Biomedicine

Lecture 13:
Nervous System I
Learning Outcomes

In today’s topic you will learn:

- The structure, function & physiology of the nervous system.
- The physiology of nerve impulses.
- Neurotransmitters and their activities.
- Some common degenerative & neurotransmitter pathologies of the nervous system.
The Nervous System

- A network of fibres which span the body, co-ordinating a diverse range of voluntary and involuntary actions.

- Transmits signals between different parts of the body.

- Rapidly responds to changes within the internal and external environment.

- Works alongside the endocrine system to maintain homeostasis.

- Contains two main divisions:
  1. **Central nervous system (CNS)**
     - Consists of brain & spinal cord
  2. **Peripheral nervous system (PNS)**
     - Peripheral nerves (all nerves not in the CNS)
Functions

SENSORY:
• **Detects** internal and external environmental changes (e.g. pH, sensation/touch)
• Information is carried by sensory (afferent) neurons.

INTEGRATION:
• **Processes** sensory information by analysing, storing & making decisions.
• Abundant in the brain (allows ‘perception’)
• Carried by interneurons

MOTOR:
• Produces a **response** to sensory information (perception) to effect change.
• Impulse carried by motor (efferent) neurons.
• The PNS includes all nervous tissue located outside the CNS.

• The PNS can be further subdivided into the somatic nervous system and autonomic nervous system.

• The somatic nervous system conveys sensory information from head, limbs etc. and motor signals to skeletal muscles only (hence voluntary).
Autonomic Nervous System

- Works automatically and involuntarily to maintain homeostasis.
- The hypothalamus is the highest control centre over autonomic motor neurons.
- Affects organs, glands, cardiac and smooth muscles.

**Two branches:**
1. **Sympathetic**
   - ‘Fight or flight’ response
   - Thoraco-lumbar innervation

2. **Parasympathetic**
   - ‘Rest and digest’
   - Cranio-sacral innervation
# Autonomic Nervous System

<table>
<thead>
<tr>
<th>Structure</th>
<th>Sympathetic</th>
<th>Parasympathetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye (pupil)</td>
<td>Dilation</td>
<td>Constriction</td>
</tr>
<tr>
<td>Lungs</td>
<td>Bronchodilation</td>
<td>Bronchoconstriction</td>
</tr>
<tr>
<td>Heart</td>
<td>Heart rate &amp; blood pressure increased</td>
<td>Heart rate &amp; blood pressure decreased</td>
</tr>
<tr>
<td>Gastrointestinal Tract</td>
<td>Decreased motility and secretions</td>
<td>Increased motility and secretions</td>
</tr>
<tr>
<td>Liver</td>
<td>Conversion of glycogen to glucose</td>
<td>Glycogen synthesis</td>
</tr>
<tr>
<td>Adrenal glands</td>
<td>Releases Adrenaline &amp; Noradrenaline</td>
<td>No involvement</td>
</tr>
</tbody>
</table>
Autonomic Nervous System:

• The sympathetic & parasympathetic divisions generally have opposite effects.

• For example, whilst parasympathetic activity increases GIT peristalsis and secretions, sympathetic activity reduces it.

• Note the locations of nerve origin on the diagram: thoraco-lumbar vs. cranio-sacral.
Enteric Nervous System

- The ‘Brain’ of the GIT, containing around 100 million neurons.
- Functions independently but regulated by the autonomic nervous system.
- Interacts extensively with the CNS.
- Links with the CNS via the sympathetic and parasympathetic nerve fibres (Vagus nerve) – involuntary.

1. **Sensory neurons** monitor chemical changes (via chemo-receptors) in the GI tract and stretching (stretch receptors) of its walls.

2. **Motor neurons** govern motility and secretions of the GI tract and associated glands.

3. **Interneurons** connect the 2 plexuses.
Histology

- *glia = “glue”*

Nervous tissue contains two types of cells:

1. **Neurons:**
   - Process and transmit information.
   - Structural and functional units of the nervous system.
   - Electrically excitable.
   - Lots of different types of neurons (most diverse cell type in the body).

2. **Neuroglia (glial cells):**
   - Supporting cells that nourish, support and protect neurons.
   - There are 6 types of glial cell.
   - More numerous than neurons (90% of brain volume)
Nerves & Neurons

- A ‘nerve’ is a bundle of one or more neurons.

Neurons can contain the following parts:
- Cell body
- Dendrites
- Axon
- Myelin sheath & nodes of ranvier
- Terminal endings

- Neurons possess electrical excitability: the ability to create a nerve impulse or “action potential”

- A stimulus is anything able to generate an action potential. The stimulus can be internal or external.
Cell Body & Dendrites

- Cell bodies consists of a nucleus and cell organelles.

