


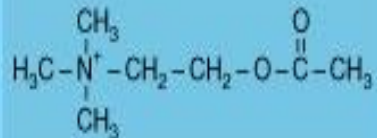


Neurotransmitters

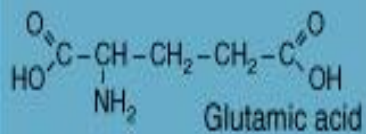
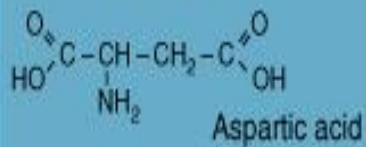
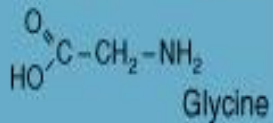
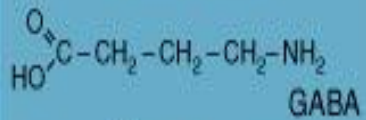
Dr. Amer Khazal Al-Hasan

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- **Neurotransmitters** are the chemicals which allow the transmission of signals from one neuron to the next across synapses.
 - found at the axon endings of motor neurons, where they stimulate the muscle fibers.
 - produced by some glands such as the pituitary and the adrenal glands.

Acetylcholine

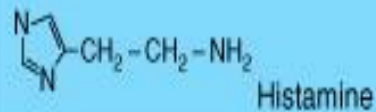
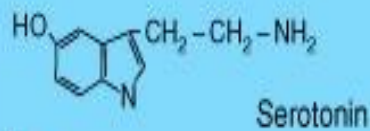
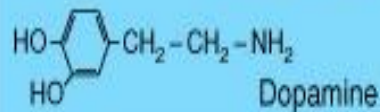
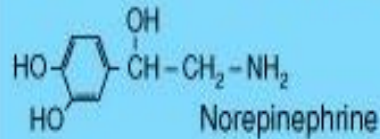
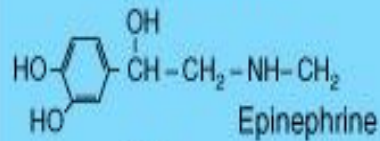


Amino acids

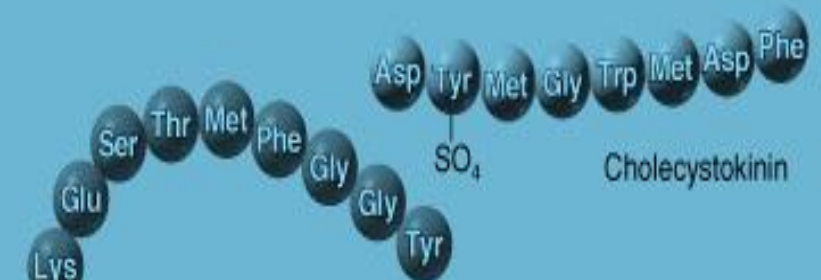
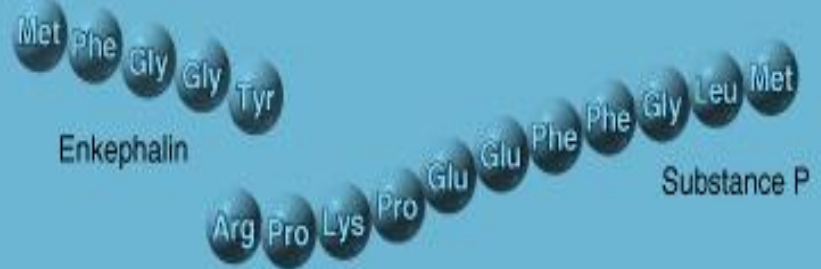


