
- Compulsion, difficult to resist

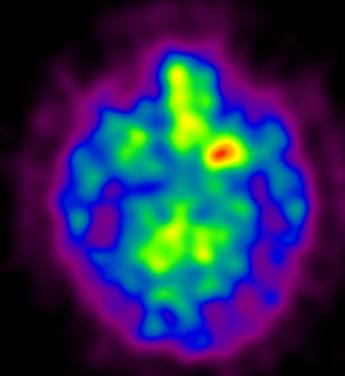
Amygdala



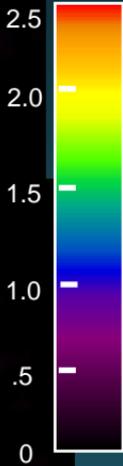
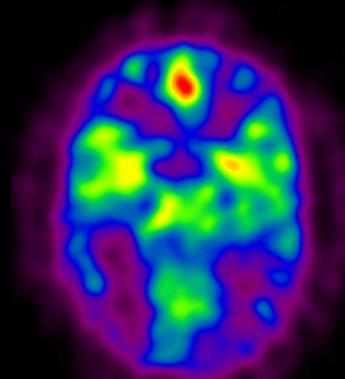
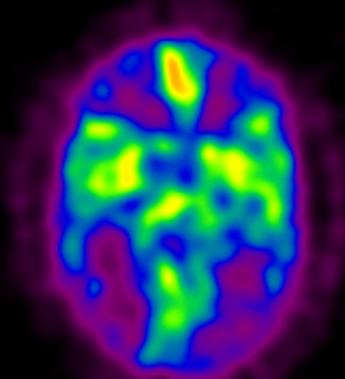
Nature Video



Cocaine Video



Anterior Cingulate

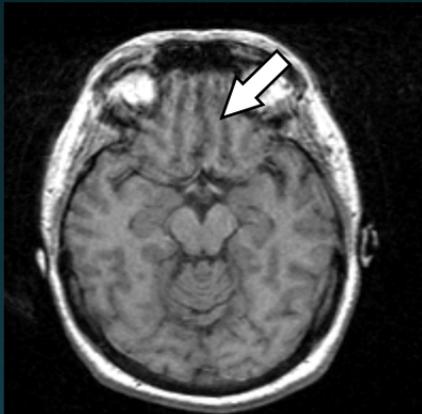


Pt. 30023

Childress '97

Cocaine Pt. 30023

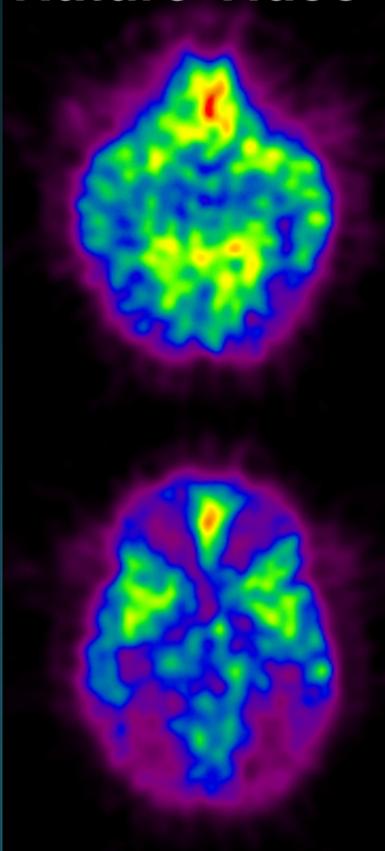
Orbitofrontal



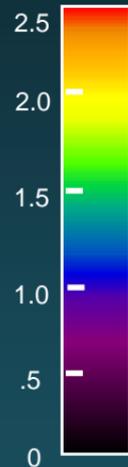
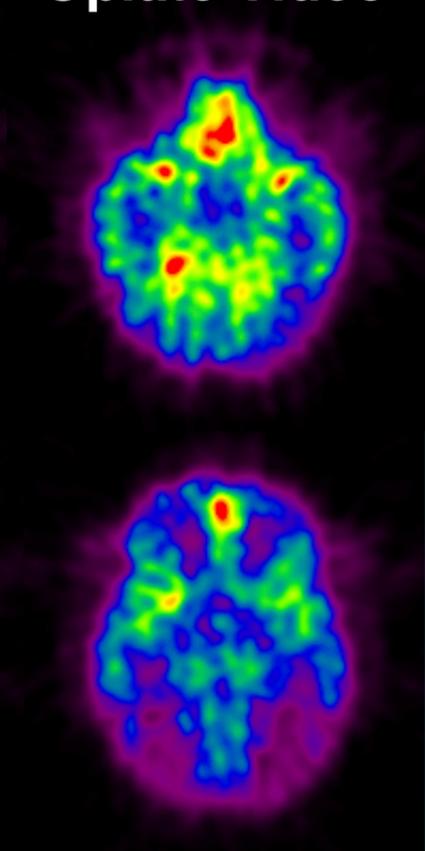
Anterior Cingulate