- Cell bodies are known collectively as **grey matter**.

- Collections of cell bodies clustered together are referred to as:
  - **Nuclei** in the CNS – form structural and functional groups in the brain.
  - **Ganglia** in the PNS.

- **Dendrites are the receiving portion of the cell.** They communicate with other neurons/dendrites.

  *dendrites = “little trees”*
Axons

- A long, thin cylindrical projection that carries nerve impulses towards another neuron, away from the cell body.

- Length varies from <1mm (CNS) to approx. 1m (sciatic nerve).

- Covered by a membrane called the axolemma.

- The ends are called axon terminals.

- Axon bundles are called **tracts** in the CNS, **nerves** in the PNS.

- If injured, axons can regenerate at a rate of 1-2mm per day.
Myelin Sheath

- A multi-layered lipid & protein covering around the axons.
- Formed by neuroglia (schwann cells & oligodendrocytes) in the embryo, continuing through childhood and peaking in adolescence.
- Each cell wraps about 1mm of length repeatedly (up to 100 layers).
- Gaps in myelin sheath are called nodes of ranvier.
- Covered axons are termed myelinated.
- Electrically insulates the axon and increases speed of nerve impulse conduction.
- Supports regeneration of axons in the peripheral NS.
Grey & White matter:

- When observing a region of the brain or spinal cord, some regions appear white whilst others appear grey.

- **Grey matter** is mostly composed of cell bodies. It also contains dendrites and unmyelinated axons.

- **White matter** is composed primarily of myelinated axons. The whitish colour of myelin is what gives the region its name.
Activity: Label the neuron

Label the following features on the diagram:

1. Dendrites
2. Myelin sheath
3. Cell body
4. Nucleus
5. Terminal endings
6. Axon
7. Nodes of ranvier
Neuroglia

- Also known as ‘glial cells’. They are non-excitatory.

- **Surround and bind the neurons.** Neurons would not function without glial cells.

- Far smaller than neurons, but up to 50x as many.
- Can multiply and divide (unlike neurons).

- After trauma, glia will fill spaces left by damaged neurons (important concept when considering malignant growth of tumours → gliomas).

**Functions:**
- Surround neurons and hold them in place.
- Supply nutrients and oxygen to neurons.
- Destroy pathogens and remove dead neurons.
Neuroglia

There are six types of neuroglia:

• 4 in the central nervous system:
  Astrocytes, oligodendrocytes, microglia & ependymal cells.

• 2 in the peripheral nervous system:
  Schwann cells and Satellite cells.

Astrocytes:

• Star-shaped with branching processes.
• Most numerous and largest neuroglia (in CNS).

• Hold neurons to their blood supply (physical support).
• Contribute to the blood brain barrier.
Neuroglia in CNS

Oligodendrocytes:
• Glial cells that **myelinate axons of neurons in the CNS.**

Microglia:
• Derived from **monocytes** that migrate to the CNS before birth.
  • Resident immune cells of the brain: **phagocytic.**
  • Mobile in the brain and multiply when the brain is damaged.

Ependymal cells:
• Endothelial & epithelial cells which line the walls of the:
  • 4 Ventricles of the cerebrum
  • Central canal of spinal cord
• **Make cerebrospinal fluid (CSF) and beat their cilia to circulate CSF.**

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**Schwann cells:**
- Schwann cells produce myelin sheaths around the axons of neurons in the peripheral NS.
- This insulates the axon, increases the speed of nerve impulse conduction and participates in axon regeneration.
- Most dendrite connections & myelination completed by age of 3 – malnutrition in infancy = irreversible damage.
- The unmyelinated gaps along a neuron are called Node’s of Ravier – increasing speed of nerve conduction.

**Satellite cells:**
- Surround the cell bodies of neurons in PNS ganglia.
  Provide structural support & assist in substance exchange.
Neurons are electrically excitable.

There are 2 types of electrical signal in a neuron:

<table>
<thead>
<tr>
<th>Graded potential</th>
<th>Action potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>• For short distance communication</td>
<td>• For long distance communication</td>
</tr>
<tr>
<td>• Occur in dendrites and cell body</td>
<td>• Propagated down axon</td>
</tr>
<tr>
<td>• Amplitude proportional to strength of stimulus (no threshold)</td>
<td>• All-or-nothing (has threshold)</td>
</tr>
<tr>
<td>• Longer duration (few milliseconds to secs)</td>
<td>• Shorter duration (3-5 milliseconds)</td>
</tr>
</tbody>
</table>

Graded and action potentials are facilitated by two characteristics:

1. Specific ion channels can open and close when stimulated, changing the potential & creating an electrical current.
2. An electrical difference across the membrane of the cell (‘resting potential’)

Ion = electrically charged particle eg. a+
Nerve impulses - Ion channels

• These are transport channels for ions created by trans-membrane proteins within the neuronal membranes.

