KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

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Module:
Biological Foundations of Mental Health

Week 1:
Introduction to brain anatomy

Topic 3:
Microanatomy of the nervous system
Part 2 of 3

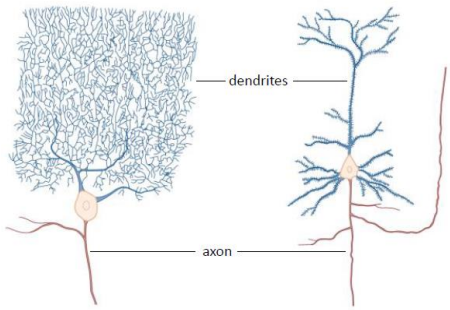
Part 2

Cell structures and function

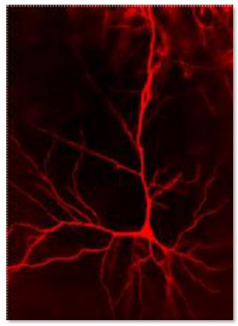
Neuronal morphology

Neuronal morphology is refined during development to fit specific functions.

The extent of dendritic branching reflects the neuron's required level of input.



Cerebellar Purkinje neuron



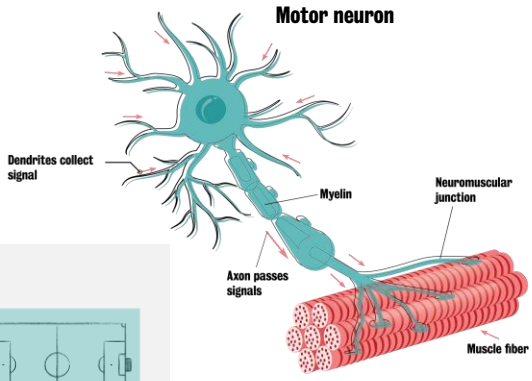
Cortical pyramidal neurons

Neuronal axons

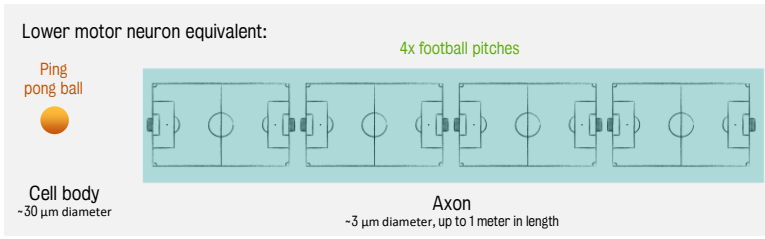
Axonal length determines the distance of output in the network.

Motor neurons exhibit incredibly long axons.

- Longest axon from lower motor neuron cell body in spinal cord to control the muscles in your big toe = 1 meter

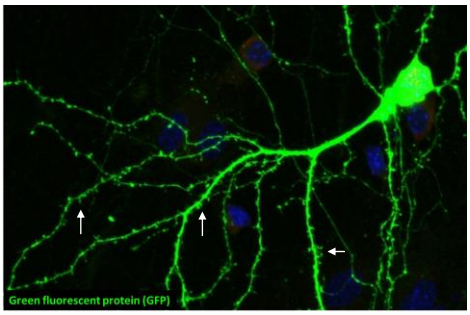


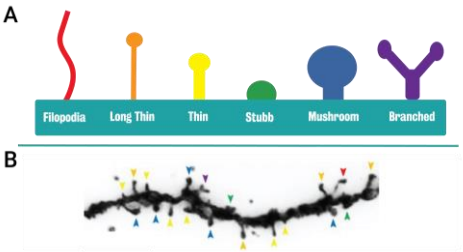
Lower motor neuron equivalent:



Neuronal dendritic spines

Dendritic spines – small protrusions on dendrites which form the postsynaptic side of a synapse, receiving input from another neuron





- variable forms from long and thin to mushroom-shaped
- spines with larger surface area form stronger, more stable synapses
- spines are 'plastic' - increase in size during learning and memory

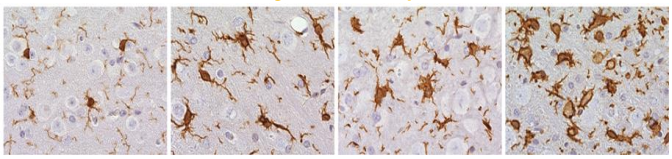
Microglial morphology

Microglia change morphology when they become activated or 'reactive':

