# Lecture 6

**Neurotransmission**

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## Varieties of Neurotransmitters

- Over 50 different kinds identified
- Some are inhibitory at one location and excitatory at another
- More than one neurotransmitter may be active at a single synapse
- No simple one-to-one relationship between a single neurotransmitter and a single behavior

## Small-Molecule Transmitters

- Class of quick-acting neurotransmitters
- Synthesized from dietary nutrients and packaged ready for use in axon terminals
- Examples:
    - Acetylcholine (ACh)
    - Amines
        - Norepinephrine (NE)
        - Epinephrine (EP)
        - Serotonin (5-HT)
    - Amino Acids
        - Glutamate (Glu)

        - Gamma-aminobutyric (GABA)
        - Glycine (Gly)

## Glutamate and GABA

- Most important neurotransmitters for information transmission in the CNS
- Glutamate
    - Usually excitatory
- GABA
    - Usually inhibitory

## Peptide Transmitters

- Act as hormones that respond to stress
- Enable a mother to bond with her infant
- Regulate eating, drinking, pleasure and pain
- Contribute to learning
- Opiates such as morphine and heroin mimic the actions of natural brain peptides

## Transmitter Gases

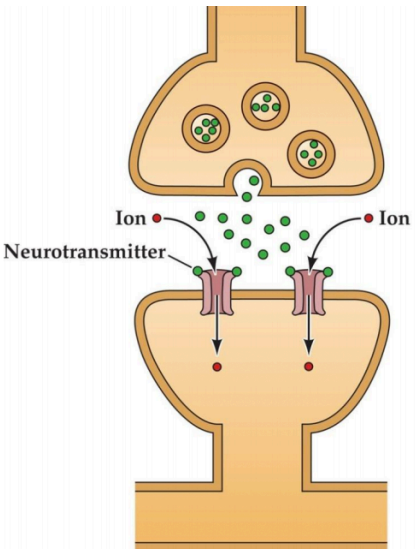
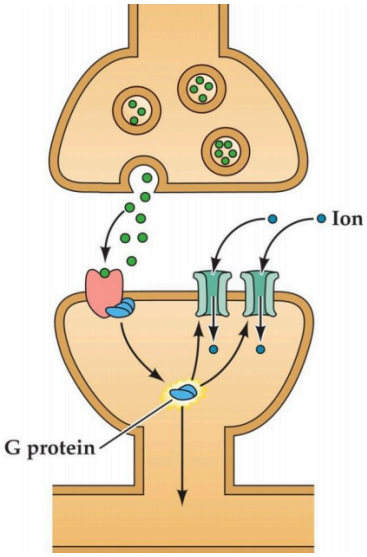
- Neither stored in synaptic vesicles nor released from them
- Synthesized in cell, as needed
- Easily crosses cell membrane
- E.g., Nitric Oxide (NO)
    - Viagra enhances the effects of this neurotransmitter in the blood vessels in the penis

## Postsynaptic Neuron

- Interprets the chemical message
- On postsynaptic side, a neurotransmitter may
    - Depolarize the postsynaptic membrane
        - Causing excitatory action on the postsynaptic neuron
        - EPSP (Excitatory PostSynaptic Potential)
    - Hyperpolarize the post synaptic membrane
        - Causing inhibitory action on the post synaptic neuron
        - IPSP (Inhibitory PostSynaptic Potential)
    - Initiate other chemical reactions that
        - Modulate either the excitatory or inhibitory effect **or**
        - Influence other functions of the receiving neuron

## Receptors

- Receptor proteins recognize transmitters and their mimics
- Two basic kinds of neurotransmitter receptors

| **Ionotropic** | **Metabotropic** |
| --- | --- |
| Fast | Slow |
| Quickly change shape | When activated they alter chemical reactions in the cell |
| Open or close an ion channel when the transmitter molecule binds | Use a system of *second messengers* to open ion channels |
|  |  |

## Learning: Changes in Synapses

- Presynaptic Neuron
    - Increased axonal transport
    - Increase size or area of terminal
    - Increase in number of synaptic vesicles
    - Increase in density of contact zones
    - Change in size of synaptic cleft

- Postsynaptic Neuron
    - Increase in size or area of spine
    - Change in stem length and width
    - Increase in protein transport for spine construction

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# Activating Systems in the CNS

## Cholinergic System

- Acetylcholine
- Produced in the Basal forebrain nuclei and Midbrain nuclei
- Active in maintaining attention
- Important for learning and memory, specially in adults
- A decrease in cholinergic activity is seen in Alzheimer's Disease

## Noradrenergic System

- Noradrenaline (Norepinephrine)
- Produced in the Locus coeruleus
- Plays a role in learning memory (particularly in adults)
- Important in emotional processing
- Has been implied in different neurological disorders
    - Depression (less)
    - ADHD (less)
    - Mania (excess)

# Dopaminergic Systems

## Nigrostriatal Dopaminergic System

- Produced in the Substantia nigra
- Involved in movement
- Related to Parkisonism

## Mesolimbic Dopaminergic System

- Produced in the Ventral Tegmentum Area (VTA)
- Important in reward processing
- Has been linked to addiction and schitzophrenia

## 6-Hydroxydopamine (6-OHDA)

- Neurotoxin
- Destroys dopaminergic neurons

## Lesions of the Ascending Dopaminergic pathways

- Results in behavioral deficits
- Animals show
    - Sensory neglect
        - Little attention to the environment
    - Motivational deficits
        - Little interest in eating food or drinking water
    - Motor impairments
        - Difficulty initiating voluntary movements
        - Similar to Parkinson's

## Drug Abuse

- Drugs that are abused increase mesolimbic dopamine activity, either directly or indirectly
- Drugs that blunt abuse and addiction decrease mesolimbic dopamine activity

### Serotonergic System

- Serotonin
- Plays a role in
    - Wakefulness
    - Learning
    - Mood
- Might be related to OCD and schitzophrenia

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# Parkinson's

- First described in 1817 by James Parkinson
- It is a *hypokinetic* movement disorder
- Symptoms arise due to the loss of nigrostriatal dopaminergic neurons
- As a result, the inhibitory output of the basal ganglia is abnormally high
- Incorrect coordination of movement
- Symptoms
    - Diminished facial expressions

    - Lack of smooth movements
    - Movement initiation is difficult (akinesia)
    - Reduced velocity and amplitude of movements (bradykinesia)
    - Tremor at rest
    - Impaired balance

## The Frozen Addicts

- 1982: Several young drug addicts were admitted to a hospital with symptoms resembling parkinson's
- Their symptoms responded to L-DOPA
- The heroin they consumer was contaminated with MPTP
- Injection of MPTP to rats and nice had no effect but in monkeys it resulted in "parkinson's"

## Causes

- While the symptoms arise from the death of the dopaminergic neurons, it is not known what causes this
- Recently it has been suggested that it could present a genetic component
    - Mutations in 3 genes have been implicated in rare forms of the disease but this doesn't account for most of the cases of PD
- These genes could be therapeutic targets in the future

## Treatments

- Administration of L-DOPA
    - A dopamine precursor

    - Caveat: The dose had to be constantly increased and it becomes ineffective after ~5 years
- Surgical lesioning
    - Lesioning of specific areas of the basal ganglia can increase the ability of the person to move
- Deep brain stimulation
- Stem cells