Drugs, The Brain, and Behavior

John Nyby

Department of Biological Sciences

Lehigh University

What is a drug?

Difficult to define

Know it when you see it

Neuroactive vs Non-Neuroactive drugs

Two major categories of neuroactive drugs:

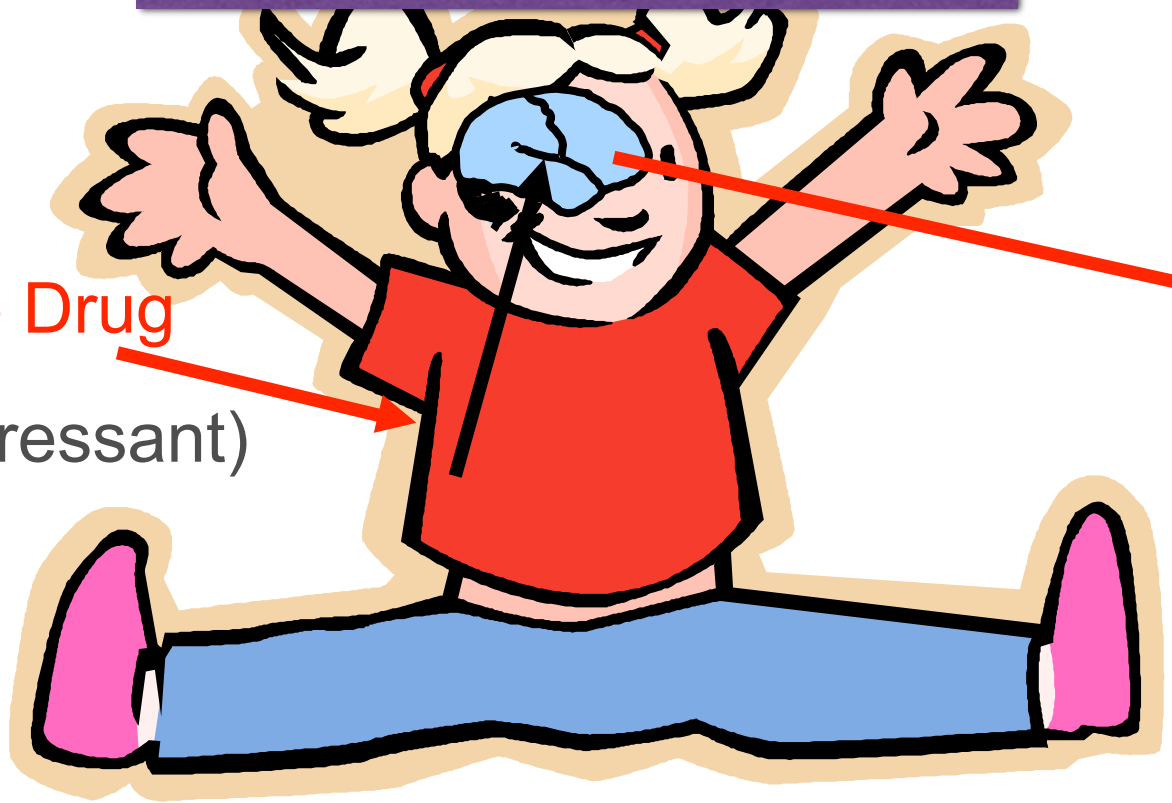
Therapeutic Drugs

Recreational Drugs (Drugs of Abuse)

Both types of neuroactive drugs affect neural functioning and behavior

How does a drug affect behavior

Neural Circuits Altered



Neuroactive Drug

(Antidepressant)

Behavioral Outcome

(Capable of positive emotions)

Different Levels at which drug effects in the brain can be studied

Molecular events → Cellular Events → Intercellular Events → Organismal Events

"Good" Therapeutic Drugs vs "Bad" Addictive drugs

No clear boundary!

Even the best therapeutic drugs have undesirable side effects

Many therapeutic drugs can be addictive and deadly (i.e. "bad") under the right circumstances

Which drug causes the most overdose deaths/year?

