Nerve tissue & Nervous system

Nerve tissue & Nervous system

- The most complex system
- Network of many billions Nerve cell (neuron)
- Supporting cell (glial cell)

Anatomical organization:

- Central nervous system

brain & spinal cord

- Peripheral nervous system

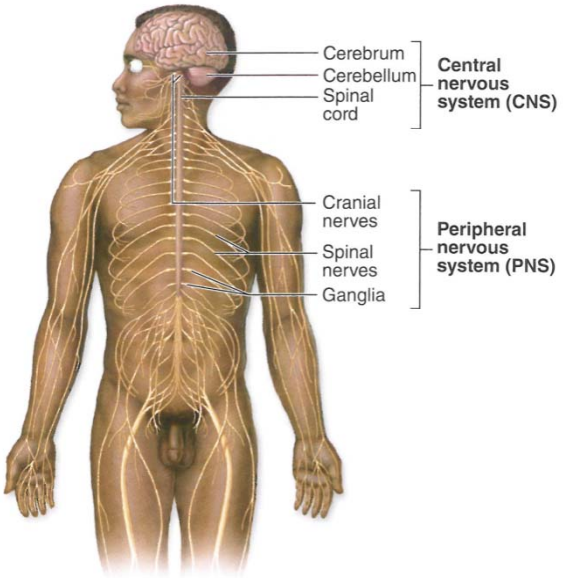
cranial & spinal peripheral nerves & ganglia

Cells:

- Neuron (numerous long processes)
- Glial cells (short processes)

- Stimuli
- Excitable (irritable)
- Membrane depolarization
- Potential action
- Depolarization wave (Nerve impulse)

FIGURE **9–1** **The general organization of the nervous system.**



Components of the nervous system are subdivided both structurally and functionally. Major structural divisions (shown here) are the **CNS**, which includes the brain and spinal cord, and the **PNS**, which is composed of nerves and ganglia. Functional categories are the **sensory (afferent)** and **motor (efferent)** divisions. Sensory nerves are further subdivided into voluntary **somatic** and involuntary or **visceral** components. Motor nerves are subdivided into **voluntary (somatic)** and **involuntary (autonomic)** components. The array of autonomic motor nerves is often called the **autonomic nervous system**.

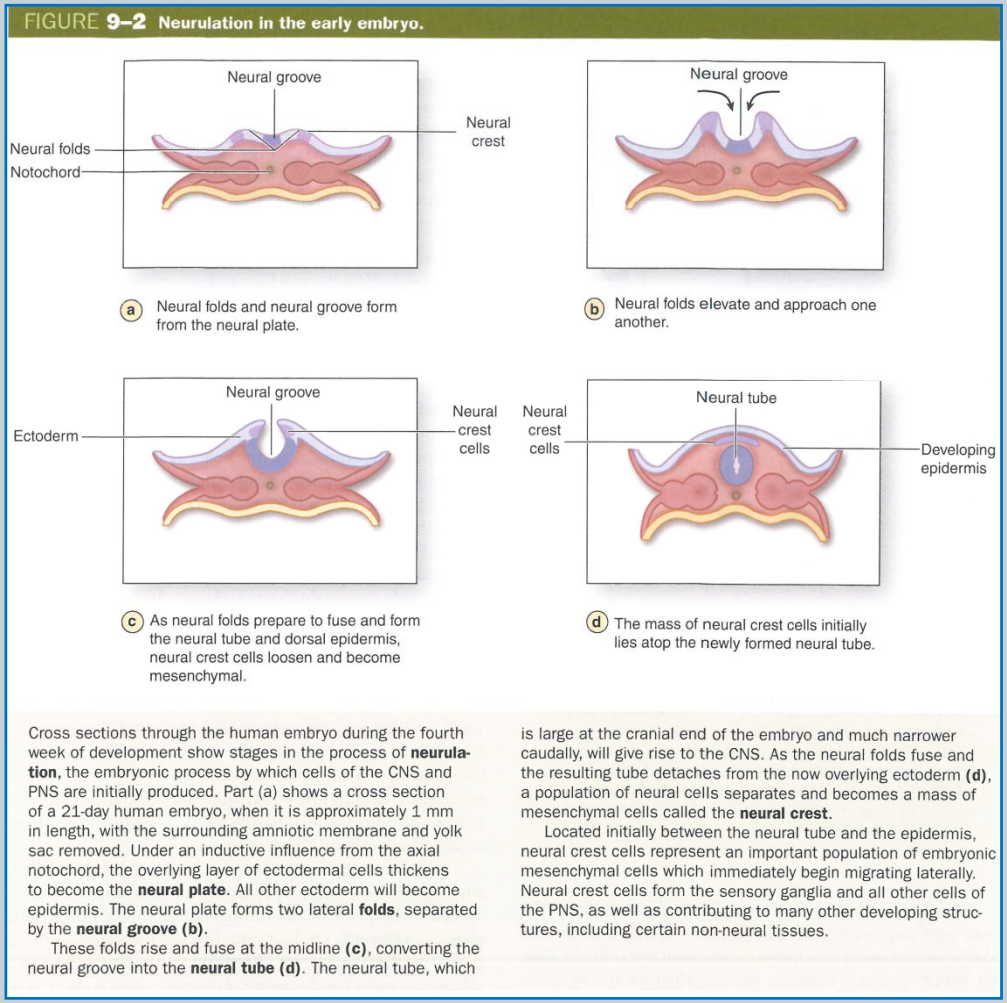
Development of nerve tissue

- Ectoderm
- Third week
- Notochord
- Ectoderm thickness
- Neural plate
- Neural groove
- Neural fold
- Neural tube

Forms CNS

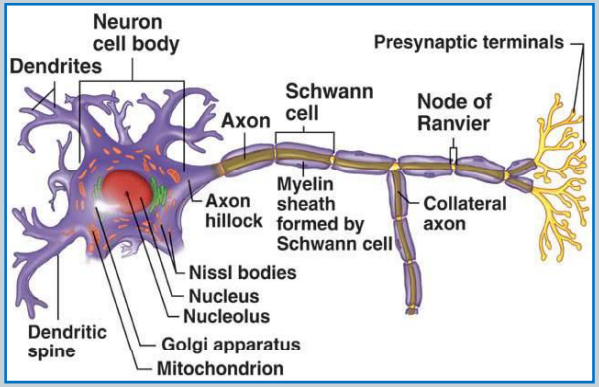
- Neural crest (mesenchyme)

