



BIOCHEMISTRY OF NERVOUS SYSTEM I

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Advanced Clinical Biochemistry II (MA 416)

Summer Semester

Lecture Three

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Outlines

- Objectives
- Introduction of NS
- Autonomous NS
- CSF and its properties
- Transport of molecules across BBB
- Neurotransmitters and the metabolism
- Summary
- References

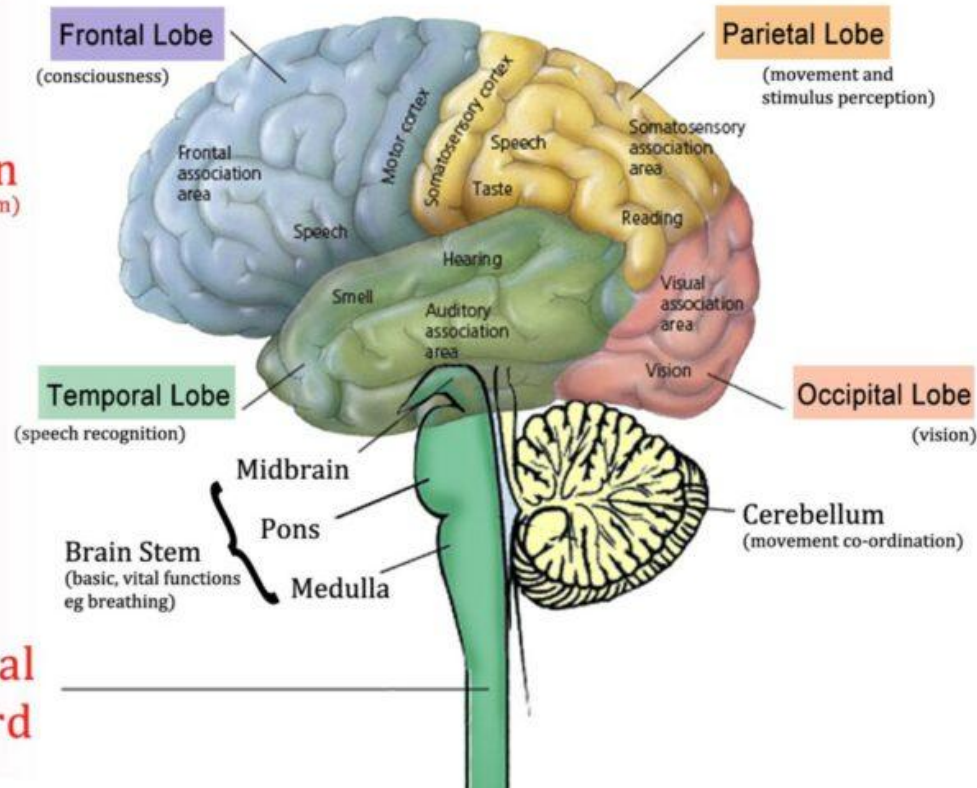


Objectives

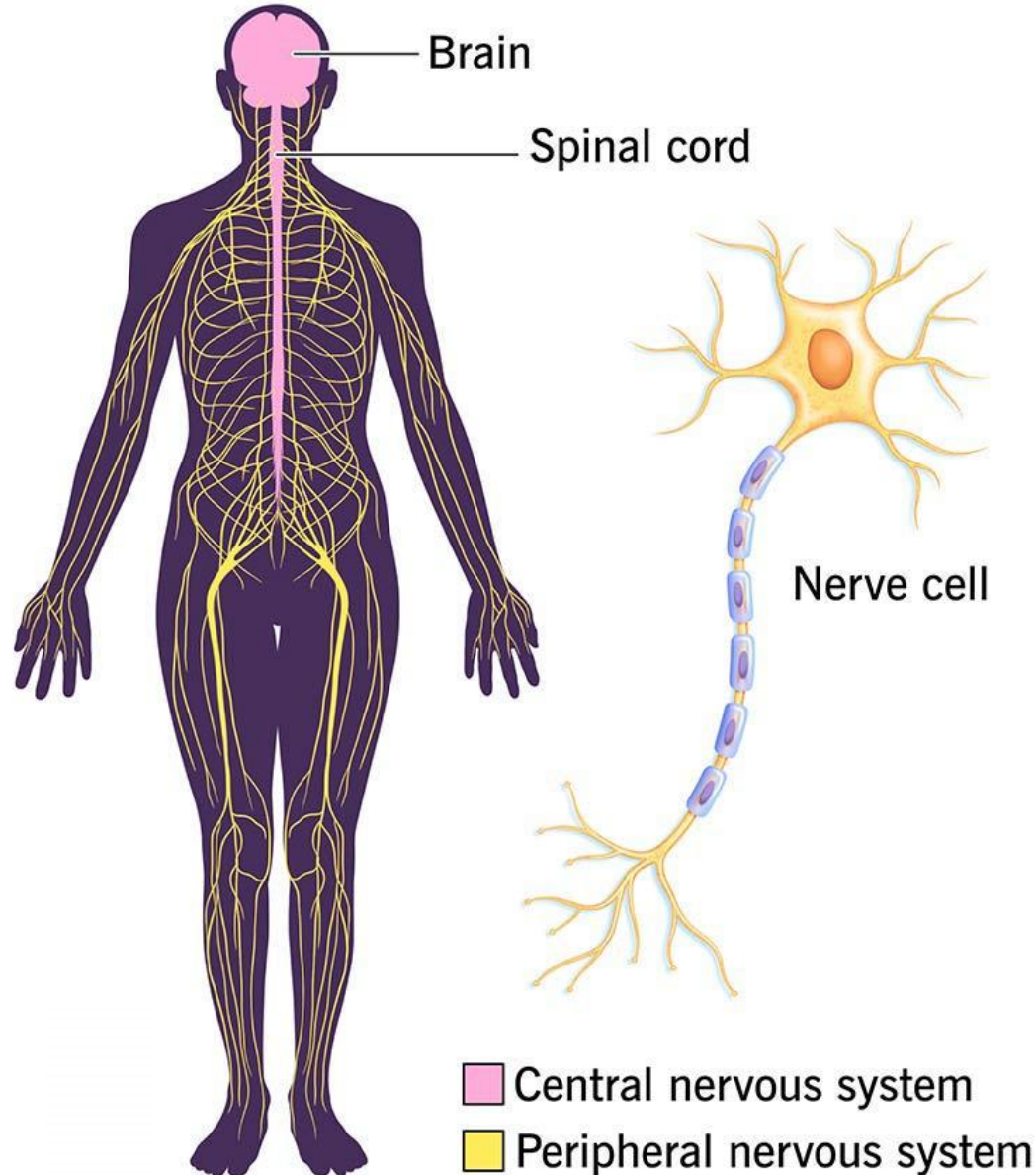
- **At the end of this lesson, the students should be able to:**
 - Understand the general concept of the nervous system.
 - Understand the biochemistry behind the workings of the nervous system.
 - Understand how biomolecules are transported across the blood-brain barrier.
 - Understand the metabolism of neurotransmitters.