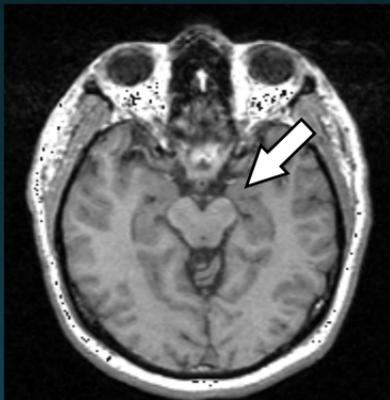
Nature Video



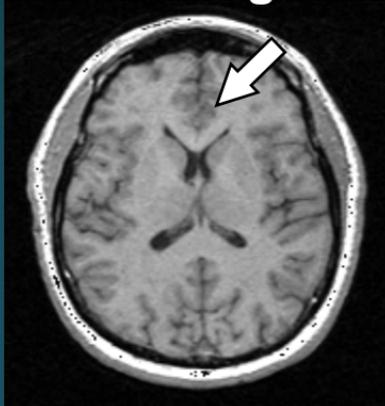
Opiate Video



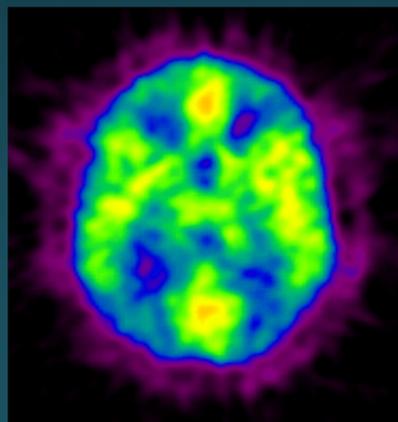
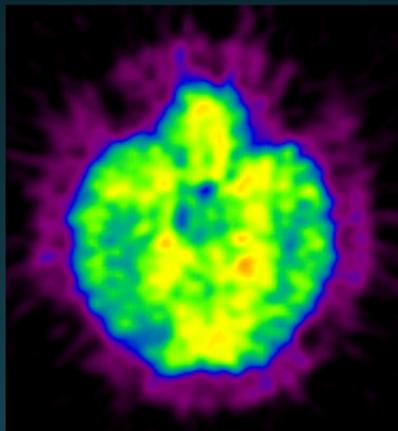
Amygdala



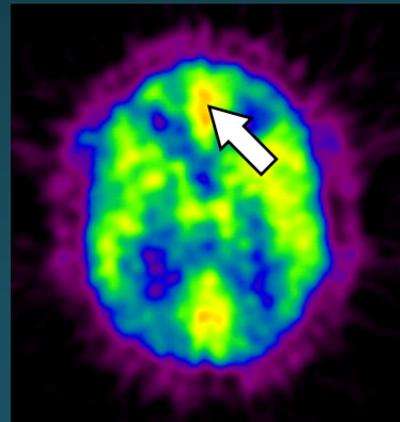
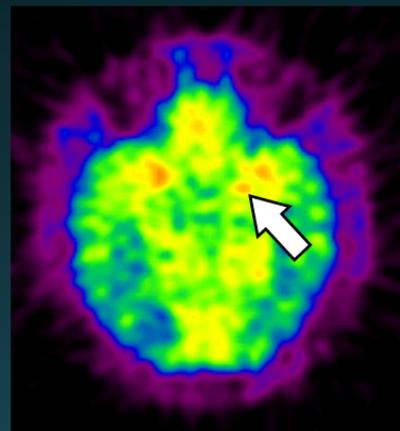
Anterior Cingulate

