

**Class of 2029**

# **Introduction to the Nervous System**

PPOM1

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# Introduction to the Nervous System

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- Nervous system connections to... muscles, organs & glands, etc
- Neural control of behavior – *neural activity creates behavior (sensory & motor; cognitive & emotional, visceral, etc)*
- Changes in the brain (anatomical/physiological) cause behavioral change (development, aging, disease, injury, learning)
- Treatments for brain diseases must change the brain (back to normal or to stop further dysfunction)     *ex. – neurodegeneration, demyelination, etc*

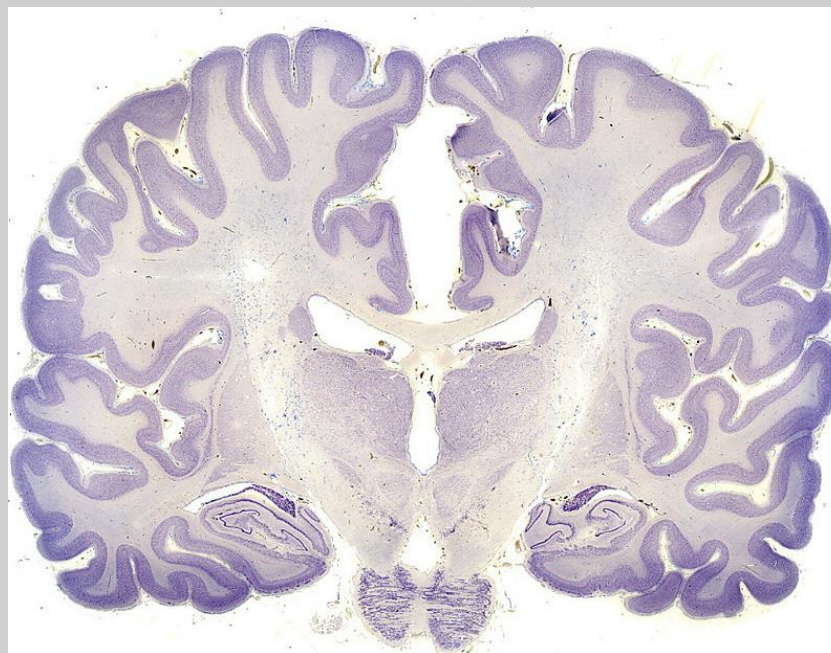
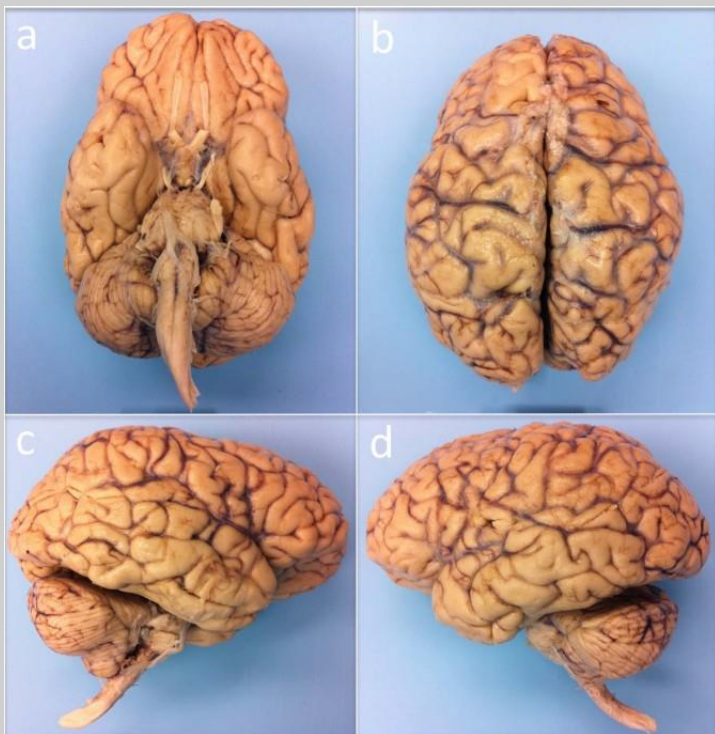


# Cells of the Central Nervous System: NEURONS

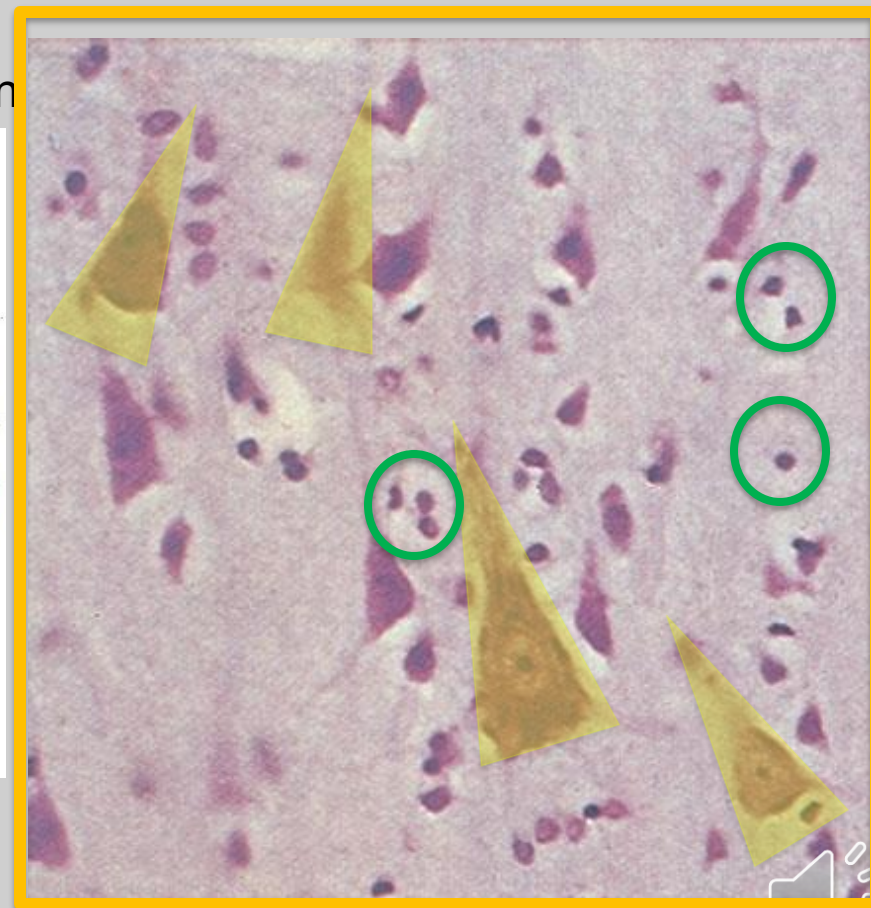
- characterized by the presence of soma (intracellular organelles), branching dendrites (often w/ spines), axon initial segment, branching axon, and axon terminals (synapses)
- electrically excitable cells that can release and respond to neurotransmitters via neuronal connections/synapses
- almost all neurons produced before birth and almost entirely non-renewable.

## Clinical correlate:

Neurodegeneration or neuronal injury (stroke) results in permanent loss of neurons.