More overdose deaths/year from prescription opiates than heroin (5x) and cocaine (2x) combined

Two US Federal Agencies decide if a drug is good or bad

- Food and Drug Administration (FDA) decides if drug is therapeutic (i.e. good)
- Drug Enforcement Administration (DEA) decides whether a drug is illegal (i.e. bad).

A "bad" drug in the US can be a "good" drug in other countries

Neuroactive Drugs Work by Altering Chemical Signaling in the Brain

Two Classes of Chemical Signals in the brain

- Neurotransmitters
- Neurohormones

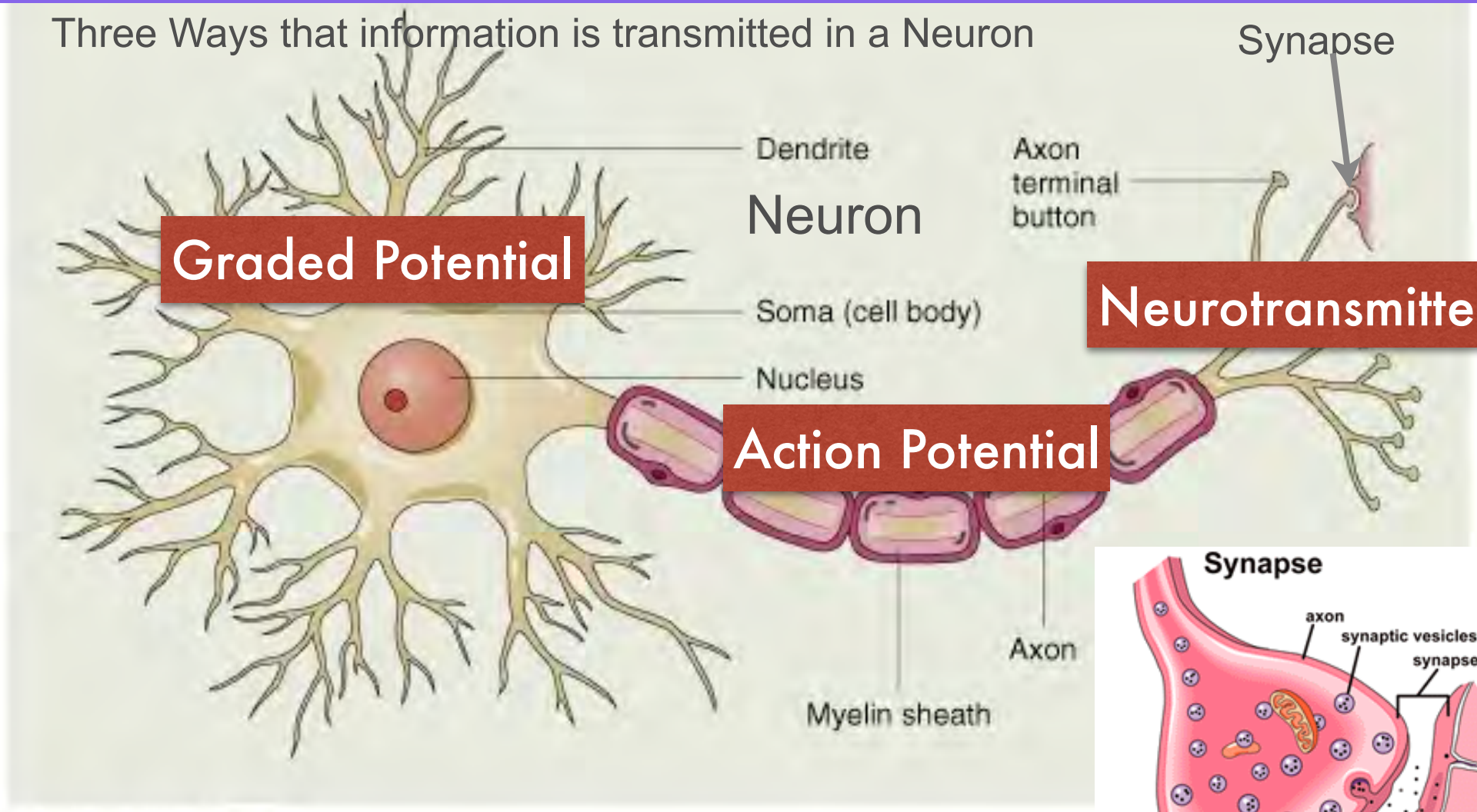
Two Ways a Drug Affects Neural Signaling