• When ion channels open they allow specific ions to move through the membrane across a concentration gradient e.g. Na\(^+\) channels allow Na\(^+\) through.

• Channels open in response to a stimulus which changes the permeability of the membrane to Na\(^+\) & K\(^+\).

• Stimuli include changes in voltage, chemicals (hormones), mechanical pressure and light.

Video (watch at home): www.youtube.com/watch?v=OZG8M_IdA1M
Nerve impulses – Resting potential

- Neurons at rest possess an electrochemical gradient across the cell membrane.

- **This is created by a build up of negative ions on the inside of the cell membrane, relative to the extracellular fluid which contains more positive ions.**

- Separation of charges across a cell membrane creates potential energy.

- This resting potential is approximately **-70mV**.

- Cells exhibiting a membrane potential are said to be polarised or “charged”.

\[mV = \text{millivolts}\]
The extracellular fluid is rich in Na\(^+\) and Cl\(^-\) ions and carries a positive charge.

The intracellular fluid is rich in K\(^+\) and large negatively charged proteins and phosphates which cannot leave the cell. Thus carries a negative charge inside the cell.

As the Na\(^+\) and Cl\(^-\) try to move back to equalise the charge, the separation of charges is maintained by the sodium-potassium pump which pumps 3 Na\(^+\) out for every 2 K\(^+\) it pumps back in (using ATP).
Nerve impulses – Action potential

• An action potential is the formation of a nerve impulse.

• It is a series of events which reverse the membrane potential and then restore it to its resting state.

• It is then propagated down the axon in an “all-or-nothing” fashion meaning there is no reduction of the signal as it travels down the axon.

• Occurs in 2 phases:
  1. Depolarisation: The negative membrane potential (-70mV) becomes less negative, reaches zero, and then becomes positive.

  2. Repolarisation: The membrane is then restored to its resting potential of (-70mV).

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**Action potential: Depolarisation**

- Triggered by stimulation of a nerve ending.
- Depolarisation must reach a **threshold value** (-55mv) in order to generate an action potential.
- $\text{Na}^+$ channels open allowing $\text{Na}^+$ to flood into the cell up to about +30mV (so at the peak of the action potential, the inside of the membrane is 30mV more positive than the outside)
- Positive charge builds up inside the cell.
Action potential: Repolarisation

- $K^+$ channels open much more slowly than $Na^+$ channels so just as the $Na^+$ channels are closing the $K^+$ channels open.
- This allows $K^+$ to flood out of the cell, restoring the membrane potential to $-70\text{mV}$. 

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Action potential: Refractory period

- Period of time after repolarisation in which a nerve cannot generate another action potential because Na\(^+\) & K\(^+\) are on the wrong sides of the membrane.

- During this period the Na-K pump pumps 3 Na\(^+\) out and 2 K\(^+\) back into the cell to restore the resting potential.

- **Absolute refractory period**: Even a strong impulse cannot generate an action potential.

- **Relative refractory period**: Larger than normal stimulus needed to generate an action potential.

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Refractory = resistant to a stimulus

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Nerve impulse video: [www.youtube.com/watch?v=fHRC8SILcH0](https://www.youtube.com/watch?v=fHRC8SILcH0)
Unmyelinated axons

Conduction is the movement of the nerve impulse along the axon of a neuron.

Unmyelinated axons:
- No myelin sheath around the nerve.
- The membrane becomes depolarised in a **continuous conduction** away from the cell body down the axon.
- Step-by-step depolarisation & repolarisation of each adjacent segment of plasma membrane.
- Occurs in one direction only.
Myelinated axons

- Myelin is an insulator, preventing the ionic currents from crossing the membranes.

- Instead, at the **Nodes of Ranvier**, there are high concentrations of Na⁺ gates hence the current appears to jump from node to node (saltatory conduction).

- Action potentials ‘leap’ across long segments of the myelinated axon, leading to much faster conduction.

- **Saltatory conduction** is far more energy efficient, with less ATP needed for the sodium-potassium pumps.

