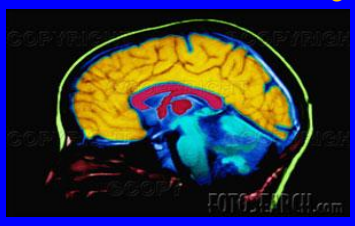
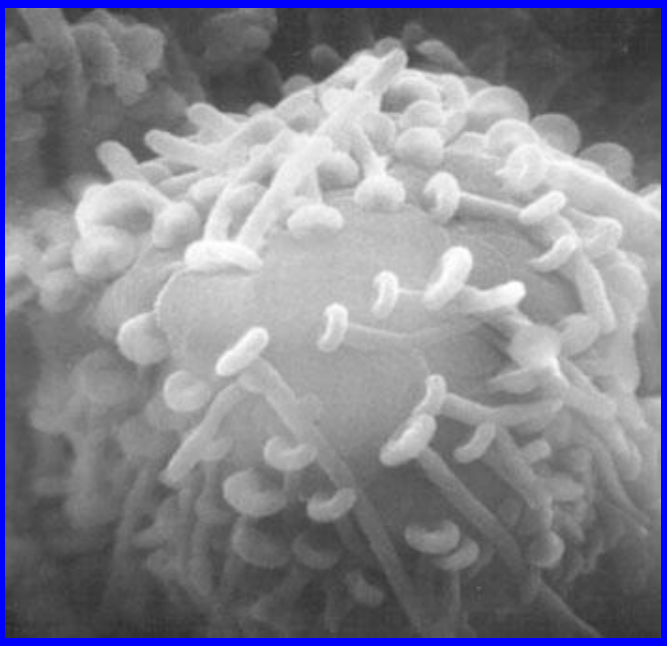
Neurobiology of Addiction and Recovery



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

Population	Rate	Exposure Time
Asian	1-3%	4-6K Years
U. S.	10-12%	
Native American	50-80%	400 Years

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

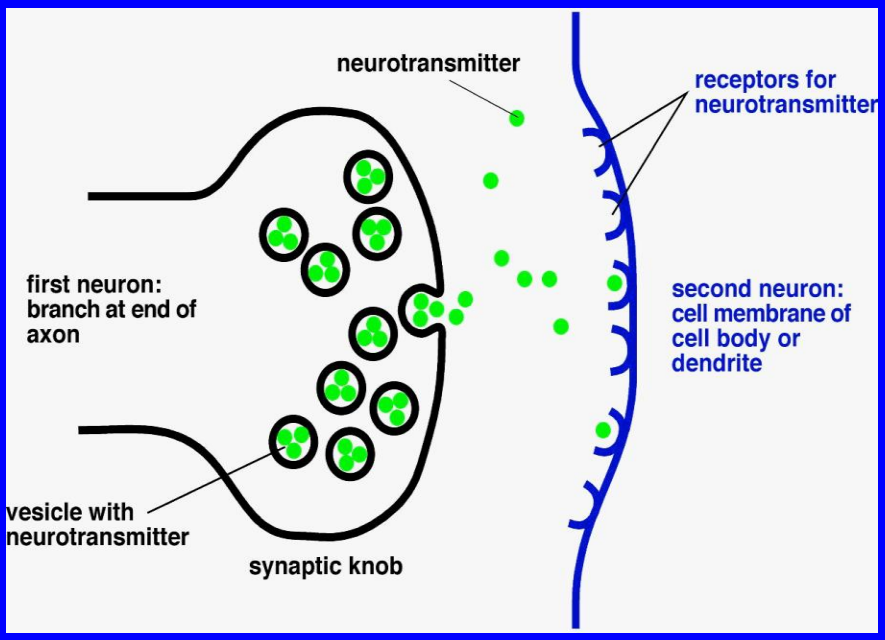
- Twin Studies:
  - Male monozygotic: 60% concordance rate
  - Male dizygotic: 39% concordance rate

