The most evil disease imaginable …

- Wouldn’t look like a “disease” at all
- Genetic, but with variable penetrance (genotype ≠ phenotype)
- Repulsive symptoms easily confused with “willful badness”
- Self-deception as a clinical feature
- Poor prognosis in many, but most will get better
- Chronic and relapsing condition (not acute, rarely “cured”)
- Culturally & politically divisive (would tap into society’s deepest prejudices, stigma, superstitions and attack its core values)
- Would only submit to “weird” solutions: peer support, patient accountability, personal evaluation, and spiritual growth (not just a medication or surgery)
Leading Causes of Death

1. Heart Disease
2. Cancer
3. Chronic Lower Pulmonary Disease
4. Hypertension/Stroke
5. Accidents
10. Suicide
12. Liver Disease/Cirrhosis

Big Questions

• How does heredity fit in?
• Why do addicts put drugs over things that really matter?
• How do we define addiction? (Who is an addict?)
• Why do addicts relapse?
• What is the primary cause of addiction?
• Where did the child/spouse/friend/employee that I love/value go?
Is Addiction Really a “Disease?”
“Choice” vs. “Disease”

- Free Will exists
- Responsibility
- Can stop
- Punishment and Coercion DO work
- BEHAVIORS

- No Free Will
- No Responsibility
- Can’t stop
- Punishment and Coercion DON’T work
- SYMPTOMS
The Prosecutors Challenges

1. The Outrage Argument
   How dare you call addiction a “disease” – addicts are liars, cheats and thieves

2. The Disease Nosology Argument
   Pedophiles have a disease – they suffer from pedophilia

3. The “Punishment Works” Argument
   Most people quit when the consequences get bad enough

4. The Accountability Argument
   What’s to keep the addict from running to “disease” as an excuse for bad behavior?

5. The “First Choice” Argument
   The addict never should have taken that first drug/drink

6. The Problem of Evil Argument
   You’re just trying to explain away bad behavior
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
- Risk Taking
- Novelty-seeking
- Impulsivity
- Empathy/Narcissism
- Memory/Stress/Trauma
- Social Status
Ways to define “Disease”

- By “fiat”
- Normative
- Biostatistical

- **Pathophysiological** a disease is a cellular defect in an organ or organ system that leads to observable, measurable signs and symptoms
The “Disease Model”
Organ → Defect → Symptoms
Femur → Fracture
Pancreas → Islet Cell Death
   No Insulin
       2. Blurred Vision
       3. Coma
       4. etc.
       1. Screaming
       2. Bleeding
       3. Deformity
       4. Disability
If ever we could fit addiction into this model, then it would win admission into "The Disease Club".
And now, we finally can ...
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 fits the “Disease Model!”
Environment
- Pathogens
- Chemicals
- Smoking
- Diet
- Sun exposure

Epigenetic, post-genomic and regulatory events
- Gene rearrangements
- Messenger RNA splicing and/or editing
- Retroviral sequences
- Methylation
- MicroRNAs

Genome allelic variants
- Single nucleotide polymorphisms
- Copy number variation
- Insertion/deletion polymorphisms
- Disease modifier genes
- Disease susceptibility genes
Addiction is a disorder of ... 

5. ... CHOICE  (motivation)
4. ... STRESS  (anti-reward system)
3. ... MEMORY  (learning)
2. ... REWARD  (hedonic system)
1. ... GENES  (vulnerability)
Five Theories of Addiction

5. Pathology of Motivation and Choice (Kalivas & Volkow)
4. Stress and Allostasis (Koob & LeMoal)
3. Pathology of Learning & Memory (Hyman, Everitt & Robbins)
2. Incentive-sensitization of Reward (Robinson & Berridge)
1. Genetic Vulnerability (Schuckit et al)
“Blindsight”

- Occurs in normally sighted people who sustain brain damage to the higher visual processing areas.
- Their experience is “blindness”.
- Yet they can “see things” (kind of).
- They can reliably guess which direction a stimulus is moving.
- Reason: lower visual processing areas in the brain are still intact.
“Blindsight”

Reminds us of two features of the brain:

1. That much of brain processing is outside our awareness of it (it is “unconscious”)

AND

2. Conscious experiences are “constructs” (different levels of brain processing coming together and experienced as a unified “whole”)
Consciousness

- A “layered construct”
- Different levels of brain processing take place in different areas of the brain are assembled into a unified conscious experience
- Conscious awareness increases with increasing neural complexity (i.e. as you go up the evolutionary chain and get more complex brains, you get greater levels of consciousness/awareness)
- In brain disease states, the “constructs” the brain creates can become unraveled
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
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*
Individual characteristics that predict high vulnerability to drug-seeking behavior

- High stress reactivity
- High novelty-induced locomotor activity
- High novelty-seeking
- High trait impulsivity
Conditions associated with deficits in impulsive control

- Adolescence
- Alcohol use disorders
- Substance abuse
- ADHD
- Conduct disorder / Anti-social personality disorder
- Depression
Addiction is a disorder of ...

