11

Physiology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

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Doctor

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Functional Unit (Neuron):

Neuron is almost similar to all cells , has cell body which has almost all the organelles in any cell except the centrosome (or centriole) because centrosomes are needed for cell division while neurons don't divide , once the cell dies it will not be able to regenerate, so that it is well protected in our bodies b

1) The skull (protecting neurons forming the brain).

2) Vertebral column (protecting neurons forming the spinal cord) .

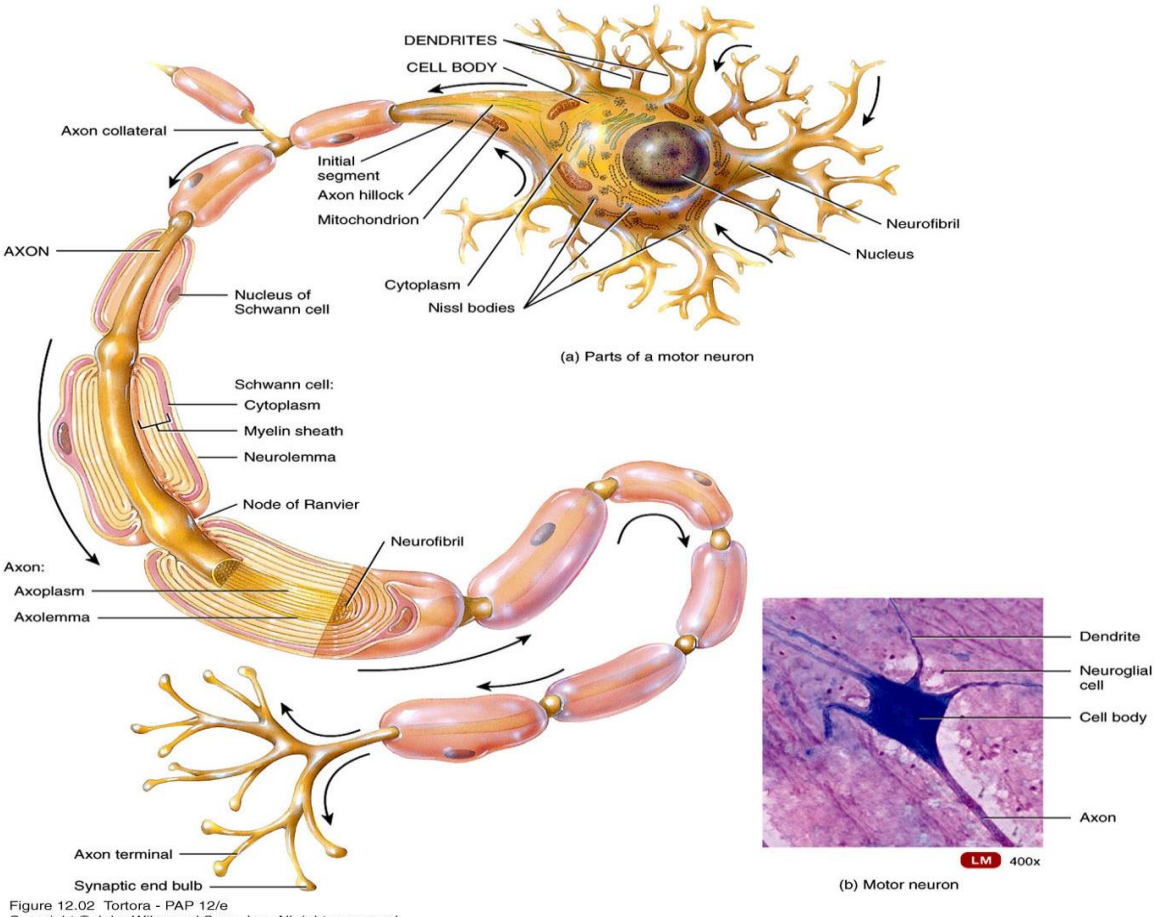

Figure 12.02 Tortora - PAP 12/e
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After studying the last figure, the neuron consists of:

1.cell body that has almost all organelles and the main function is the synthesis of proteins.

-Nissl bodies: (Nissl is the first substance describing cell bodies) large granular bodies ,found in neurons. These granules are of rough endoplasmic reticulum (RER) with rosettes of free ribosomes and are the site of protein synthesis. (not very important don't waste your time on it)

-Proteins: they are formed at the ER then transported to the Golgi apparatus for packaging (vesicles that bud from Golgi apparatus to the cytoplasm)

And once we need these proteins in the axonal terminals it just go through the axon by a mechanism called **"axonal transport"** which is a very slow mechanism (around 2 mm per day) and that's why proteins that are synthesized in the soma(cell body) are very precious and important.