- Nerves also propagate action potentials slower at lower temperatures (hence icing an injury can reduce pain).
## Nerve Conduction

<table>
<thead>
<tr>
<th>Continuous conduction</th>
<th>Saltatory conduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmyelinated</td>
<td>Myelinated</td>
</tr>
<tr>
<td>Step-by-step depolarisation spread</td>
<td>‘Leaps’ of depolarisation</td>
</tr>
<tr>
<td>Slower</td>
<td>Faster</td>
</tr>
<tr>
<td>Less energy efficient</td>
<td>More energy efficient</td>
</tr>
</tbody>
</table>

### Local anaesthetics:
Block the Na⁺ gates from opening therefore stopping an action potential from being formed, inhibiting the nerve from being able to transmit the pain message.
Synapses

- Neurons are not continuous, they have gaps between them called synapses.

- The ends of axon terminals are called synaptic end bulbs.

- The space between the synaptic end bulbs and the post-synaptic neuron is the synaptic cleft, which is filled with interstitial fluid.

- The nerve impulse is carried across the synaptic cleft by nerve messengers – neurotransmitters. These are stored in synaptic vesicles.

- In electrical synapses, the synaptic end bulbs and next neuron are connected by tubes. These are gap junctions (found in visceral smooth muscle & cardiac muscle).
A typical chemical synapse transmits a signal as follows:

1. Nerve impulse arrives at synaptic end bulb.

2. The depolarisation phase causes calcium (Ca\(^{2+}\)) channels to open, sending Ca\(^{2+}\) into the synaptic bulb.

3. Increase of concentration of Ca\(^{2+}\) causes exocytosis of synaptic vesicles: neurotransmitters are released into the synaptic cleft.

4. The neurotransmitters diffuse across the synapse and bind to receptors on the post-synaptic neuron.

5. This opens the ion channels on the post-synaptic neuron allowing ions to flow across the membrane.

6. The change in ion concentration creates a post-synaptic potential, that then triggers an graded or action potential in the post-synaptic nerve.
Synapse:

1. Nerve impulse arrives
2. Ca\(^{2+}\) channels open
3. Exocytosis of synaptic vesicles & release of neurotransmitter
4. Neurotransmitter binds to receptors on post-synaptic neuron
5. This opens the ion channels on the post-synaptic neuron
6. Action potential in the post-synaptic nerve.

Neurotransmitter travels across synaptic cleft in 1,000,000th of a second!

Video (watch at home):
www.youtube.com/watch?v=VitFvNvRIIY

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Neurotransmitters

• A neurotransmitter (NT) is a chemical messenger that gets released from a pre-synaptic terminal which causes an effect in the post-synaptic cell.

• More than 100 have been identified so far. Many NTs co-exist together in one end bulb.

• Neurotransmitters are broadly categorised into 3 main types:

  1. **Amino Acids** e.g. glutamate, GABA, aspartate etc.
  2. **Monoamines** e.g. adrenaline, dopamine, serotonin etc.
  3. **Peptides** (neuropeptides) e.g. endorphins, substance P etc.
  4. **Unique molecules** e.g. acetylcholine.
Neurotransmitters

- One way to classify neurotransmitters is whether they have an **excitatory** or **inhibitory action** on a post-synaptic neuron:

<table>
<thead>
<tr>
<th>Excitatory</th>
<th>Inhibitory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes depolarisation of the post-synaptic neuron</td>
<td>Causes hyperpolarisation of the post-synaptic neuron</td>
</tr>
<tr>
<td>Opens the Na(^+) ion channels</td>
<td>Opens the K(^+) or Cl(^-) ion channels</td>
</tr>
<tr>
<td>Inner membrane becomes more positive</td>
<td>Inner membrane becomes more negative</td>
</tr>
</tbody>
</table>

- Neurotransmitters can be excitatory in one tissue type and inhibitory in another.

- **Following a nerve impulse the neurotransmitters need to be inactivated and removed** for the process to be able to start again:
  - This can occur by **diffusion, degradation by enzymes** (eg. acetylcholinesterase) or through **re-uptake by terminal bulb** (eg. epinephrine)
# Neurotransmitters: Amino Acids

## Glutamate

<table>
<thead>
<tr>
<th>Type of neurotransmitter:</th>
<th>Amino acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary action:</td>
<td>Excitatory, opens Na(^+) channels</td>
</tr>
<tr>
<td>Location:</td>
<td>CNS</td>
</tr>
<tr>
<td>Role:</td>
<td>Major excitatory neurotransmitter in the brain</td>
</tr>
<tr>
<td>Removal:</td>
<td>Re-uptake.</td>
</tr>
</tbody>
</table>