Monoamines

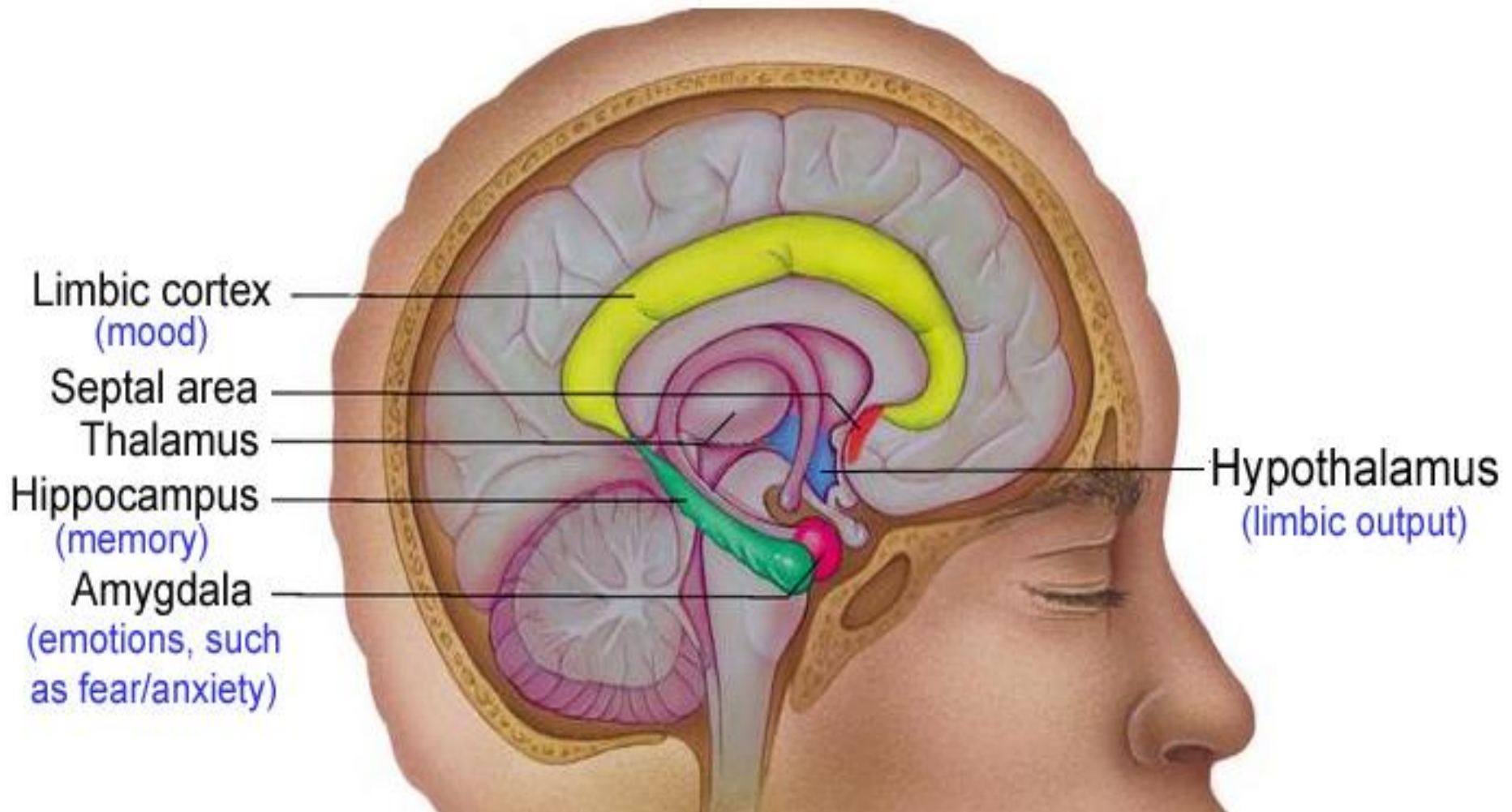
Catecholamines





Neuropeptides



Limbic System



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- They are chemicals that communicate information throughout our brain and body.
 - The brain uses neurotransmitters to tell your heart to beat, your lungs to breathe, and your stomach to digest.
 - They can also affect mood, sleep, concentration, weight, and can cause adverse symptoms when they are out of balance.

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- Different types of cells secrete different neurotransmitters.
 - Each brain chemical works in widely spread but fairly specific brain locations and may have a different effect according to where it is activated.
 - All of the major neurotransmitters are made from amino acids except acetylcholine. Some 60 neurotransmitters have been identified.

