Neurobiology of Addiction

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What is Addiction?

- Addiction is a chronic, relapsing, and treatable brain disorder.
- Compulsive drug seeking and use in spite of serious consequences
Three Stage Model of Addiction

Stage 1
Binge / Intoxication

Stage 2
Withdrawal / Negative Mood

Stage 3
Preoccupation / Anticipation
Three Stage Model of Addiction

1. **Binge / Intoxication**
   - Associated with positive reinforcement & motivational learning
   - Associating cues with reward delivery

**Stage 1**
Binge / Intoxication

*E.g., Cat on Catnip*
What does ↑ dopamine signal?

↑ Value of future reward / of work to gain the reward
↑ Motivation to obtain reward
↑ WANT

— Evolved out of survival —
Dopamine is released in response to many types of rewards

Food

Sex

Amphetamine

Cocaine

Nicotine

Di Chiara and Imperato, PNAS 1988, Slides NIDA
Drugs of abuse can be more reinforcing than natural rewards

Drugs of abuse can release up to 10 times the amount of DA that natural rewards do

**Overstimulation of the reward circuit:**
- Leads to an increase in the drive to obtain drugs over natural rewards
DA neurons will eventually fire in response to cues that predict the reward.

Conditioned stimuli paired formerly paired with the drug elicit DA release:
- Trigger craving
- Increase motivation to seek out drug
- May lead to binge use
Three Stage Model of Addiction

1. **Stage 1**
   - Binge / Intoxication

2. **Stage 2**
   - Withdrawal / Negative Mood
     - Associated with negative reinforcement and increases in stress

3. **Stage 3**
   - Preoccupation / Anticipation

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Koob & Le Moal 2008
Neuroadaptations as a result of *prolonged* drug use: Dopamine

- At baseline, dopamine receptor concentration is reduced to compensate for the frequent, large dopamine surges elicited by drug use.

*Volkow et al 2009*
Normal

Reward Circuits

Prolonged Drug Use

Reward Circuits

- Dopamine
- Dopamine Receptor

*Elevated Reward Threshold
**Normal**

**Reward Circuits**

**Prolonged Drug Use**

**Reward Circuits**
Stress Systems
Dysregulated

HPA/Stress Axis

Hypothalamus

CRF

Anterior Pituitary

ACTH

Adrenal Cortex

CORT

Baseline Normal Feeling

*Negative Motivational / Affective state

Low CRF

High CRF
Stress Systems

Dysregulated

HPA/Stress Axis

Hypothalamus

CRF

Anterior Pituitary

ACTH

Adrenal Cortex

CORT

Baseline Normal Feeling

*Negative Motivational / Affective state

Low CRF

High CRF

DYSPHORIA
Stress Systems

Dysregulated

HPA/Stress Axis

Hypothalamus

CRF

Anterior Pituitary

ACTH

Adrenal Cortex

CORT

Baseline Normal Feeling

*Negative Motivational / Affective state

Low CRF

High CRF
Long-term Result of Neuroadaptations

Baseline
Normal
Feeling

Amount of drug needed to feel normal
Three Stage Model of Addiction

Stage 1
Binge / Intoxication

Stage 2
Withdrawal / Negative Mood

Stage 3
Preoccupation / Anticipation

3. Preoccupation & Anticipation
   - Associated with changes to executive functioning

Koob & Le Moal 2008
Normal

Control

Automatic

STOP

STOP

Brain Illustration
Iowa Gambling Task
Iowa Gambling Task

- **GOOD**
  - **WINS**: Small, Frequent
  - **LOSSES**: Moderate, Rare
Iowa Gambling Task

- **WINS**: Large, Rare
- **LOSSES**: Large, Frequent
Iowa Gambling Task

**GOOD**
- **WINS:** Small, Frequent
- **LOSSES:** Moderate, Rare

**BAD**
- **WINS:** Large, Rare
- **LOSSES:** Large, Frequent
Iowa Gambling Task

- **BAD**
  - **WINS:** Large, Rare
  - **LOSSES:** Large, Frequent

*Bechara 2008*
What happens if there is PFC dysfunction?

Bechara 2008
What happens if there is PFC dysfunction?
What happens if there is PFC dysfunction?

Control

Automatic

STOP

Control

Cocaine Abuser
What happens if there is PFC dysfunction?
Summary:

Why is it so difficult to quit?
Thank you

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