## Gamma-aminobutyric acid ‘GABA’ (& Glycine)

<table>
<thead>
<tr>
<th>Type of neurotransmitter:</th>
<th>Amino acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary action:</td>
<td>Inhibitory (prevents neural over-activity)</td>
</tr>
<tr>
<td>Location:</td>
<td>CNS, especially interneurons (up to 1/3 brain synapses use GABA)</td>
</tr>
<tr>
<td>Role:</td>
<td>Major inhibitory neurotransmitter</td>
</tr>
<tr>
<td>Removal:</td>
<td>Re-uptake.</td>
</tr>
<tr>
<td>Pharmacology:</td>
<td>Diazepam reduces firing in brain by enhancing actions of GABA.</td>
</tr>
</tbody>
</table>
Adrenaline and Noradrenaline

<table>
<thead>
<tr>
<th>Type of neurotransmitter:</th>
<th>Monoamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Produced from:</td>
<td>Tyrosine</td>
</tr>
<tr>
<td>Primary action:</td>
<td><strong>Excitatory</strong>, opens Na(^+) channels</td>
</tr>
<tr>
<td>Location:</td>
<td>Sympathetic NS, motor neurons, brain &amp; adrenal medulla.</td>
</tr>
<tr>
<td>Role:</td>
<td>Major <strong>excitatory</strong> neurotransmitter (<em>also hormones</em>)</td>
</tr>
<tr>
<td>Removal:</td>
<td>Re-uptake or degradation by enzymes <strong>monoamine oxidase (MAO)</strong> &amp; <strong>catechol-oxygen-methyl transferase (COMT)</strong>.</td>
</tr>
</tbody>
</table>

**Questions:**

Where are the hormones adrenaline & noradrenaline produced? By what cells? What are the effects of these hormones?
# Neurotransmitters: Monoamines

## Dopamine

<table>
<thead>
<tr>
<th>Type of neurotransmitter:</th>
<th>Monoamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary action:</td>
<td>Excitatory &amp; inhibitory</td>
</tr>
<tr>
<td>Location:</td>
<td>Brain (primarily substantia nigra → muscle tone &amp; movement)</td>
</tr>
<tr>
<td>Role:</td>
<td>Reward mechanisms in brain, motor activity, mood, motivation</td>
</tr>
<tr>
<td>Removal:</td>
<td>Re-uptake or degradation by enzymes MAO &amp; COMT.</td>
</tr>
<tr>
<td>Associated disorders:</td>
<td>Parkinson’s disease, schizophrenia</td>
</tr>
</tbody>
</table>

## Serotonin (5-Hydroxytryptamine):

<table>
<thead>
<tr>
<th>Type of neurotransmitter:</th>
<th>Monoamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Produced from:</td>
<td>Tryptophan</td>
</tr>
<tr>
<td>Location:</td>
<td>Digestive tract, brainstem, thrombocytes, pineal gland.</td>
</tr>
<tr>
<td>Role:</td>
<td>Intestinal mobility, mood, attention, sleep, eating, pain regulation</td>
</tr>
<tr>
<td>Removal:</td>
<td>Re-uptake or degradation by the enzyme MAO.</td>
</tr>
</tbody>
</table>
Neurotransmitters: Neuropeptides

Neuropeptides:
• Small proteins acting as neurotransmitters and hormones.

• Common neuropeptides: enkephalins, endorphins, dynorphins & substance P.

• They may act as neuromodulators - substances that do not propagate nerve impulses directly, but instead exert regulatory effects on synaptic receptors.

• Enkephalins, endorphins and dynorphins are opioids (body’s natural analgesics).

• Substance P enhances the feeling of pain.

neuro- = nerve
peptide = protein
analgesic = pain killer

Exercise stimulates the release of opioids
# Neurotransmitters: Other

## Acetylcholine:

<table>
<thead>
<tr>
<th>Primary action:</th>
<th>Excitatory (<em>inhibitory in the vagus nerve</em>).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location:</td>
<td>Major NT of autonomic nervous system, CNS, neuromuscular junction and the parasympathetic NS.</td>
</tr>
<tr>
<td>Role:</td>
<td>Muscle contractions, cognition.</td>
</tr>
<tr>
<td>Removal:</td>
<td>Degraded by the enzyme acetylcholinesterase.</td>
</tr>
<tr>
<td>Associated disorders:</td>
<td>Alzheimer’s, <em>botulinum</em> toxin (‘botox’) blocks Ach.</td>
</tr>
</tbody>
</table>

## Nitric Oxide (NO):

<table>
<thead>
<tr>
<th>Primary action:</th>
<th>Excitatory.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formed from:</td>
<td>Arginine.</td>
</tr>
<tr>
<td>Role:</td>
<td>Vasodilation. Exists for less than 10 seconds before becoming inactive.</td>
</tr>
<tr>
<td>Pharmacology:</td>
<td>Used for angina (GTN). Viagra enhances the effect of NO.</td>
</tr>
</tbody>
</table>
Neurotransmitter breakdown enzymes

**Monoamine oxidase (MAO) enzyme:**
Found in neurons and astrocytes
Catalyses the breakdown of **monoamines**:
- Serotonin
- Adrenaline
- Noradrenaline
- Dopamine

**Catechol-O-methyl transferase (COMT):**
Catalyses the breakdown of:
- Adrenaline
- Noradrenaline
- Dopamine

**COMT inhibitors** are found in many dietary compounds incl. green tea
COMT and MAO enzymes are highly polymorphic (vary from individual to individual)

catalyse = to accelerate a chemical reaction
Nerve sensation: Touch

• Touch excites a graded potential in the sensory nerve endings in your fingers (Meissner’s corpuscles).