Forms PNS & other non neuronal cells



Neuron

- Functional unit
- Neurolemma

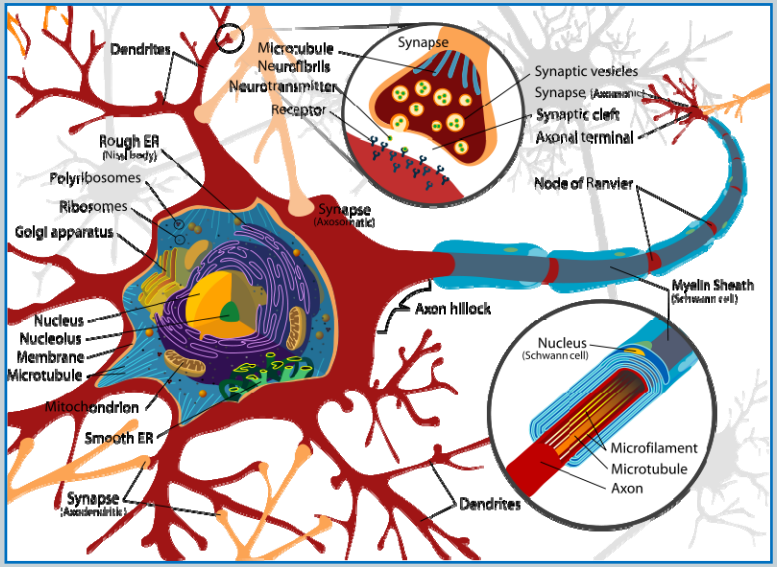


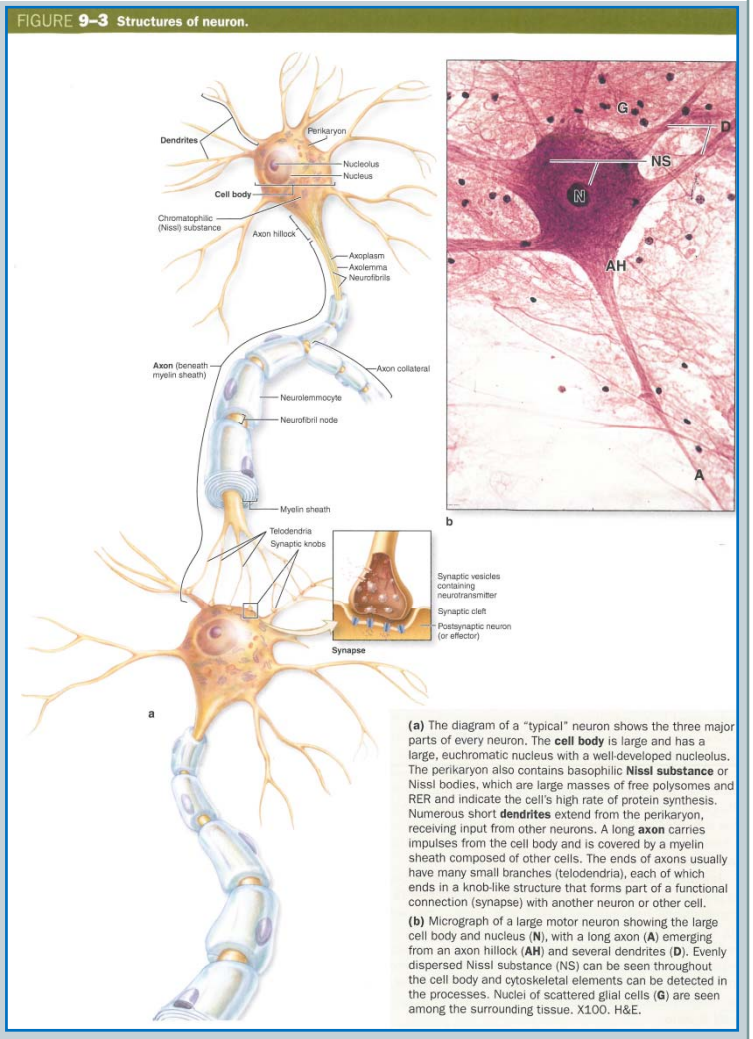
Neurons parts:

- Cell body (perikaryon)