[https://brains.anatomy.msu.edu/brains/human/coronal/2060\\_cell.html](https://brains.anatomy.msu.edu/brains/human/coronal/2060_cell.html)

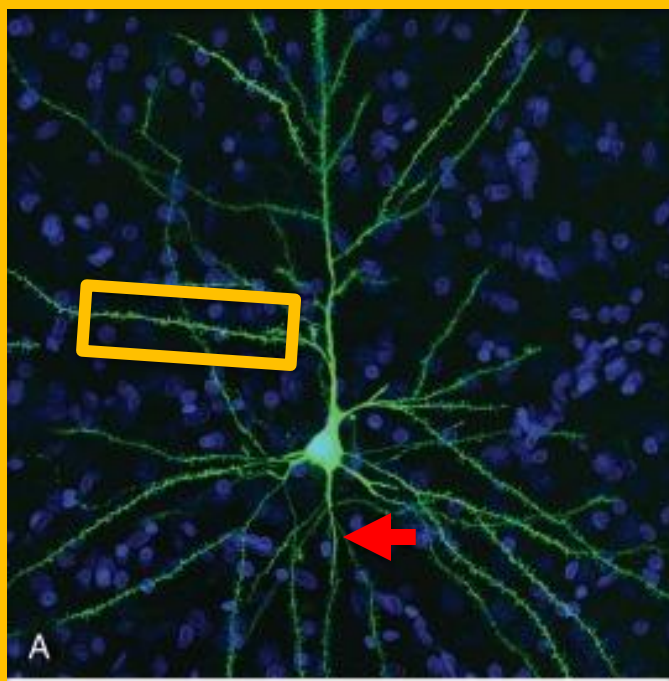


Edlow, B.L., Mareyam, A., Horn, A. *et al.* 7 Tesla MRI of the *ex vivo* human brain at 100 micron resolution. *Sci Data* 6, 244 (2019).  
<https://doi.org/10.1038/s41597-019-0254-8>

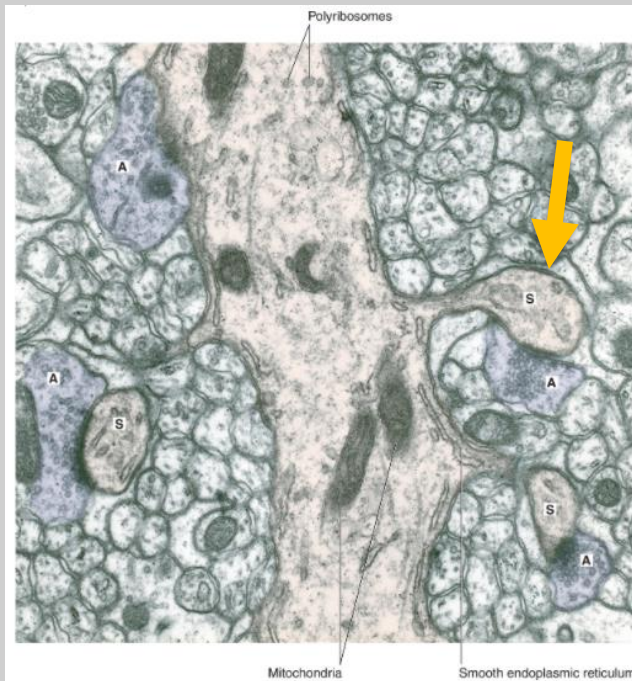


# Parts of NEURONS: Dendrites & dendritic spines

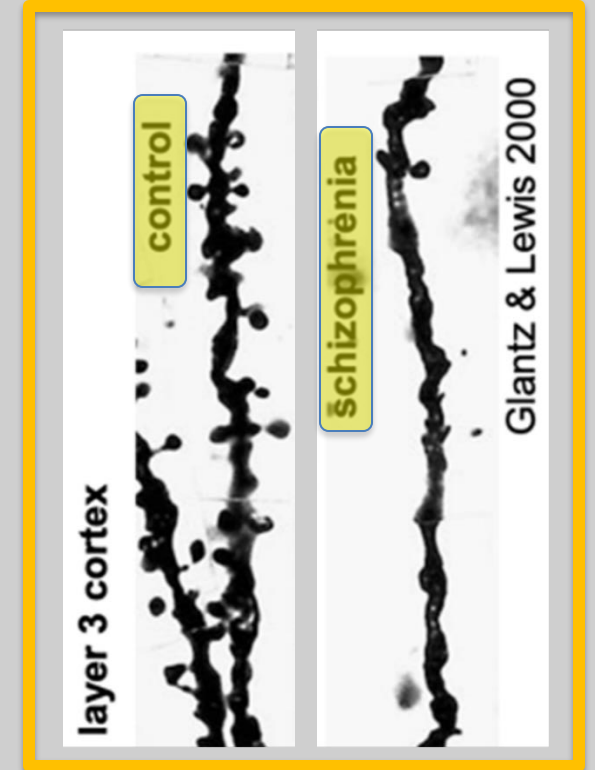
- spines found on the dendrites of many neurons such as neocortical neurons, Purkinje neurons, etc.
- synapses are preferentially made on spines



Human neocortical neuron (Benavides-Piccione et al. *Cerebral Cortex* 2013)



•Estomih Mtui MD, Gregory Gruener MD, MBA and Peter Dockery BSc, PhD Fitzgerald's *Clinical Neuroanatomy and Neuroscience*, 6, 63-74



## Clinical correlate:

*FMRP* gene - that causes Fragile X syndrome- is important in dendritic spine development.  
Patients with Fragile X syndrome have **increased** numbers of spines on neocortical neuron dendrites.

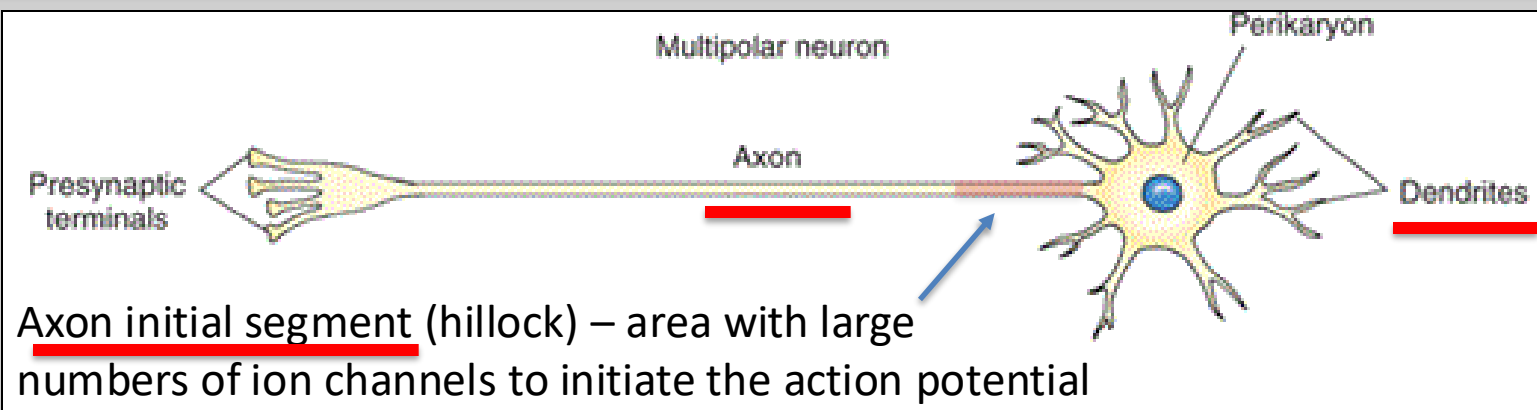
## Clinical correlate:

Dendritic spines are **decreased** in neocortical neurons of patients w/ schizophrenia.  
Mechanisms still unknown.