• The graded potential triggers the axon of a sensory neuron to form an action potential which travels into the CNS.

• Neurotransmitters are released at nerve synapses where there are interneurons.

• Perception occurs in the brain (primary somatosensory area) where you interpret touch.
Nerve sensation

- ‘Spinal nerves’ carry impulses to and from the spinal cord. There are 31 pairs of spinal nerves.

- The spinal nerve is named based on the spinal level it originates from. Eg. L5

- Spinal nerves combine to form ‘peripheral nerves’, such as the sciatic nerve.

- If a spinal nerve is injured (eg. By disc prolapse, bone spur, tumour), it can cause pain and altered sensation (tingling/numbness) in the associated distribution. This distribution is called a dermatome.
Neuroregeneration

• Neurons have limited powers of regeneration.

Peripheral Nervous System (PNS):
• Peripheral nerve fibres do regenerate if Schwann cell and cell body are intact, and scarring doesn’t occur too quickly.
• The success of regeneration depends on extent of injury.

Central Nervous System (CNS):
• CNS nerve fibres cannot regenerate in mammals.
• Oligodendrocytes and astrocytes inhibit re-growth so scar tissue is formed instead.
• After the foetal period there is an absence of growth stimulating factors
• Clean up of debris is slow (no macrophages)
Neuroplasticity

• The nervous system is dynamic and capable of change.

• Synapses can be modified by learning and experience known as “synaptic plasticity”.

• In the brain this occurs in key areas such as the hippocampus (part of the emotional brain), cerebellum and neocortex.

• Neurons can produce new dendrites or alter their shape.

• New synapses are formed throughout life.

• New neurons and synapses have even been shown to form in starvation, to increase brain capacity to find food.

neuro = nerve
plasticity = capacity to change
Neural Circuits

• The CNS contains billions of neurons that are connected by neural circuits.

• These connections are strengthened with repetitive use (pruning and myelination during brain development).

• Behaviours are strengthened circuits (or patterns) that have become hardwired, but can be rewired.

• Neuroplasticity – remodeling of neural circuits in response to internal and external stimuli.
Applying concepts

- Each tissue in the body has its own nerve supply (innervation).
- Electrical flow differs based on the structure.
- The flow of electricity and health are directly related. Meaning that disruption to nerve signalling would interfere with the health of the structure it supplies (and vice versa).
- Electrical flow means there is an electromagnetic field.
- The concept of energy flow is essential. External and internal factors can disrupt this energy (electrical flow).

Using the knowledge you have learnt so far today, how might this happen?
Summary Quiz!

1. Explain what is meant by the Peripheral Nervous System (PNS)
2. Name the parts of a neuron
3. Explain the function of microglia
4. Explain the function of Schwann cells.
5. Describe the movement of sodium during depolarisation
6. What is the charge present at resting potential?
7. What is meant by all-or-nothing in relation to action potentials?
8. Define the term ‘synapse’
9. Is GABA an excitatory or inhibitory neurotransmitter?
10. What is the role of the neurotransmitter dopamine?
Carpal Tunnel Syndrome

CAUSES:

• Overuse – using vibrating tools.
• Fluid retention: pregnancy / menopause.
• Secondary to: RA, diabetes mellitus, hypothyroidism, acromegaly.
• Congenital predisposition – small carpal tunnel.
• Trauma (swelling), tumour or fracture in wrist.

The median nerve becomes compressed in carpal tunnel syndrome.
SIGNS & SYMPTOMS:
• Tingling, numbness or pain in the median nerve distribution.
• Symptoms are often worse at night and can wake patient.
• Weakness of grip and weak opposition of thumb.
• Muscle wasting at base of the thumb (sensory symptoms 1st)

DIAGNOSIS:
• Tinel’s test & Phalen’s test.
• Nerve conduction studies.

To relieve symptoms patients may hang hand out of bed or shake their hand.