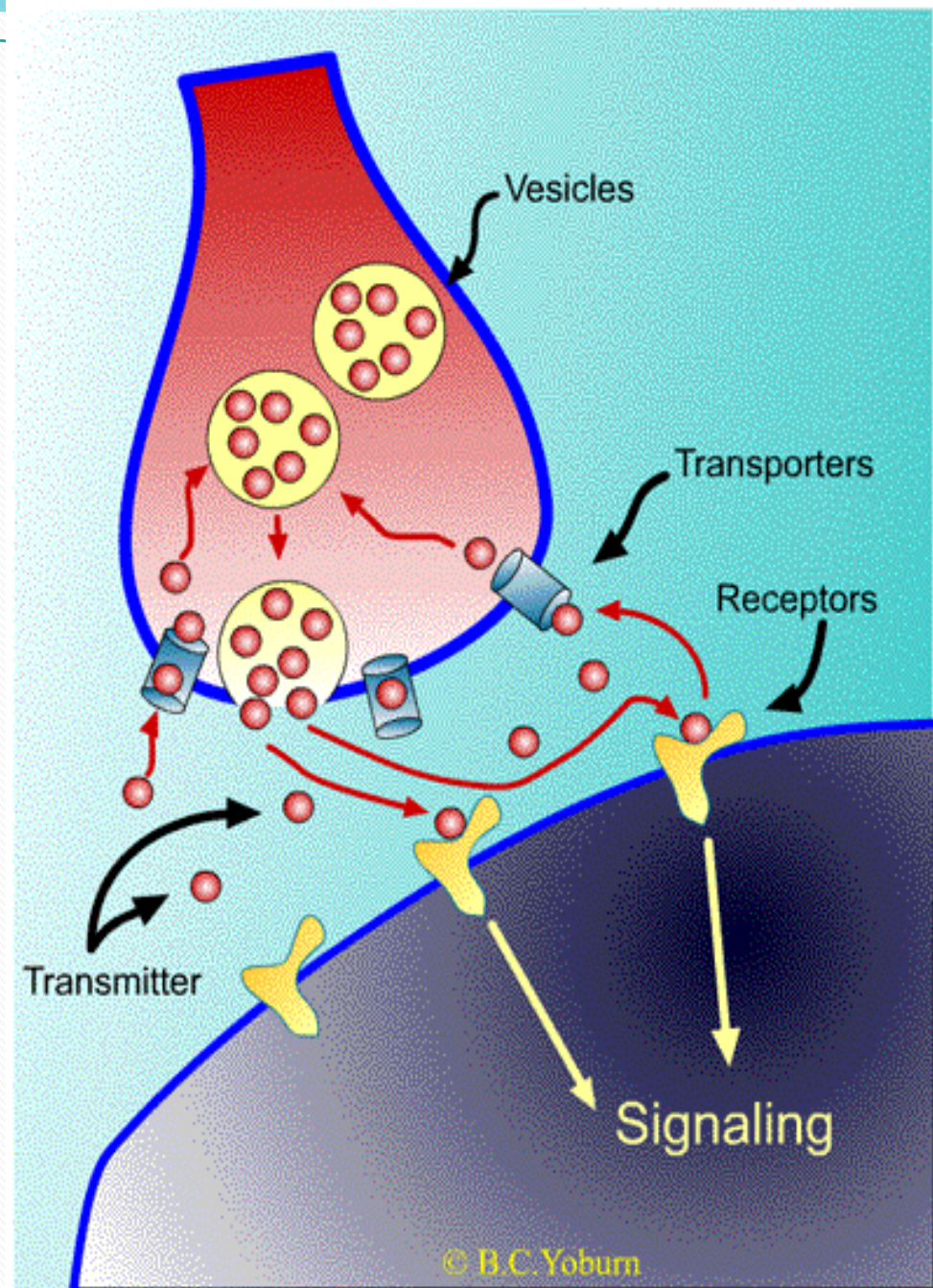



Neurotransmitter levels can be depleted many ways.


- Stress, poor diet, neurotoxins
- genetic predisposition
- drug (prescription and recreational)
- alcohol and caffeine usage can cause these levels to be out of optimal range.

The neurotransmitters are stored in tiny sac-like structures called vesicles at the end of axons.

When an impulse, or nerve signal, reaches the end of the axon, the vesicles release a neurotransmitter into the small space between the adjoining cells (synaptic gap).




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- Enzymes concerned with the synthesis of neurotransmitters are present both in the cell body and in the nerve ending.
 - A portion of neurotransmitter is produced in the cell body and transported to the nerve ending.