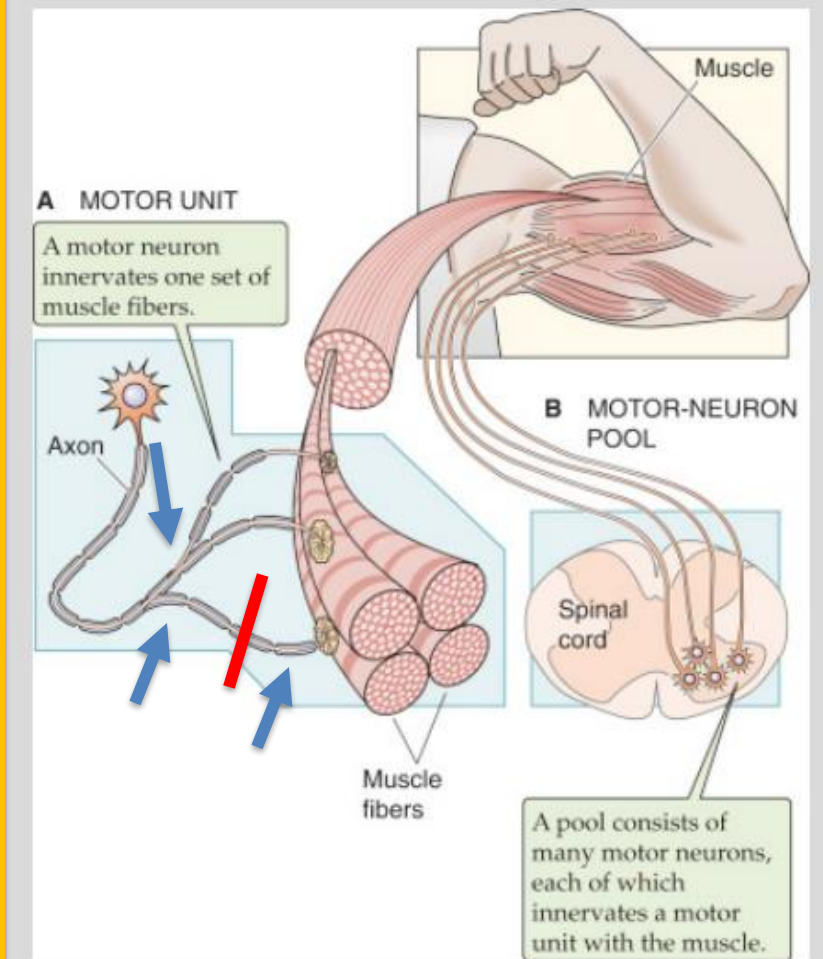


# Parts of a NEURON: Axon, branches, terminals

- axons found on nearly all neurons
- axons can vary widely in length, shape, and number of branches (emanating from axon initial segment/hillock).
- axon terminals make “contact” with other neurons or muscle and form synapses
- communicating “wires” of neurons that do the “talking”



Ch.5, Essential Neuroscience 2<sup>nd</sup> ed. Wolters Kluwer/Lippincott Williams



Medical Physiology by Boron and Boulpaep, Ch.9

## Clinical correlate:

Severed or injured axons of neurons in the PNS can often grow back. Wallerian degeneration is the process of degenerating of axon distal to injury.



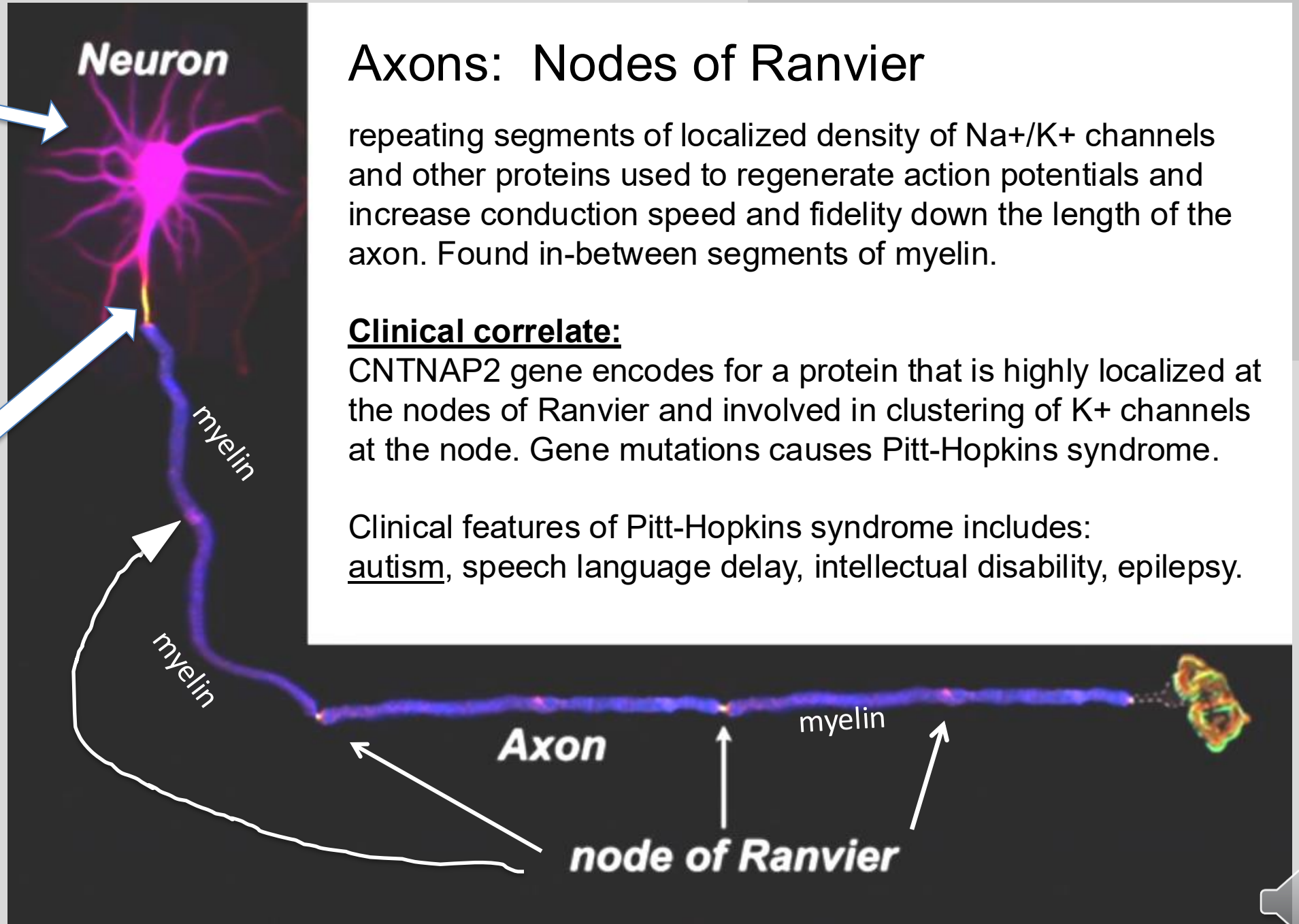
Cell body and  
dendrites

**Neuron**

Yellow shows areas on  
axon where  $\text{Na}^+$  are  
localized.

High expression at the  
axon initial segment

And at nodes of  
Ranvier



## Axons: Nodes of Ranvier

repeating segments of localized density of  $\text{Na}^+/\text{K}^+$  channels and other proteins used to regenerate action potentials and increase conduction speed and fidelity down the length of the axon. Found in-between segments of myelin.

### Clinical correlate:

CNTNAP2 gene encodes for a protein that is highly localized at the nodes of Ranvier and involved in clustering of  $\text{K}^+$  channels at the node. Gene mutations causes Pitt-Hopkins syndrome.

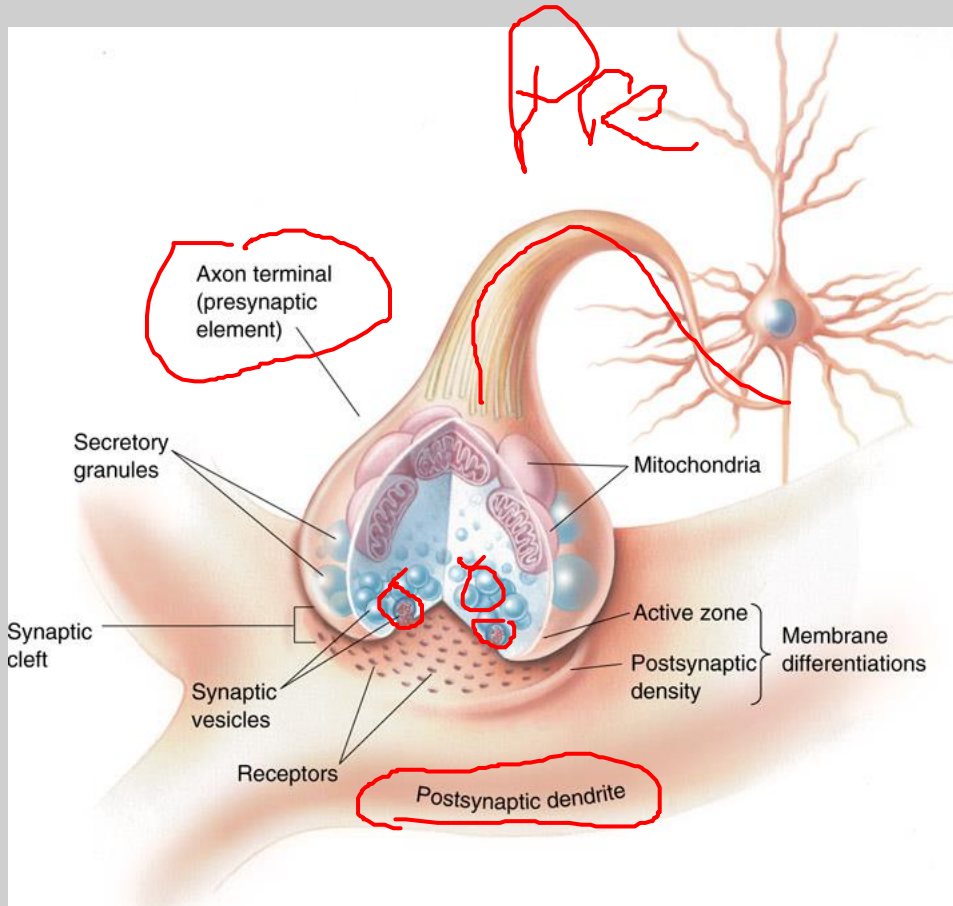
Clinical features of Pitt-Hopkins syndrome includes:  
autism, speech language delay, intellectual disability, epilepsy.



