Module:
Biological Foundations of Mental Health

Week 1
Introduction to brain anatomy

Topic 3
Microanatomy of the nervous system – Part 1 of 3

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Hi, my name is Dr Sarah Mizielinska, and I specialise in the neuronal cell biology of dementia. In this topic, we will be delving into the microanatomy of the nervous system.

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Part 1, neurons and glia.

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In 1906, Ramóny Cajal and Camillo Golgi were jointly awarded the Nobel Prize in physiology and medicine for their discovery that the brain is not a single continuous entity but composed of individual cellular units. We now know that during development, the cells of the nervous system differentiate into two major cell types: neurons – the cells responsible for fast communication along large networks – and the supporting glial subtypes.

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Neurons communicate by passing electrical signals along their elongated form and they're converting this into a chemical signal to activate an electrical signal in the next neural network. Information travels at different speeds in different neurons, ranging from 1 mile per hour, the speed of a tortoise, to 268 miles an hour, which is faster than most Formula 1 racing cars.

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Neurons are not homogeneous, they come in many forms specialised for their particular function within the nervous system. On the left, we have a classical neuron which both receives signals from and sends signals to other neurons and has a long, extended shape. However, some neurons can both receive signals and send signals

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to other cell types. For example, sensory neurons can be activated by changes in the skin cells, and lower motor neurons can stimulate muscle movement. Some neurons, such as interneurons, can actually send and receive signals with multiple other neurons.

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Even within brain regions, neurons can vary widely. For example, in the cerebellum, the brain region that primarily coordinates movement, there is a dense lobe structure. The dense layer in these lobes is generated by millions of small granule cell neurons, which feed into one of the largest types of neuron in the brain, the Purkinje cells, with other interspersed basket and Golgi neurons.

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But neurons do not function in isolation, they are supported by multiple types of glia. Those that directly interact with neurons – oligodendrocytes, astrocytes, microglia – and ependymal cells, who line the ventricles of the brain and the central canal of the spinal cord (similar to epithelial/skin cells). We will now go through each of these cell types one by one.

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Astrocytes have many known functions, including distribution of nutrients from the blood supply to neurons, maintenance of extracellular ionic balance and tissue repair. They can also regulate synaptic activity by direct contact with synapses, in what is known as the 'tripartite synapse', and signal between each other independently of neurons via gap junctions – small gaps in the cell membrane that leak charged ions. For further reading, you can see Santello et al. (2019) *Nature Neuroscience*.

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Microglia, as inferred by the name, are smaller than astrocytes and function as the resident immune cells of the brain. In this function, they clear debris, recruit other cells to sites of damage and aid in tissue repair. In addition to debris clearance, they can also degrade synapses – which is essential for synaptic pruning during development but may make matters worse by preventing recovery when neurons undergo chronic stress during disease. For further reading for this, you can see Lannes et al. (2017) *Oncotarget*.

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The next type of glia, oligodendrocytes, play the same role in the brain as Schwann cells in the periphery. They wrap their processes around neuronal axons secreting the lipid myelin, generating a protective myelin sheath. This sheath also increases the speed of neuronal signalling by insulating the passing of electrical charge along the axon, in a process called saltatory conduction. Recent data also shows that oligodendrocytes also provide metabolic support to neurons, aided by their proximity. Demyelinating diseases, like multiple sclerosis, cause degeneration of the myelin sheath, preventing the brain communicating adequately with the body.

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We have now seen that many different cell types contribute to the proper functioning of the brain and, therefore, it is not surprising that dysfunction of any of these cell types can lead to disease. Neurons and glia cohabit in a very delicate balance. Neuroinflammation is the activation of glia within a nervous system. This neuroinflammation

may initially be a defence response to threat, to protect neurons. But chronic activation can lead to the over or aberrant activation of astrocytes and microglia and toxicity to neurons. Altered function of astrocytes and oligodendrocytes can also directly disturb synaptic transmission. Therefore, these changes can result in vulnerability of neurons both in neurodevelopmental and neurodegenerative diseases.

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