Introduction

- Many neurological disorders have a biochemical basis or are associated with disturbances of metabolism.
- The study of the chemical basis of diseases affecting CNS and PNS is termed neurochemistry.
- Many generalized disorders of metabolism affect the CNS.



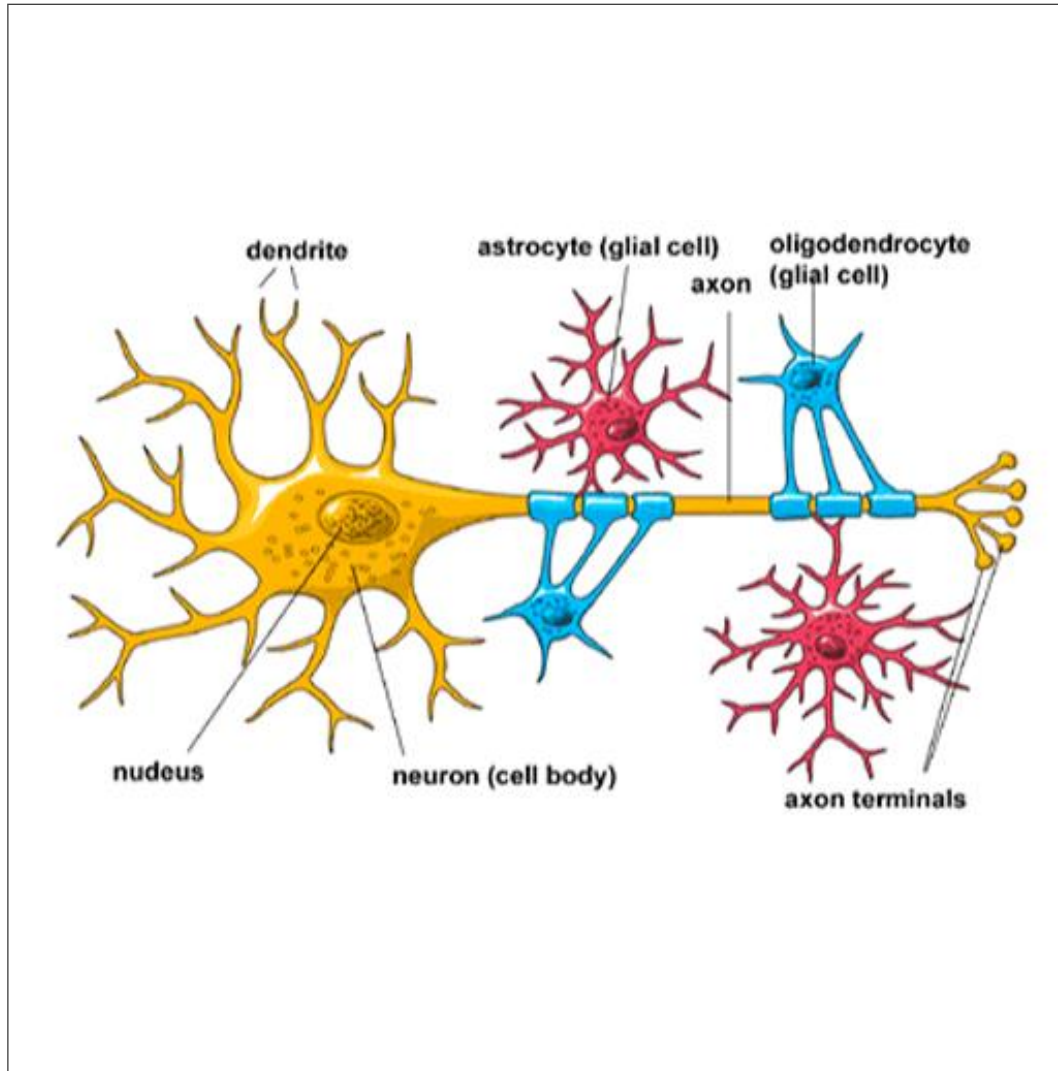
Nervous system



Nervous system

- The human nervous system comprises two main parts **Central and Peripheral Nervous System**):
- **CNS**: This includes the brain and spinal cord. The CNS is responsible for processing information, coordinating responses, and controlling voluntary and involuntary actions.
- **PNS**: This consists of nerve fibers that connect the CNS to every other part of the body. It includes motor neurons (for voluntary movement) and the autonomic nervous system (which regulates involuntary activities).