Median nerve sensory distribution:

Tinels & Phalens: www.youtube.com/watch?v=yQ1GE4RiJLw
Carpal Tunnel Syndrome

ALLOPATHIC TREATMENT:
• Anti-inflammatory drugs, corticosteroid injection, splinting the wrist, physiotherapy.
• Surgery (cutting transverse carpal ligament)

ALTERNATIVE TREATMENT:
• Treat the cause!
• Herbs for pain, inflammation & swelling. Nutrition.
• Acupuncture, homeopathy (arnica, ruta), vit. B₆, Osteopathy.

COMPLICATIONS:
• In chronic and / or untreated cases, the muscles at the base of the thumb may degenerate.

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Bell’s Palsy

- The nerve that controls the facial muscles (facial nerve) becomes inflamed or compressed.

- A type of mononeuropathy → damage to a single nerve or nerve group.

CAUSES:
- Viral e.g. Herpes simplex, surgery, injury or autoimmune.

SIGNS & SYMPTOMS:
- Sudden unilateral weakness or paralysis of the facial muscles.
- Cannot close affected eye (can lead to corneal/conjunctiva damage).
- Loss of taste and intolerance to loud noise if severe.

TREATMENT:
- **Allopathic:** Dependent on cause. Acyclovir, cortisone.
- **Alternative:** Treat cause: herbs & nutrients to support nerve function, antiviral, anti-inflammatory diet. acupuncture, homeopathy.
Guillain-Barre Syndrome

- A form of **post-infectious neuritis**.
- Many different variants.
- A **demyelinating condition**.
- Associated with acute, ascending, progressive inflammation and demyelination of peripheral nerves.

**CAUSES:**
- Auto-immune. Antibodies formed against virus cross react with glycolipids in myelin – molecular mimicry.
- Can be triggered 1-3 weeks after respiratory infection or following vaccination eg. Influenza.

\[ \text{neur(o) = nerve} \]
\[ \text{-it is = inflamed} \]
\[ \text{de- = removal} \]
\[ \text{-myelinating = myelin} \]
Guillain-Barre Syndrome

SIGNS & SYMPTOMS:
• Sudden, progressive, bilateral, ascending paralysis.
• Paraesthesia and sensory changes.
• Neuropathic pain into legs.

DIAGNOSIS:
• Nerve conduction studies, lumbar puncture, antibodies.

ALLOPATHIC TREATMENT:
• Emergency care - respirator, intensive care.
• Plasma exchange.

COMPLICATION:
• Death by heart or respiratory failure.
Multiple Sclerosis (MS)

- An autoimmune inflammatory disease causing demyelination of axons in CNS neurons with damage.
- Multiple areas of sclerosis (scar tissue) form along axons which disrupts nerve conduction.
- Usually occurs between 20-50 years of age, affecting women (2:1) to men.
- Most MS follows a relapsing-remitting pattern (85%). Other patterns are progressive.

CAUSES:
- Unknown.
- Genetic susceptibility & environmental trigger, dietary risk factors. Slightly increased risk with family history.
MS affects nerves that are highly myelinated, such as the optic nerve

Multiple Sclerosis (MS)

SIGN & SYMPTOMS:

- **Visual symptoms** are common: Blindness, loss of vision of one eye and occasional pain (neuritis). Double vision and nystagmus (jerking of eyeball).

- Deafness and loss of balance.

- Burning, pulling sensations.

- Tingling and loss of sensations.

- Bladder urgency and incontinence.

- Cognitive changes and depression.

- Impotence in men.
Multiple Sclerosis (MS)

PROGNOSIS:
• Depends on disease patter. Progressive types have a poor prognosis.

DIAGNOSIS:
• No definite test: based on clinical findings, MRI ophthalmoscopy and CSF analysis.

TREATMENT:
• **Allopathic:** Immunomodulatory therapies: Corticosteroids, interferon-beta, physiotherapy. Symptom management.

• **Alternative:** Lifestyle & diet are important in prolonging remission. Anti-inflammatory diet. Herbal medicine for autoimmune & antiviral conditions. Low-grade exercise.

Optic nerve de-myelination as seen via opthamoscopy
Motor Neuron Disease (MND)

• Progressive degeneration of motor neurons in the spinal cord, motor cortex & brain stem

• Current hypotheses focus on an abnormality of mitochondrial function causing oxidative stress in motor neurons.

• Most common form is Amyotrophic Lateral Sclerosis (ALS).

• Sensory and cognitive function normally remains intact.

• Age of onset is typically >40yrs (highest incidence 50-70yrs).
  • More commonly affects men.

CAUSES
• Unknown, although suspected link with genetics & environmental toxin exposure.
Motor Neuron Disease (MND)

SIGNS & SYMPTOMS
- Typically presents as weakness in upper limbs → dropping objects or difficulty manipulating objects.
- Wasting of hand muscles & tremor of limbs at rest.
- Later stages can affect the legs (tripping), cause slurred speech, dyspnoea, difficulty swallowing.