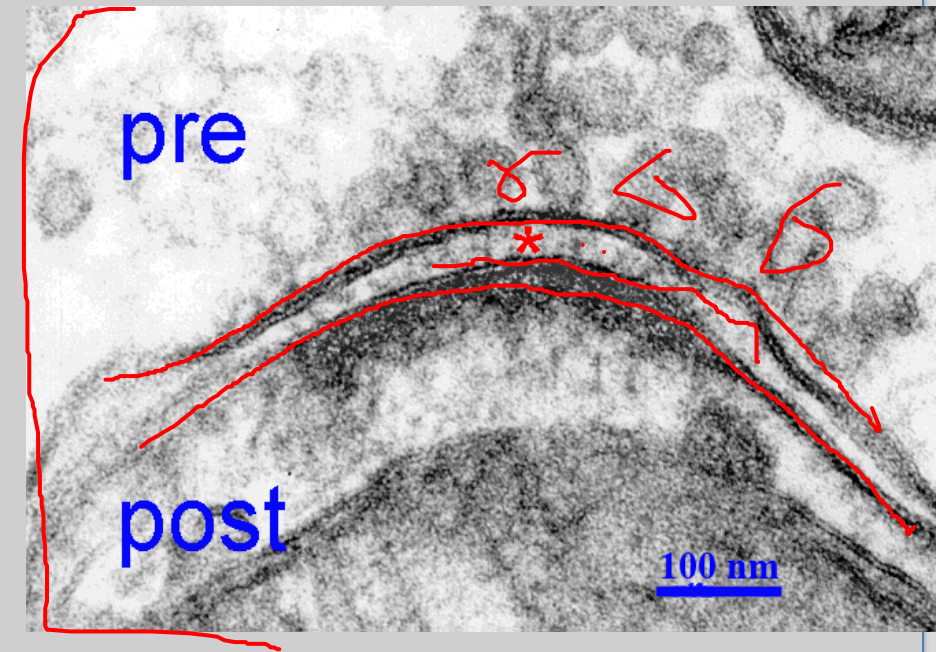
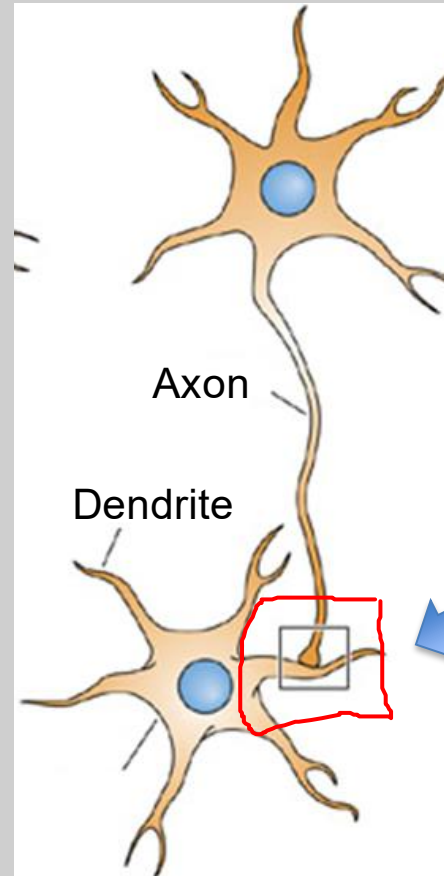


Axon terminal (terminal bouton) forms the chemical synapse!

- site where neurons functionally communicate with one another via neurotransmitter release.



- Most common type of synapse
- Slower form of neural communication but still pretty fast ~1-5ms



Presynaptic neuron – sending info/message

Postsynaptic neuron – receiving message

Clinical correlates – so many!

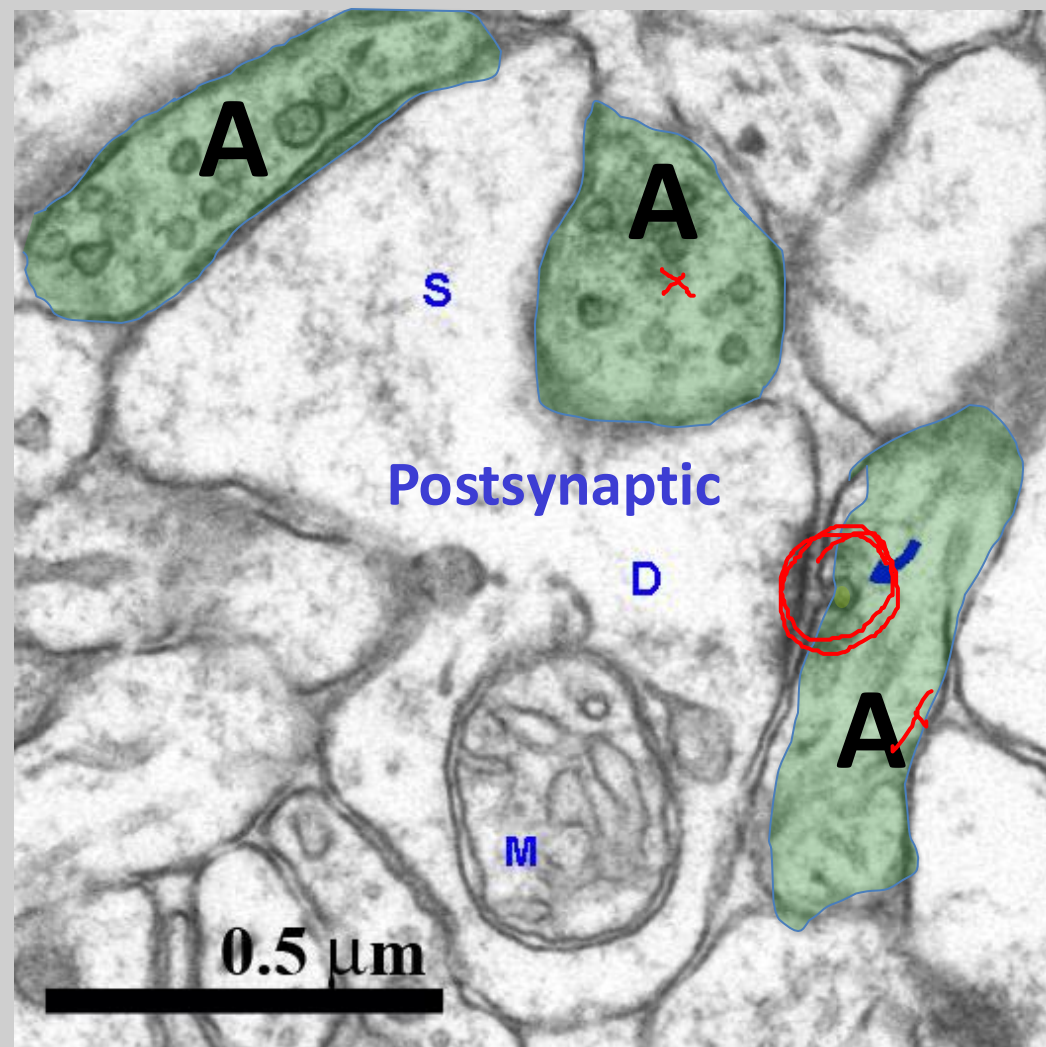
- neuro/psych disorders
- drugs of abuse/addiction
- sleep/wake, hunger/satiety
- SHANK3 mutations & autism