Nucleus & organelles

- Dendrites
- Axon





Neuron classification according number of processes

- **Multipolar neuron**

Most of neurons

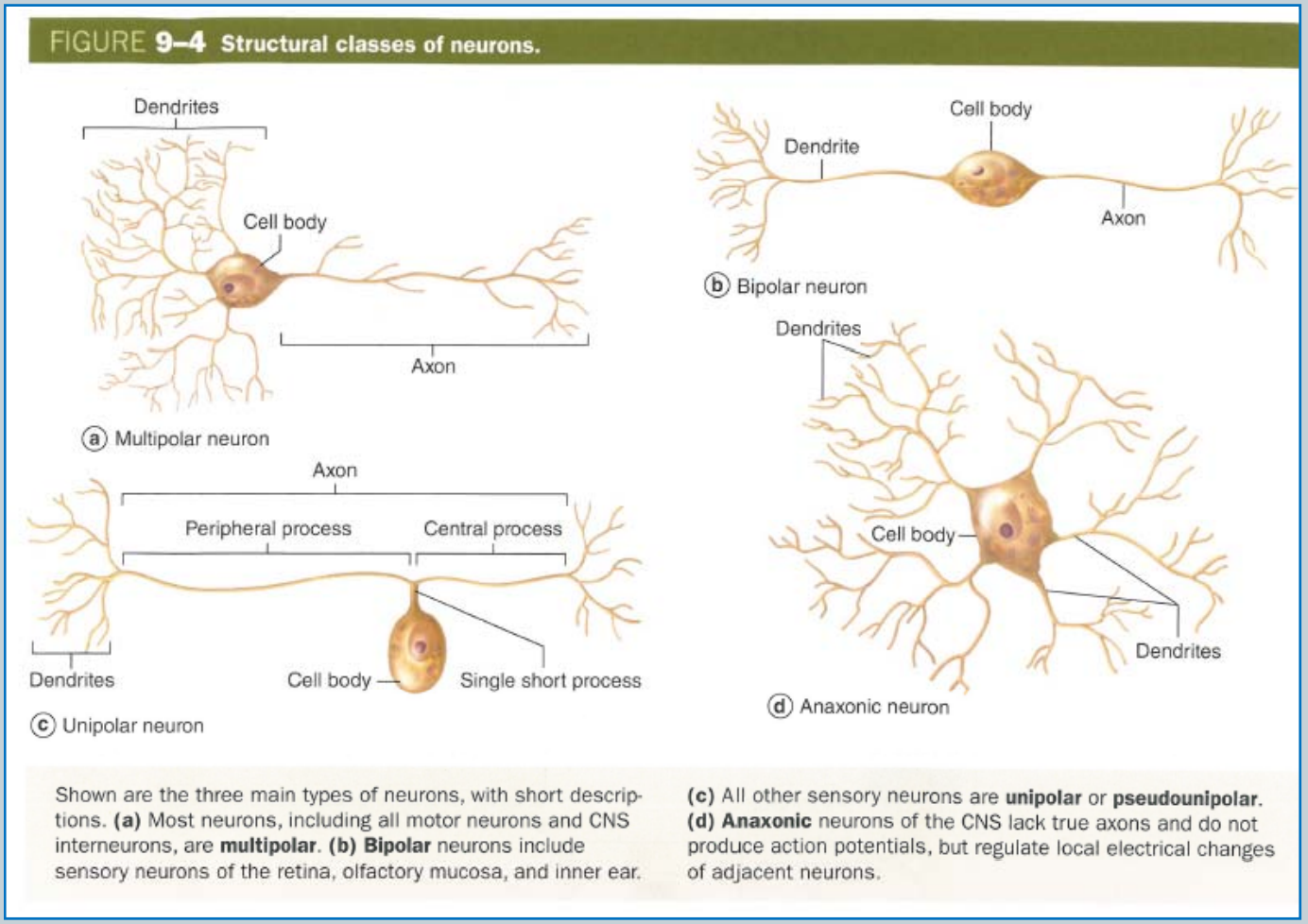
- **Bipolar neuron**

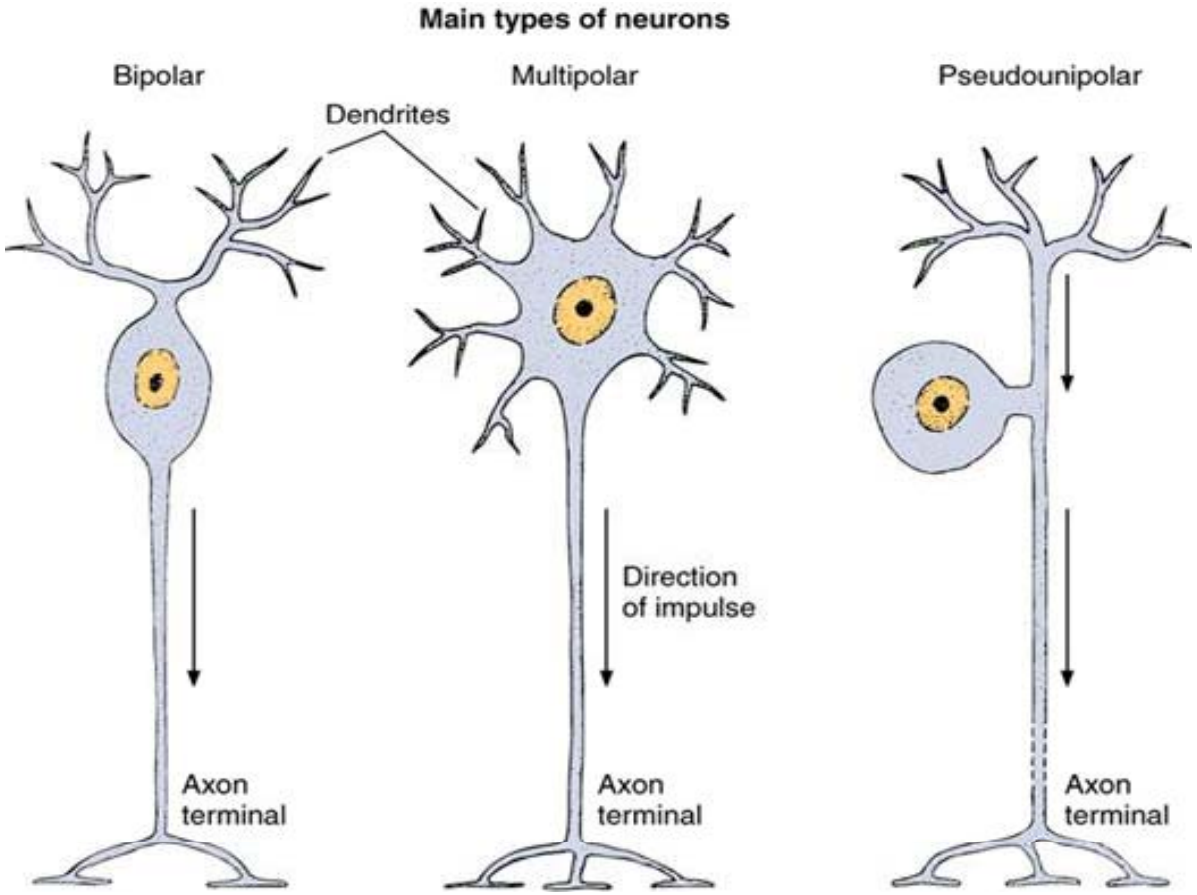
Retina
Olfactory mucosa
Cochlear & vestibular ganglia

- **Unipolar neuron**

Spinal ganglia (sensory)
Most cranial ganglia

- **Anaxonic neurons**




Main types of neurons
Bipolar
Multipolar
Pseudounipolar
Dendrites
Direction of impulse
Axon terminal
Axon terminal
Axon terminal

Neuron classification according to function

- **Sensory neurons** (afferent)

- **Motor neurons** (efferent)

1. Somatic motor
2. Autonomic motor

- **Interneurons** (CNS & retina)

99% of all neurons in CNS

In CNS:
Gray matter
White matter

Parkinson disease

- Slowly processing
- Muscular activity defects
- Tremor
- Reduced facial muscle activity
- Balance loss
- Dopamine producing neurons Apoptosis
- Substantia nigra (CNS)
- L-dopa treatment

>> MEDICAL APPLICATION

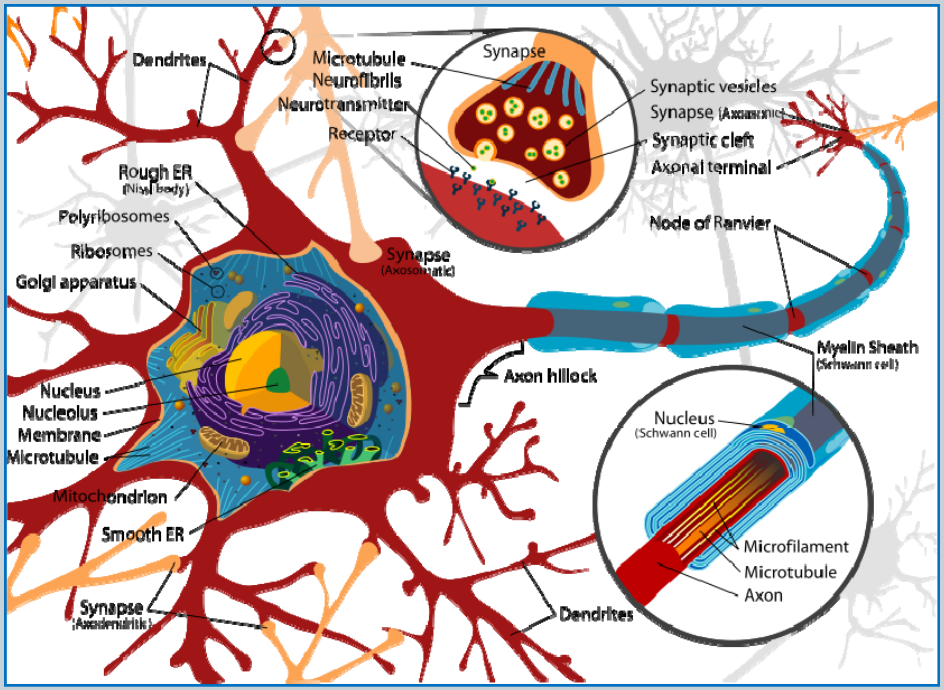
Parkinson disease is a slowly progressing disorder affecting muscular activity characterized by tremors, reduced activity of the facial muscles, loss of balance, and postural stiffness. It is caused by gradual loss by apoptosis of dopamine-producing neurons whose cell bodies lie within the nuclei of the CNS substantia nigra. Parkinson disease is treated with **L-dopa** (L-3,4-dihydroxyphenylalanine), a precursor of dopamine which augments the declining production of this neurotransmitter.

Perikaryon

- Very large spherical & euchromatic nucleus
- Prominent nucleoli
- Well developed RER
- Polysomes (chromatophilic substance or nissl bodies)
- Golgi apparatus
- Mitochondria (also in axon)
- Intermediate filaments (neurofilaments)

Silver staining

- Microtubules
- lipofuscin



Dendrites

- Short & divided process (tree branch)
- Each Purkinje cell with 200,000 axon

- **Dendritic spine**

Short & broad process (actin dependent)