- Agonist for chemical signal
- Antagonist for chemical Signal

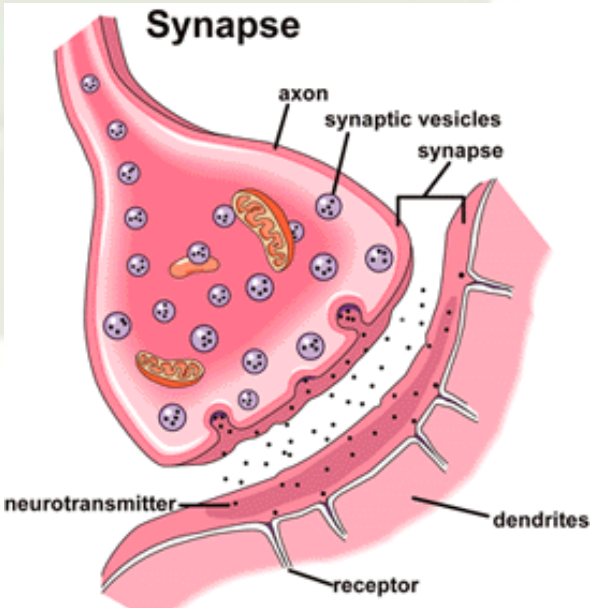
In order to understand drug action must have a good understanding of chemical signaling in brain

Neuronal communication

Three Ways that information is transmitted in a Neuron



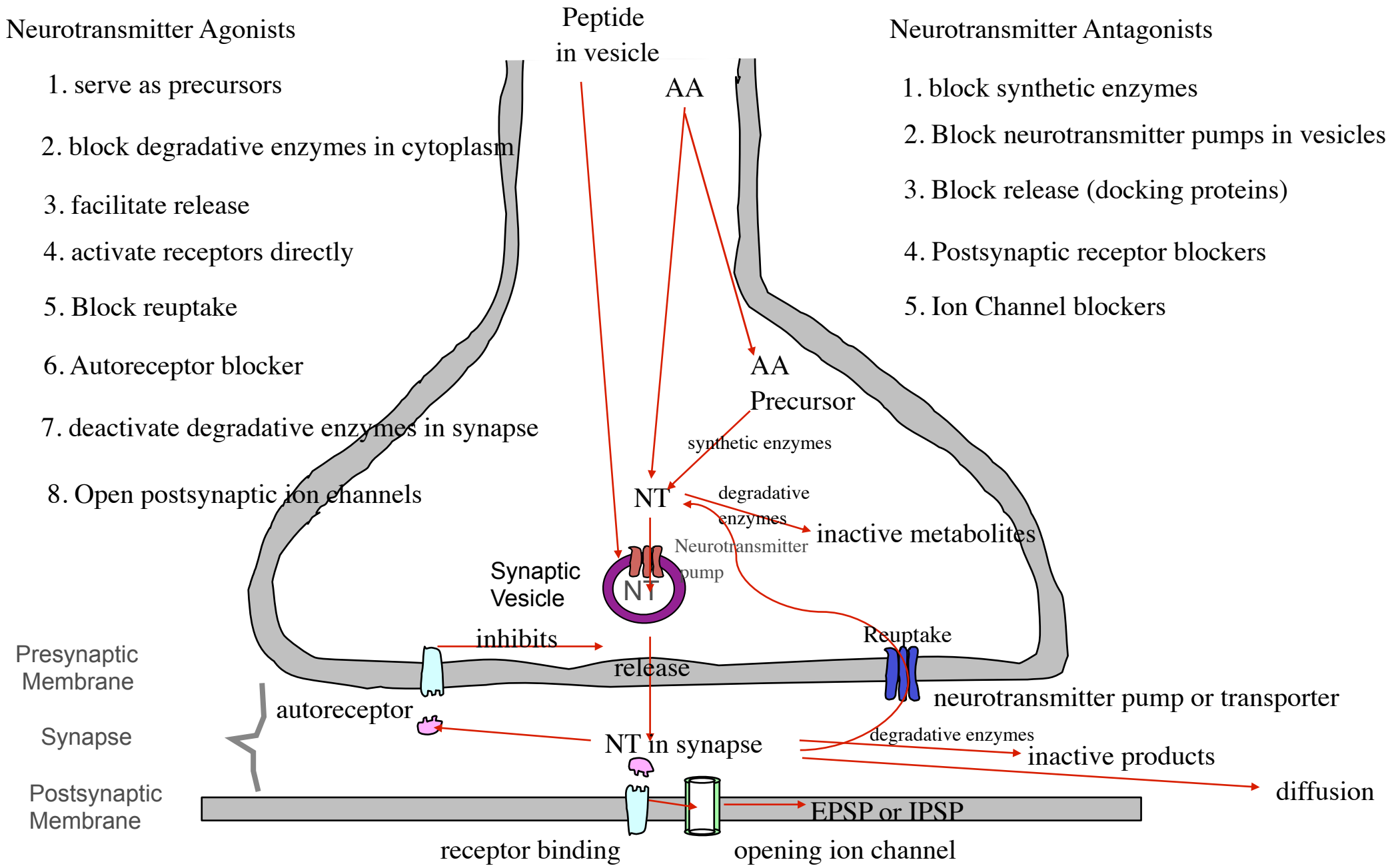
© 2000 John Wiley & Sons, Inc.