5.

4.

3.

2.

1. ... GENES (vulnerability)
Genetic Vulnerability vs Resilience

- Genetic differences determine "low responders" vs. "high responders" to the effects of alcohol (low responders are more likely to become alcoholics).
- There are genetic differences in how people respond to methylphenidate (Ritalin) injections (some like it, some don't care) implying different vulnerabilities.
- For addicts, drugs really do "feel" different than they do to non-addicts.

Mark Schuckit, MD
U.C. San Diego
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
Epigenetics

- Modifications (DNA methylation, Histone acetylation) that affect 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
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.
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.
ACE reduction reliably predicts simultaneous decrease in all of these conditions.

Population attributable risk

MAGNITUDE OF THE SOLUTION
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 (hedonic system)
1. GENES (vulnerability)
Midbrain

- Associated with vision, hearing, motor control, sleep/wake cycle, arousal, temperature regulation, and reward
- Tectum
  - Inf & Sup Colliculi
- Tegmentum
  - Ventral Tegmental Area
  - PAG, Red Nucleus, RF, SN
- Cerebral Peduncles
Midbrain Pathways

**Mesolimbic Pathway**
VTA $\rightarrow$ NA $\rightarrow$ PFC/ACC/OFC

**Mesocortical Pathway**
VTA $\rightarrow$ NA $\rightarrow$ PFC/Insular Ctx

**Mesostriatal Pathway**
SN/VTA $\rightarrow$ Striatum/Extended

**Amygdala**

**Mesodiencephalic Pathway**
VTA $\rightarrow$ thalamus/hypothalamus

**Mesorhombencephalic Pathway**
VTA $\rightarrow$ PAG/Reticular Formation
Striatum

- Planning & modulating movement pathways
- Activated by aversive and rewarding stimuli, novel and intense stimuli, and cues for such stimuli
- Dorsal Striatum
  - Caudate
  - Putamen
- Ventral Striatum
  - Nucleus accumbens
James Olds, PhD (1922 - 1976)

• Discovery of the reward system in the midbrain
• Mice will avidly self-administer electric currents to the Septal Areas
• They prefer the electrical stimulation over other survival rewards such as food

Olds and Milner: *Mice self-administer electric stimulation to the septal areas of the brain*

**NEW #1: DRUG!!**

2. **EAT !!**
3. **KILL !! (defend)**
4. **SEX !!**
Olds and Milner: Mice self-administer electric stimulation to the septal areas of the brain

• To the exclusion of all other survival behaviors
• To the point of death
Mice can get addicted to drugs!
Mice get addicted to drugs, but …

• Mice don’t weigh moral consequences
• Mice don’t consult their “Mouse God”
• Mice aren’t sociopaths
• Mice don’t have bad parents
• There are no “Mice Gangs”
Addiction: the manipulation of a DA-releasing chemical or behavior to cope with stress

NEW #1: DRUG!!

2. EAT !!
3. KILL !! (defend)
4. SEX !!

1. Hyperprioritization (Drug = Survival)
2. .
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 salience (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”.
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
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

The Full Spectrum of Addiction

- Alcohol & Sedative/Hypnotics
- Opiates/Opioids
- Cocaine
- Amphetamines
- Entactogens (MDMA)
- Entheogens/Hallucinogens
- Dissociants (PCP, Ketamine)
- Cannabinoids
- Inhalants
- Nicotine
- Caffeine
- Anabolic-Androgenic Steroids
- Food (Bulimia & Binge Eating)
- Sex
- Relationships
- Other People
  (“Codependency,” Control)
- Gambling
- Cults
- Performance
  (“Work-aholism”)
- Collection/Accumulation
  (“Shop-aholism”)
- Rage/Violence
- Media/Entertainment
Functionally…

Dopamine D2 Receptors are Decreased by Addiction

Cocaine
Meth
Alcohol
Heroin

Control
Addicted

DA D2 Receptor Availability
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
Relapse

• Three things that are known to evoke relapse in humans:
  1. Brief exposure to drug itself (DA release in NAc)
    drug-induced reinstatement
  2.
  3.
Old definition of “addiction”
Addiction: the manipulation of a DA-releasing chemical or behavior to cope with stress

NEW #1: DRUG!!