Neurons and Glia Cells



- **Neurons:** These specialized cells transmit chemical signals in nerve transmission.
- They play a crucial role in communication within the nervous system.
- **Glial Cells:** These cells support and protect neurons. They are essential for maintaining the health and function of the nervous system.

The Autonomic Nervous System

Sympathetic NS

Norepinephrine and Epinephrine

Fight, Flight or Freeze

Increases

- Heart rate
- Respiratory rate
- Blood pressure
- Pupil dilation

Decreases

- Digestion
- Urine production

Parasympathetic NS

Acetylcholine

Rest and Digest

Increases

- Digestion

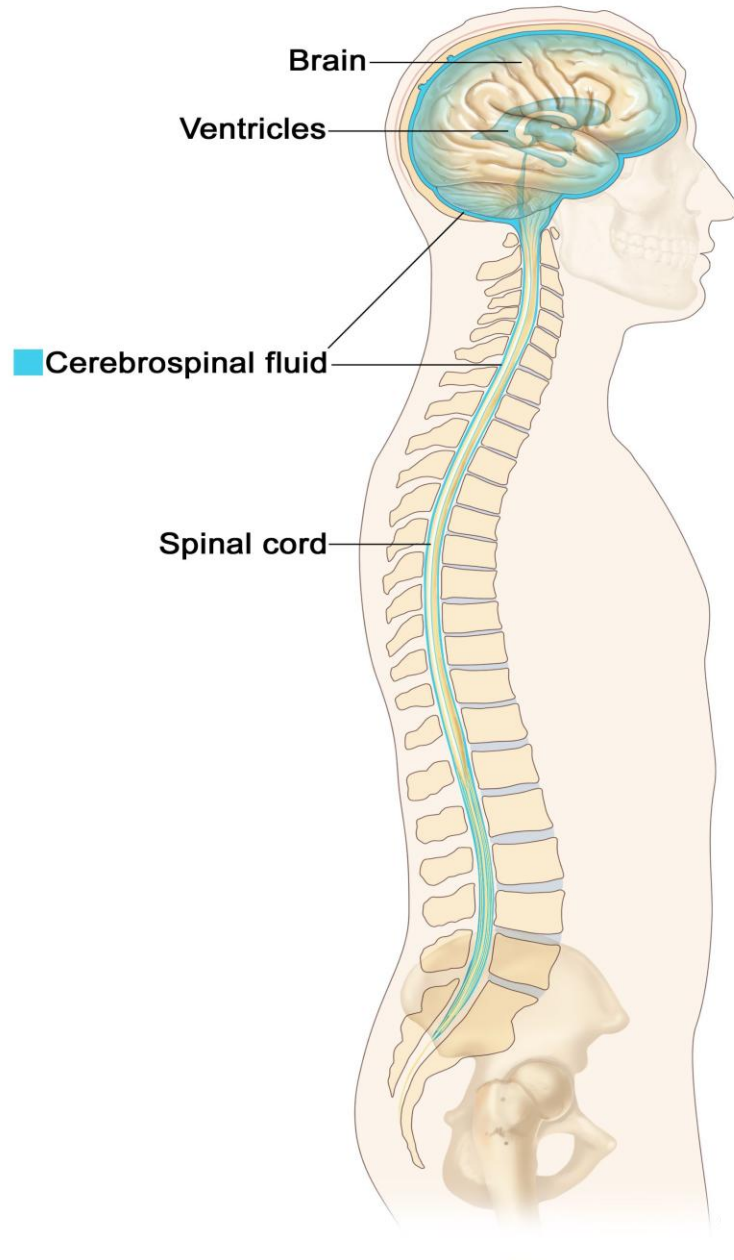
Decreases

- Heart rate
- Respiratory rate
- Blood pressure
- Pupil dilation



Autonomous Nervous System

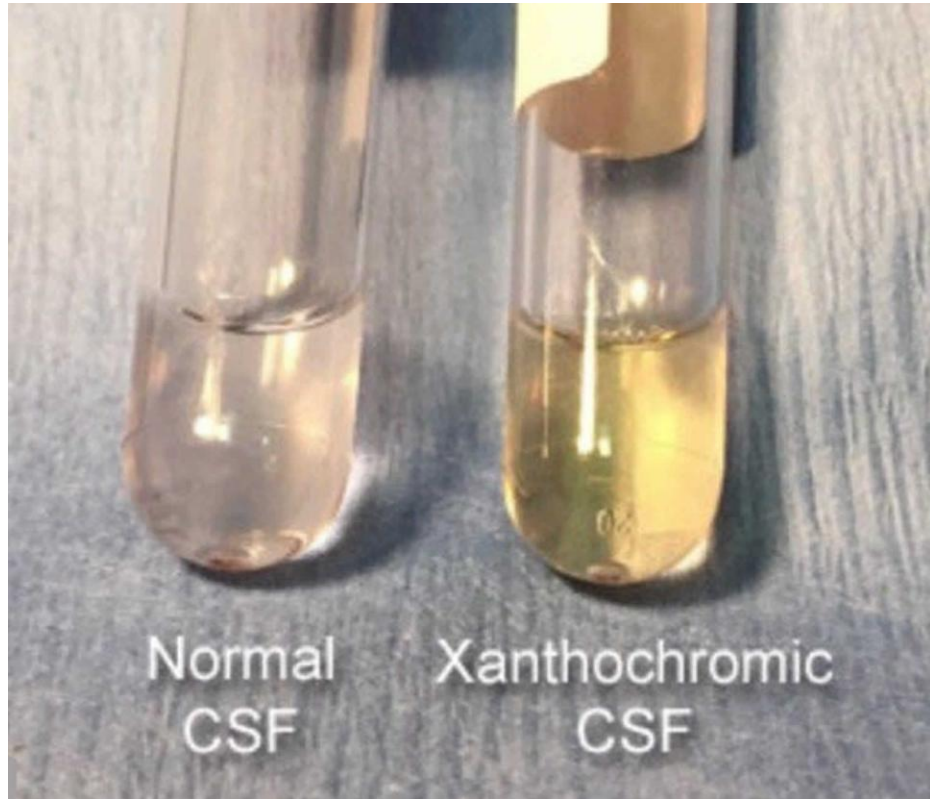
- The autonomic nervous system controls involuntary activities, and it includes:
- **Sympathetic Nervous System:** Responsible for the “fight or flight” response.