Most neuroactive drugs act by altering synaptic transmission

Generalized Synapse (Major Drug Events)

Most neurotransmitters are either AA's, modified AA's, or peptides



Why are Some Neuroactive Drugs Addictive?

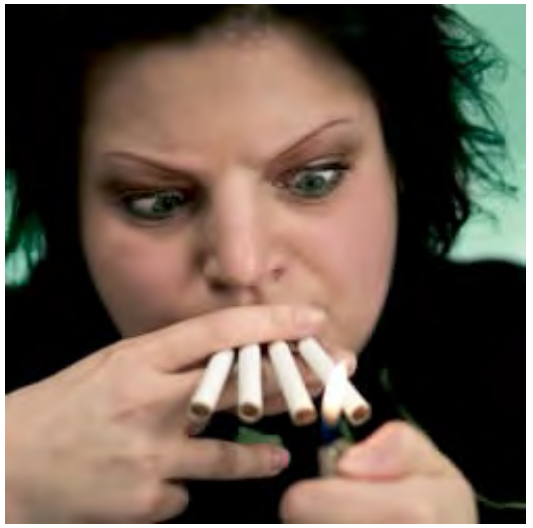
Hallmark of addiction is compulsive drug use

Older Model of Addiction

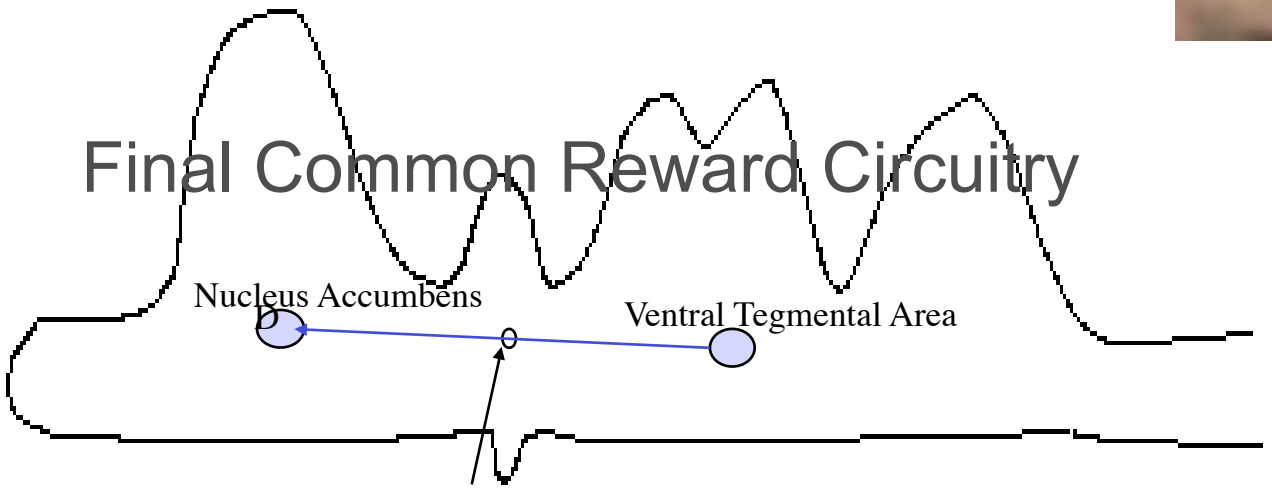
Tolerance and Withdrawal

Problem With Older Model

Newer Model of Addiction



Final Common Reward Circuitry



Tegmentostriatal branch of Mesolimbic/Mesocortical Pathway

Effects of Different Drugs of Abuse

Type of Drug	Major Synaptic Effects
Amphetamine, Methamphetamine	Promote DA release Inhibit Dopamine and NE Reuptake
Cocaine	Reverses Dopamine Reuptake Transporter
Heroin, Morphine,Codeine	Activate endogenous opiate receptors
Alcohol, Benzodiazepines & Barbiturates	$GABA_A$ agonist (allosteric modulators)
Caffeine	Blocks adenosine receptors
Nicotine	Activates Acetylcholine nicotinic receptors
Marijuana (THC)	Activates endogenous cannabinoid receptors

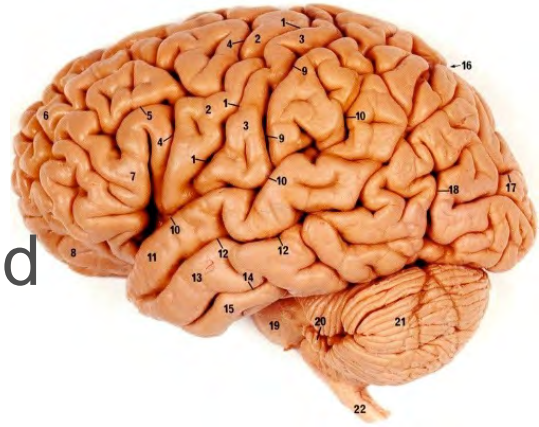
All Drugs of Abuse cause dopamine release in the nucleus accumbens!! (either directly or indirectly)