2. EAT !!
3. KILL !! (defend)
4. SEX !!

1. Hyperprioritization (Drug = Survival)
2.  
A line is crossed …

NON-ADDICT  ADDICT

(non-user)  (experimenter)  (user)  (abuser)

DRUG = DRUG  DRUG = SURVIVAL
**DSM-IV Criteria for Substance Abuse**

- **RECURRENT SUBSTANCE USE** leading to failure to fulfill major role obligations (work, school, home)
- **RECURRENT SUBSTANCE USE** in physically hazardous situations (impaired driving, operating machinery, in the work place)
- **RECURRENT SUBSTANCE USE** with related legal problems
- **CONTINUED SUBSTANCE USE** despite social/interpersonal conflict
- Person has never before met the criteria for Substance Dependence
DSM-IV Criteria for Substance Dependence
(I’M A TOWN DRUNK)

- INABILITY (to cut down)
- MORE DRUG USED (than intended)
- A LOT OF TIME (spent obtaining, using & recovering from using the drug)
- TOLERANCE
- OLD ACTIVITIES, FRIENDS & FAMILY MEMBERS (given up in favor of the drug)
- WITHDRAWAL
- NEGATIVE CONSEQUENCES (have no effect on the pattern of drug use)
A spectrum of diagnosis ...

NON-ADDICT \(\rightarrow\) ABUSER \(\rightarrow\) ADDICT

(non-user) \(\rightarrow\) (heavy user) \(\rightarrow\) (abuser)

DRUG = DRUG
DRUG = VITAL
DRUG = SURVIVAL
DSM-5 Criteria for “Substance Use Disorder”
“FLIP A SWITCH” (2 or more in the last year)

- **FAILURE TO FULFILL** (major work, school, & home obligations due to drug use)
- **LARGER AMOUNTS** (of drug used over) **LONGER PERIODS** (than intended)
- **INABILITY** (to cut down or control drug use)
- **PHYSICAL & PSYCHOLOGICAL PROBLEMS** (due to drug does not curtail use)
- **A LOT OF TIME** (spent obtaining, using & recovering from drug use)
- **SOCIAL & INTERPERSONAL PROBLEMS** (due to drug does not curtail use)
- **WITHDRAWAL**
- **IMPORTANT ACTIVITIES** (are given up in favor of the drug)
- **TOLERANCE**
- **CRAVING**
- **HAZARDOUS** (situations occur involving drug use)
Relapse

Three things that are known to evoke relapse in humans:

1. Brief exposure to drug itself (DA release in NAc) - drug-induced reinstatement
2. Exposure to drug cues (GLU release in bAmyg/Hipp) - cue-induced reinstatement
3. 
Addiction is a disorder of …

5.
4.
3. … MEMORY (learning)
2. … REWARD (hedonic system)
1. … GENES (vulnerability)
The Memory System

Hippocampus

Amygdala
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)
<table>
<thead>
<tr>
<th><strong>DOPAMINE (DA)</strong></th>
<th><strong>GLUTAMATE (Glu)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• All drugs of abuse and potential compulsive behaviors INCREASE DA</td>
<td>• All drugs of abuse and potential compulsive behaviors EFFECT Glu</td>
</tr>
<tr>
<td>• Reward salience</td>
<td>• Drug memories &amp; seeking</td>
</tr>
<tr>
<td>• “this is important!”</td>
<td>• “OK, I’ll remember”</td>
</tr>
<tr>
<td>• “I really want this!”</td>
<td>• “Fine, go and get it”</td>
</tr>
<tr>
<td>• Rostral (toward the nose) projections:</td>
<td>• Caudal (toward the tail) projections:</td>
</tr>
<tr>
<td>• PFC &lt; NA &lt; VTA</td>
<td>• PFC &gt; NA</td>
</tr>
</tbody>
</table>
The hypofrontal/craving brain state represents an imbalance between 2 brain drives.