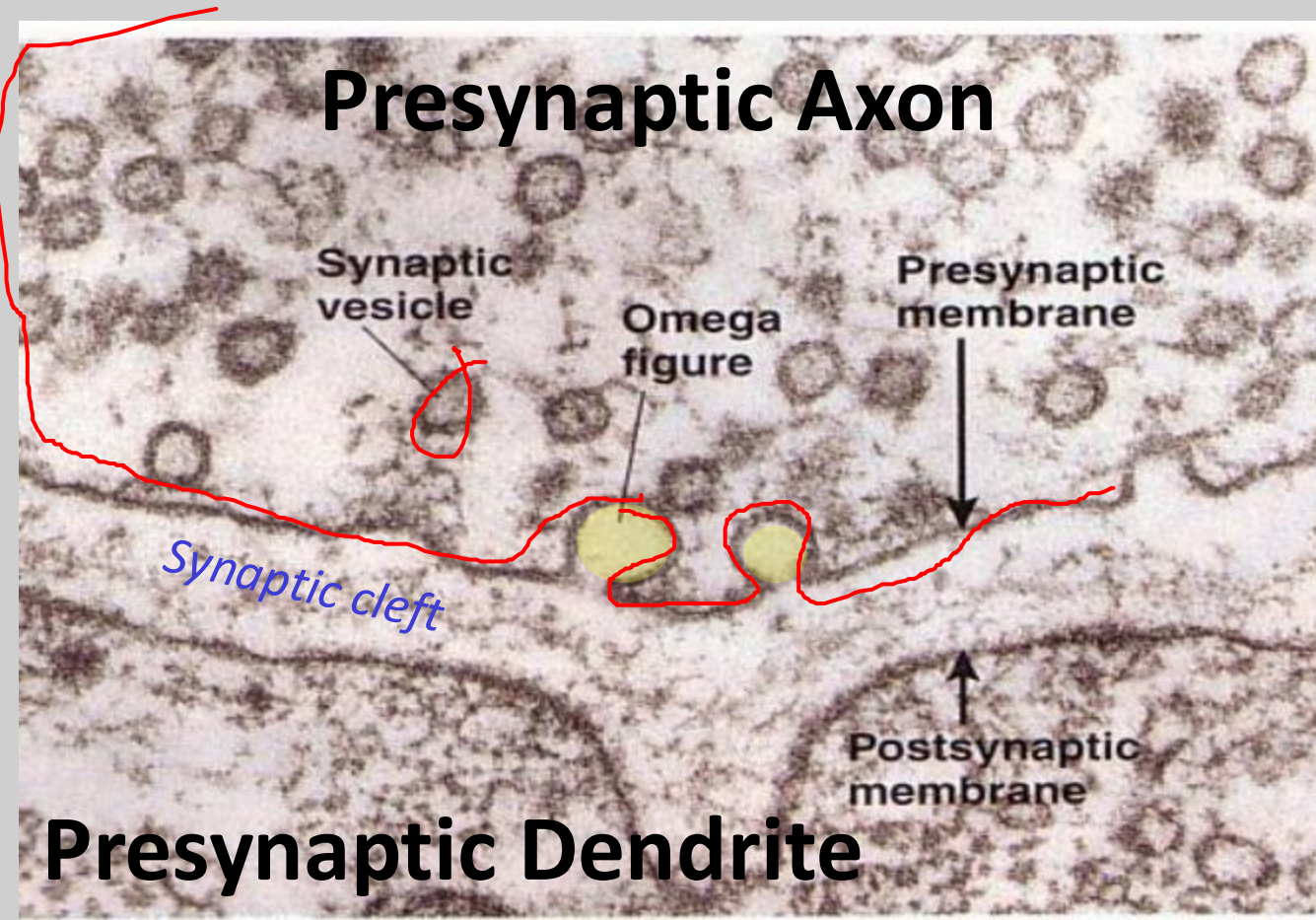


# Electron micrograph of the chemical synapse

- omega shapes structures show endocytosis of neurotransmitters



S = dendritic spine    D = dendrite    A = axon



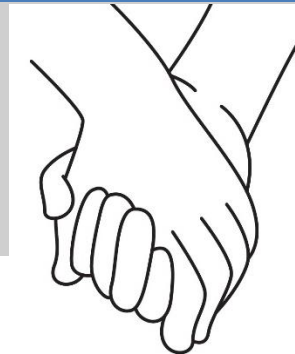
Heuser JE, Society for Neuroscience Symposia Vol 2; SFN 1997



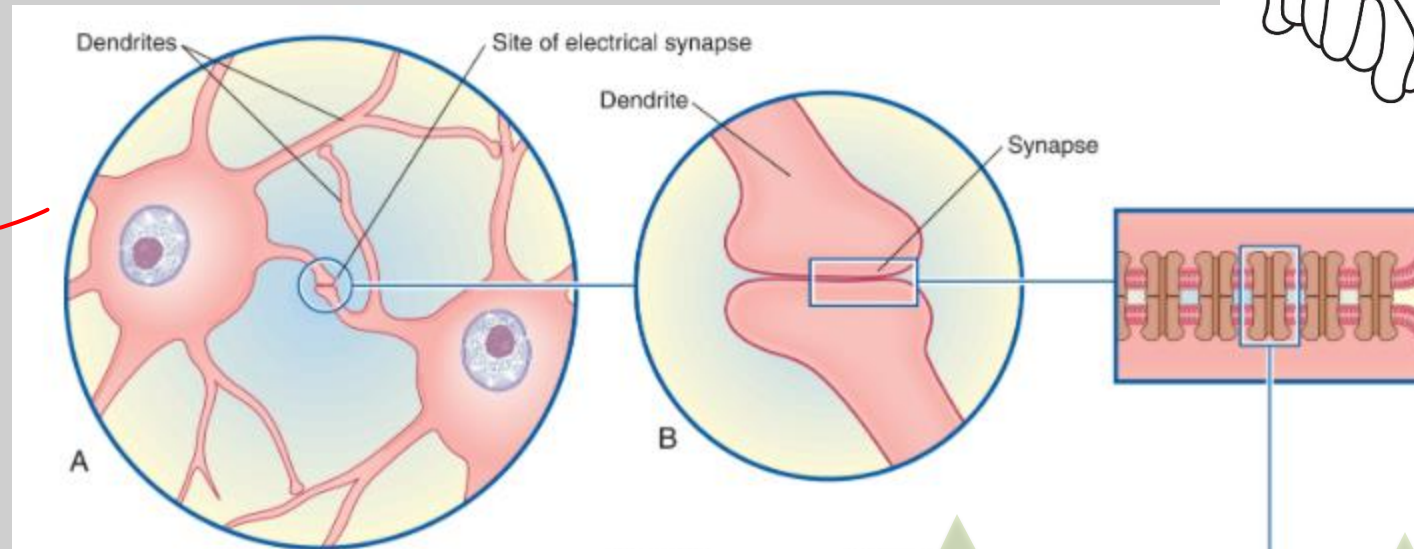
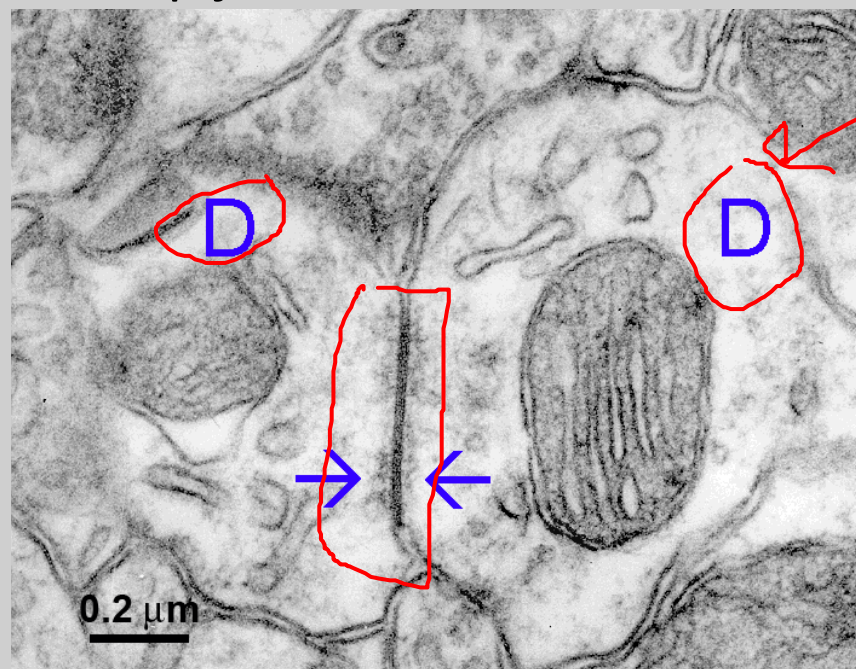


