

# 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

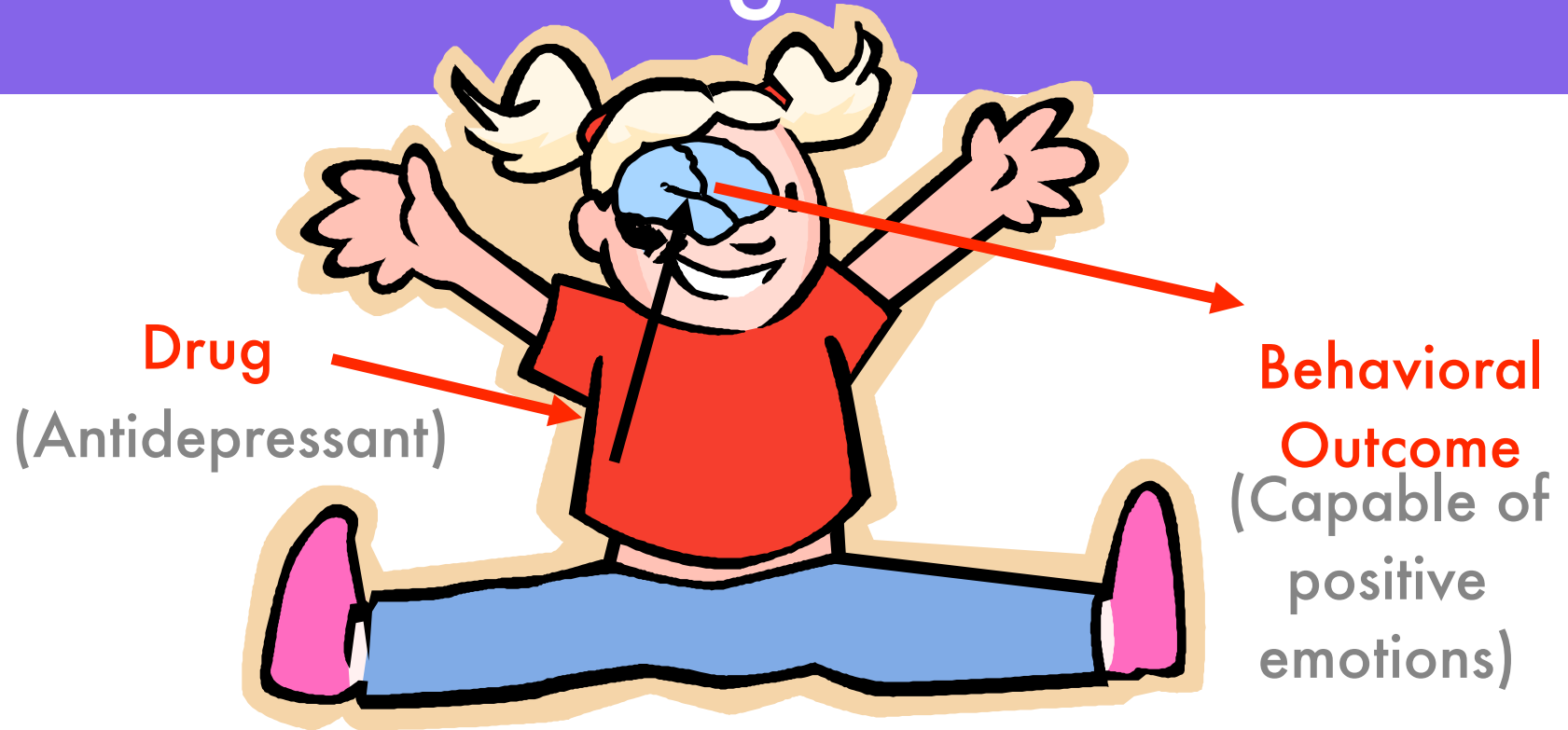
Two major types of neuroactive drugs:

Psychotherapeutic Drugs

Drugs of Abuse

Both types of drugs affect behavior

# How does a drug affect behavior



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

Molecular  
events



Cellular  
Events



Organismal  
Events

# “Good” Therapeutic Drugs vs “Bad” Addictive drugs

No clear boundary!

All “good” drugs have undesirable side effects

Many “good” drugs can be addictive (i.e. “bad”) under the right circumstances (i.e. Rush Limbaugh and oxycontin)

How does Drug Enforcement Administration (DEA) decide whether a drug is a “good” therapeutic drug or a “bad” illegal drug.