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

THERE’S TOO MUCH OF THIS

**Cortico-Striatal Circuit**
- “NOT GO!”
- Organized, Attentive
- Sensitive to consequences
- Well-planned
- Socially appropriate

THERE’S TOO LITTLE OF THIS
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
Relapse

• Three things that are known to evoke relapse in humans:
  
  1. Brief exposure to drug itself (DA release)
     drug-induced reinstatement
  
  2. Exposure to drug cues (GLU release in bAmyg/Hipp)
     cue-induced reinstatement
  
  3. Stress (CRF release in CeAmyg & BNST)
     stress-induced reinstatement
Addiction is a disorder of ... 

5.  
4.  ... STRESS (anti-reward system) 
3.  ... MEMORY (learning) 
2.  ... REWARD (hedonic system) 
1.  ... GENES (vulnerability)
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
HPA Axis

- Hypothalamus
  - CRH (Corticotropin Releasing Hormone)
  - Corticotropin Releasing Hormone

- Anterior Pituitary
  - ACTH (Adrenocorticotropic Hormone)
  - Adrenocorticotropic Hormone

- Adrenal Cortex
  - CORT
  - Negative Feedback
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)
Drugs cause Dopamine Surges in the midbrain reward system
Addiction: the manipulation of a DA-releasing chemical or behavior to cope with stress

NEW #1: DRUG!!

2. EAT !!
3. KILL !! (defend)
4. SEX !!

1. Hyperprioritization (Drug = Survival)
2. Utility (Drug = Stress Coping)
George Koob, PhD
Chair, Neurobiology of Addictive Disorders
Scripps Neurosciences Institute
Hedonic Allostasis Theory (Koob & LeMoal)

- With continued drug use and withdrawal, the “anti-reward” system is recruited to counter-balance excess Dopamine (with 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 a desperate attempt to maintain stability
- Current Rx/Tx focus: CRF1-antagonists as anti-craving drugs
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
- Racial and ethnic variables correlate with remission rates
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
Social dominance in monkeys: dopamine D₂ receptors and cocaine self-administration

Drake Morgan¹, Kathleen A. Grant¹, H. Donald Gage², Robert H. Mach¹,², Jay R. Kaplan³, Osric Prioleau¹, Susan H. Nader¹, Nancy Buchheimer², Richard L. Ehrenkauffer³ and Michael A. Nader¹,²

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Disruption of the dopaminergic system has been implicated in the etiology of many pathological conditions, including drug addiction. Here we used positron emission tomography (PET) imaging to study brain dopaminergic function in individually housed and in socially housed cynomolgus macaques (n = 20). Whereas the monkeys did not differ during individual housing, social housing increased the amount or availability of dopamine D₂ receptors in dominant monkeys and produced no change in subordinate monkeys. These neurobiological changes had an important behavioral influence as demonstrated by the finding that cocaine functioned as a reinforcer in subordinate but not dominant monkeys. These data demonstrate that alterations in an organism’s environment can produce profound biological changes that have important behavioral associations, including vulnerability to cocaine addiction.
• Dominant and Submissive monkeys (i.e. monkeys exposed to social defeat) have differences in DAD2 receptors
• If offered cocaine, dominant monkeys are less likely to acquire regular self-administration
• But submissive monkeys acquire cocaine self-administration rapidly …
• … and cocaine reinstatement occurs quickly in submissive monkeys if exposed to social defeat stress (they relapse immediately - even in the absence of physical stress)
• SDS is an example of “loss of agency” dys-stress
• Question: Is socially dominating “treatment” inviting relapse?
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
Now that the midbrain has found what securing survival …

… how does it motivate the individual to repeat that behavior?
Craving / Drug Seeking

- Not quite as conscious as deliberative acts
- More automatic - like driving a car home from work without really thinking about it
- “I was vaguely aware that what I was doing was not too smart”
- “There I was again with a drink in my hand thinking that this time things would be different”
Addiction is a disorder of ...