Brain cortex 10^{14}

Information processing

Silver staining

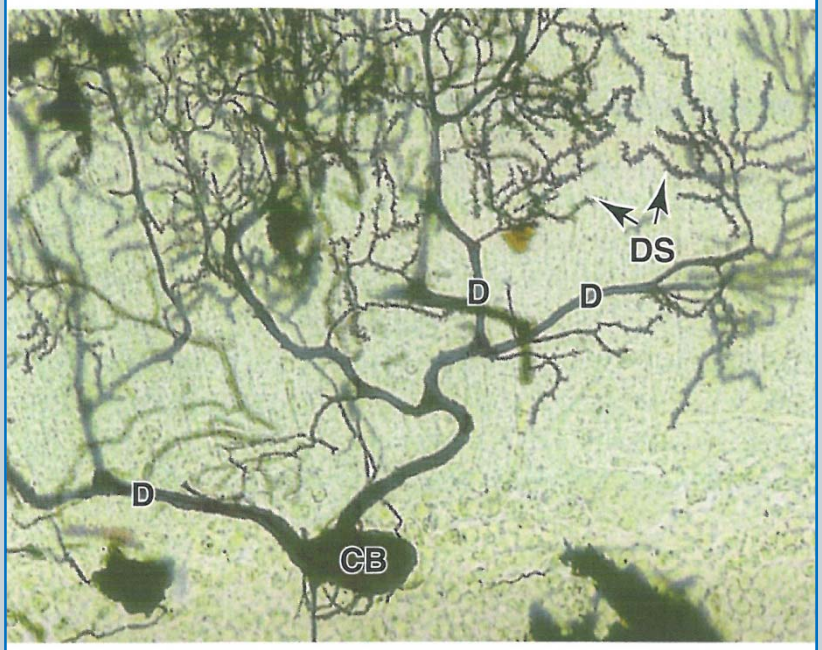
- **Neural plasticity**

Adaptation

Learning

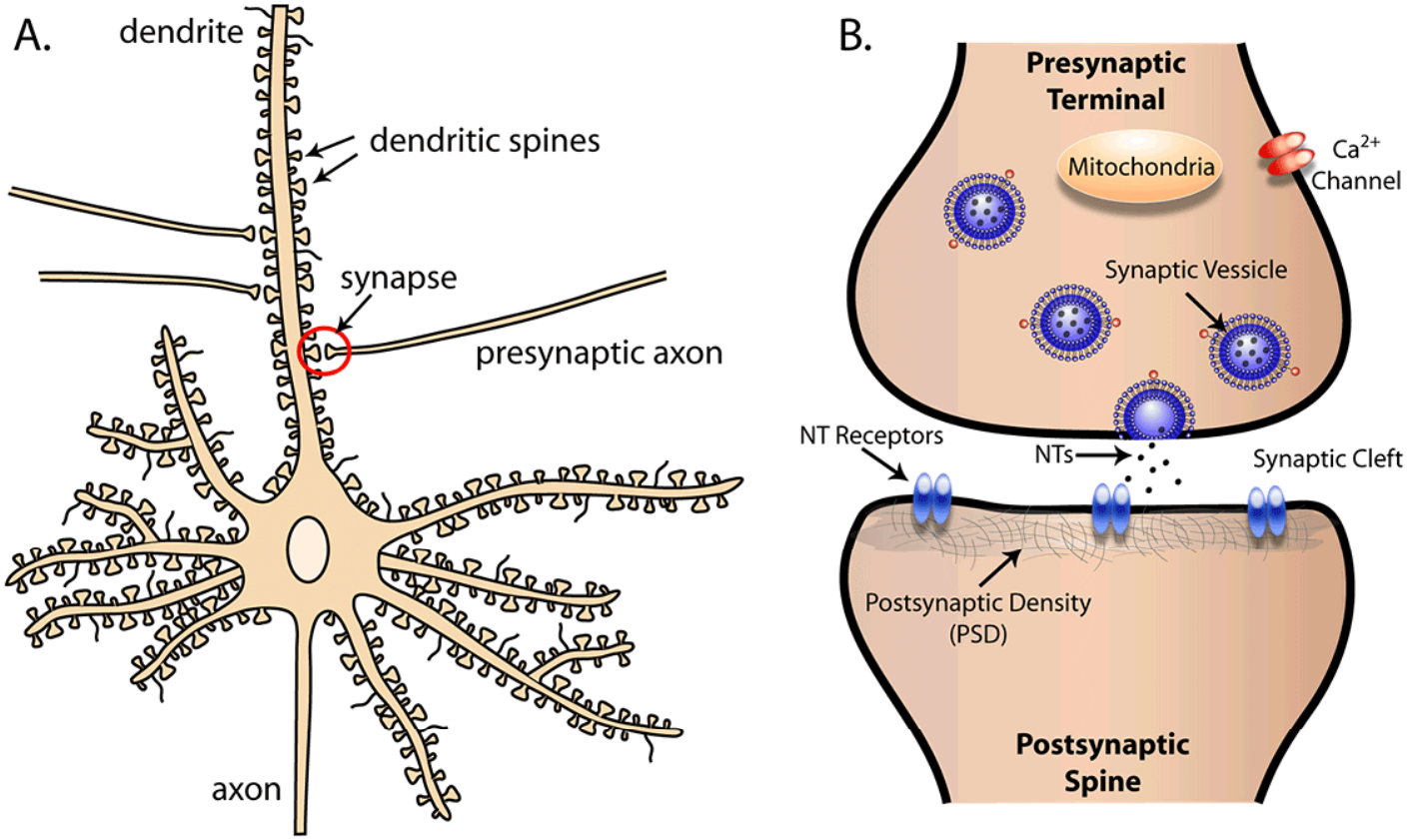
Memory

FIGURE **9–5** **Dendrites and dendritic spines.**



The large Purkinje neuron in this silver-impregnated section of cerebellum has many dendrites (**D**) emerging from its cell body (**CB**) and forming branches. The small dendritic branches have many short projecting dendritic spines (**DS**) spaced closely along their length, each of which is a site of a synapse with another neuron. X650. Silver stain.

Background: Dendrites and dendritic spines



Axon

- Axon hillock (initial segment)
- Axolemma
- Axoplasm

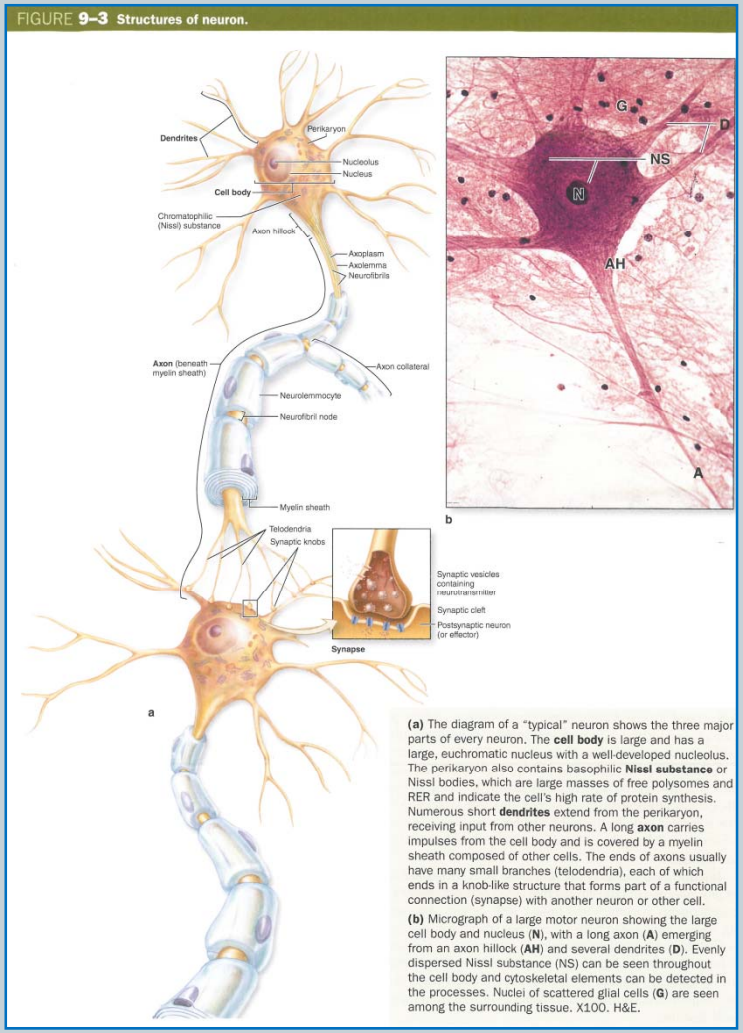
- Terminal arborization
- Collateral
- Terminal bouton