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

# Psychoactive Drugs Work by Altering Chemical Signaling in the Brain

Two Ways a Drug Affects Neural Signaling

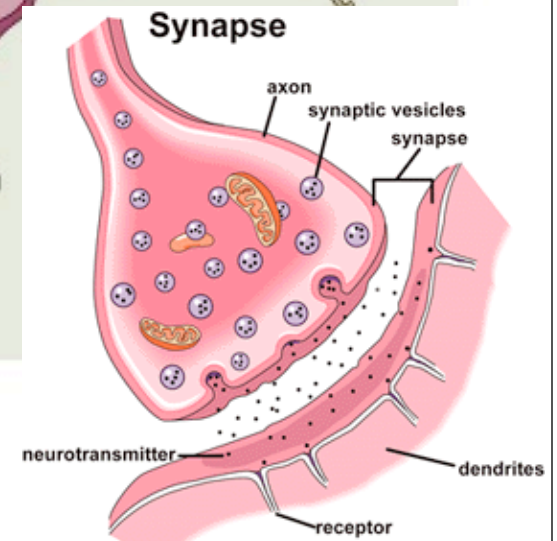
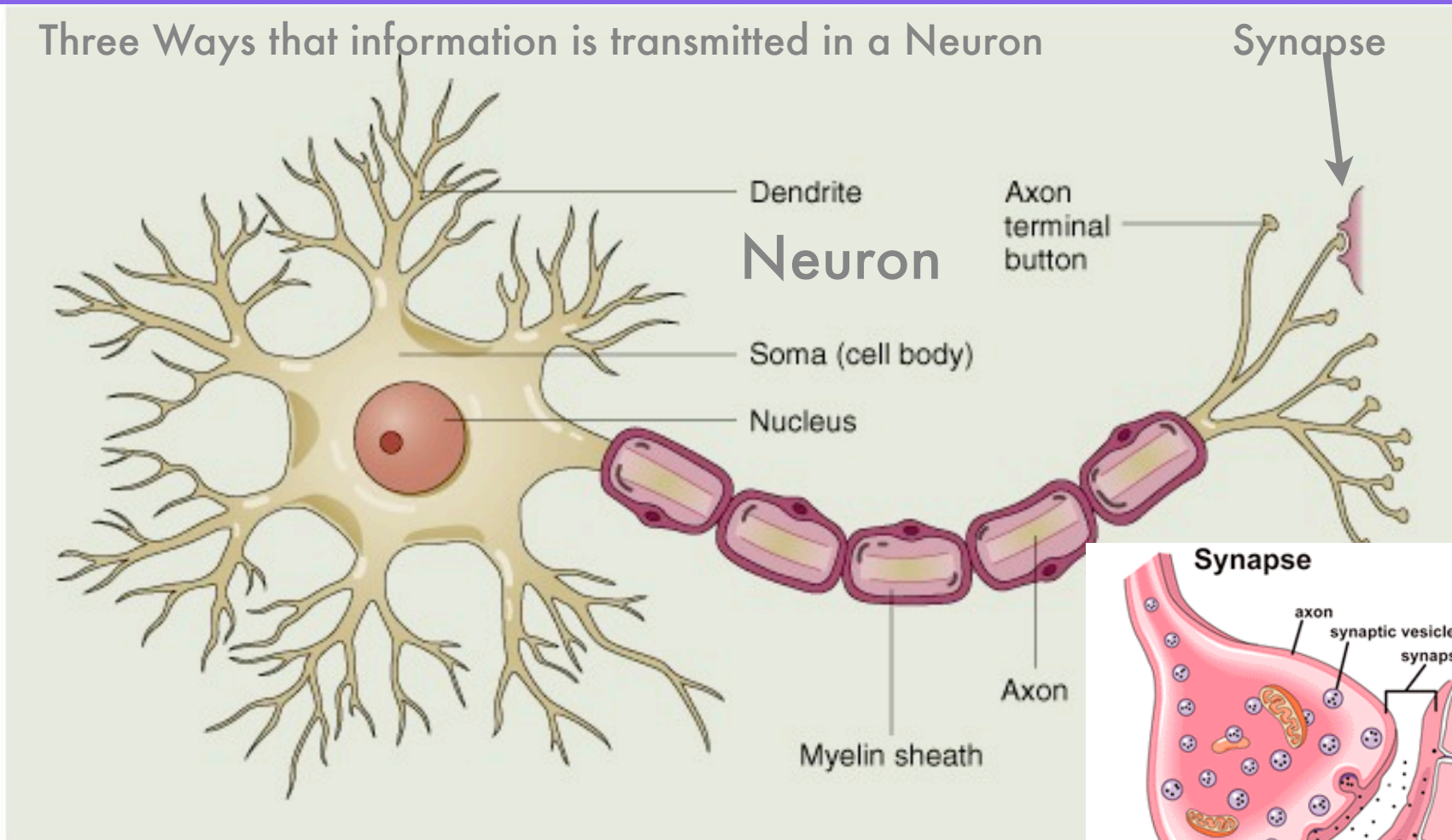
Agonist for chemical signal