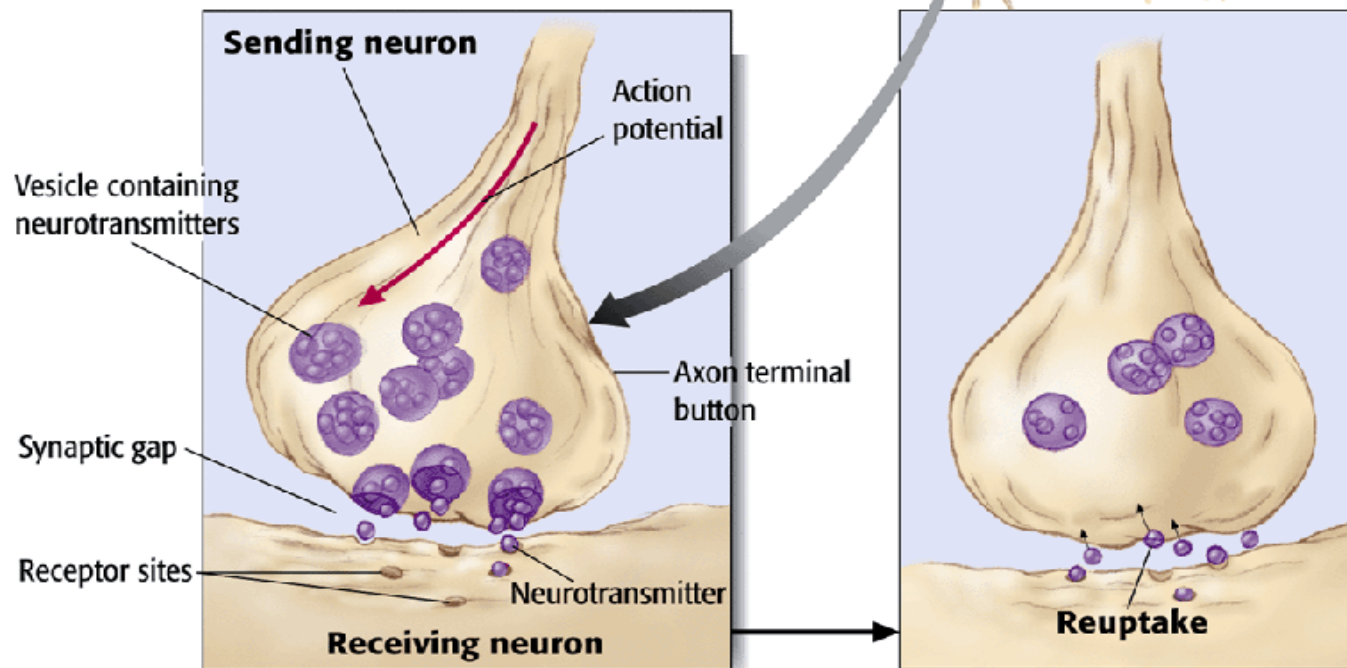
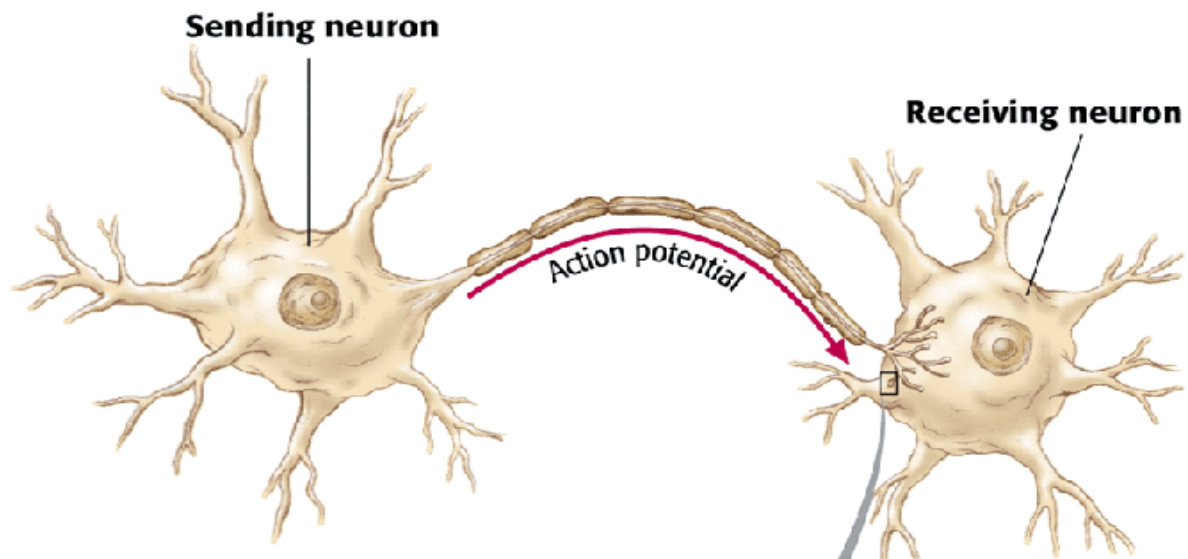


