Machinery of the Mind

How High-risk Choices Redesign the Brain

Key Concepts

- Brain and Mind are reciprocal
- Brain/Mind Functions intertwine
- We are “hardwired” and we have “software”
- Your brain changes all the time

Six Brain—Mind Functions

- Reward & Tolerance
- Memory & Learning
- Salience & Sensitization
- Impulsivity & Restraint
- Decision Making
- Stress/Relaxation
- Withdrawal
- Loss of Control

The Growing Cycle

Addictive Agent

Homeostasis

Administration
Reward Rebound

While “buzzed,” drunk or high, the brain’s reward threshold is lowered:
- Friends seem friendlier
- Humor seems funnier
- Normal pleasures are more pleasurable

What’s the problem?

Reward Rebound

- Following the “high,” the reward threshold is temporarily raised.

Reward Rebound

As the brain’s reward and motivational systems “rebound” – a higher reward threshold means life becomes overall less rewarding

The Growing Cycle

- Acute Euphoric Reward
- Positive Reinforcement
- Homeostasis
- Addictive Agent
- Administration
Euphoric Reward

• We are wired for pleasure – glutamate, GABA, serotonin, enkephalin & endorphin (dopamine?)
• Reward is good - making life satisfying
• Reward shapes our behavior every day
• This is part of our homeostatic norm

What’s bad about feeling good?

Euphoric Reward

What’s bad about feeling good?

• Drug reward is abnormal
  – effects even in healthy, satisfied animals
  – meets no obvious physical need
  – can produce physical need
  – not diminished by quenching
  – nor enhanced by deprivation (early)

Euphoric Reward

What’s bad about feeling good?

• Because the reward is abnormal, it causes abnormal
  Neuroadaptation

• The Brain starts to change in unusual ways

The Growing Cycle

Addictive Agent
Administration

Euphoric Reward
Positive Reinforcement
Neuroadaptations
Tolerance
Reward & Tolerance
- Drug tolerance is a normal, unavoidable process because of the nature of reward
- Increasing tolerance to pleasure does not always increase tolerance to other effects, including health problems

Neuroadaptation: Tolerance
- Tissue tolerance - change in the brain
  - Altered neurochemical production
  - Altered neurochemical activity
  - Altered genetic activity
  - Drug specific changes in receptors
  - Drug specific changes in transporters
  - Let’s use nicotine and cocaine as examples of different mechanisms

The Growing Cycle
- Addictive Agent
- Administration
- Euphoric Reward
- Positive Reinforcement
- Neuroadaptations
  - Tolerance
  - Memory & Learning

Memory & Learning
- Memory and Learning are intertwined, normal brain activities
- Gated through the hippocampus...
There are various Memory functions mapped to various brain regions:

- Declarative (factual)
- Perceptual (sensory)
- Procedural (motor skills)
- Episodic (autobiographic)
- Conditioned Incentive (emotional memory of pain/pleasure)

High risk alcohol and drug choices impact all memory formation through the release of dopamine, glutamate, serotonin and others:

- Declarative (factual)
- Perceptual (sensory)
- Procedural (motor skills)
- Episodic (autobiographic)
- Conditioned Incentive (emotional memory of pain/pleasure)

The purpose of Memory is NOT to recall the past.

The purpose of Memory is to PREDICT the FUTURE!

Let me repeat that!

We all predict the future based on our memory of the past.

What future here?
Memory is hijacked
• Should build motivation for life-enhancing pain/pleasure experiences in memory.
• Weak drug-paired signals take on strength to become drug cues.

Memory is hijacked.
• Responding to minor cues, the brain senses opportunity,
• Revving up motivation to repeat drug use, regardless of the outcome (not our "thinking brain")

The Growing Cycle
Addictive Agent 
Positive Reinforcement
Euphoric Reward

Salience & Sensitization
The brain has a normal system to prioritize stimuli
• Sensitization: "behavioral, physiological or cellular response to a stimulus that is augmented as a result of previous exposure to that stimulus"
• Reinforcement of the behavior
• VTA, Nucleus accumbens, frontal cortex

The brain has a normal system to prioritize stimuli
• Sensitization: "behavioral, physiological or cellular response to a stimulus that is augmented as a result of previous exposure to that stimulus"
• Reinforcement of the behavior
• VTA, Nucleus accumbens, frontal cortex

Memory & Learning
Memory & Learning

Memory & Learning

Memory & Learning

Memory & Learning

Copyright © 2012 Prevention Research Institute
All rights reserved – No reproduction without written permission
**Altered Gene Expression**

Society is coming to realize that our genes affect our behavior. What they don’t yet appreciate is that our behavior changes genetic expression in the brain.

(C) Prevention Research Institute, 2010. All rights reserved.

**Salience & Sensitization**

- The brain measures the potential for pain and pleasure based on memory.
- Opportunities for each provoke a dopamine spike, especially if we are wrong in our predictions.
- This helps us learn what needs attention and what does not.

(C) Prevention Research Institute, 2010. All rights reserved.

**Salience & Sensitization**

- Your inaccurate prediction made a more powerful learning experience AND made this a reward cue. Illustrates how easily we modify our feelings, beliefs and behaviors based on just a chance of reward.