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

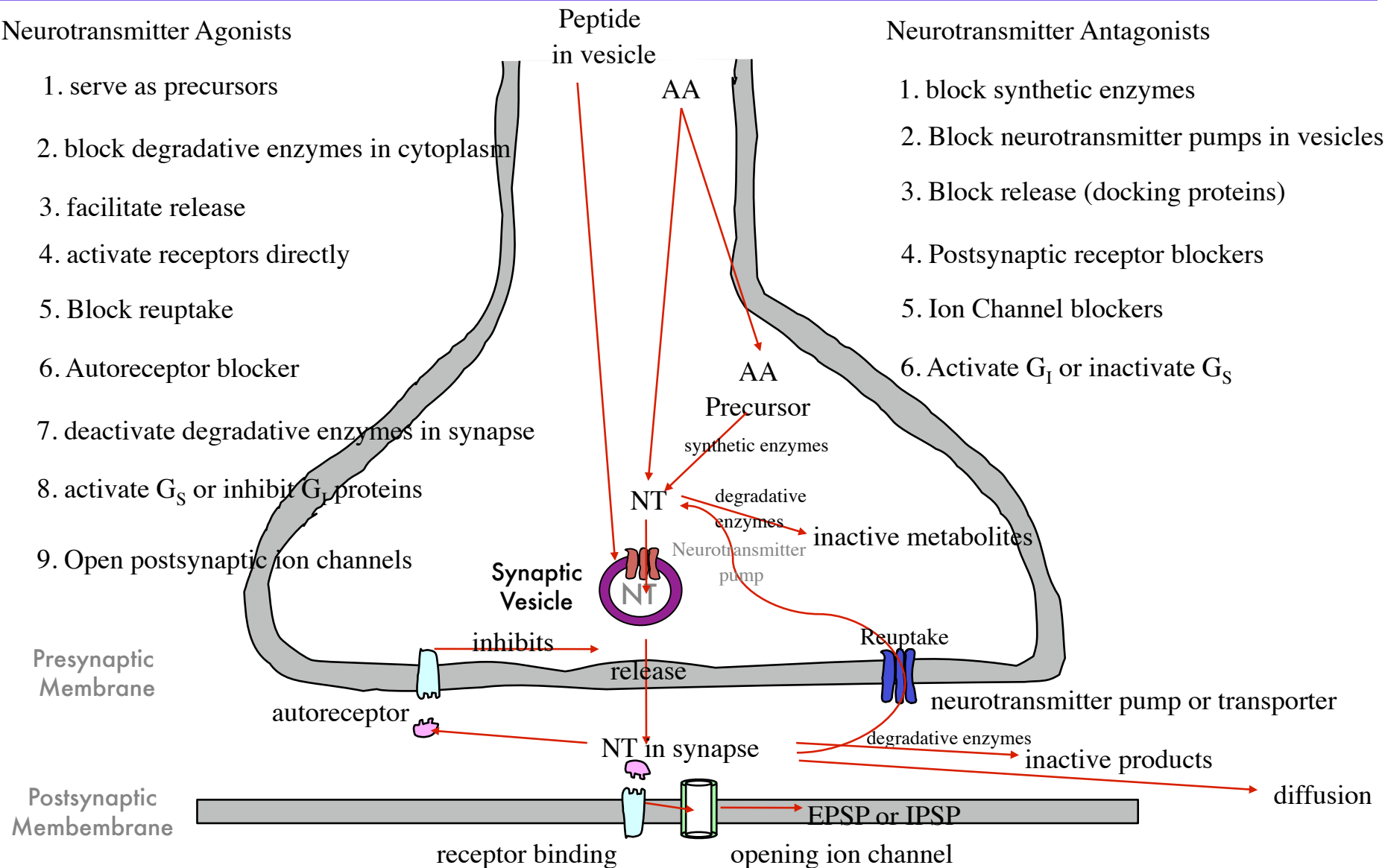
# Generalized Synapse (Major Drug Events)