Neurotransmitters diffuse across the synapse and bind to receptors in the receiving cell that are specific for the neurotransmitter. The kinds of reactions that occur in the receiving cell may vary:

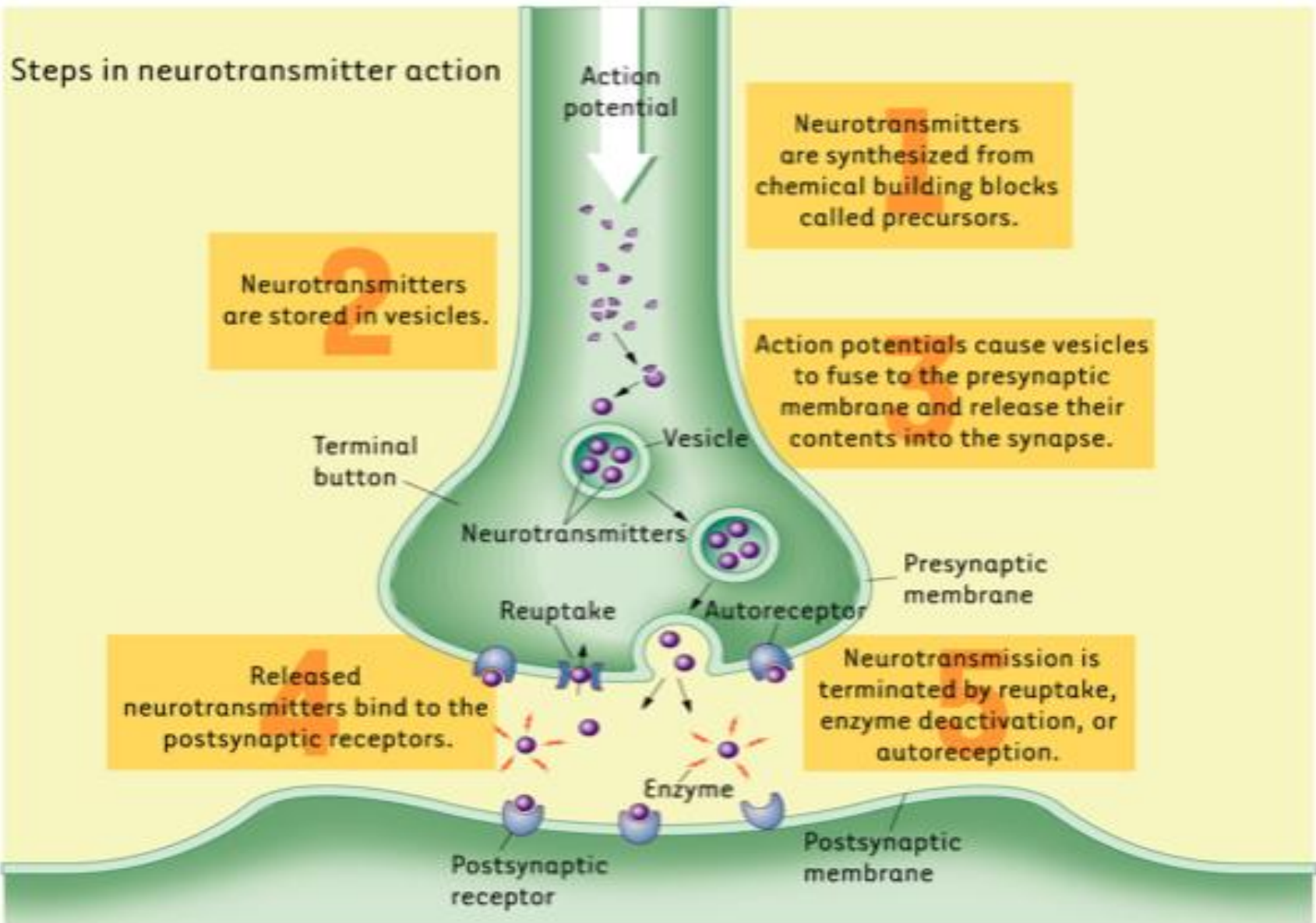
- The cell may be excited and an action potential is set up and the impulse is transmitted
- or the opposite effect may occur, and the cell will be inhibited from transmitting the impulse because it becomes hyperpolarized.