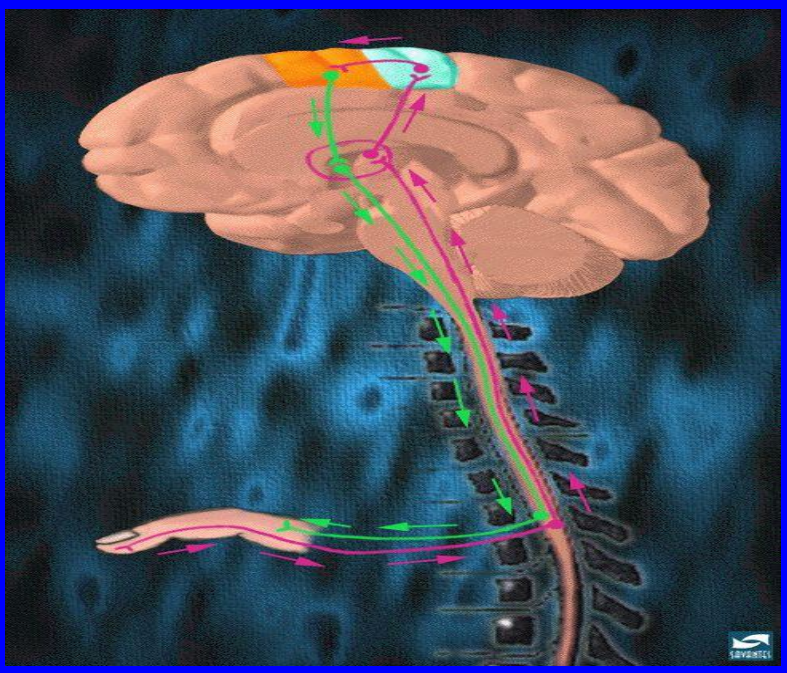
Genetic Influences in Addiction

- 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

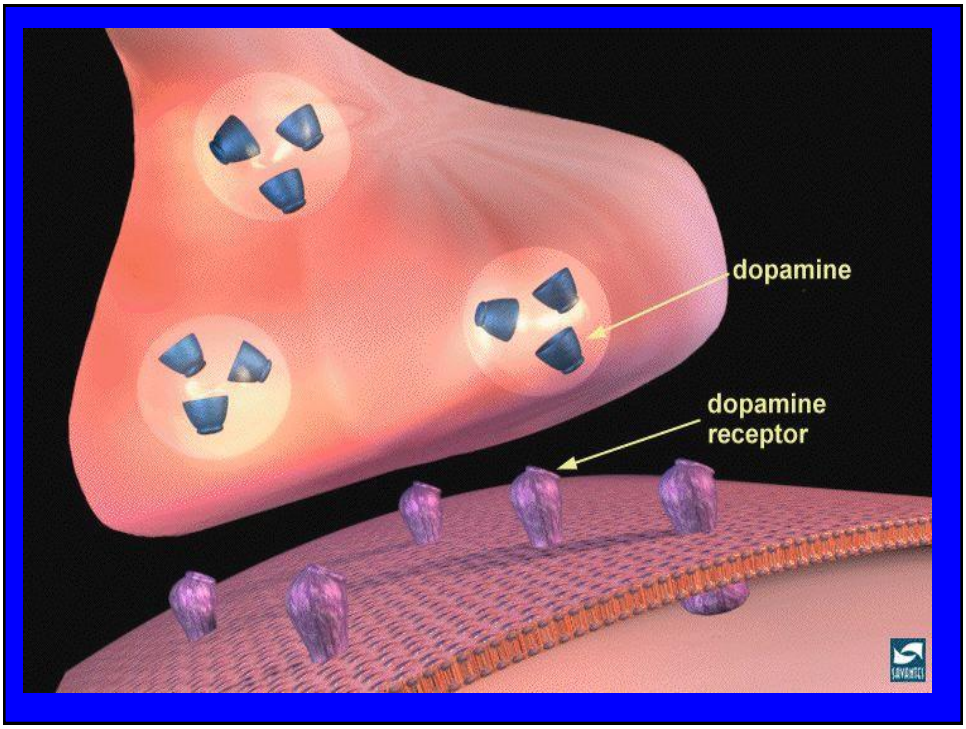
- Neurons are pathways not physically connected.
- They communicate with chemical messengers.
- Neurons control: thoughts, moods, behavior, memory, emotion, sleep, aggression, desire, movement, etc.