- **Parasympathetic Nervous System:** Involved in relaxation and energy conservation.
- **Enteric Nervous System:** Semi-independent, regulating gastrointestinal processes.



Cerebrospinal fluid

- **CSF** is a clear, colorless fluid found within the tissue that surrounds the brain & spinal cord of all vertebrates.
- **CSF** (blue) is made by tissue that lines the ventricles (hollow spaces) in the brain.
- It flows in and around the brain and spinal cord to help cushion them from injury and provide nutrients.

Appearance of CSF

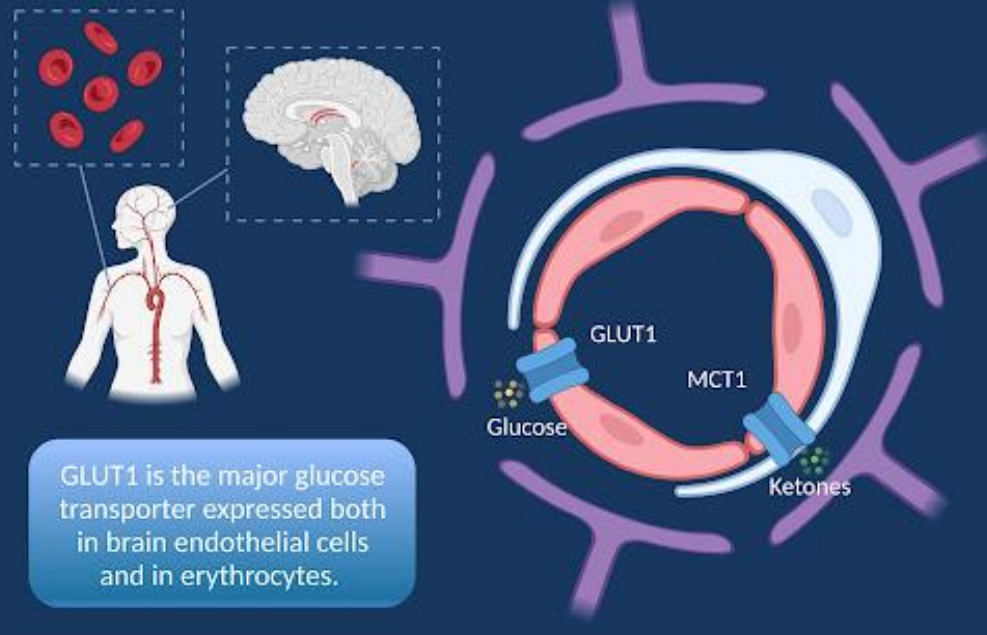


- CSF is normally clear and colorless. Turbidity is usually due to leucocytes, but it may be due to microorganisms.
- Blood-stained CSF may indicate a recent hemorrhage or damage to a blood vessel during specimen collection.
- Xanthochromia (yellow color) is most often due to previous hemorrhage into the CSF, but it may indicate high protein in CSF.
- The CSF may be yellow in jaundiced patients.