- The number and kind of neurotransmitter molecules received by the receptor cell, as well as the kind of receptor, determines whether the effect will be to stimulate or to inhibit.
- Neurotransmitters function by changing the permeability of the cell membrane to various ions such as sodium and potassium. If an excess of sodium ions flow into the nerve cell, an impulse is generated. If an excess of potassium ions flow out, the impulse is inhibited.

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- If neurotransmitters were allowed to operate over a long period of time, the results would be disastrous for the organism since there would be a constant overload of messages being sent. One way in which the problem is solved is through enzymes which break down the neurotransmitter very rapidly.



Neurotransmitters



Types of Neurotransmitters

- There are two kinds of neurotransmitters
EXCITATORY and **INHIBITORY**
- Excitatory neurotransmitters excite, stimulate the brain.
- Inhibitory neurotransmitters those that calm the brain and help create balance. balance mood and are easily depleted when the excitatory neurotransmitters are overactive.

Neurotransmitter Molecules

- Neurotransmitters can be broadly split into two groups :
classical' small molecule neurotransmitters
and the relatively
larger neuropeptide neurotransmitters.
- Within the category of small molecule neurotransmitters, the biogenic amines (dopamine, noradrenaline, serotonin and histamine) are often referred to as a 'discrete group' because of their similarity in terms of their chemical properties.

Small molecule neurotransmitters

Type	Neurotransmitter	Postsynaptic effect
Amino acids	Acetylcholine	Excitatory
	Gamma aminobutyric acid GABA	Inhibitory
	Glycine	Inhibitory
	Glutamate	Excitatory
Biogenic amines	Aspartate	Excitatory
	Dopamine	Inhibitory
	Nor adrenaline	Excitatory
	Serotonin	Inhibitory
	Histamine	Excitatory

Neuropeptide neurotransmitters

Corticotropin releasing hormone

Corticotropin (ACTH)

Beta-endorphin

Substance P

Neurotensin


Somatostatin

Bradykinin

Vasopressin

Angiotensin II

Nitric oxide

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- This acquired knowledge about the neurotransmitters has led to the development of successful products (Drugs) for many brain disorders including :
 - epilepsy
 - schizophrenia
 - Parkinson's disease
 - depression, anxiety disorders and migraine .

ACETYLCHOLINE

- Acetylcholine was the first neurotransmitter to be discovered.
- It is responsible for much of the stimulation of muscles, including the muscles of the gastro-intestinal system.
- It is also found in sensory neurons and in the autonomic nervous system, and has a part in scheduling REM (dream) sleep.


- Acetylcholine is transmitted within **cholinergic pathways** that are concentrated mainly in specific regions of the brainstem and are thought to be involved in cognitive functions, especially memory. Severe damage to these pathways is the probable cause of Alzheimer's disease.
- There is a link between acetylcholine and Alzheimer's disease: There is something on the order of a 90% loss of acetylcholine in the brains of people suffering from Alzheimer's, which is a major cause of senility.

- Outside the brain, acetylcholine is the main neurotransmitter in the **parasympathetic nervous system** – the system that controls functions such as:
 - heart rate
 - digestion
 - secretion of saliva
 - bladder function.
- The plant poisons **curare** cause paralysis by blocking the acetylcholine receptor sites of muscle cells.
- The well-known poison **botulin** works by preventing the vesicles in the axon ending from releasing acetylcholine, causing paralysis.

SEROTONIN

- **SEROTONIN** is an inhibitory neurotransmitter – which means that it does not stimulate the brain.
- Adequate amounts of serotonin are necessary for a stable **mood** and to balance any excessive excitatory (stimulating) neurotransmitter firing in the brain.
- If you use stimulant medications or **caffeine** in your daily regimen – it can cause a depletion of serotonin over time.

