The Brain and Recovery:
An Update on the Neuroscience of Addiction

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Boise State University
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Is Addiction Really a “Disease?”
Discrepant findings
the Disease Model has to explain . . .

- **Robins (Vietnam Vets):** drug use is situational
- **Alexander (Rat Park):** it’s not the drug that causes addiction, it’s the environment
- **Heyman:** most people with addiction do NOT progress or die – most stop when they get older and start making better choices
- **Lewis:** addiction is a learned habit that can be unlearned; a developmental disorder not a disease
Gene Heyman, PhD

- Addiction is not a chronic disease
- Most addicts do stop on their own, without treatment, and do not display relapse chronicity
- Remission ("maturing out") is the rule, not the exception
- Addicts do not need lifelong treatment
- Remission rates lower for legal drugs than illegal drugs
Long-Term Course of Opioid Addiction

Yih-Ing Hser, Ph.D.
UCLA Integrated Substance Abuse Programs
Addiction Seminar (Psychiatry 434)

Supported by the National Institute on Drug Abuse
(P30 DA016383)
Longitudinal Approach to Study Drug Use over Time

Life-course Drug Use Career

- Protective Factor: e.g., family support
- Protective Factor: occurrence of positive life events (e.g., got married, got employed)
- Risk Factors: e.g., crime involvement

Estimated trajectory of Drug use

Trajectories of drug use are heterogeneous among individuals and can be classified as several distinctive trajectory groups.

Age

Age
A “Disease” of Volition

• Could such a thing exist? (ontologic argument)
• What would happen if such a thing existed? (teleologic argument)
• What is the nature of volition/free will/choice?
• Is there something special (non-material) about “choice?”
• If so, what is it?
• If not, how is “choice” realized in the brain?
What goes into a “choice?”

- Valuation and Framing
- Risk-taking, Novelty-seeking and Impulsivity
- Genetic vulnerability vs resilience
- Empathy vs. Narcissism
- Memory, Stress and Trauma (and Epigenetics)
- Social Status/Social Defeat
Addiction is a disorder in the brain’s hedonic system (pleasure sense) …
... resulting in a failure to correctly assess future value and uncertainty (likelihood) ...
… undermining the individual’s decision-making capacity (choice) and self-awareness (insight).
ASAM Addiction Definition (Aug 2011)

A stress-induced (HPA axis), genetically-mediated (polymorphisms, epigenetic mechs.) primary, chronic and relapsing brain disease of reward (nucleus accumbens), memory (hippocampus & amygdala), motivation and related circuitry (ACC, basal forebrain) that alters motivational hierarchies such that addictive behaviors supplant healthy, self-care behaviors.
Addiction is a disorder of ...

1. GENES (vulnerability) - polymorphisms, epigenetic changes
2. REWARD (incentive salience) - dopamine, dopamine receptors
3. MEMORY (habits, cues) - glutamate, synaptic remodeling
4. STRESS (anti-reward system) - HPA axis
5. CHOICE (motivation, insight) - OFC, ACC, PFC, IC
From the “Disease Model” of Addiction to a “Public Health Model” of Recovery …

The Public Health Model of Recovery

- life course
- educational opportunity
- housing
- identity
- societal context
- disparity
- family
- social support
- occupation
- cultural context
- faith, meaning and purpose
- political context

The Disease Model of Addiction

- mental health
- medication
- primary care
- detox & treatment
Anterior Cingulate Cortex (ACC)

- Works with OFC: decision-making based on reward values
- But also generates new actions based on past rewards/punishments
- Appreciation and valuation of social cues
- MRI: active in tasks requiring empathy and trust
Prefrontal Cortex (PFC)

- EXECUTIVE DECISION-MAKING
- Motivation for goal-directed activity
- Planning and problem-solving
- Attention to tasks
- Inhibition of impulsive responses
- Weighing consequences of future actions
- Flexibility of responses (rule shifting)
- Reflective decision-making

*Gives us the capacity to use past experience and knowledge to make sense of our current behavior*
Insular Cortex (IC)

- Abrupt cigarette smoking cessation with IC lesions (Naqvi et al)
- Important in emotional awareness, empathy, interoceptive representation
- Impairment is one part of craving
Orbitofrontal Cortex (OFC)

- Decision-making guided by rewards
- Integrates sensory and emotional information from lower limbic structures
- Flexible assignment of value to environmental stimuli to motivate or inhibit choices & actions
- Self-monitoring and social responding
The Brain is a Bayesian Calculator

Rev. Thomas Bayes (1701 – 1761)

\[ P(A|B) = \frac{P(B|A) P(A)}{P(B)} \]
choice

alcoholic

Outcome 1

v1 = x
p1 = 1

Outcome 2

v2 = y
p2 = 1

Outcome 3

given

v3 >> v4
p3 >> p4
In addiction, the brain’s ability to correctly calculate
1. value
and
2. probability
becomes severely biased.