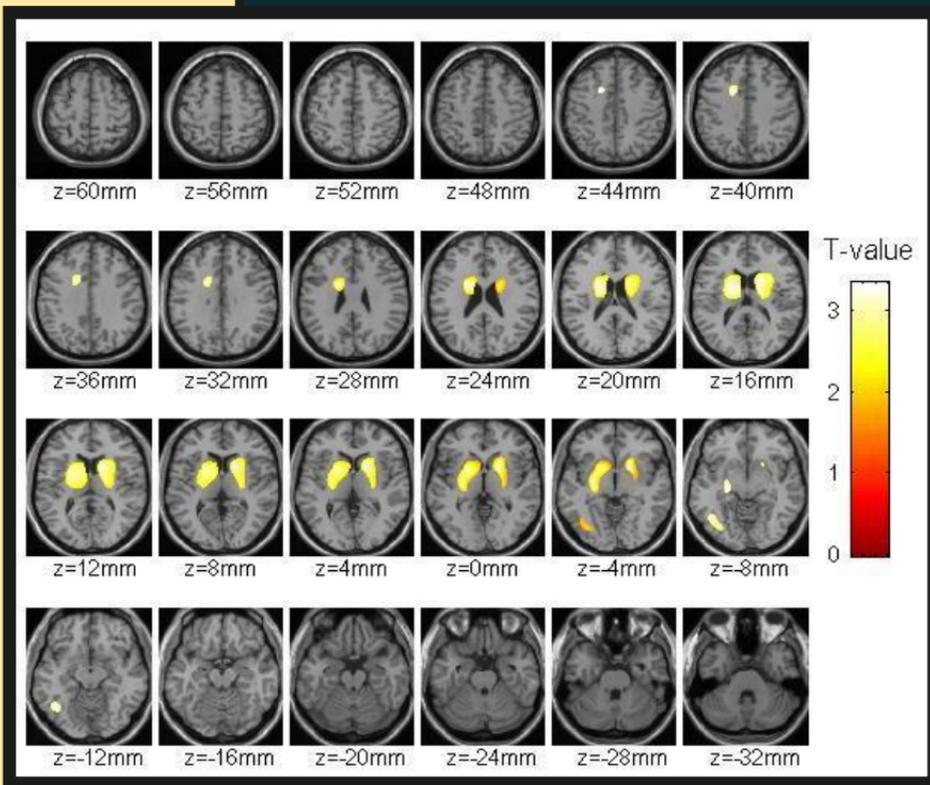
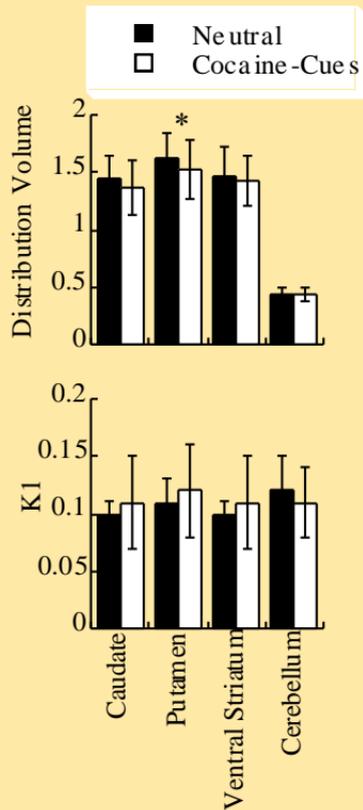


Nature Video



Sexual Video





Conditioned drug effects

Craving

Autonomic (HR, Skin Temp, GSR)

Regional CBF

Regional Brain Metabolism

Neurotransmitter release (DA)

Immediate early genes (c Fos)

Discussion Questions

- If addiction is a brain disease?
- If so, where is the lesion?
- How can you compare drug taking which is voluntary behavior to diabetes which is completely involuntary?

Post-Lecture Exam

Question 1

1. After starting to smoke a cigarette, at about what time does the plasma nicotine level peak?
 - a. **5 Seconds**
 - b. **30 Seconds**
 - c. **1 minute**
 - d. **2 minutes**
 - e. **3 minutes**

Question 2

2. On PET scan, which of the following yields the least intense activity in the anterior cingulate?
- a. Opiates
 - b. A Sex Video
 - c. Cocaine
 - d. They are all roughly equal

Question 3

3. Which pair of drugs lead to a sharp spike in dopamine levels within 1 hour of administration?
- a. Amphetamines and Nicotine
 - b. Nicotine and Cocaine
 - c. Opiates and Cocaine
 - d. Canabinoids and Cocaine
 - e. Amphetamines and Opiates

Question 4

4. Which is not involved in acquired tolerance?
- a. Pharmacokinetics
 - b. Behavioral Factors
 - c. Pharmacodynamics
 - d. Gene Transcription
 - c. Conditioning

Answers to Questions

Pre-Test

1. e. all of the above
2. e. all of the above
3. e. all of the above
4. a. tobacco

Answers to Questions

Post-Test

1. d. two minutes
2. b. sex video
3. a. amphetamines and nicotine
4. d. gene transcription