# Neurons are “connected” to one another at the synapse

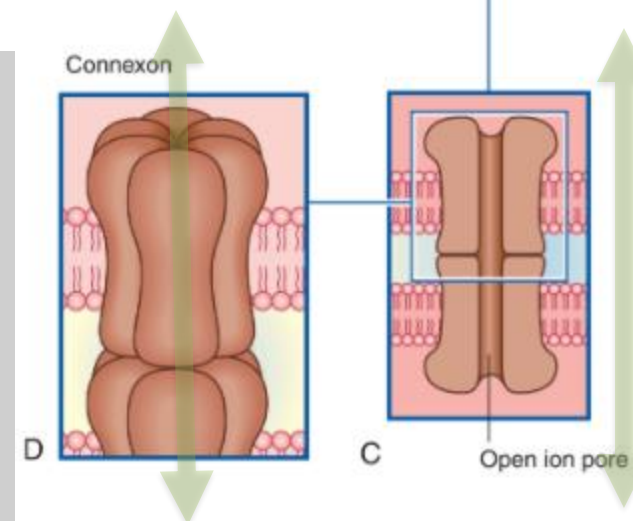
- the site where neurons functionally communicate with one another



## Electrical synapses: Gap junctions/Connexons



Gap junctions allow direct ion & small molecule flow from one neuron to the other. Usually bidirectional.

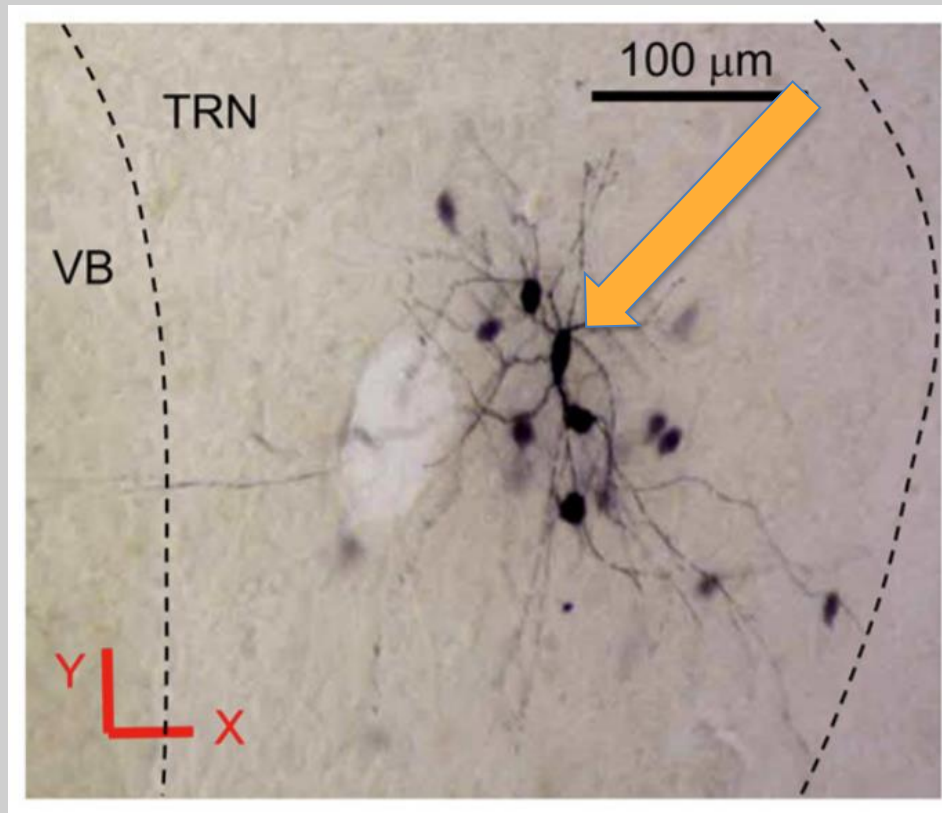


### Clinical correlate:

Certain connexins expressed in specific cell types.  
~30 disease due to connexin gene mutations.

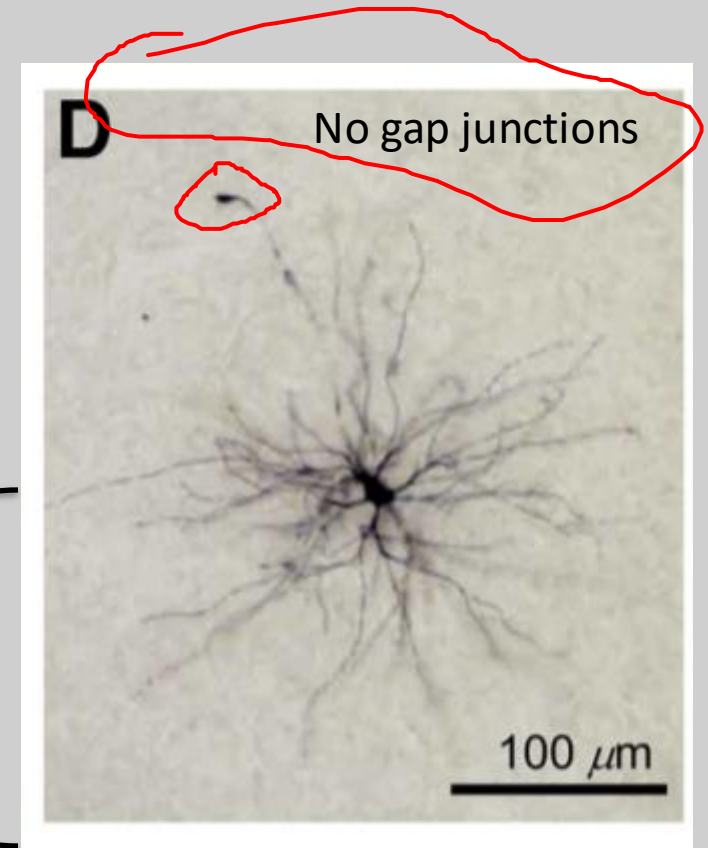


# Gap junctions & Electrical synapses in neurons



Inject dye into neuron labeled with orange arrow and dye travels through gap junctions to label neurons that are connected via electric synapses

Injection of dye only labels one neuron because the cell does not have any gap junctions.



Lee et al. J Neurosci. 2014 Sep 24;34(39):13170-82. doi: 10.1523/JNEUROSCI.0562-14.2014.