This means that people in early recovery have a hard time assessing
likelihood of future harm

... or RISK
Addiction is a disorder of ...

1. GENES (vulnerability)
   polymorphisms
   epigenetic changes
# Heritability of Addiction

(from twin studies)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Heritability</th>
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<tbody>
<tr>
<td>Alcohol</td>
<td>48 – 66%</td>
</tr>
<tr>
<td>Cannabis</td>
<td>51 – 59%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>42 – 79%</td>
</tr>
<tr>
<td>Opioids</td>
<td>23 – 49%</td>
</tr>
<tr>
<td>Nicotine</td>
<td>33 – 71%</td>
</tr>
<tr>
<td>Gambling</td>
<td>49%</td>
</tr>
</tbody>
</table>

- Heritability: an aggregate measure of the variability of a characteristic due to genetics vs environment (the risk due to genes – “risk genes”)
- First-order family members of a person with SUD have a 4 – 8 x increased risk of developing SUD
- Applies to populations, not individuals (that would be inheritance)
- Probabalistic, not deterministic

Shifts from adolescence (environment) to young adulthood (genetics)

COMT gene & Impulsiveness

- Polymorphism at VAL-158-MET gene for catechol-O-methyltransferase influences impulsive decision-making style
- Individuals homozygous for more active 158-VAL allele have an increased tendency to choose immediate over delayed rewards
- Genetic variation that contributes to impulsivity and may increase risk of addiction
Delay Discounting

we tend to discount the value of a reinforcer depending on how long we have to wait for it.
Epigenetics

- Modifications (DNA methylation, Histone acetylation) that effect gene expression
- Tells the cell what genes to express
- Heritable (but reversible) changes in gene expression due to environmental factors
- Allows passage of information from generation to generation that is not encoded in DNA
- Inheritance without DNA sequence change
Epigenetics

- Overkalix study: Starvation during adolescence increased the prevalence of diabetes in grandchildren.
- Holocaust survivors with PTSD: their children also had PTSD without having been exposed to trauma.
- A mechanism exists to transmit environmental exposure information from one generation to the next to the next.
EPIGENETIC MECHANISMS are affected by these factors and processes:
- Development (in utero, childhood)
- Environmental chemicals
- Drugs/Pharmaceuticals
- Aging
- Diet

DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.

Histones are proteins around which DNA can wind for compaction and gene regulation.

HEALTH ENDPOINTS
- Cancer
- Autoimmune disease
- Mental disorders
- Diabetes

Histone modification
The binding of epigenetic factors to histone “tails” alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.
Strategies to deal with the GENETIC (VULNERABILITY) component of addiction

- Careful framing (vulnerability > adaptation)
- Adaptive strategies
- Risk assessment and stratification for all future medications
- Pharmacogenomics
Addiction is a disorder of …

5.
4.
3.

2. REWARD (incentive salience)  dopamine  dopamine receptors
1. GENES (vulnerability)  polymorphisms  epigenetic changes
Addiction is a disorder in the brain’s hedonic system (pleasure sense) …
Addiction Neurochemical #1: Dopamine

- All drugs of abuse and potential compulsive behaviors release Dopamine
- Dopamine is the first chemical in the cascade of chemicals that generate a rewarding experience
- DA is the chemical of **saliency** (survival importance)
- DA is more about “wanting” than “liking”
- DA is more about expectation than consummation
- DA signals **reward prediction error** - it tells the brain when something is “better than expected”
DA NAc neurons do more than encode receipt of reward

- Expectancy of reward
- Amount of reward
- Delay of reward
- Errors in reward prediction
- Motivation for drug seeking
- Contribute to synaptic neuroplasticity that underlies the acquisition of addictive behaviors

Drugs cause Dopamine Surges in the midbrain reward system.
Incentive-Sensitization (Robinson & Berridge)