2.**The axon:** In some neurons it is surrounded by a lipid layers of membrane ,so we have first the membrane of the axon which is phospholipid bilayer, then we have schwann cells that surround axon membranes and form the myelin (in this case we have a myelinated neurons) but there are some areas that are interrupted (this areas without myelin called nodes of ranvieer)

-The main function of the myelin: to isolate the axon so it is very hard to produce action potential here - action potentials are produced whithin nonmyelinated areas- so action potential seems to be jumping from one ranvieer nodes to another.

-SOME AXONS ARE UNMYLINATED.

3.**The axon hillock** :the area between the cell body and the axon and it is a nonmyelinated area, which has the largest density of voltage gated Na+ channels which are very important in A.P ,as a result the threshold is the lowest here (lowest means nearest to the rest potential) ,Also A.P can be produced in the cell body , as it still contains voltage gated Na+ channels but in smaller amounts, However within dendrites, A.P can't be produced (Almost don't contain any voltage gated Na+ channel)

4**.axon terminals, knobs, buttons :** Contains chemical substances that are released upon stimulus.

-these chemical substances mediate the transfer of the impulse from the first neuron to the second neuron-that's why they are called neurotransmitters-

Note: we have some organelles in the axon and the axon terminal like mitochondria - because we need energy in the axonal transport- (but we don't have any ER there).

Transmission of Receptor Information to the Brain (by neuron)

➢The larger the nerve fiber diameter the faster the rate of transmission of the signal because the larger the neuron the lesser the resistance, velocity of transmission can be as fast as 120 m/sec or as slow as 0.5 m/sec .

Remember: Velocity of transmission depends on:

1.diameter of the nerve fiber. 2.myelination of the nerve fiber

➢Nerve fiber classification:

➢type A - myelinated fibers of varying sizes, generally fast transmission speed.

the diameter here is between (1-20) micrometer and the speed rate from 6 to 120 m/sec. It subdivided into:

1-alpha(α): the largest one, so it is the fastest - The larger the nerve fiber diameter the faster the rate of transmission-.

2-beta(β): smaller than α

3-gama(γ): smaller than β

4-delta(δ): the smallest one, then it is the slowest in type A.

➢type B- partially myelinated neurons (3-14m/sec speed). -it is found excessively in the autonomic nervous system -

➢type C - unmyelinated fibers, small with slow transmission speed, the diameter is (0.5-2) micrometer and the speed is 0.5 to 2 m/s .

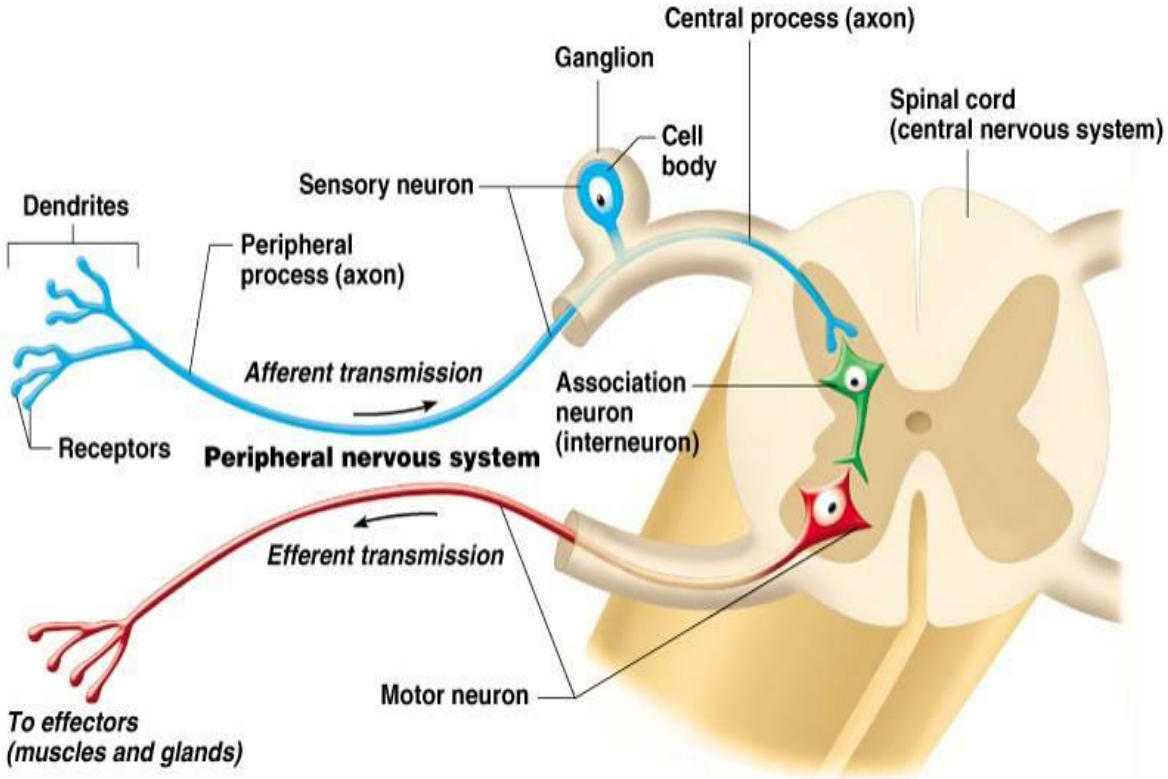
-So, the types of Nerve Fiber:
1-Myelinated fibers: Type A (types I, II and III)
- A α, - A β, - A γ, - Aδ.
2-Unmyelinated Fibers: Type C (type IV)