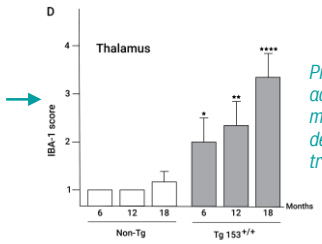
- microglia progressively become round and phagocytic
- reactive microglia release more cytokines to attract more microglia to the site of perceived injury
- in phagocytic mode, they engulf any perceived debris, which can include synapses

Morphology can be used to score and infer neuroinflammation:

Mouse brain stained with anti-microglial (Iba1) antibody



1. Ramified (normal)
2. Reactive
3. Ameboid
4. Phagocytic

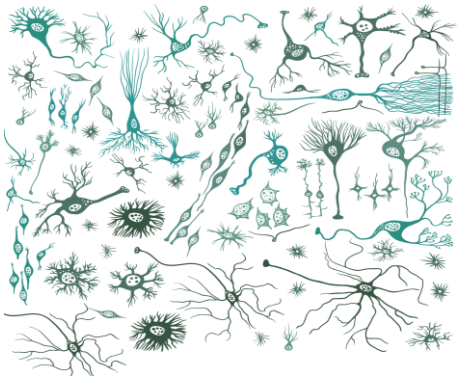


Progressive microglial activation in a mouse model of frontotemporal dementia (versus non-transgenic control mice)

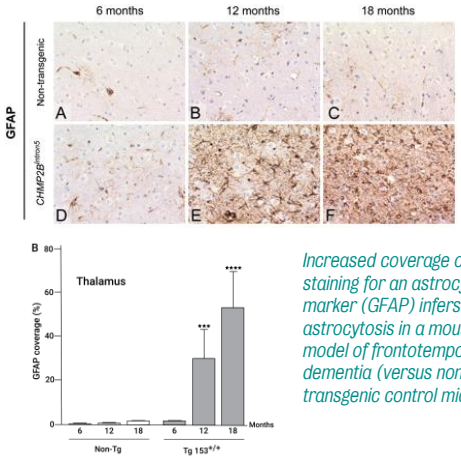
Ghazi-Noori et al., 2012

Astrocytic morphology

Astrocytic morphology is highly variable even at rest.



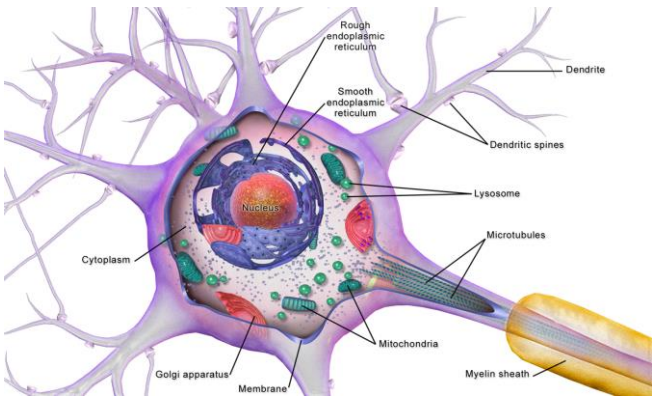
- activation is therefore often inferred through astrocytosis
- **astrocytosis** is an increased number of cells in a given location (due to recruitment or proliferation)



Increased coverage of staining for an astrocytic marker (GFAP) infers astrocytosis in a mouse model of frontotemporal dementia (versus non-transgenic control mice)

Ghazi-Noori et al., 2012

Neuronal substructures and their functions



Nucleus – genetic information store

Endoplasmic reticulum –proteins produced, sorted and processed for delivery to their required location

Golgi apparatus – additional sorting and processing centre

Mitochondria – energy generator (also has roles in calcium buffering and cell signalling)

Lysosome –degrades proteins and organelles when faulty

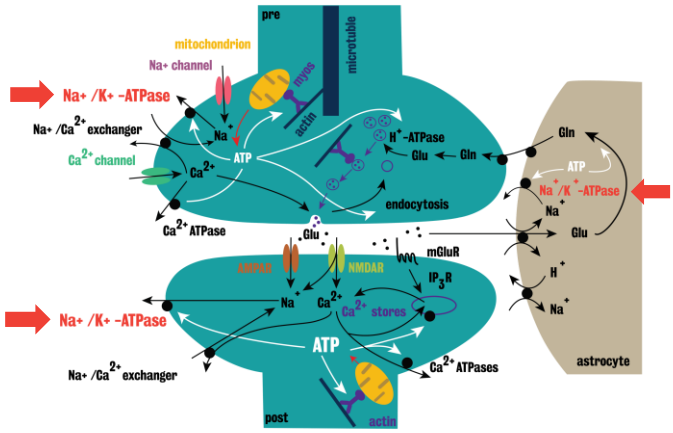
Cell membrane – lipid bilayer containing receptors for cellular communication

For a video introduction to these concepts, please visit https://www.youtube.com/watch?v=URUJD5NEXC8

Unique features of a neuron (1)

Neurons have an unusually high energy demand.