## Neurotransmitter Agonists

1. serve as precursors
2. block degradative enzymes in cytoplasm
3. facilitate release
4. activate receptors directly
5. Block reuptake
6. Autoreceptor blocker
7. deactivate degradative enzymes in synapse
8. activate  $G_s$  or inhibit  $G_i$  proteins
9. Open postsynaptic ion channels

## Neurotransmitter Antagonists

1. block synthetic enzymes
2. Block neurotransmitter pumps in vesicles
3. Block release (docking proteins)
4. Postsynaptic receptor blockers
5. Ion Channel blockers
6. Activate  $G_i$  or inactivate  $G_s$



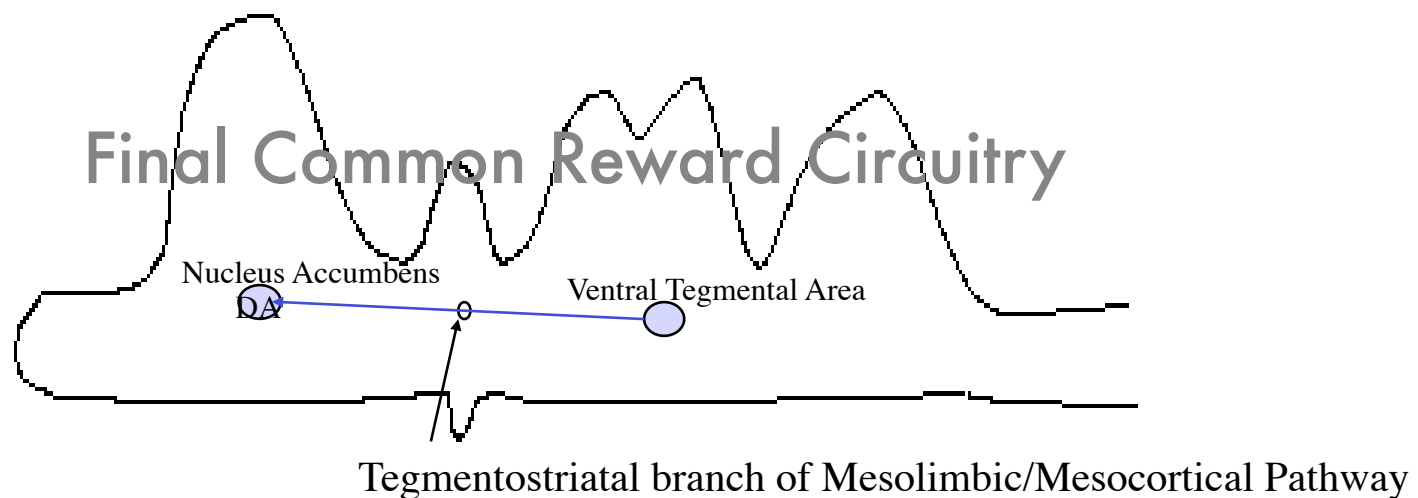
# Why are Some Neuroactive Drugs addictive?

Older Model of Addiction

Tolerance and Withdrawal

Problem With Older Model

Newer Model of Addiction





# 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 <sub>A</sub> agonist (allosteric modulators)
Caffeine	Blocks adenosine receptors
Nicotine	Activates Acetylcholine nicotinic receptors
Marijuana (THC)	Activates endogenous cannabinoid receptors

# Some diseases that are malfunctions in neurosecretion in the brain

Diseases are mainly diseases of modulatory neurotransmitters, defects in GA 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

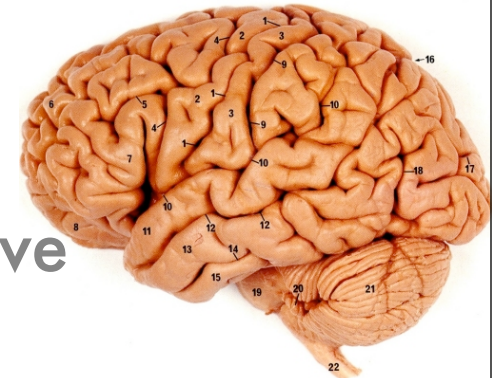
Must first learn how Brain works

Bios 120: Biology Core III: Integrative and Comparative

Bios 276: Central Nervous System and Behavior

Bios 390: Neuropharmacology

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



*Any* Questions?