-We cannot say that types I is the same as type Aα (they are not the same) while

we can say that type c and type IV are the same.

Please check slide 5 and notice that we have an overlapping between Aα , - Aβ , - Aγ ,- Aδ ,and each one is found somewhere in the body.

Neuron classification-function classification-



Sensory neuron =afferent neuron: the neuron that carry the impulse to the CAN.

, Motor neuron=efferent neuron: the neuron that carry the impulse from the CNA to the effectors.

, association neuron (interneuron): the neuron that associate the motor neuron with the sensory neuron.

So, it is like this!:

Sensory(afferent) neuron---association neuron (interneuron) in the spinal cord---Motor(efferent) neuron.

Structural Classification of Neurons

1.**multipolar neuron:** a lot of projections(dendrites+axon) from the soma (cell body) - the most common type of neurons in our bodies.

2.**bipolar neuron:** the soma in the middle and has two projections, in one side we have the dendrites and in the other side we have the axon. (visual sensory neurons)

3.unipolar neuron: the soma has one projection that divided to dendrites and the axon. Found in olfactory system(smell).

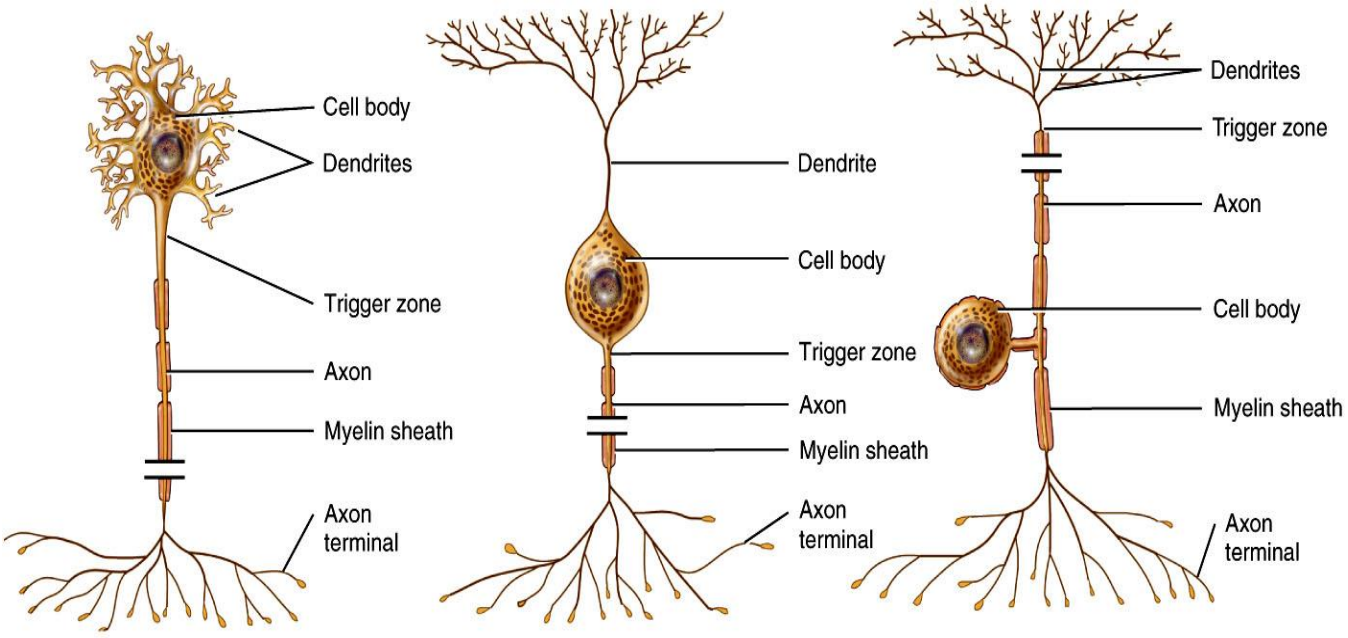


Figure 12.03 Tortora - PAP 12/e
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Neurotransmitters