- the human brain = 2% of body mass, but uses about 20% of the oxygen consumed (in the resting body)
- biggest energy (ATP) demand = sodium-potassium ATP pump (Na^+/K^+-ATPase), which maintains the. electrical equilibrium of the neuronal cell membrane
- other demands include recycling neurotransmitters and calcium (Ca^{2+}) buffering



Key energy demands at neuronal synapse (Harris et al., 2012)

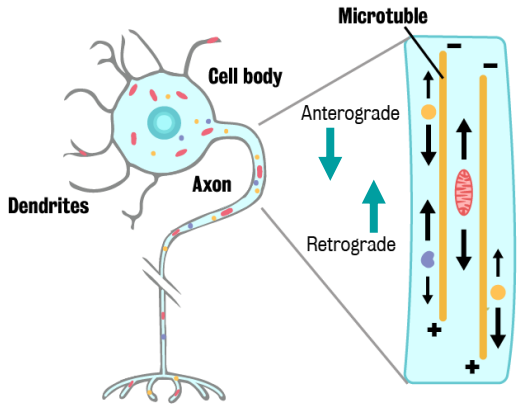
Unique features of a neuron (2)

Neurons need to transport cargo along long distances due to their extended morphology.

- though the majority of proteins and mitochondria are produced next to the nucleus, they are often required at distant sites, eg synapses
- cargo needs to be transported back to the soma for recycling and signalling
- transport occurs along microtubules

anterograde = away from the cell body

retrograde = towards the cell body



Saxton & Hollenbeck, 2014

A note on cellular transport

Neuronal transport exists in a balance between anterograde and retrograde transport.

Example

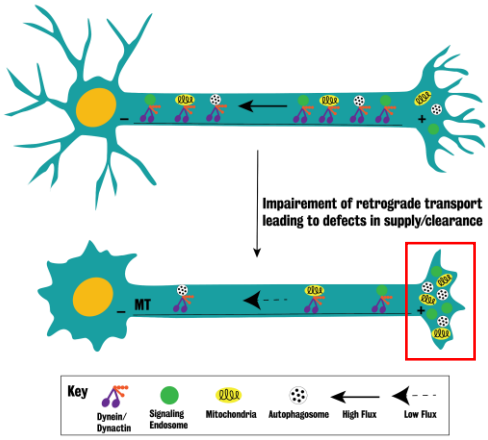
A small impairment in retrograde transport in motor neurons

↓

Build up of dysfunctional components at the synapse

↓

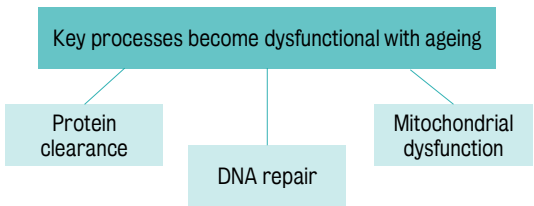
Disruption of normal synaptic function



Unique features of a neuron (3)

Neurons are vulnerable to stress.

- we have limited capacity to generate new neurons
- neurons cannot undergo cell division (post-mitotic) for growth or repair
- neurons become vulnerable with age as cell components deteriorate



Selective vulnerability of distinct neuronal populations/brain regions in different neurological diseases is probably due to differences in the resistance of particular neurons to different cell/network stressors.

Figures

Slide 5

https://bodytomy.com/motor-neurons-location-structure-function (redrawn)

Slide 6

Mizielinska personal research image

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0107591

Slide 7+8

https://academic.oup.com/brain/article/135/3/819/1746712#86267722 (Mizielinska author on this paper)

Slide 8

https://www.sciencedirect.com/science/article/pii/S0165017309001295#fig1 (redrawn)

Slide 9

https://commons.wikimedia.org/wiki/File:Neuron_Cell_Body.png

Slide 10

https://www.cell.com/neuron/comments/S0896-6273(12)00756-8 (redrawn)

Slide 11

http://jcs.biologists.org/content/125/9/2095 (redrawn)

Slide 12

https://www.sciencedirect.com/science/article/pii/S0166223610000524 (redrawn)

End of part 2