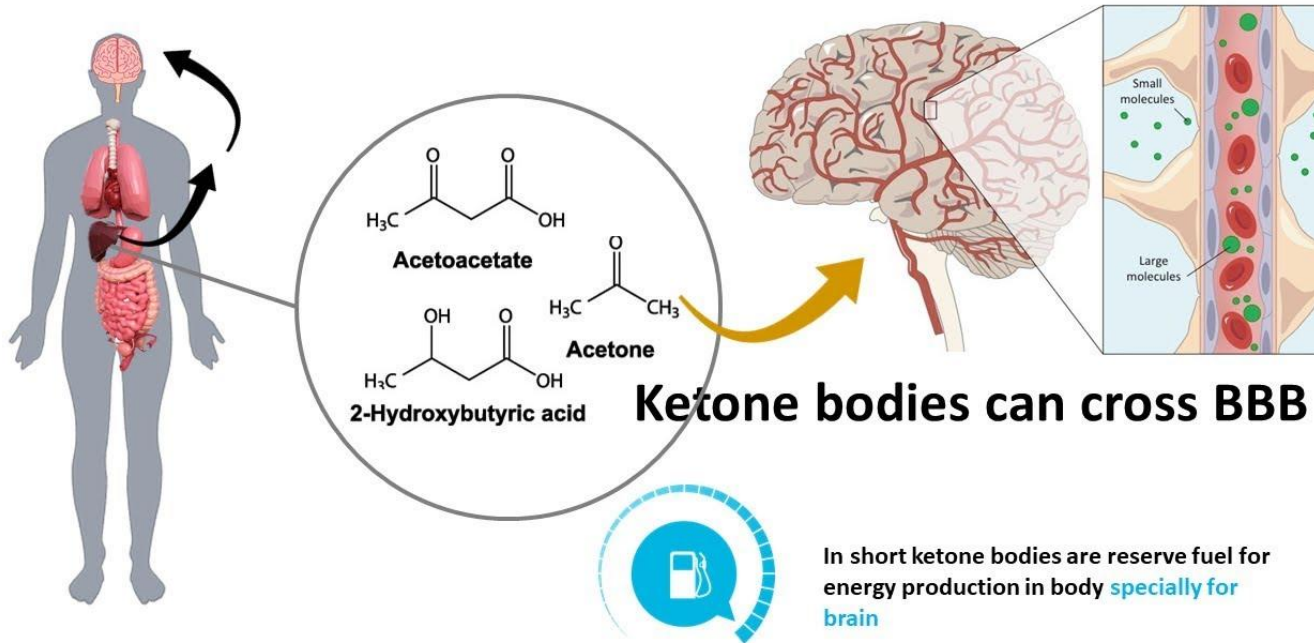
Transport through BBB

- A large number of compounds are transported through endothelial capillaries by facilitated diffusion.
- Fuels Glucose: The principal fuel of the brain is transported through endothelial membranes by facilitated diffusion via GLUT-1.
- At blood glucose of 60 m/dl, glucose is reduced to below K_m of GLUT-1 leading to the appearance of symptoms of hypoglycemia

GLUT1 in the blood-brain barrier (BBB)

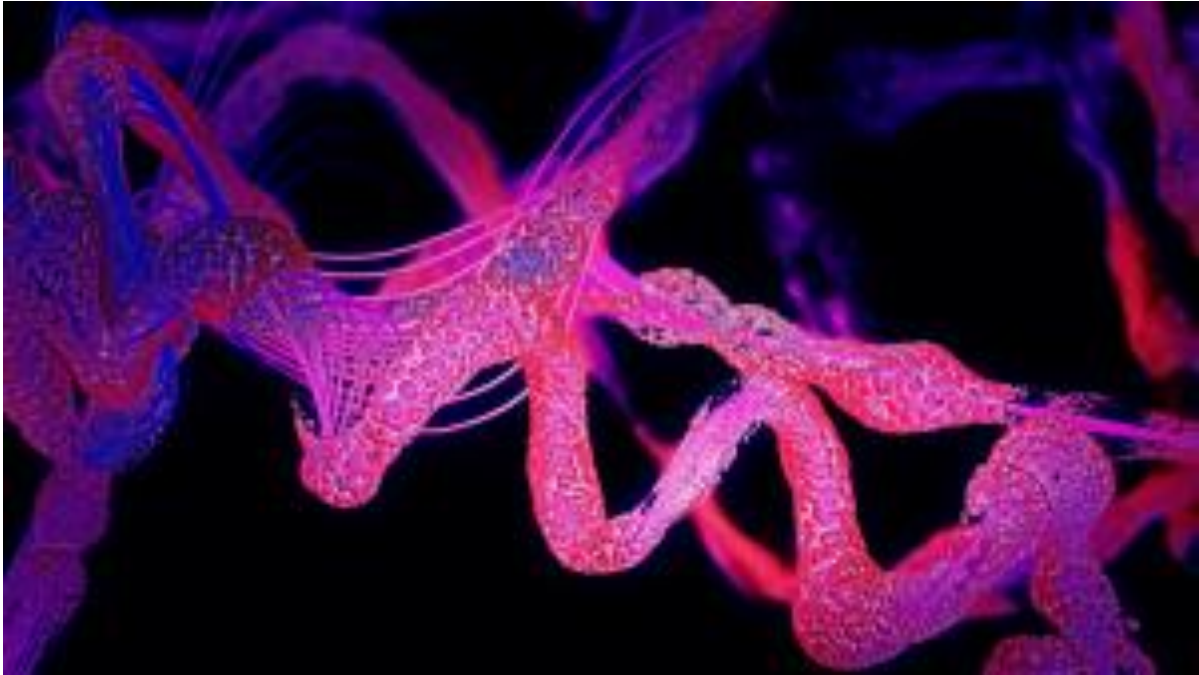


Ketone bodies and its metabolism



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- Others: as ketone bodies by another transport system When blood levels of KB are elevated (during starvation).
- KBs are important fuels for the brain during prolonged starvation Non-essential fatty acids (of diet or lipolysis) do not cross BBB
- Essential fatty acids (linoleic & linolenic) can pass BBB