❖Chemical substances that function as synaptic transmitters and found in the axonal terminals. They are classified in two main types:

1. **Small molecules**:

rapidly acting transmitters: secreted in large amount and for a short duration. Each neuron has only one kind of these NT.

If one neuron contains acetylcholine, we will not be able to find another kind in it (just acetylcholine)

❖Examples: acetylcholine, norepinephrine, dopamine, serotonin, GABA, glycine, glutamate, NO

2. **Neuropeptides** (Neuromodulators) :

❖more potent than small molecule transmitters, cause more prolonged actions.

**Peptides=proteins and these proteins are produced in the soma then they are transported to the axonal terminal by the axonal transport which is very slow (precious), so they are secreted in smaller quantity, but their duration of action is long.

Each neuron may have one or more Neuropeptides.

They are never secreted alone -they are secreted with the small molecule rapidly acting transmitters. (co secreted)

Examples: endorphins, enkephalins, VIP, ect.

-Some neuropeptides are hypothalamic (a specific area in the brain) releasing hormones , such as : TRH(Thyrotropin Releasing Hormones), LHRH, ect.

- Also they could be pituitary (a gland in the brain) peptides such as : ACTH, prolactin, vasopressin, ect.

Comparison between Small Molecules and Neuropeptides Neurotransmitters (NT)

Small Molecules	*Neuropeptides*
rapidly acting	slowly acting
Each neuron has only one kind of these NT.	Each neuron may have one or more NP
short lived action (short duration)	prolonged time of action
Small molecules NT are secreted in larger amounts	They are secreted in smaller quantities
vesicles are recycled .	The vesicles aren't recycled, because they are produced in the soma,therefore, vesicles are coming from far away from stoma.
They could be formed at the presynaptic terminals.	They are synthesized in the soma.

The small molecule rapidly acting NT has IV classes:-

Table 45–1

Small-Molecule, Rapidly Acting Transmitters

Class I
- Acetylcholine

Class II: The Amines
- Norepinephrine
- Epinephrine
- Dopamine
- Serotonin
- Histamine

Class III: Amino Acids
- Gamma-aminobutyric acid (GABA)
- Glycine
- Glutamate
- Aspartate

Class IV
- Nitric oxide (NO)

Class II:

The amines: derivative from amino acids.

1)Tyrosine based (epinephrine, norepinephrine, dopamine),
2)tryptophan based (serotonin),
3) histidine based (histamine)

Class IV: gases such as , Nitric oxide (NO), carbon monoxide (CO) (they exit the cells quickly because they are lipid-soluble and for the same reason they can easily enter the postsynaptic membrane and bind to it's receptors **inside the neuron**,they usually work (GMP) .

Some notes about Neuropeptides:-

Table 45–2

Neuropeptide, Slowly Acting Transmitters or Growth Factors

Hypothalamic-releasing hormones
- Thyrotropin-releasing hormone
- Luteinizing hormone–releasing hormone
- Somatostatin (growth hormone inhibitory factor)

Pituitary peptides
- Adrenocorticotropic hormone (ACTH)
- β-Endorphin
- α-Melanocyte-stimulating hormone
- Prolactin
- Luteinizing hormone
- Thyrotropin
- Growth hormone
- Vasopressin
- Oxytocin

Peptides that act on gut and brain
- Leucine enkephalin
- Methionine enkephalin
- Substance P
- Gastrin
- Cholecystokinin
- Vasoactive intestinal polypeptide (VIP)
- Nerve growth factor
- Brain-derived neurotropic factor
- Neurotensin
- Insulin
- Glucagon

From other tissues
- Angiotensin II
- Bradykinin
- Carnosine
- Sleep peptides
- Calcitonin