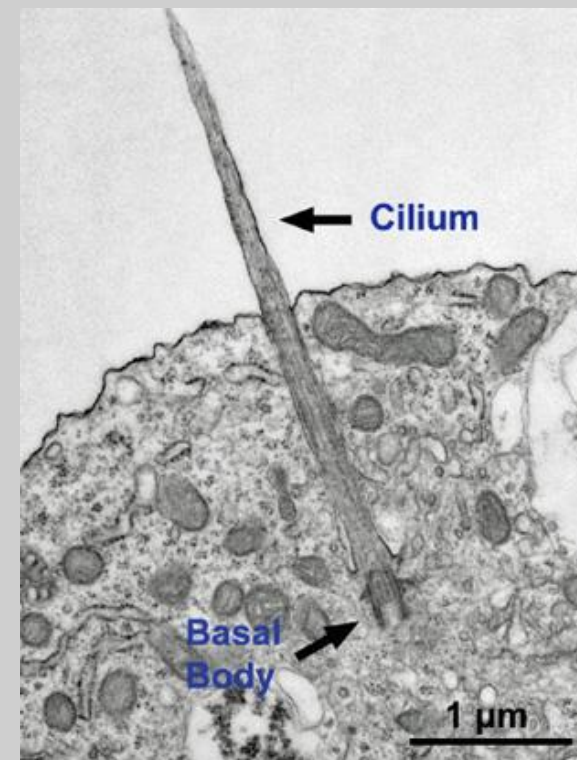
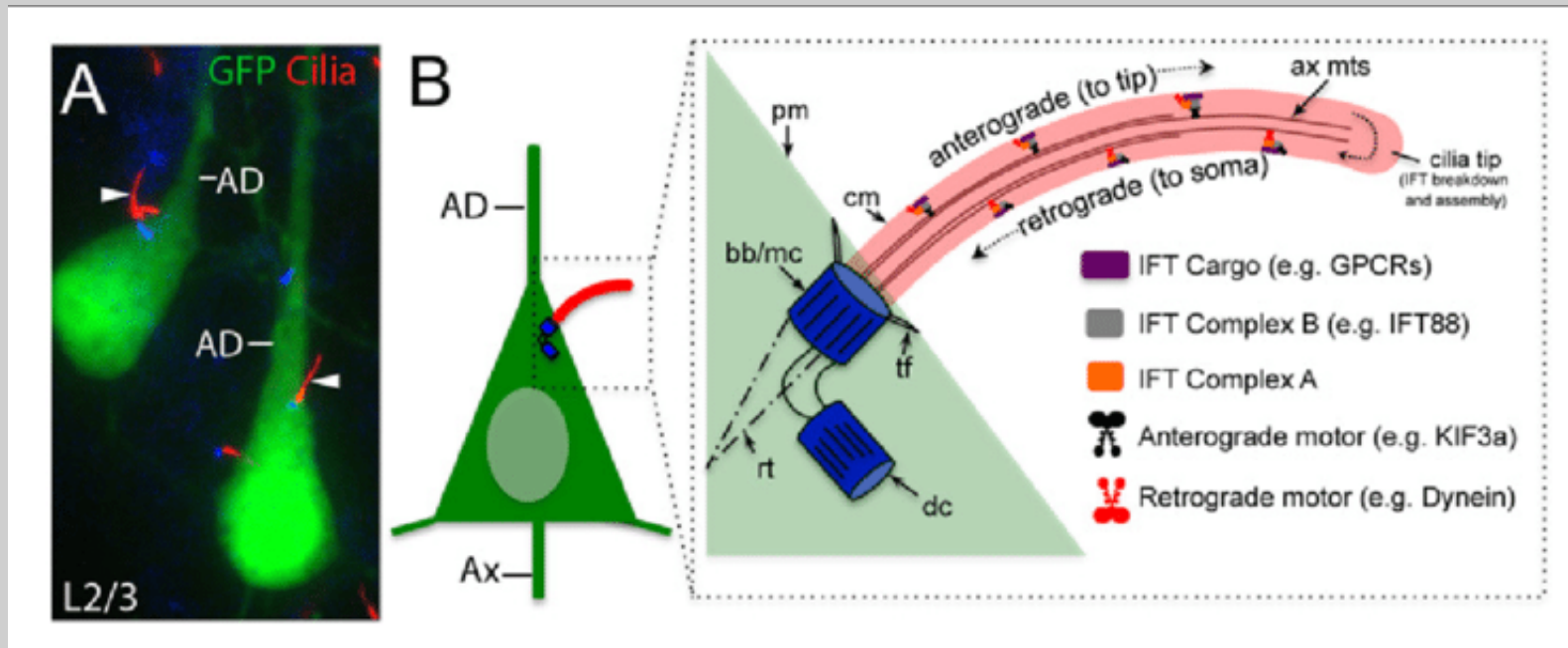
- Gap junctions allow direct ion & small molecule flow from one neuron to the other.
- Usually bidirectional
- Fastest type of neural communication <1ms





# Neuronal Cilia

- every neuron has a cilium (~2-4 $\mu$ m long) which generally emerges from the cell body
- function of the cilium is poorly understood



**Clinical correlate:** serious neurodevelopmental disorders are associated with mutation of Genes important for cilia development.

ARL13B gene mutation causes defects in cilia development and Joubert Syndrome – characterized by midbrain & hindbrain malformations, intellectual disability, retinal dystrophy, cystic renal disease, congenital hepatic fibrosis and polydactyly



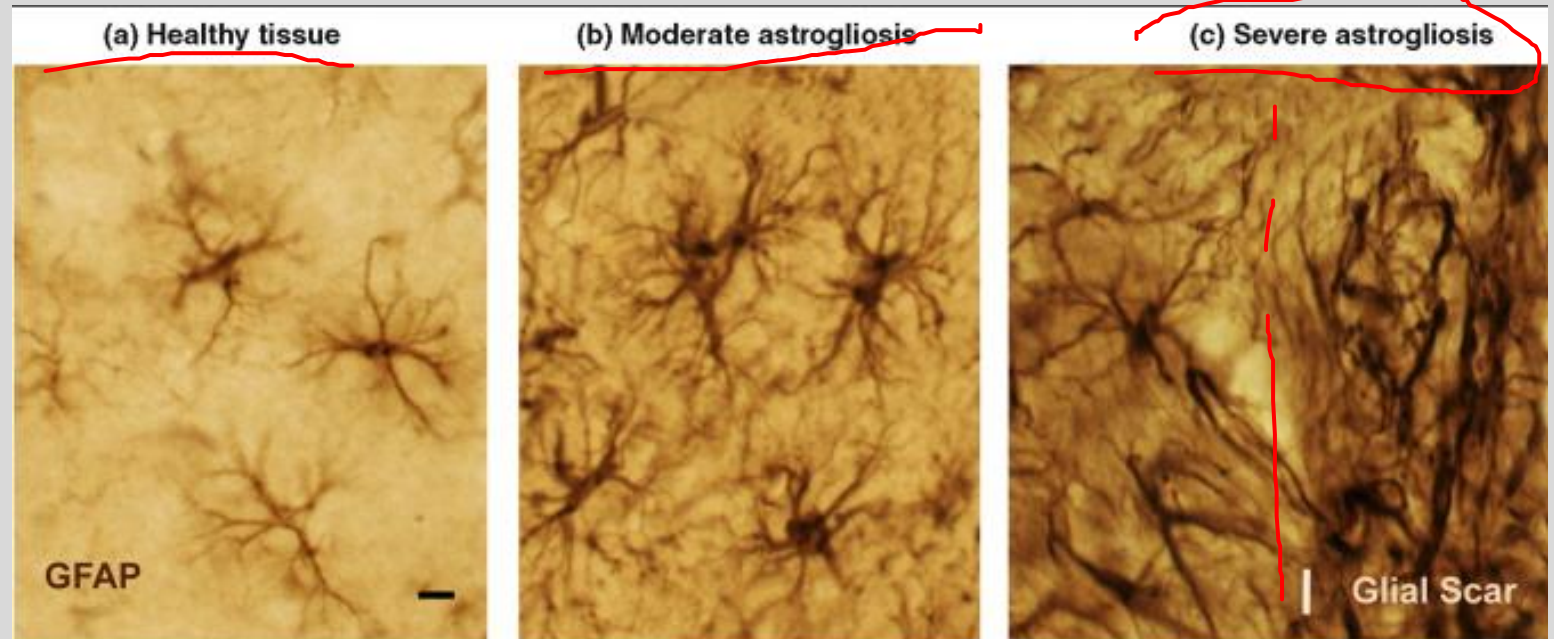
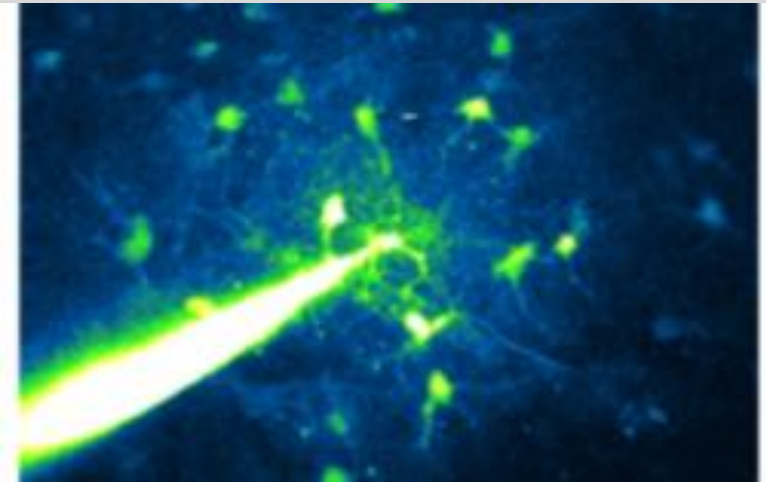
# Gap junctions & Electrical synapses in Astrocytes

