Neurobiology of Addiction and Recovery

R. Dewayne Book, M.D.
Medical Director
Fellowship Hall
Greensboro, North Carolina

Addiction

- Drug Addiction results from adaptations in specific brain neurons caused by repeated exposure to a drug of abuse.
Addiction

- These adaptations produce the behaviors that define an addicted state:
  - Dependence
  - Tolerance
  - Sensitization
  - Craving

How Common is Substance Use?

- As many as 85-90% of adults in U.S. use alcohol or other mood altering chemicals.
- What Percentage Are Addicted?
  - 10-12%
- What makes these people different?

Different Populations

<table>
<thead>
<tr>
<th>Population</th>
<th>Rate</th>
<th>Exposure Time</th>
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</thead>
<tbody>
<tr>
<td>Asian</td>
<td>1-3%</td>
<td>4-6K Years</td>
</tr>
<tr>
<td>U. S.</td>
<td>10-12%</td>
<td></td>
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<tr>
<td>Native American</td>
<td>50-80%</td>
<td>400 Years</td>
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Why such large differences in nationality?
What Accounts for this Difference?

- 50% of Asians lack one form of aldehyde dehydrogenase
  - Accumulation of acetaldehyde
  - Facial flushing
  - Tachycardia
  - Burning sensation in stomach
  - Severe headache

Electrophysiological Markers

- EEG in alcohol-naive sons of alcoholics shows:
  - Decreased p300
  - Decreased theta waves

Pre-Morbid Differences

- First time drinkers' report of the intensity of euphoria
- Family History Positive (FHP) report greater euphoria with alcohol exposure than Family History Negative (FHN)
Pre-Morbid Differences

- First time drinkers’ report of negative effects of acute alcohol exposure
- FHP report less negative effects than FHN
  - Less body sway, less nausea, less disorientation
  - Weaker warning system

What Are Genes?

- Genes are inherited chemical recipes for proteins.
- Genes tell cells how much of each protein is needed when and where and under what circumstances.

Genetic Influences in Addiction

- Family Studies show:
  - Children of alcoholics show 3-4 times increased risk of addiction
Genetic Influences in Addiction

- Twin Studies:
  - Male monozygotic: 60% concordance rate
  - Male dizygotic: 39% concordance rate

- Adoptions Studies:
  - Adoption Studies show that non-alcoholic adoptive parenting did not change risk of developing alcoholism
  - Sons of alcoholics are FOUR times more likely to be alcoholic than sons of non-alcoholics

How Organisms Work

- Neurons are pathways not physically connected.
- They communicate with chemical messengers.
- Neurons control: thoughts, moods, behavior, memory, emotion, sleep, aggression, desire, movement, etc.
Neurotransmitters are Proteins

- Neurotransmitters allow neurons to communicate with each other:
  - Dopamine – reward/stimulation
  - Serotonin – mood, sleep, appetite
  - GABA – sedative, anti-anxiety
  - Endorphins – natural pain killers
The “right” combination of neurotransmitters will lead to a sense of well being. A sense of unease might result from a lack of the “right” combination of neurotransmitters.
**Sense of Well-Being**

- If the genetic recipe is deficient in one or more of the neurotransmitters, then a neurotransmitter or “reward deficiency” syndrome may result.

**Addiction = Reward Deficiency Syndrome**

- A decrease of endogenous neurotransmitters leads to a sense of incompleteness, decreased pain tolerance, uneasiness, anxiety.
- A person genetically or environmentally programmed to have a neurotransmitter deficiency is at increased risk of finding “the answer” in a chemical of abuse.
Neurobiology of Addiction

- Chemicals are chosen to be abused based on their action on the brain:
  - Dopamine - reward/stimulation
  - Serotonin - natural antidepressant
  - GABA - sedative anti-anxiety
  - Endorphins - pain killers

- Substances of Abuse mimic the effects of natural neurotransmitters:
  - Cocaine/Amphetamine - dopamine
  - THC - serotonin
  - Benzodiazepine - GABA
  - Heroin/Opiates - endorphins, enkephalins
  - Alcohol - ALL

- The artificial release of dopamine occurs in levels never seen in nature.
- The brain tries to adapt by making the dopamine less effective (tolerance).
Once the cell has adapted, it becomes less responsive. The cells are now left with insufficient neurotransmitters to function. These changes drive the craving for more drug.

**Neurobiology of Addiction**

- Dopamine deprivation produces:
  - Chronic unpleasant feelings
  - Depression
  - Loss of motivation
  - The need to take the drug to feel better
  - Addicts now use just to feel "normal", not to feel high
Neurobiology of Addiction

- In humans, the amygdala is more important in craving. If people have a lesion in a section of the amygdala, they no longer link pleasure to its causes.

- Over-stimulation leads to down-regulation of D2 dopamine receptor.

- The degree of this reduction lessens over time but is still present a year and a half after withdrawal.

- Over-stimulation of a system leads to depletion.

- Addiction leads to decreased dopamine, which leads to more dysphoria, resulting in craving.

- NOW the Solution is the Problem!
Neurobiology of Addiction

- PET scans show that when addicts feel a craving, there is a high level of activation in a strip of areas ranging from the amygdala and the anterior cingulate to the tip of both temporal lobes (mesolimbic system).

- The highest risk of relapse for cocaine addicts is during the third and fourth week of abstinence.
- PET images show even lower levels of activity in the mesolimbic dopamine system during this time.
- The addict is almost back to normal after a year or so, but not completely.

Neurobiology of Addiction

- If addiction means the brain has changed, then the task is to change the brain back to normal.
- This doesn’t mean treatment has to be biological.
- Behavioral treatments can change the brain as well.
Neurobiology of Addiction

- One day there might be a drug specific neurochemical cocktail for each addictive drug that would break the cycle of craving.