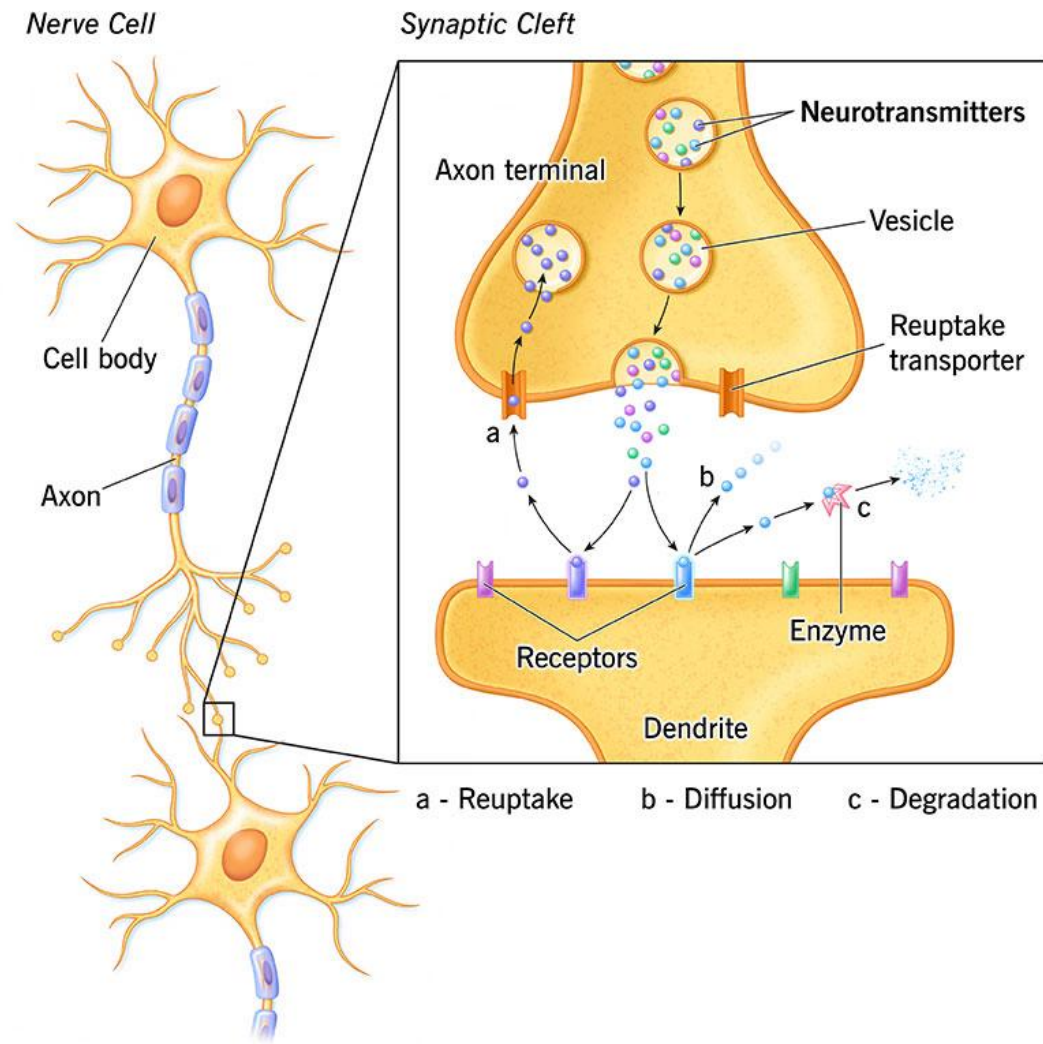
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- Amino acids are transported by amino acid transporters, and are used in the brain for the synthesis of:
 - Proteins of CNS and Neurotransmitters.
- Types of transported amino acids:
 - Long neutral amino acids (by single amino acid transporters). Essential: Phe, Leu, Isoleucine, Val, Try, Met.
 - Small neutral amino acids (entry is markedly restricted as their influx markedly changes the content of neurotransmitters). Nonessential: Alanine, Glycine, Proline



Interaction

- What are the two main divisions of ANS
- Differentiate between neuron and glia cells in terms of their function
- What are the biochemical functions of CSF
- What are the possible causes of xanthochromia?
- Explain the role of GLUT1 in the CNS



Metabolism of Neurotransmitters

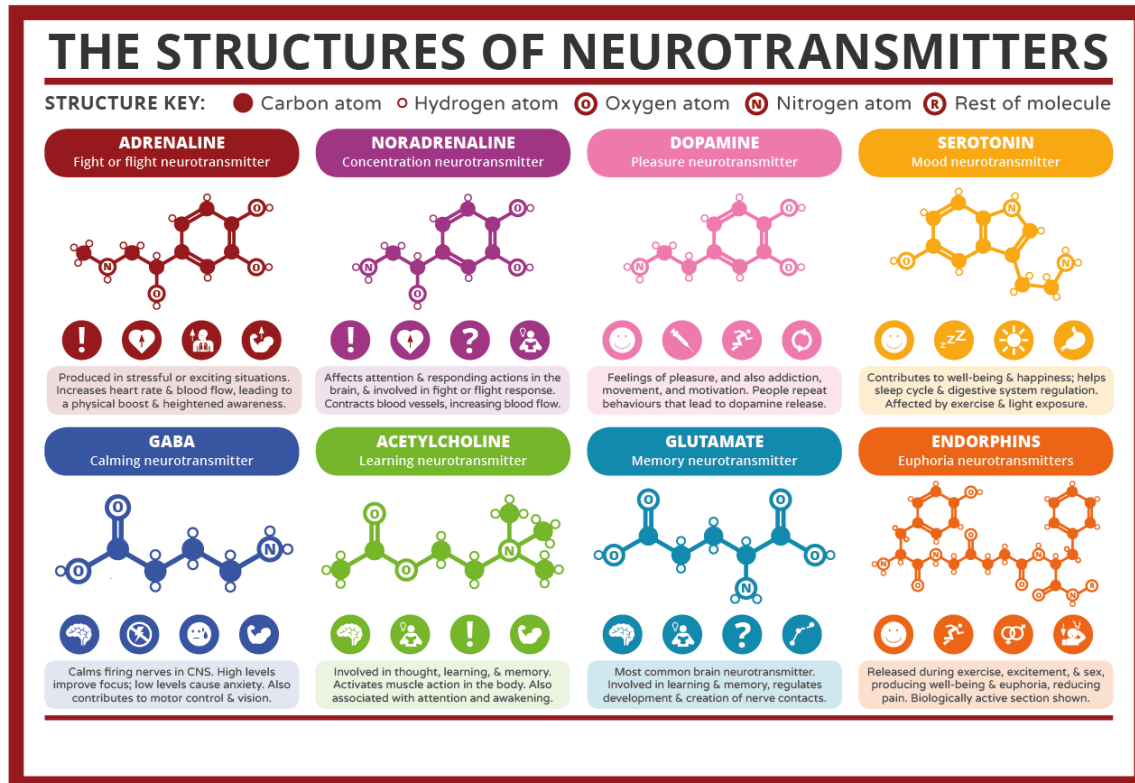
- Neurotransmitters are chemicals released at synapses for the transmission of nerve impulses.
- Generally, each neuron synthesizes only those neurotransmitters that it uses for transmission through synapses.
- The neuronal tracts are often identified by their neurotransmitters.