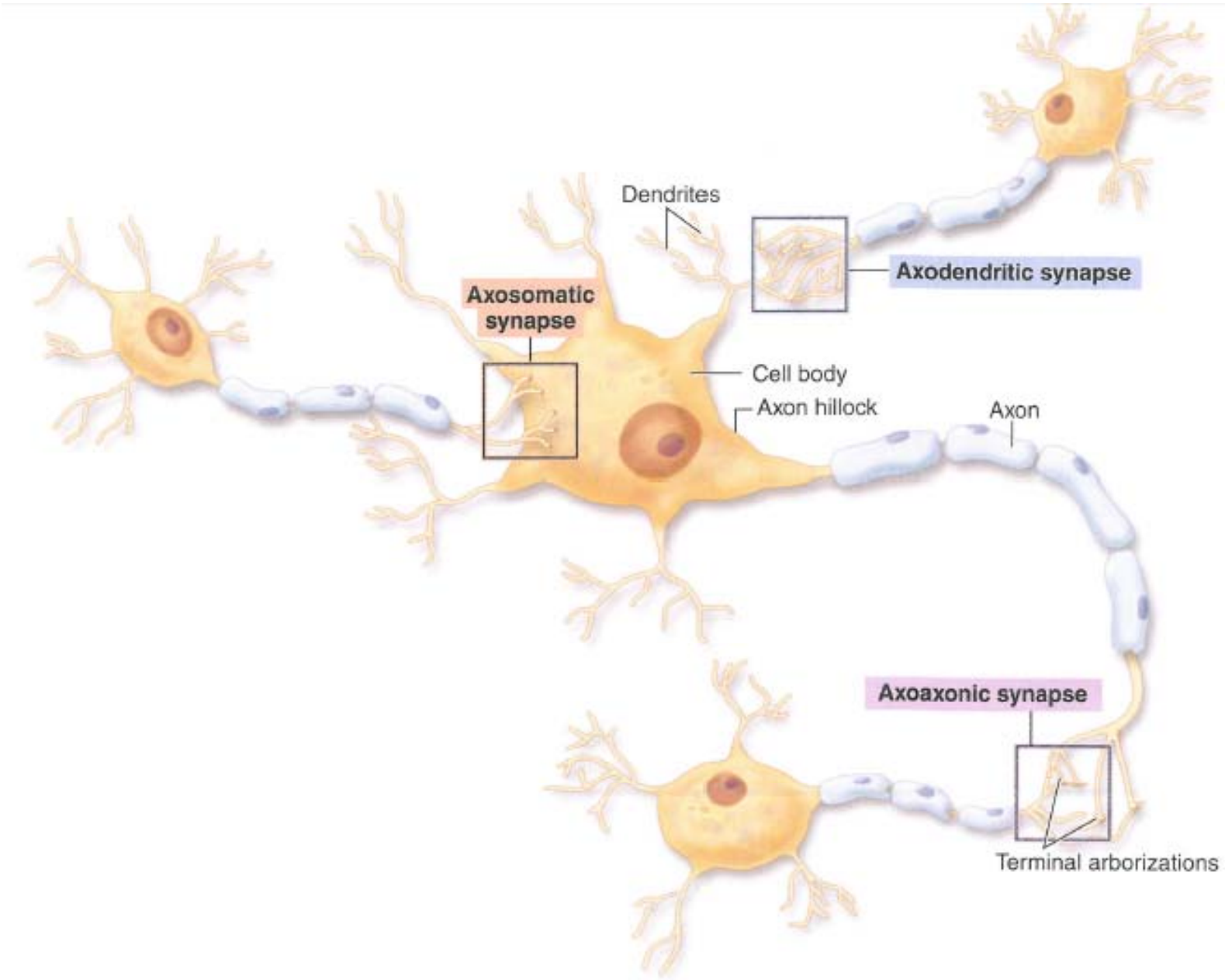
- Anterograde transport
- Retrograde transport

- Nerve impulse (action potential)
- Voltage gated Na+ K+ channels
- Resting potential
- Refractory period

>> MEDICAL APPLICATION

Most **local anesthetics** are low-molecular-weight molecules that bind to the voltage-gated sodium channels of the axolemma, interfering with sodium ion influx and, consequently, inhibiting the action potential responsible for the nerve impulse.




Dendrites
Axodendritic synapse
Axosomatic synapse
Cell body
Axon hillock
Axon
Axoaxonic synapse
Terminal arborizations

Synapthic communication

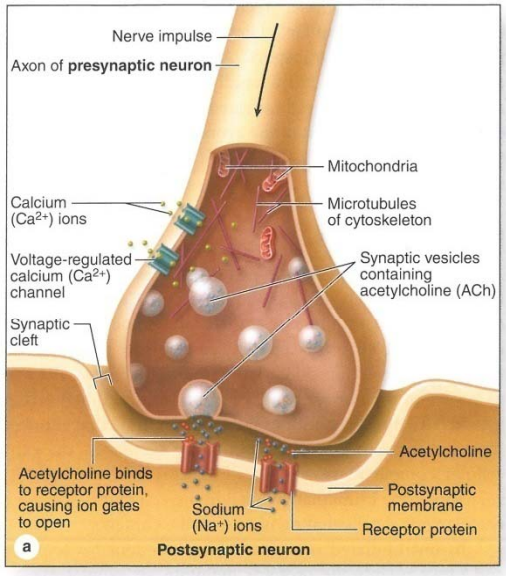
- Presynaptic cell
- Postsynaptic cell
- Neurotransmiters

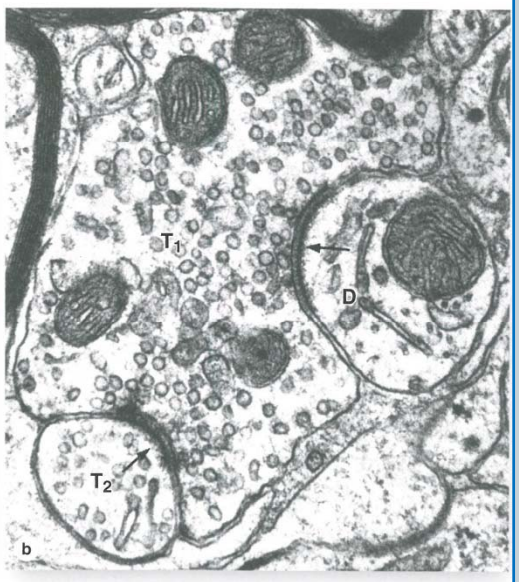
- Terminal bouton (synaptic vesicle)
- Synaptic cleft

- Excitatory synapse
- Inhibitory synapse

- Axosomatic synapse
- Axodendritic synapse
- Axoaxonic synapse

FIGURE 9–6 Major components of a synapse.



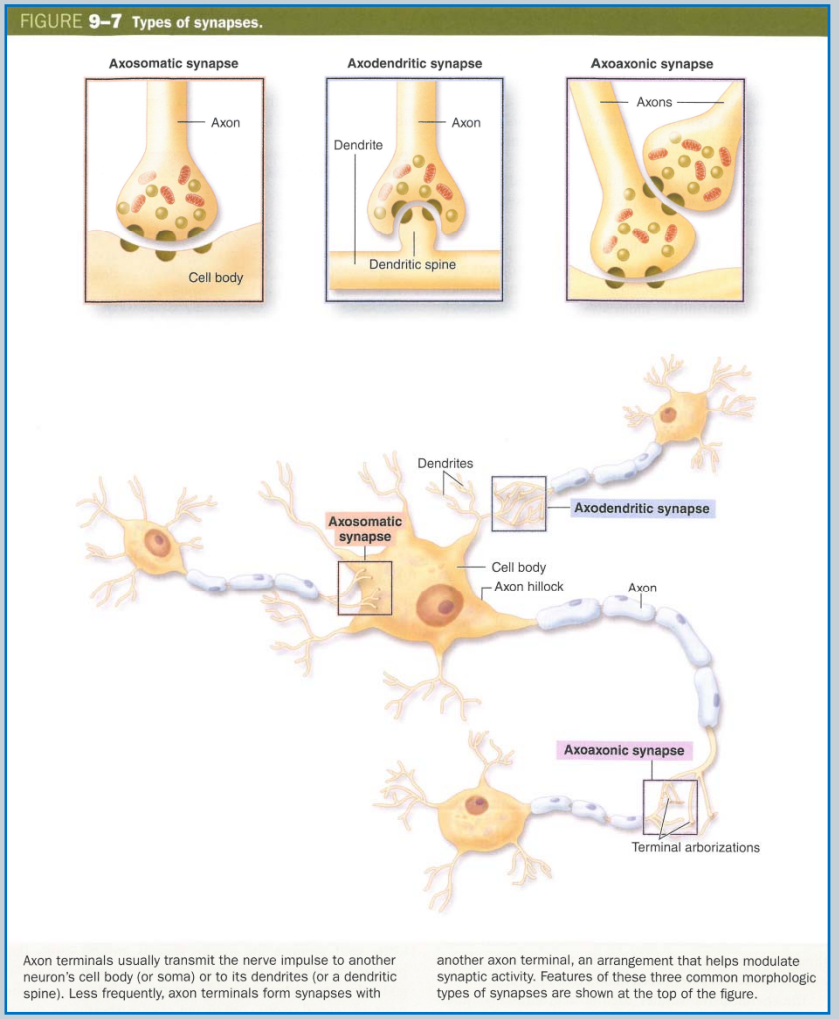


(a) Diagram showing a synapse releasing neurotransmitters by exocytosis from the terminal bouton. Presynaptic terminals always contain a large number of **synaptic vesicles** containing neurotransmitters, numerous **mitochondria**, and smooth ER as a source of new membrane. Some neurotransmitters are synthesized in the cell body and then transported in vesicles to the presynaptic terminal. Upon arrival of a nerve impulse, voltage-regulated Ca^{2+} channels permit Ca^{2+} entry, which triggers neurotransmitter release into the synaptic cleft. Excess membrane accumulating at the presynaptic region as a result of exocytosis is recycled by clathrin-mediated endocytosis, which is not depicted here.