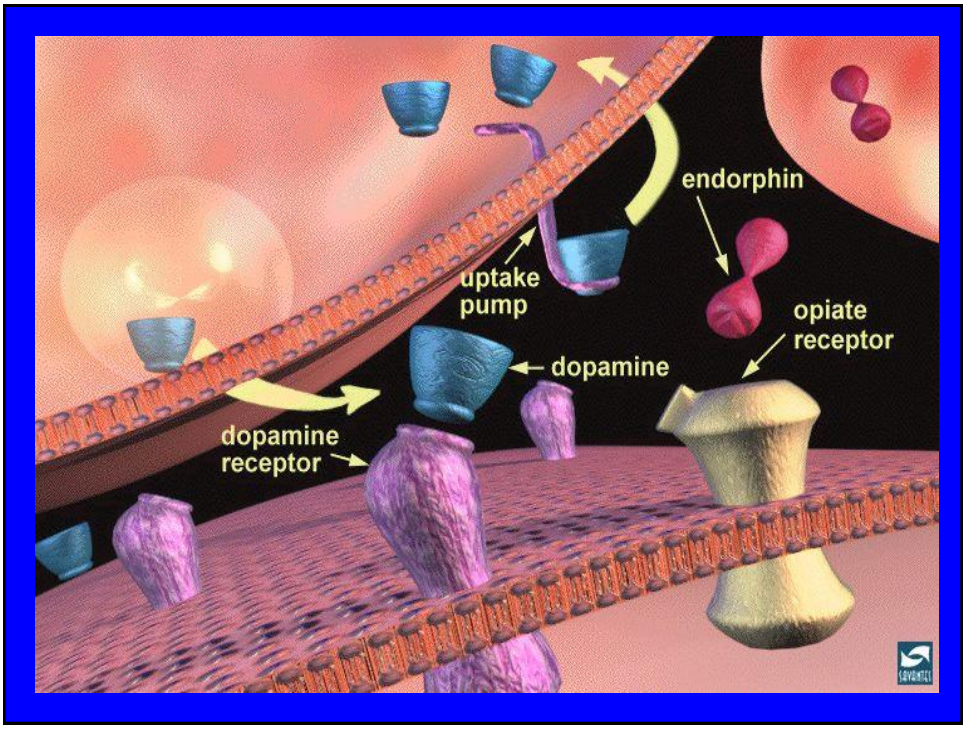




Neurotransmitters are Proteins

- Neurotransmitters allow neurons to communicate with each other:
  - Dopamine – reward/stimulation
  - Serotonin – mood, sleep, appetite
  - GABA – sedative, anti-anxiety
  - Endorphins – natural pain killers