- Distinguished between a “liking” and a “wanting” role for Dopamine (it’s more about “wanting”)
- Created hyper-dopaminergic Dopamine Transporter “knock-down” mice (mice with increased synaptic Dopamine)
- Observed increased intake of reinforcing substances in these mice and greater thwarting of obstacles to get them (i.e. more “wanting”)
- But did not observe greater “liking” of these substances by these mice
Dopamine-Releasing Chemicals

- Alcohol & Sedative/Hypnotics
- Opiates/Opioids
- Cocaine
- Amphetamines
- Entactogens (MDMA)
- Entheogens/Hallucinogens
- Dissociants (PCP, Ketamine)
- Cannabinoids
- Inhalants
- Nicotine
- Caffeine
- Anabolic-Androgenic Steroids
Dopamine-Releasing Behaviors

- Food (Bulimia & Binge Eating)
- Sex
- Relationships
- Other People ("Codependency," Control)
- Gambling
- Cults
- Performance ("Work-aholism")
- Collection/Accumulation ("Shop-aholism")
- Rage/Violence
- Media/Entertainment
The Full Spectrum of Addiction

- Alcohol & Sedative/Hypnotics
- Opiates/Opioids
- Cocaine
- Amphetamines
- Entactogens (MDMA)
- Entheogens/Hallucinogens
- Dissociants (PCP, Ketamine)
- Cannabinoids
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- Rage/Violence
- Media/Entertainment
Functionally…

Dopamine D2 Receptors are Decreased by Addiction
Correlations Between D2 Receptors in Striatum and Brain Glucose Metabolism

Cocaine Abusers

r = 0.7, p < 0.001

DA D2 Receptors (Ratio Index)

METH Abusers

r = 0.7, p < 0.005

DA D2 Receptors (Bmax/kd)
# Periodic Table of the Intoxicants

<table>
<thead>
<tr>
<th>Periodic Table</th>
<th>Intoxicant</th>
<th>Compound</th>
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</thead>
<tbody>
<tr>
<td><strong>Al</strong></td>
<td>ethanol</td>
<td>phenethylamine</td>
</tr>
<tr>
<td><strong>Mj</strong></td>
<td>cannabis</td>
<td>cannabinol</td>
</tr>
<tr>
<td><strong>Cb</strong></td>
<td>hashish</td>
<td>delta-9-tetrahydrocannabinol</td>
</tr>
<tr>
<td><strong>Ha</strong></td>
<td>synthetic cannabinoids</td>
<td>synthetic cannabinoids</td>
</tr>
<tr>
<td><strong>Sp</strong></td>
<td>salvia</td>
<td>salvinorin</td>
</tr>
<tr>
<td><strong>Pc</strong></td>
<td>ketamine</td>
<td>ketamine</td>
</tr>
<tr>
<td><strong>K</strong></td>
<td>nitrous oxide</td>
<td>nitrous oxide</td>
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<tr>
<td><strong>No</strong></td>
<td>isoxsuprane</td>
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<td><strong>Sa</strong></td>
<td>tramadol</td>
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<td><strong>Ly</strong></td>
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<td><strong>Sm</strong></td>
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<td>alfentanil</td>
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<tr>
<td><strong>So</strong></td>
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<td><strong>Lu</strong></td>
<td>chloroform</td>
<td>chloroform</td>
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<td><strong>Ch</strong></td>
<td>benzodiazepines</td>
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<td><strong>G</strong></td>
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<td><strong>Q</strong></td>
<td>antipsychotics</td>
<td>antipsychotics</td>
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<td><strong>Pb</strong></td>
<td>opioid agonists</td>
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<tr>
<td><strong>Sb</strong></td>
<td>opioid receptor antagonists</td>
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<td>oxycodone</td>
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<td>buprenorphine</td>
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<td><strong>Tz</strong></td>
<td>naloxone</td>
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<tr>
<td><strong>Xz</strong></td>
<td>naltrexone</td>
<td>naltrexone</td>
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**Kevin T. McCauley, MD**
Strategies to deal with the DOPAMINE (REWARD) component of addiction

- Daily “dopamine load” assessment
- Take out the Dopamine “spikes”
- Nicotine cessation
- Avoid cross-addiction
- Put normal Dopamine releases (normal, competing rewarding activities) back in
- Judiciously chosen medications
“Rat Park” Study (Alexander)

- Morphine consumption by rats housed in isolation vs socially
- Isolated rats drank more morphine ($n = 32$ rats)
- Both groups drank plenty of morphine, and 5 rats died of morphine overdoses (2 in the isolated group and 3 in the socially-housed group)
- Implication: morphine is more reinforcing in isolated environments and less so in enriched environments
- Study has some problems, and subsequent replication studies had mixed results
- Point taken: Housing matters
- But: how do you know “cross-addiction” didn’t occur?