- Connected to other astrocytes as well as oligodendrocytes by gap junctions
- Can respond/"react" to tissue damage and form a glial scar but role not well understood (i.e. harmful or helpful such as in spinal cord injury)

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Gap junctions in astrocytes



## Clinical correlate:

Glial fibrillary acid protein (Gfap) is the gold standard molecular marker for reactive astrocytes and is used for detection of astro-gliosis (brain injury) and tumors made up of astrocytes (i.e. astrocytoma).

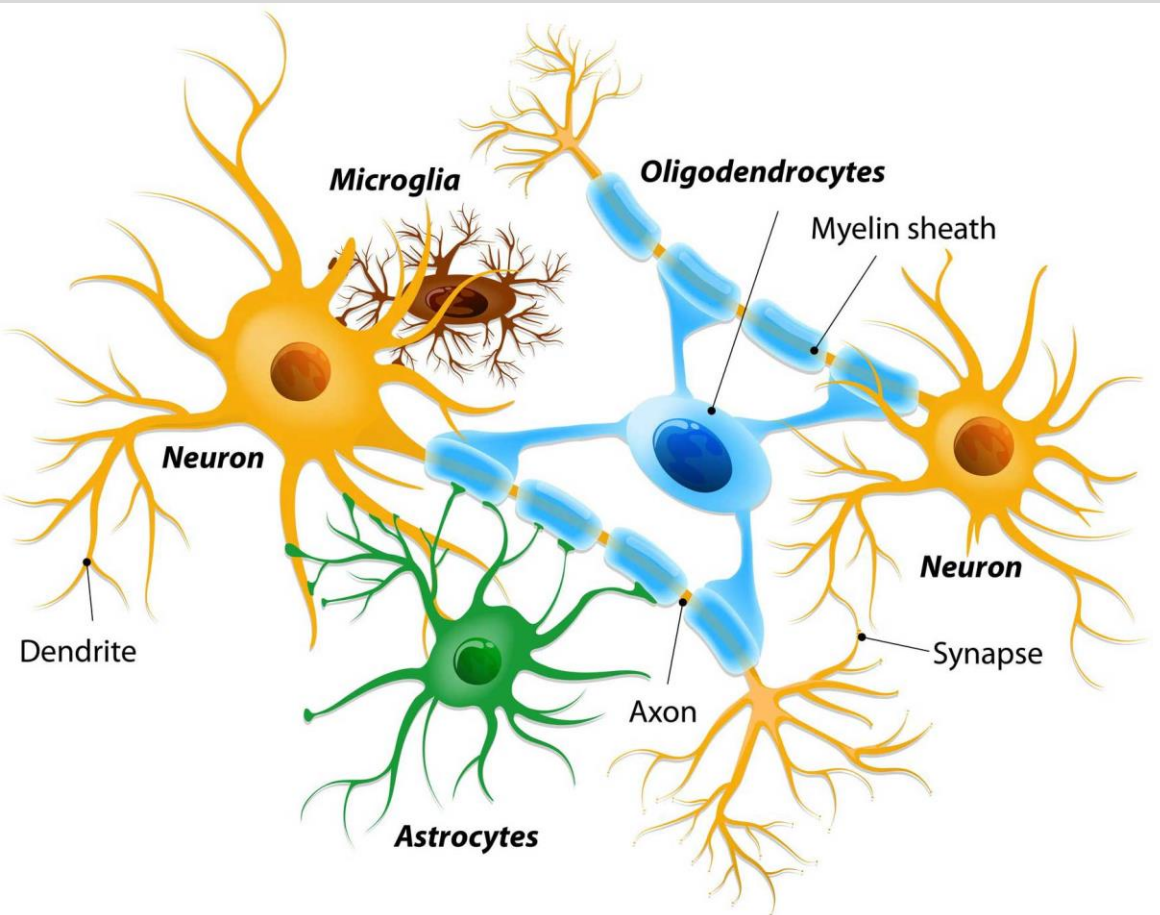
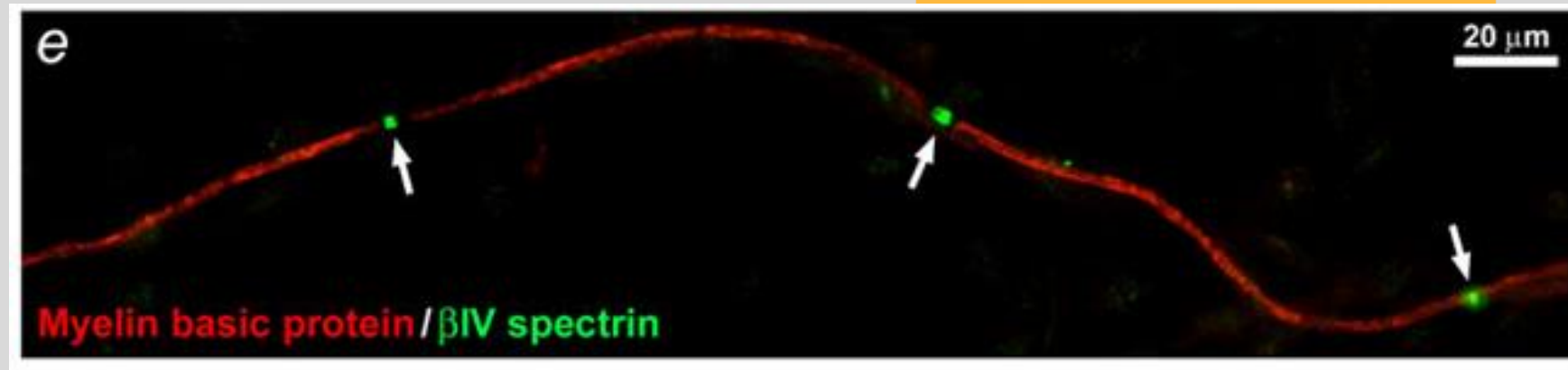
Mutation of the **GFAP** gene causes Alexander disease leukodystrophy which is characterized by childhood white matter development disruptions, and diverse symptoms such as cognitive and motor delays, loss of motor control.





Myelin found in between nodes of Ranvier

Oligodendrocytes ensheath axons from more than one neuron.  
Schwann cells ensheath only 1 neuron.



## Clinical correlates

Autoimmune disorder where patients have IgG against **MOG - myelin oligodendrocyte glycoprotein**. MOG is a glycoprotein uniquely expressed in oligodendrocytes in the CNS. **MOG antibody disorder (MOGAD)** is an idiopathic, inflammatory, demyelinating disease of the central nervous system (CNS). Diverse peripheral and central symptoms including optic neuritis (loss or blurry vision, eye pain), transverse myelitis (weakness, numbness, pain, loss of bowel or bladder control).

**Olig2** is a protein exclusively found in oligodendrocytes and is a maker for **oligodendroglioma** which can present with diverse symptoms such as headache, weakness, seizures, cognitive changes, etc.



## Non-neural & non-glial barrier cells

- Choroid plexus cells - epithelial and endothelial cells important for cerebral spinal fluid production
- Ependymal cells of the ventricles – important for circulation of the cerebral spinal fluid
- Lepto/Meningeal cells of the dura, arachnoid, and pia

Will be discussed in upcoming lectures.





- The brain controls behavior via the activity of interconnected brain cells.
- There exist diverse cell types in the brain (neurons, glia, etc) with distinct functions, morphologies (structural components), connections (synapses) and clinical significance.