dopamine
dopamine
receptor

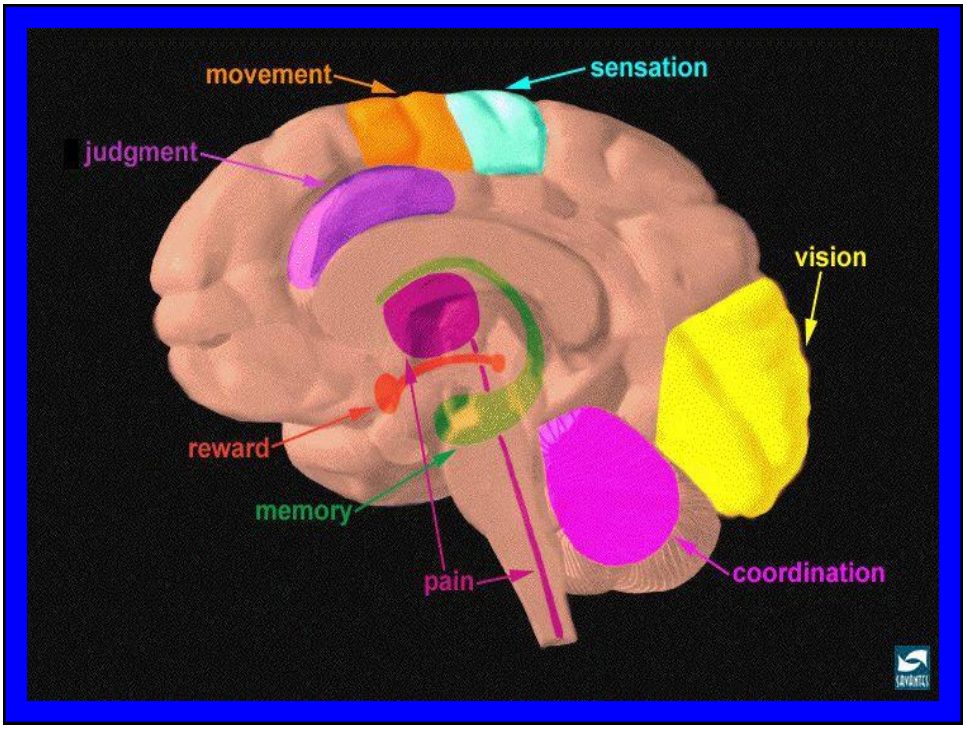

endorphin
uptake
pump
opiate
receptor
dopamine
dopamine
receptor

Sense of Well-Being

- 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

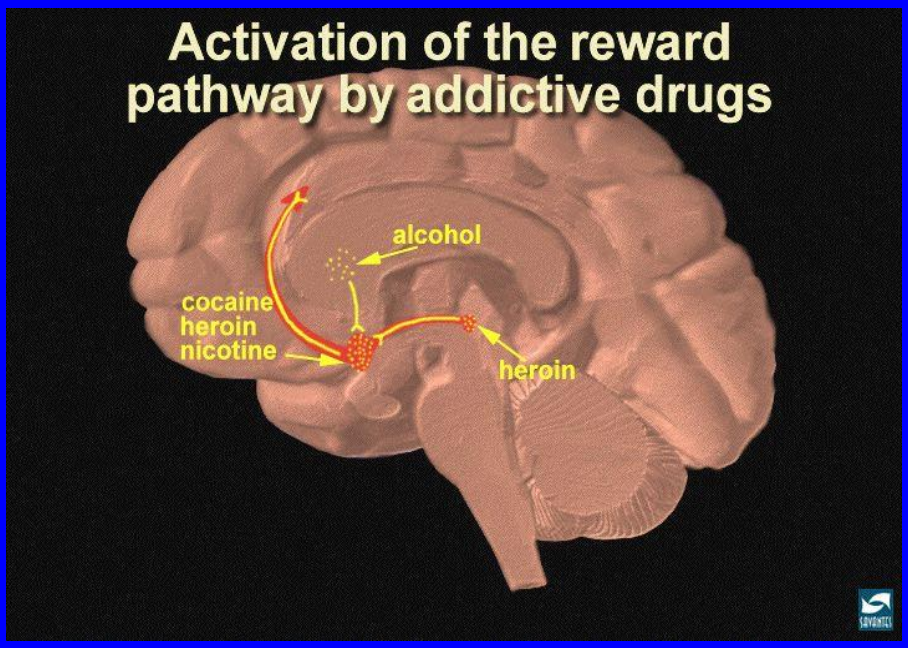
- Chemicals are chosen to be abused based on their action on the brain:
  - Dopamine - reward/stimulation
  - Serotonin - natural antidepressant
  - GABA - sedative anti-anxiety
  - Endorphins - pain killers

Neurobiology of Addiction

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

Neurobiology of Addiction

- The artificial release of dopamine occurs in levels never seen in nature.
- The brain tries to adapt by making the dopamine less effective (tolerance).



Neurobiology of Addiction

- 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.

Neurobiology of Addiction

- 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.

Neurobiology of Addiction

- 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).

Neurobiology of Addiction

- 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.