ASAM Definition: Relapse

- Persistent relapse / and risk thereof
- Even after periods of abstinence
- Triggered by:
  1. Re-exposure to drug itself *(DA release in NAc)*
      drug-induced reinstatement
  2. 
  3. 
Dopamine begins reward but quickly fades to support cues

- Drug-induced fast DA increases in the striatum (incl NAc) mediate their rewarding effects
- In addiction: drug-induced DA increases (as well as subjective rewarding effects) are markedly blunted (pharmacologic effects fade)
- In addiction: but CUE-induced DA increases in the striatum are still significant and are associated with self-reports of craving (conditioned responses strengthened)
- In addiction: lower levels of striatal DAD2Rs

Addiction is a disorder of ...

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<td>4.</td>
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</tbody>
</table>
| 3. MEMORY | (habits, cues) | glutamate 
            synaptic remodeling |
| 2. REWARD | (incentive salience) | dopamine 
                 dopamine receptors |
| 1. GENES | (vulnerability) | polymorphisms 
             epigenetic changes |
The Memory System

Hippocampus

Amygdala
• Key role in conditioned responding, especially fear
• Drives an impulsive, non-reflective response selection (decision-making)
• Active during craving
Addiction Neurochemical #2: Glutamate

• The most abundant neurochemical in the brain
• Critical in memory formation & consolidation
• All drugs of abuse and many addicting behaviors effect Glutamate which preserves drug memories and creates drug cues
• And ... glutamate is the neurochemical of "motivation" (it initiates drug seeking)
The hypofrontal/craving brain state represents an imbalance between 2 brain drives.

Amygdalar-Cortical Circuit
- “GO!”
- Impulsive
- Non-reflective
- Poorly conceived
- Socially inappropriate

Cortico-Striatal Circuit
- “DON’T GO!”
- Organized, Attentive
- Sensitive to consequences
- Well-planned
- Socially appropriate

THERE’S TOO MUCH OF THIS (Behavioral Impulsivity)
THERE’S TOO LITTLE OF THIS (Failure of Behavioral Inhibition)
Marc Lewis, PhD

the Biology of Desire
Why Addiction Is Not a Disease
Marc Lewis, PhD:
Addiction as a Developmental Stage

- Brain changes *per se* do not indicate pathology
- Plasticity and synaptic pruning (learning) are normal functions of the brain
- Addiction is a particularly deep form of learning
- Motivated repetition remolds the brain causing intense desire for drugs (craving), strong cues to repeat, over-valuation of drug, narrowing of focus,
- The very thing that got a person into addiction (plasticity) can get them out (development past addiction into recovery)
- Getting to “core issues” is important
Glutamate “spillover”

- Enduring vulnerability to relapse due to recruitment of “corticofugal” GLU projections to striatum
- Excess GLU “spills” out of the synapse to bing to extrasynaptic GLU receptors
- Changes in synaptic plasticity leads to pathologic learning and memory
- Result: impairment of inhibition of drug seeking

Peter W. Kalivas, PhD
Department of Neurosciences
Medical University of South Carolina
GLU synaptic plasticity
Transcription Factor: ΔFosB

- Mediates the structural plasticity induced in the NAc by cocaine
- Changes in number, shape and size of dendritic spines of NAc DAD1R-expressing MSNs
- Larger changes in spine density with self-admin over experimenter-admin of cocaine
- Also induced by chronic consumption of natural rewards (sucrose, high fat foods, sex, wheel running)
- “ΔFosB is both necessary and sufficient for many of the changes in the brain after chronic drug exposure”

Strategies to deal with the GLUTAMATE (MEMORY) component of addiction

- Prepare for triggers
- Avoid triggers as much as it is possible to do so (avoiding old places, playmates, etc)
- Self-talk in moments of craving (CBTx)
- Peers, behavioral barriers, frequent monitoring
- Medications
ASAM Definition: Relapse

- Persistent relapse / and risk thereof
- Even after periods of abstinence
- Triggered by:
  1. Re-exposure to drug itself (DA release in NAc)
     - drug-induced reinstatement
  2. Exposure to drug cues (GLU release in Amygdala/Hipp)
     - cue-induced reinstatement
  3. Exposure to Envir Stress (CRF release in Amygdala)
     - stress-induced reinstatement
Addiction is a disorder of ... 