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- Structurally neurotransmitters are divided into two categories:

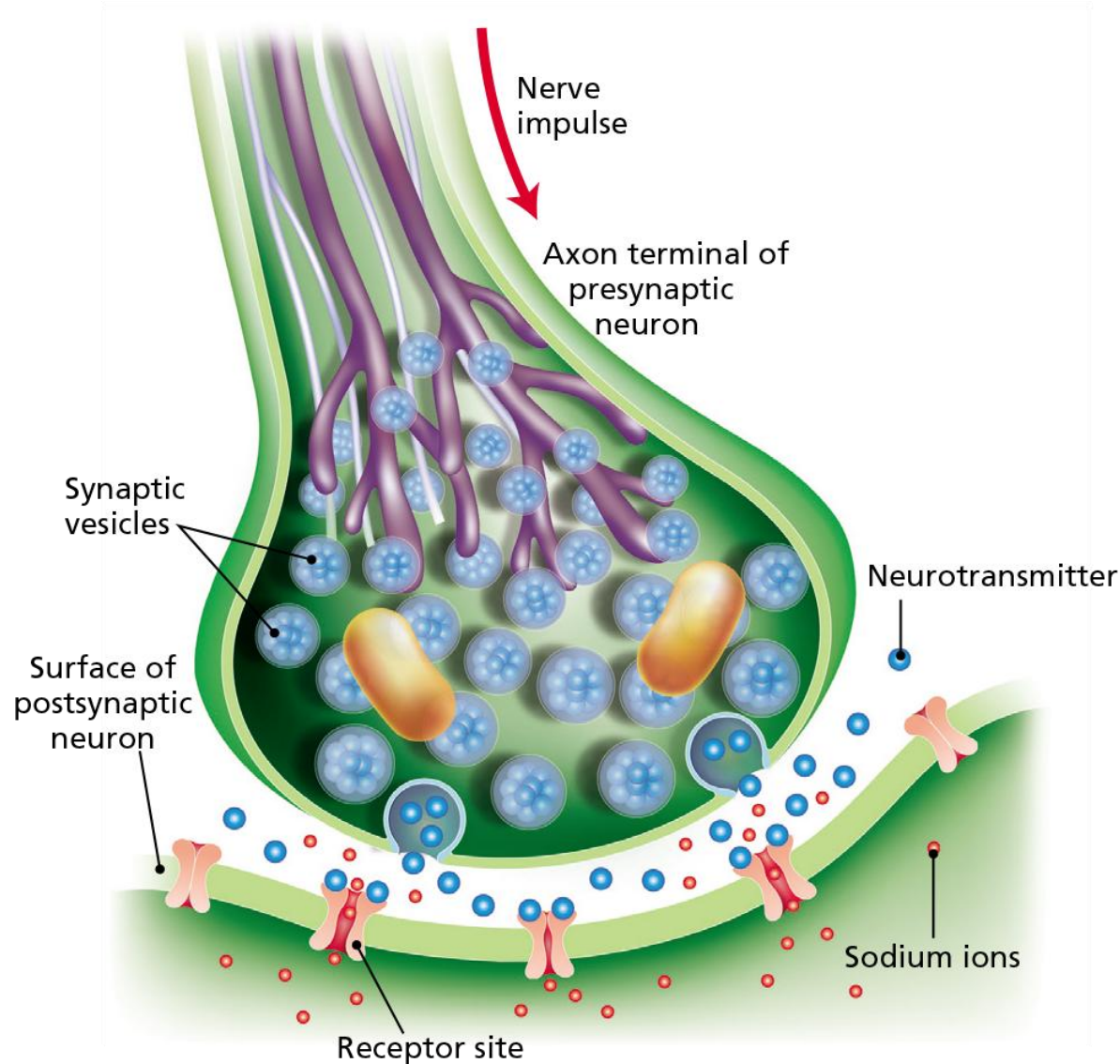
- Small nitrogen-containing neurotransmitters, e.g., neuropeptides (Targeted in CNS as endorphins or Released to circulation as GH & TSH).