5. ... CHOICE (motivation)
4. ... STRESS (anti-reward system)
3. ... MEMORY (learning)
2. ... REWARD (hedonic system)
1. ... GENES (vulnerability)
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
“Both Steering and Brakes Fail”

Four circuits:

1. **Reward**
   Overvaluation of drug/decreased value of natural reinforcers

2. **Motivation/Drive**
   Immediate rewards > delayed gratification

3. **Memory**
   Hypersalience of drug-related cues

4. **Control**
   Impaired self-awareness, bodily awareness, problem recognition
disruptive to social relationships
Diminished social competence/cognition
Impaired behavioral inhibition / impulse control

• Bechara: research on pts with vmPFC & OFC lesions

• “Myopia for the future” - cognitive impulsiveness
  - these patients prefer immediate but disadvantageous rewards over rewards that are delayed but advantageous in the long run
  - their decisions are guided primarily by immediate prospects and are **insensitive** to positive or negative future consequences (rewards or punishments)
  - they deny or are unaware of their problem

• Scans of vmPFC patients are similar to Sub Abuse pts
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
ASAM Definition: more than reward …

- Addiction encompasses more than the neurochemistry of reward
- Frontal cortex & circuits of reward/motivation/memorY fundamental to altered impulse control, altered judgment and the dysfunctional pursuit of rewards (ex. drug use despite mounting negative consequences, inability to delay gratification and inhibit impulsivity)
ASAM Definition: Genetic Vulnerabilities vs. Resiliencies

• Genetic factors account for half of the likelihood that an individual will develop addiction
• Environmental factors interact with individual biology to affect influence of genetic factors
• Likewise, acquired resiliencies can affect extent to which genetic factors exert influence
• Culture matters in how genetic vulnerabilities become actualized
ASAM Definition: Motivational, Emotional & Perceptual components

- Presence of an underlying biological deficit of reward circuits (alters reward function & reward pursuit)
- Neuroadaptation in motivational circuitry leads to impaired control
- Cognitive & affective distortions impair perceptions and compromise emotional capacities > self-deception
- Exposure to trauma overwhelm individual coping
- Distortions in meaning, purpose and values, connection to self, others, transcendent concepts
ASAM Definition: Addiction is characterized by . . .

- Inability to consistently **ABSTAIN**
- Impairment in **BEHAVIORAL CONTROL**
- **CRAVING**
- **DIMINISHED RECOGNITION** of problems with one’s behavior and interpersonal relationships
- Dysfunctional **EMOTIONAL RESPONSE**
ASAM Definition: Relapse

- Persistent relapse / and risk thereof
- Even after periods of abstinence
- Triggered by:
  1. exposure to rewarding substances
  2. exposure to environmental cues
  3. emotional stressors
ASAM Definition: Relapse

- Power of external cues to trigger craving and drug use (relapse)
- Also: trigger engagement in other addictive behaviors
- **Hippocampus**: memory of previously euphoric (& dysphoric) experiences
- **Amygdala**: motivational concentration on selecting behaviors associated with past reward-related experiences
- Relapse is common but not inevitable
ASAM Definition: Self-Deception

- Significant impairment in executive functioning
- Problems with perception, learning, impulse control, compulsivity and judgment
- Low readiness to change despite concerns expressed by others
- Lack of appreciation of magnitude of problems and complications
- PUDNC: avolitional aspect of addiction
ASAM Addiction Definition (Aug 2011)

- Addiction is more than a behavioral disorder:
  1. Behavioral manifestations & complications
  2. Cognitive changes
  3. Emotional changes
ASAM Addiction Definition (Aug 2011)

1. BEHAVIORAL
   - Excessive use at higher frequencies & amounts than intended
   - Unsuccessful attempts at control
   - Excessive time lost
   - Adverse impact on social, occupational & interpersonal functioning
   - Continued use/engagement in addictive behaviors despite persistent or recurrent physical & psychological problems
   - Narrowing of behavioral repertoire
   - Lack of ability or readiness to take consistent, ameliorative action despite recognition of problems

2. COGNITIVE

3. EMOTIONAL
ASAM Addiction Definition (Aug 2011)

1. BEHAVIORAL

2. COGNITIVE
   - Preoccupation
   - Altered evaluations of relative benefits/detriments associated with drugs
   - Inaccurate belief that problems experienced in one’s life are attributable to other causes (rather than a predictable consequence of drug use)

3. EMOTIONAL
1. BEHAVIORAL
2. COGNITIVE
3. EMOTIONAL
   • Increased anxiety, irritability, dysphoria, emotional pain & mood lability
   • Increased sensitivity to stressors (due to recruitment of brain stress systems)
   • Difficulty in identifying feelings, distinguishing between feelings and bodily arousal, and describing feelings in other people (alexithymia)
References:


Dennis ML, Scott CK. Four-year outcomes from the early re-intervention (ERI) experiment using recovery management checkups (RMCs). Drug and Alcohol Dependence 121 (2012) 10-17.