(C) Prevention Research Institute, 2010. All rights reserved.

**Salience & Sensitization**

- Linked to memory, the drug cues take on greater salience - a sensitized response.
- They gain the power to grab attention.
- They gain the power to motivate action.

(C) Prevention Research Institute, 2010. All rights reserved.
The Growing Cycle

Addictive Agent
Administration

Euphoric Reward
Positive Reinforcement

Neuroadaptations
Tolerance
Memory & Learning
Salience & Sensitization

Positive Reinforcement

Withdrawal/Rebound

—

Negative Reinforcement

Withdrawal/Rebound

The Growing Cycle

Addictive Agent
Administration

Euphoric Reward
Positive Reinforcement

Neuroadaptations
Tolerance
Memory & Learning
Salience & Sensitization

Positive Reinforcement

Withdrawal/Rebound

New Allostatic Norm

The brain's reward and motivational systems "rebound" – a higher reward threshold

• Malaise/fatigue
• Chronic irritability
• Emotional pain/depression

Withdrawal/Rebound

The brain's reward and motivational systems "rebound" – a higher reward threshold

• Less motivation for natural rewards
• Increased baseline anxiety
• Alexithymia (difficulty naming feelings - poor self-awareness/low empathy)
Withdrawal/Rebound

The brain's stress (anti-reward) systems are overactive:
- ↑ Corticotropin Releasing Factor (more stress)
- ↑ Norepinephrine (more stress)
- ↓ GABA (more stress/anxiety)
- ↓ Neuropeptide Y (more stress)
- Altered opioid production - ↑ dynorphin, ↓ endorphin (more pain, less pleasure)
- ↓ dopamine & glutamate production (less motivation, less alert, less pleasure)

Produces an internal allostatic stress state

The Growing Cycle

Addictive Agent
Administration

Euphoric Reward
Positive Reinforcement

Neuroadaptations
Tolerance
Memory & Learning
Salience & Sensitization

Negative Reinforcement
Withdrawal/Rebound
ALLOSTASIS

Stress Threshold

- A point at which we are not stressed, moving to the point where we become stressed

Reward – During the early “high,” the stress threshold is temporarily raised
• **Rebound** – After the “high” the stress threshold is temporarily lowered

• **Chronic Use leads to Chronic Rebound** – After the “high” the stress threshold remains chronically lowered

---

**Withdrawal/Rebound**

The brain's overactive stress (anti-reward) systems produce an allostatic stress state

- Life's little stresses are more stressful
- Life is less rewarding

---

**The Growing Cycle**

- Addictive Agent
- Positive Reinforcement
- Neuroadaptations
- Tolerance
- Memory & Learning
- Salience & Sensitization
- Negative Reinforcement
- Withdrawal/Rebound
- Allostatic norm
- Craving Incubation
- Stress
**Craving Incubation**

In early abstinence craving can actually increase
- ↑ ERK signaling in the amygdala
- ↑ BDNF in the bed nucleus striatum
- These increase for a period of time (weeks)...
- A period of high-risk for relapse
- Then begin to decrease

**The Growing Cycle**

- **Drug Euphoria**
  - Positive Reinforcement
  - Neuroadaptations
  - Tolerance
  - Memory & Learning
  - Sensitized Salience
- **Negative Reinforcement**
  - Withdrawal/Rebound
  - Allostatic norm
  - Craving Incubation
- Stress

**Decision Making**

Results from two interacting systems:
- Impulsive - amygdala (external cues)
- Reflective - ventromedial prefrontal cortex (internal cues)

- With a history of high-risk choices, the amygdala has an exaggerated incentive response to external drug cues
- The VMPC and other brain regions related to internal, emotional memories become blunted
- In combination, these changes produce poor decision making
Decision Making

Many alcohol, nicotine, cannabis, cocaine, methamphetamine and opioid users show poorer decision making skills while continuing use

- Not only regarding drug use, but in various life arenas
  - Legal Consequences
  - Finances
  - Health

Impulsivity & Restraint

Impulsivity: “acting suddenly in an unplanned manner to satisfy a desire”

- The changes just examined will also make it harder to control drug-cued impulses
- Lowers the threshold for signals to create a drug-related impulse
- Creates obsessive thinking about drugs
- Creates more impulsive drug behaviors
Loss of Control

Impulsivity: "acting suddenly in an unplanned manner to satisfy a desire"
Impulsive action turns into Compulsive action
Compulsive: "acting despite the desire not to take the action"
Acting on compulsion is generally followed by feelings of shame, regret and/or guilt
These add stress which can lead to more use

How Do We Heal the Machinery of the Mind?

We start by caring for and healing the brain:
Stop the High-risk Alcohol or Drug Use!

How Do We Heal the Machinery of the Mind?

We learn to:
Be Well - healthy sense of self
Play Well - relax with/out others
Work Well - meaning & productivity
Love Well - significant connections
These also work for prevention

✓ Exercise – physical & mental
✓ Good Nutrition
✓ Adequate Sleep
✓ Spirituality & Meditation
✓ Pursuing positive passions

from “A User’s Guide to the Brain” author, John J. Ratey, M.D.