(b) The TEM shows a large presynaptic terminal (T_1) filled with synaptic vesicles and asymmetric electron-dense regions around 20- to 30-nm-wide synaptic clefts (**arrows**). The postsynaptic membrane contains the neurotransmitter receptors and mechanisms to initiate an impulse at the postsynaptic neuron. The postsynaptic membrane on the right is part of a dendrite (**D**), associated with fewer vesicles of any kind, showing this to be an axodendritic synapse. On the left is another presynaptic terminal (T_2), suggesting an axoaxonic synapse with a role in modulating activity of the other terminal. X35,000.

Synapse types (morphologic classification)

- Axosomatic synapse
- Axodendritic synapse
- Axoaxonic synapse



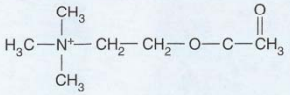
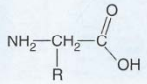
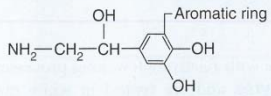
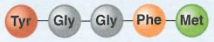
Neurotransmiters

- Acetyl choline (neuromuscular junction)
- Catecholamines (epinephrine, nor epinephrine & dopamine)
- AA(GABA, HT-5, Glutamat, Glysin)
- Small peptide (P sub. & endorphine)

>> MEDICAL APPLICATION

Levels of neurotransmitters in the synaptic cleft and available for binding postsynaptic receptors are normally regulated by several local mechanisms. **Selective serotonin reuptake inhibitors (SSRIs)**, a widely used class of drugs for treatment of depression and anxiety disorders, were designed to augment levels of this neurotransmitter at the postsynaptic membrane of serotonergic CNS synapses by specifically inhibiting its reuptake at the presynaptic membrane.

TABLE 9–1 Common neurotransmitters and their actions.

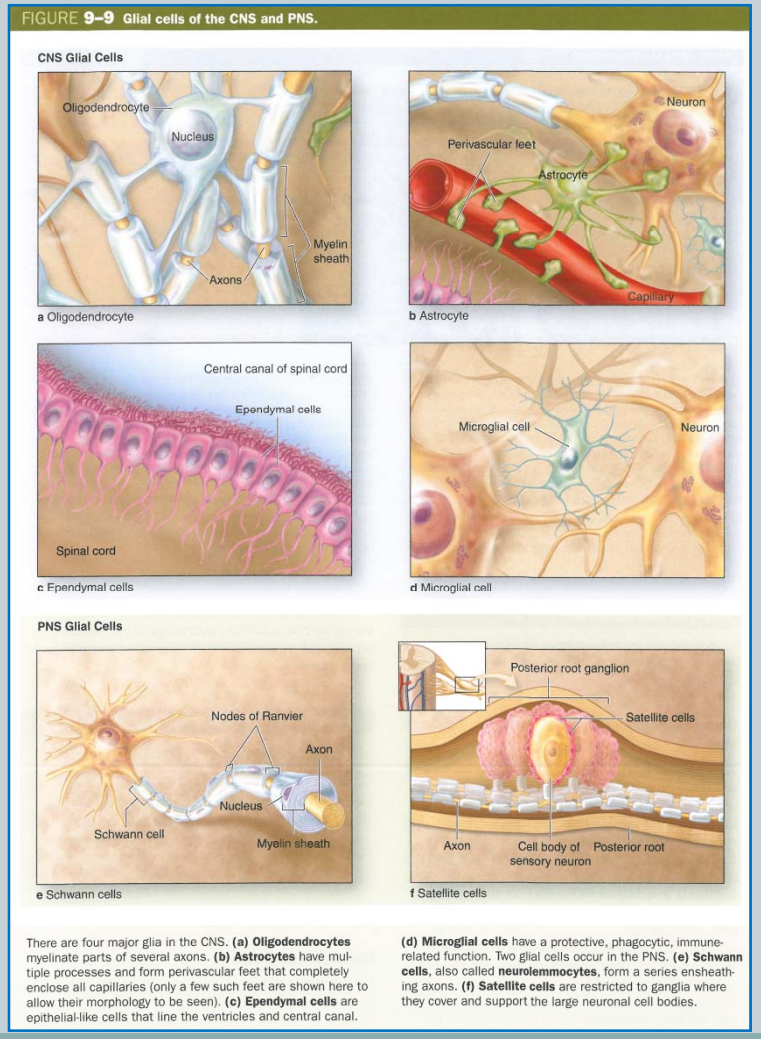
Neurotransmitter	Description/Action
ACETYLCHOLINE (ACh)	
	Chemical structure significantly different from that of other neurotransmitters; active in CNS and in both somatic and autonomic parts of PNS; binds to ACH receptors (cholinergic receptors) in PNS to open ion channels in postsymaptic membrane and stimulate muscle contraction
AMINO ACIDS	
	Molecules with both carboxyl (—COOH) and amine ($—NH_2$) groups and various R groups; act as important transmitters in the CNS
Glutamate	Excites activity in neurons to promote cognitive function in the brain (learning and memory); most common neurotransmitter in the brain; opens Na^+ channels
Gamma-aminobutyric acid (GABA)	Synthesized from glutamate; primary inhibitory neurotransmitter in the brain; also influences muscle tone; opens or closes various ion channels
Glycine	Inhibits activity between neurons in the CNS, including retina; opens Cl^- channels
MONOAMINES	
	Molecules synthesized from an amino acid by removing the carboxyl group and retaining the single amine group; also called biogenic amines
Serotonin or 5-hydroxytryptamine (5-HT)	Has various functions in the brain related to sleep, appetite, cognition (learning, memory), and mood; modulates actions of other neurotransmitters
Catecholamines	A distinct group of monoamines
Dopamine	Produces inhibitory activity in the brain; important roles in cognition (learning, memory), motivation, behavior, and mood; opens K^+ channels, closes Ca^{2+} channels
Norepinephrine (noradrenaline)	Neurotransmitter of PNS (sympathetic division of autonomic nervous system) and specific CNS regions
Epinephrine (adrenaline)	Has various effects in the CNS, especially the spinal cord, thalamus, and hypothalamus
NEUROPEPTIDES	
	Small polypeptides act as signals to assist in and modulate communication among neurons in the CNS
Enkephalin	Helps regulate response to noxious and potentially harmful stimuli
Neuropeptide Y	Involved in memory regulation and energy balance (increased food intake and decreased physical activity)
Somatostatin	Inhibits activities of neurons in specific brain areas
Substance P	Assists with pain information transmission into the brain
Cholecystokinin (CCK)	Stimulates neurons in the brain to help mediate satiation (fullness) and repress hunger
Beta-endorphin	Prevents release of pain signals from neurons and fosters a feeling of well-being
Neurotensin	Helps control and moderate the effects of dopamine
OTHERS	
Adenosine	Also part of a nucleotide, inhibits activities in certain CNS neurons
Nitric oxide	Involved in learning and memory; relaxes muscle in the digestive tract; important for relaxation of smooth muscle in blood vessels (vasodilation)

Glial cells & neuronal activity

- Neuronal survival & activity
- 10 times more
- Neural plate progenitor cells
- Small amount of connective tissue & collagen
- Cell processes network called neuropill

Glial cells (6 types):