5. 
4. STRESS (anti-reward system) HPA axis 
3. MEMORY (habits, cues) glutamate synaptic remodeling 
2. REWARD (incentive salience) dopamine dopamine receptors 
1. GENES (vulnerability) polymorphisms epigenetic changes
Childhood Trauma & Chronic Repeated Stress affect all 5 stages of SUD illness course

1. **INITIATION**: first time substance use & initial experimentation
2. **REGULAR USE**: shift from experimental to regular use
3. **ABUSE/DEPENDENCE**: escalation from regular substance use to abuse/dependence
4. **MOTIVATION TO QUIT**: behavioral & emotional control
5. **RELAPSE**: craving, negative affect

What counts as “Stress?”

- Any unpredictable or uncontrollable event that exceeds the regulatory capacity of the organism, and that threatens or could threaten and organism’s physical or psychosocial integrity.

- **Eustress:** healthy, “good” stress; perceived as a positive challenge, feelings of control/mastery, associated with meaning, hope and well-being; positive effect on healing and immunity.

- **Dystress:** “bad” stress; sustained arousal that goes unresolved; failing performance; increasing anxiety; cumulatively taxing; hysteresis.

Janos “Hans” Selye, PhD (1907-1982)
Hypothalamic-Pituitary-Adrenal (HPA) Axis

- Hypothalamus releases Corticotropin-Releasing Factor (CRF)
- CRF goes to Pituitary Gland to release ACTH (and ß-endorphin)
- Cortisol goes to Adrenal Glands to release Glucocorticoids and Cortisol
- Glucocorticoids and Cortisol mobilize the stress system
- Glucocorticoids feed-back to Hypothalamus to slow the release of CRF
Hedonic Allostasis Theory (Koob & LeMoal)

- With continued drug use and withdrawal, the “anti-reward” system is recruited to counterbalance excess Dopamine using the stress hormone CRF.
- Brain is unable to maintain normal “homeostasis.”
- So the brain reverts to “allostasis” - change of the hedonic “set point” under stress in an attempt to maintain stability.
- The result is anhedonia – an inability to find pleasure in normally pleasurable activities.
Stage 1 – Binge/Intoxication

Brain areas: Basal ganglia (VTA, NAc, DS)
Primary chemical: Dopamine
Primary process: Incentive Salience
Stage 1: Binge/Intoxication
consumption of intoxicating substance/experience of pleasurable effects
Stage 1 – Binge/Intoxication
Brain areas: Basal ganglia (VTA, NAc, DS)
Primary chemical: Dopamine
Primary process: Incentive Salience

Stage 2 – Withdrawal/Negative Affect
Brain areas: Extended Amygdala (BNST, CeA, Nas)
Primary chemicals: CRF, Dynorphin
Primary process: Reward deficit/Stress surfeit
Stage 2: Withdrawal/Negative Affect

negative emotional state in absence of substance
HPA Axis
CHRONIC, SEVERE STRESS = $\uparrow$ CRF

and $\uparrow$ CRF = $\downarrow$ DAD2 receptors

and $\downarrow$ DAD2 receptors = Anhedonia

Anhedonia: Pleasure “deafness”

(the patient is no longer able to derive normal pleasure from those things that have been pleasurable in the past)
Functionally...

Dopamine D2 Receptors are Decreased by Addiction

Cocaine

Meth

Alcohol

Heroin

Control

Addicted
Drugs cause Dopamine Surges in the midbrain reward system
Strategies to deal with the STRESS component of addiction

- Safe housing
- Recognize unconscious aspects of relapse
- Ritualistic, daily (hourly) stress management activities
- Supportive peers
- Medication (alpha- and beta-blockade)
- Minimize social dominance
Childhood Trauma & Chronic Repeated Stress affect all 5 stages of SUD illness course

1. **INITIATION:** first time substance use & initial experimentation
2. **REGULAR USE:** shift from experimental to regular use
3. **ABUSE/DEPENDENCE:** escalation from regular substance use to abuse/dependence
4. **MOTIVATION TO QUIT:** behavioral & emotional control
5. **RELAPSE:** craving, negative affect

KEY FINDINGS

In California, 61.7% of adults have experienced at least one ACE and one in six, or 16.7%, have experienced four or more ACEs. The most common ACE among California adults is emotional (or verbal) abuse.