- Low serotonin levels leads to an increased appetite for carbohydrates (starchy foods) and **trouble sleeping**, which are also associated with:
 - **depression migraines, irritable bowel syndrome**
 - **decreased immune system function.**
- Normal serotonin
 - regulation of sleep**
 - pain perception**
 - body temperature**
 - blood pressure and hormonal activity**

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- Within the brain, serotonin is localized mainly in nerve pathways emerging from the Midbrain, pons and medulla.
 - These serotonergic pathways spread extensively throughout the brainstem , the cerebral cortex and the spinal cord .
 - Largest amount of serotonin is found in the intestinal mucosa.

Gamma amino butyric acid(GABA)

- is the major inhibitory neurotransmitter that is often referred to as
- “nature’s VALIUM-like substance”.

When GABA is out of range (high or low excretion values), it is likely that an excitatory neurotransmitter is firing too often in the brain. GABA will be sent out to attempt to balance this stimulating over-firing.

- People with too little GABA tend to suffer from anxiety disorders, and drugs like Valium work by enhancing the effects of GABA.
- Lots of other drugs influence GABA receptors, including alcohol and barbiturates. If GABA is lacking in certain parts of the brain, **epilepsy** results.
- GABA is derived from glucose, which is transaminated in the Krebs's cycle to glutamine and then converted to GABA by the enzyme, **glutamic acid decarboxylase**.

Glucose

Glutamine


GABA.

HISTAMINE

- Amino acid **Histidine** is the precursor of an important neurotransmitter histamine; found in the brain.
- Histamine is present in venom and other stinging secretions.
- Histamine is a biogenic amine involved in local immune responses
- Regulate physiological function in the gut
- Triggers the inflammatory response.

- As part of an immune response to foreign pathogens, histamine is found in bound form in granules in basophils and mast cells found in nearby connective tissues. The bound form is inactive but stimuli causes its release from these granules.
- Histamine increases the permeability of the capillaries to white blood cells and other proteins, in order to allow them to engage foreign invaders in the affected tissues.
- Mast cells are especially numerous at sites of potential injury - the nose, mouth, and feet, internal body surfaces, and blood vessels.
- Another important site of histamine storage and release is the enterochromaffin-like (ECL) cell of the stomach.

- The most important pathophysiologic mechanism of mast cell and basophil histamine release is immunologic.
- Production of IgE by an Ag.
- IgE molecules attach to the surface of mast cells and basophils.
- When the same antigen re-enters into the tissue,
- Then Ag-Ab reaction occurs.
- This degranulates the mast cells and basophils.
- And histamine is released.

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- This type of histamine release produces type I or immediate allergic reaction.
 - Histamine is also produced during immune reaction mediated by IgG and IgM.
 - Chemical and mechanical stimuli can also cause its release.
 - Tissue injury and burns can also cause its release.

Mechanism of action

- Histamine exerts its actions by combining with specific cellular histamine receptors. The four histamine receptors that have been discovered are designated H₁ through H₄.

Type, Location, Function of Receptors

- **H₁ receptors:**
- Found on smooth muscle, endothelium, and central nervous system tissue.
- Causes vasodilatation, bronchoconstriction, and pain and itching due to insect stings.
- These are the primary receptors involved in allergic rhinitis symptoms, motion sickness, and sleep regulation.

- **H₂ receptors:** Found on parietal cells of stomach, brain and cardiac muscle. Primarily stimulate gastric acid secretion.
- **H₃ receptor:** Found on central nervous system and to a lesser extent on peripheral nervous system tissue.
- **H₄ receptor:** Found on primarily in the basophils and in the bone marrow. also found on thymus, small intestine, spleen and colon.
- Plays a role in chemotaxis.

Actions of Histamine

- **Cardiovascular system:**


1. Vasodilatation of arterioles and pre capillary sphincters. This decreases the peripheral vascular resistance and leads to severe fall in both systolic and diastolic blood pressures.
2. Increased permeability of vessels. This produces urticaria and laryngeal edema(triple response- Flare, wheal and pain).
3. Increase heart rate.

- **Bronchial smooth muscles:**

It causes broncho-constriction.

- **GIT:**

1. Causes contraction of Smooth muscles of GIT.
2. Causes HCl secretion.

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- **Nervous system:**
 - Histaminergic neurons occur in the posterior hypothalamus whose axons project to all parts of the brain.
1. Histamine plays a role in arousal, pain threshold, regulation of blood pressure.
 2. Histamine has got no clinical applications, but agents that interfere with the action of histamine have important therapeutic applications.