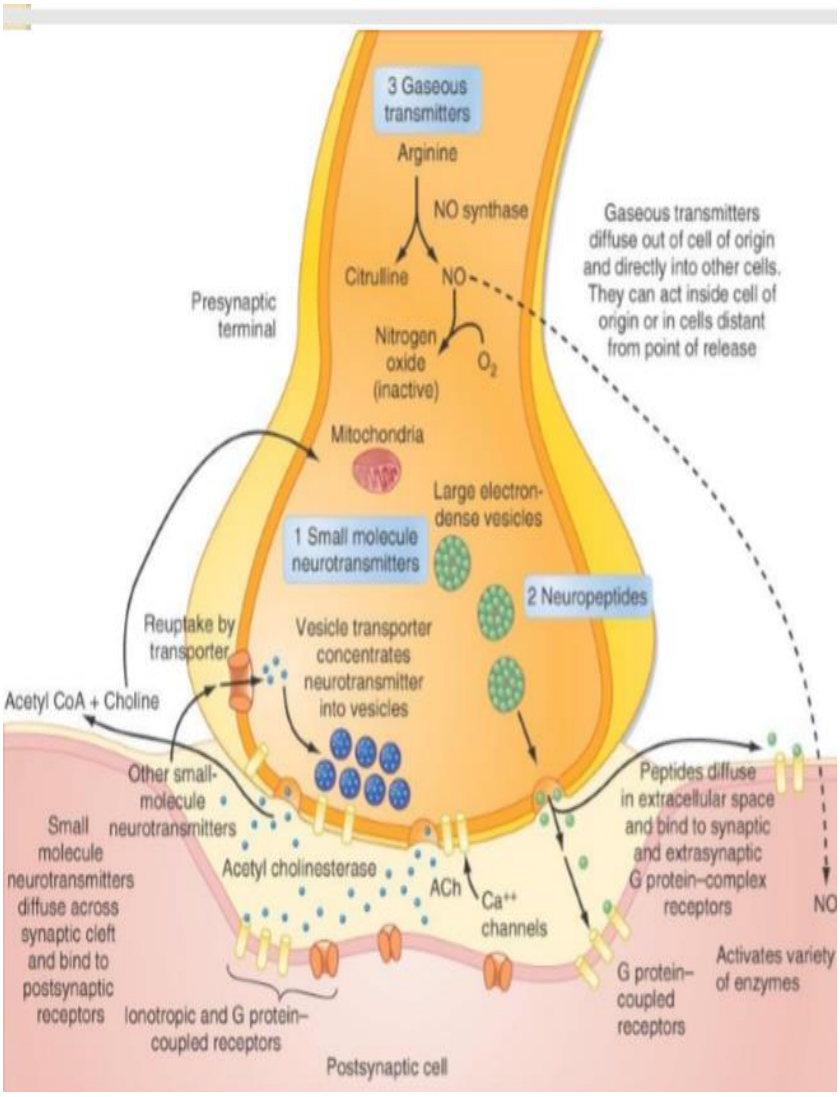
Not very important…

TRH- Thyrotropin-releasing hormone is the smallest NT, consist of 3 amino acids (tripeptides).

Leucine and methionine enkephalins are termed endogenous opioid, as they are synthesized in the body(endogenous) and bind to the body's opioid receptors (opioid is a drug derived from opium; like morphine)

Removal of Neurotransmitter:

when the action potential reaches the axonal terminals (knobs), it stimulates the opening of the voltage gated calcium channels present there, which leads to calcium influx, this influx causes the vesicles containing the neurotransmitters to dock and fuse with the presynaptic membrane and thus releasing the neurotransmitters into the synaptic cleft (active exocytosis) then they bind to receptors in the postsynaptic neuron, these receptors are usually ionotropic (they are channels by themselves)



The synapse might be between axon and soma , axosomatic synapse or between axon and dendrites axodendritic synapse,

or between axon and axon ,axoaxonic synapse.

At the end of this process we can terminate the action of the NT by :

1.**diffusion**: move down concentration gradient (from the synaptic cleft to the pre-synaptic neuron)

2**. Enzymatic degradation:** by enzymes such as, Acetylcholinesterase for (Ach)(small molecules), peptidases for neuropeptides, monoamine oxidase and Catechol-O-methyltransferase (COMT) which breaks down epinephrine and norepinephrine.(small molecules) -these enzymes are found in the postsynaptic neurons-

To make Ach (acetylcholine) more efficient >>we can use a drug to inhibit Acetylcholinesterase (block Acetylcholinesterase receptor) so Ach will work for longer time.

3**. Uptake by neurons or glia cells:** reuptake by neuron and other cells is an active process (need ATP,active).

<u>Prozac</u> (antidepressant drug) :-it inhibist the re-uptake of **serotonin** and keeps serotonin working for longer time, serotonin is important to keep us away from depression.