Most common ACEs among California Adults

- 34.9% Emotional (or verbal) abuse
- 26.7% Parental separation or divorce
- 26.1% Substance abuse by household member
- 19.9% Physical abuse
- 17.5% Witness to domestic violence
- 15.0% Household member with mental illness
- 11.4% Sexual abuse
- 9.3% Neglect
- 6.8% Incarcerated household member

Prevalence of number of ACEs among California adults
Vietnam Vets Study (Robins, 1975)

- High prevalence of heroin use in US soldiers in Vietnam
- On returning to the US, they did not continue heroin use
- Drug use was situational
- Argument against addiction being a disease
Gene Heyman, PhD

- Addiction is not a chronic disease
- Most addicts do stop on their own, without treatment, and do not display relapse chronicity
- Remission ("maturing out") is the rule, not the exception
- Addicts do not need lifelong treatment
- Remission rates lower for legal drugs than illegal drugs
What if we deal only with individuals at risk?

FIGURE 5. Schematic representation of the number of people in the New York City metropolitan area who were directly affected by the September 11, 2001, attacks, those who were not, and the number of cases of PTSD in each group in the first 6 months after September 11th.

PTSD=posttraumatic stress disorder.

TOWARD RESILIENCE

TRAUMA

RESILIENCE is one path among many!

90% PEOPLE EXPERIENCE TRAUMA in their LIVES

GENES

STOCHASTICITY (RANDOMNESS)

COMMUNITY

SHIFT THE CURVE!
Longitudinal Approach to Study Drug Use over Time

Life-course Drug Use Career

- Protective Factor: e.g. family support
  - Protective Factor: occurrence of positive life events, e.g. got married, got employed

- Risk Factors: e.g. crime involvement

Estimated trajectory of Drug use

Trajectories of drug use are heterogeneous among individuals and can be classified as several distinctive trajectory groups

Age

Age
Stage 3: Preoccupation/Anticipation

Drug seeking after a period of abstinence
Stage 1 – Binge/Intoxication
Brain areas: Basal ganglia (VTA, NAc, DS)
Primary chemical: Dopamine
Primary process: Incentive Salience

Stage 2 – Withdrawal/Negative Affect
Brain areas: Extended Amygdala (BNST, CeA, Nas)
Primary chemicals: CRF, Dynorphin
Primary process: Reward deficit/Stress surfeit

Stage 3 – Preoccupation/Intoxication
Brain areas: Prefrontal Cortex
Primary chemical: Glutamate
Primary process: Executive function deficits
Addiction is a disorder of ...
Correlations Between D2 Receptors in Striatum and Brain Glucose Metabolism

Cocaine Abusers

OFC

DA D2 Receptors (Ratio Index)

METH Abusers

OFC

DA D2 Receptors (Bmax/kd)
damage to Orbitofrontal Cortex (OFC)

- Causes a loss of a crucial behavioral guidance system
- Responses are impulsive and inappropriate
- Deficits of self-regulation
- Inability to properly assign value to rewards (such as money vs. drugs)
- Tendency to choose small & immediate rewards over larger but delayed rewards
**damage to** Anterior Cingulate Cortex (ACC)

- Just as with OFC damage: causes a loss of a crucial behavioral guidance system
- Inflexibility/Inability to respond to errors in the past with regard to rewards/punishments
- Deficits in social responding due to decreased awareness of social cues
**damage to** Prefrontal Cortex (PFC)

- **FAILURE OF EXECUTIVE FUNCTIONING**
  - Premature, unduly risky, poorly conceived actions
  - Rapid, impulsive responses without reflection or premeditation
  - Urgency
  - Sensation seeking
  - Expressed emotions inappropriate to the situation
  - Deficits in attention
  - Lack of perseverance
  - Insensitivity to consequences
Strategies to deal with the FRONTAL CORTEX (CHOICE) component of addiction

- Medical/craving/psychiatric stabilization
- Abstinence
- Peer support (small, single-gender, long-term)
- Agency-building exercises
- Service work, working with newcomers
- Purposeful, meaningful goals
- Subject > Object
ASAM Addiction Definition (Aug 2011)

A stress-induced (HPA axis), genetically-mediated (polymorphisms, epigenetic mechs.) primary, chronic and relapsing brain disease of reward (nucleus accumbens), memory (hippocampus & amygdala), motivation and related circuitry (ACC, basal forebrain) that alters motivational hierarchies such that addictive behaviors supplant healthy, self-care behaviors.
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