1. Oligodendrocyte
2. Astrocyte
3. Ependymal cell
4. Microglia
5. Schwann cell
6. Satellite cell



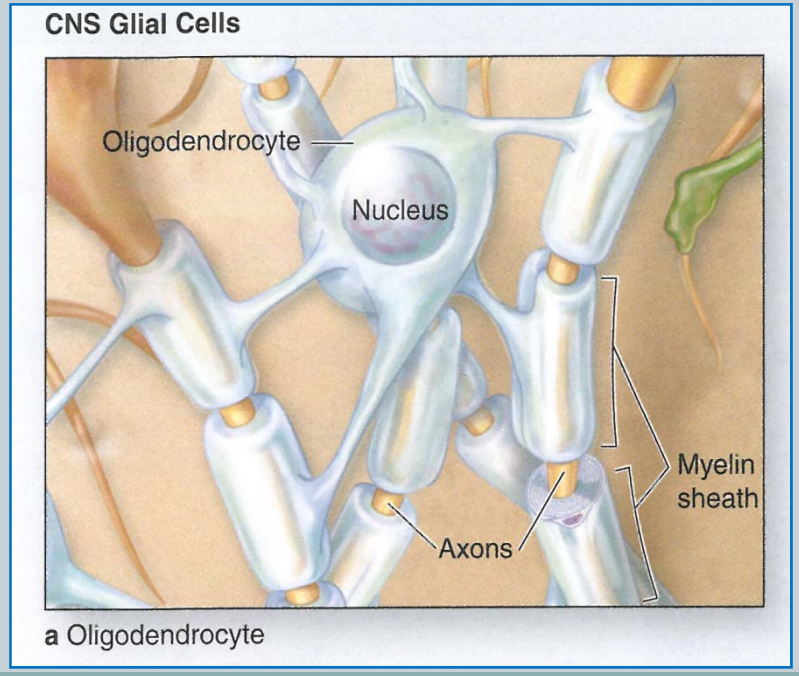
Glial cells characteristics

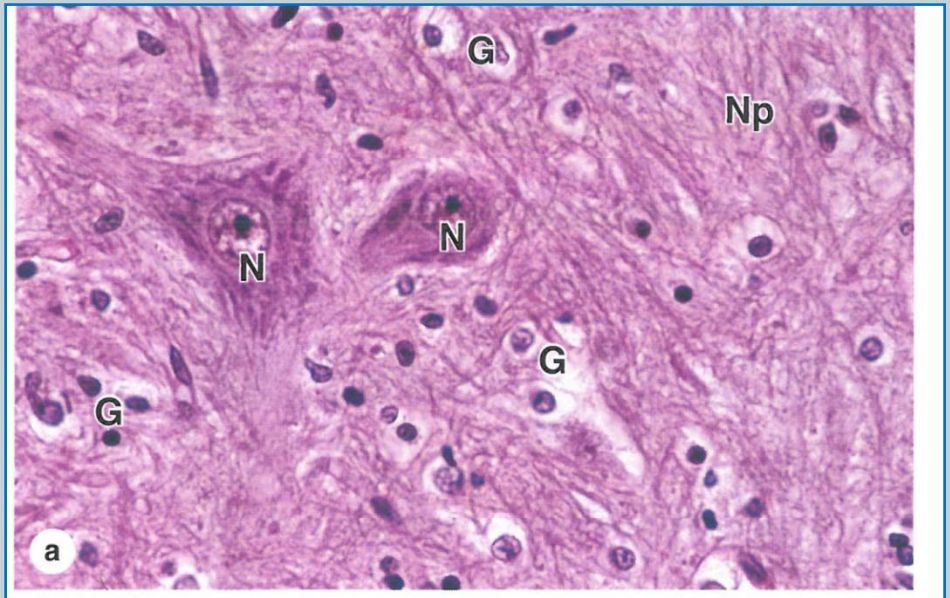
TABLE 9–2 Origin, location and principal functions of neuroglial cells.

Glial Cell Type	Origin	Location	Main Functions
Oligodendrocyte	Neural tube	CNS	Myelin production, electrical insulation
Schwann cell (Neurolemmocyte)	Neural crest	Peripheral nerves	Myelin production, electrical insulation
Astrocyte	Neural tube	CNS	Structural and metabolic support of neurons; BBB; repair processes
Satellite cells (of ganglia)	Neural crest	Peripheral ganglia	Structural and metabolic support for neuronal cell bodies
Ependymal cell	Neural tube	Line ventricles and central canal of CNS	Aid production and movement of CSF
Microglia	Bone marrow (monocytes)	CNS	Defense and immune-related activities

Oligodendrocyte

- Myelin sheaths around axons in CNS
- Most glial cells in CNS whit matter
- Small cells
- Rounded & condensed nuclei
- Unstained cytoplasm (Golgi apparatus)





(a) Most neuronal cell bodies (**N**) in the CNS are larger than the much more numerous glial cells (**G**) that surround them. The various types of glial cells and their relationships with neurons are difficult to distinguish by most routine light microscopic methods. However, **oligodendrocytes** have condensed, rounded nuclei and unstained cytoplasm due to very abundant Golgi complexes, which stain poorly and are very likely represented by the

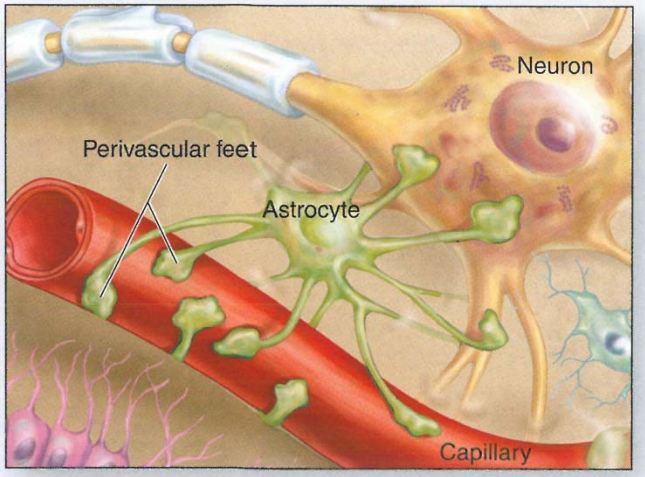
Astrocyte

- In CNS only
- most glial cells
- Most diverse type

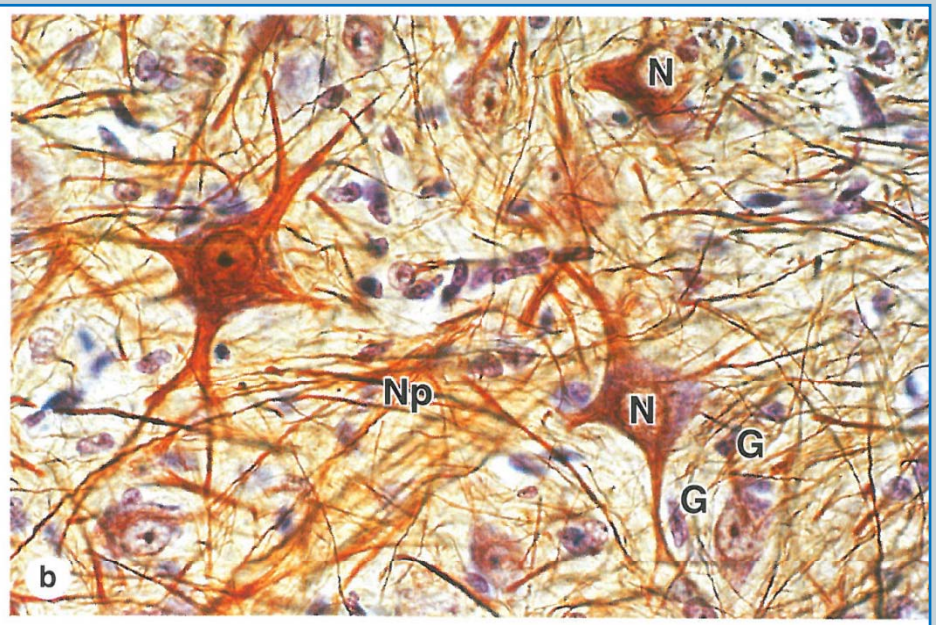
Astrocyte types:

1. Fibrous astrocyte in white matter
2. Protoplasmic astrocyte gray matter

- GFAP(Intermediated filaments)



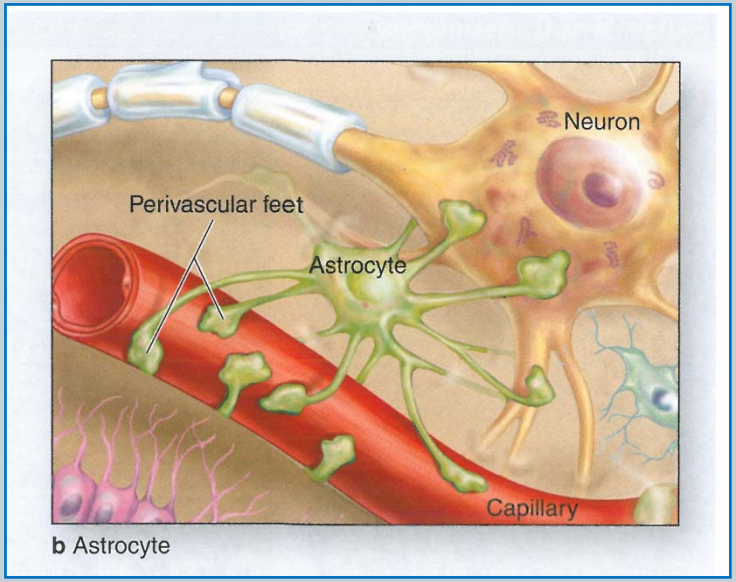
b Astrocyte



cells with those properties seen here. The other glial cells seen here similar in overall size, but with very little cytoplasm and more elongated or oval nuclei, are mostly **astrocytes**. Routine H&E staining does not allow neuropill to stand out well. X200. H&E. **(b)** With the use of gold staining for neurofibrils, **neuropil (Np)** is more apparent. X200. Gold chloride and hematoxylin.

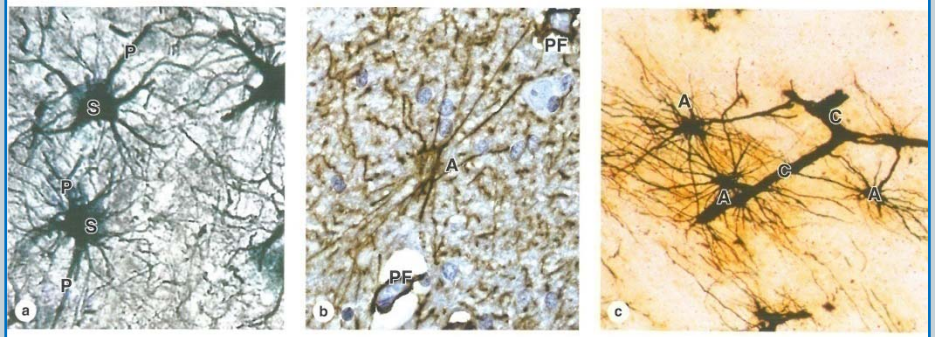
Astrocyte function

1. Regulation of Ion concentration
2. Guiding & supporting movement of developing neurons
3. Forming perivascular feet (BBB)
4. Metabolic exchange & neuron nurishment
5. Synapse covering
6. Glial limiting mem. Formation (exterior CNS)



b Astrocyte

FIGURE 9–10 Astrocytes.

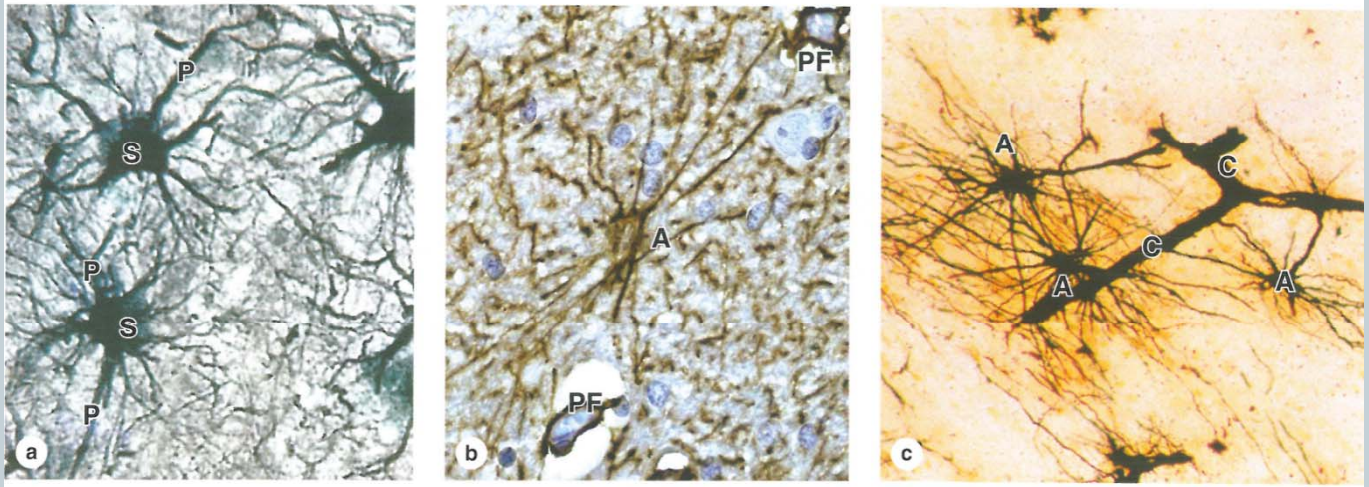


(a) Astrocytes are the most abundant glial cells of the CNS and are characterized by numerous cytoplasmic processes (**P**) radiating from the glial cell body or soma (**S**). Astrocytic processes are not seen with routine light microscope staining but are easily seen after gold staining. Morphology of the processes allows astrocytes to be classified as fibrous (relatively few and straight processes) or protoplasmic (numerous branching processes), but functional differences between these types are not clear. X500. Gold chloride.

(b) All astrocytic processes contain intermediate filaments of GFAP, and antibodies against this protein provide a simple method to stain these cells, as seen here in a fibrous astrocyte (**A**) and its processes. The small pieces of other GFAP-positive processes in the neuropil around this cell give an idea of the density of this glial cell and its processes in the CNS. Astrocytes are an important part of the blood-brain barrier (BBB), regulating entry of molecules and ions from blood into CNS tissue. Capillaries at the extreme upper right and lower left corners are enclosed by GFAP-positive perivascular feet (**PF**) at the ends of numerous astrocytic processes. X500. Anti-GFAP immunoperoxidase and hematoxylin counterstain.

(c) A length of capillary (**C**) is shown here completely covered by silver-stained terminal processes extending from astrocytes (**A**). X400. Rio Hortega silver.

FIGURE **9–10** **Astrocytes.**



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(c) A length of capillary (**C**) is shown here completely covered by silver-stained terminal processes extending from astrocytes (**A**). X400. Rio Hortega silver.

Astrocytomas

- Astrocyte
- GFAP

>> MEDICAL APPLICATION

Most brain tumors are **astrocytomas** derived from those glial cells and characterized pathologically by their expression of GFAP.

Alzheimer disease

- Dementia
- Perikaryon & synapses
- Neurofibrillary tangles
- Tau pr. In:
- Perikaryon & Axon hillock
- Neuritic plaque
- B-Amyloid:
- around neuronal region

>> MEDICAL APPLICATION

Alzheimer disease, a common type of dementia in the elderly, affects both neuronal perikarya and synapses within the cerebrum. Functional defects are due to **neurofibrillary tangles**, which are accumulations of tau protein associated with microtubules of the neuronal perikaryon and axon hillock regions, and **neuritic plaques**, which are dense aggregates of β-amyloid protein that form around the outside of these neuronal regions.