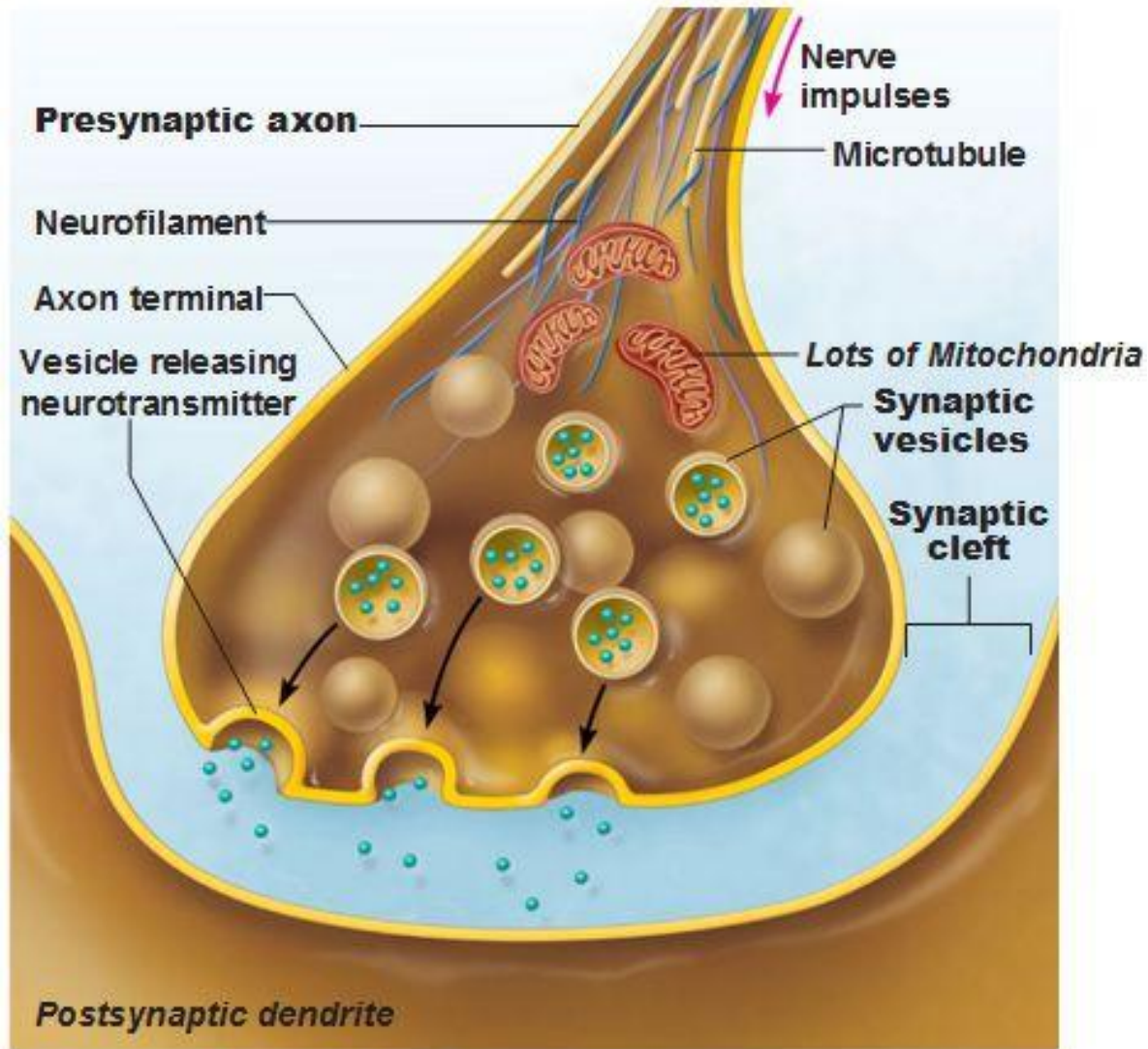
- Major small nitrogen-containing neurotransmitters such as Glutamate, GABA, Glycine, Acetylcholine, Dopamine, Norepinephrine, Serotonin, Histamine, In addition to epinephrine, aspartate, nitric oxide



Neurotransmitter synthesis

- Neurotransmitters are mostly synthesized in the presynaptic terminal.
- They are synthesized from amino acids, Intermediates of glycolysis, and Intermediates of TCA.
- Once synthesized, they are stored in vesicles (by active uptake)





Cont.

- Neurotransmitters are released in response to nerve impulses which causes an influx of Ca^{2+} to the presynaptic terminal.
- neurotransmitters undergo exocytosis into synaptic cleft and binds to receptors on the postsynaptic membrane to elicit action.
- They also undergo termination through reuptake from the presynaptic terminal (or by glial cells) Or/ Enzymatic inactivation (in the pre or postsynaptic terminals)

Summary

- Understanding neurological disorders requires biochemical and neurochemical knowledge.
- Autonomic Nervous System, controls involuntary activities through the sympathetic (fight-or-flight), parasympathetic (relaxation), and enteric (digestive regulation) systems.
- Cerebrospinal Fluid (CSF) is a clear fluid surrounding the brain & spinal cord, acting as a cushion and nutrient provider. It is normally clear and colorless; turbidity indicates infection, while xanthochromia (yellowing) suggests hemorrhage or high protein content.
- Various compounds cross the BBB via facilitated diffusion, including glucose (via GLUT-1) and ketone bodies during starvation.
- Neurotransmitters (glutamate, GABA, dopamine, serotonin) are chemical messengers released at synapses, synthesized only by neurons.
- They are synthesized and stored in vesicles, then released via Ca^{2+} -dependent exocytosis, bind to postsynaptic receptors, and are terminated by reuptake or enzymatic breakdown.



Next Lecture

◦ **Biochemistry of Nervous system II**

References

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