Some diseases treated with therapeutic drugs

Diseases are mainly diseases of **regional** modulatory neurotransmitters, defects in Glutamic Acid or GABA often fatal

Disorder	Neurotransmitter Malfunction	Problem	Drug Treatment
Schizophrenia	Dopamine	Receptor Hypersensitivity	Dopamine antagonists
ADHD or ADD	Dopamine	Receptor insensitivity	Dopamine agonists
Parkinson's Disease	Dopamine	Neuron Degeneration	Dopamine agonists
Depression	Serotonin/Norepinephrine	Receptor insensitivity	Serotonin/ Norepinephrine agonists
Obsessive/ Compulsive Disorder	Serotonin	Receptor insensitivity	Serotonin agonists
Manic/Depressive Disorder	Serotonin?	Receptor hypersensitivity?	Lithium
Alzheimer's Disease	Acetylcholine	Neuron Degeneration	Acetylcholine agonists

Learning More about Drug Effects in the Brain at Lehigh



Must first learn how Brain works

Bios 120: Biology Core III: Integrative and Comparative

Bios 276: Central Nervous System and Behavior

Bios 315: Neuropharmacology

Bios 366: Diseases of the Nervous System

Most students taking these courses major in BNS, Biology, Molecular Biology, or Biochemistry

Any Questions?