TREATMENT:
- **Allopathic:** Currently no cure, specialist treatment & care.
- **Alternative:** An anti-inflammatory diet, herbs & nutrients to support nerve function. Homeopathy & acupuncture.

PROGNOSIS:
- Death by respiratory failure - typically, within 3-5yrs.
Alzheimer’s disease

- Neurodegenerative disease of the cerebral cortex.
- Associated with abnormal protein deposition, atrophy of neurons and less acetylcholine.
- The hippocampus is among the areas first affected, which is important for memories. The amygdala is often affected later and is a key centre for emotions & memories.
- Whilst progressing, additional regions of brain become affected.
- It is the most common type of dementia (50%)
- ‘Early onset’ before age 65, ‘Late onset’ after age 65.

CAUSE:
- Aluminium toxicity – vaccines (blood brain barrier degenerates).
- Idiopathic, genetic links.
Alzheimer’s disease

- Brain deterioration is thought to begin decades before symptoms become evident.
- Global neuron atrophy (& hence brain shrinkage) with disrupted cell communication (Ach).

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Alzheimer’s disease

SIGNS AND SYMPTOMS:

Early stages:
• Slight memory loss (especially short term)
• Repeated questions
• Confusion.
• Decreased initiative (lose interest in hobbies, reduced hygiene)
• Faulty judgement

Later stages:
• Significant memory loss (eventually long-term memory).
• Subtle changes in higher order functions i.e. understand jokes.
• Mood disturbances: agitation & aggression
• “Loss of sense of self” - autobiography (left hippocampus)
• Difficulty with language, unsteadiness, depression.
ALLOPATHIC TREATMENT:
• Medication to improve the symptoms & slow down the development. *Acetylcholinesterase inhibitors* or increase glutamate.
• Psychological treatments such as cognitive stimulation.

ALTERNATIVE TREATMENT:
• Nutrition is essential in prevention and support of this condition - deficiencies need to addressed, antioxidants & other nerve supporting nutrients. Herbs such as Ginkgo and *Turmeric* can be very helpful. Regular exercise.

PROGNOSIS:
• People with Alzheimer's disease live for around 8 to 10 years on average after they start to develop symptoms.
‘Elevated brain Aluminium & early onset Alzheimer’s disease in an individual occupationally exposed to Aluminium: a case report’

- Study in 2014 finds high aluminium levels in the brain of an Alzheimer’s victim, following eight years of occupational exposure to aluminium dust. Scientists conclude that this case suggests the olfactory system & lungs play a prominent role in the accumulation of Aluminium in the Brain.

- Aluminium is neurotoxic, targeting your CNS, which can lead to serious immunological and neurodegenerative disorders.
  - Small amounts of Aluminium inhaled through your nose & mouth and absorbed from vaccines, can accumulate over time, especially in your bones & brain.
  - Recent studies show that aluminium contamination in food, drugs & consumer products is much worse than previously thought.

Available at:  
Parkinson’s disease

- A progressive neurological movement disorder affecting movement.

- Caused by loss of dopaminergic neurons in the substantia nigra: an area of the midbrain that regulates movement (and reward).

- Affecting approx. 1% of individuals over 60 years of age.

CAUSES:
- Idiopathic.
- Toxic environmental factors: i.e. carbon monoxide, manganese poisoning, exposure to pesticides & herbicides. Genetics.
- May develop after encephalitis.
Parkinson’s disease

PATHOPHYSIOLOGY:
2 major neuropathological findings in the medical model:

1. **Degeneration of dopaminergic neurons in the substantia nigra** (midbrain) causing dopamine deficiency leaving patients less able to direct or control their movement.

2. **Accumulation of abnormal proteins** (Lewy Bodies) within neurons.

Substantia nigra
“black substance” – has a darker appearance due to high levels of neuromelanin in dopaminergic neurons.
Parkinson’s disease

SIGNS & SYMPTOMS:

- **Bradykinesia**: Short shuffling steps (difficulty stopping/start­ing).
- **Resting tremor** (“pill rolling”).
- Stopped/flexed posture.
- Lack of normal subconscious movements (swinging arms).
- **Muscle rigidity**, mask-like face, low voice.

brady- = slow
Kinesia =
ALLOPATHIC TREATMENT:

• Dopamine replacement (Levodopa/L-DOPA)
  • Doesn’t cross blood brain barrier very well so high doses needed, side effects can lead to abnormal movements.

• Deep brain stimulation: Implantation of electrodes in other basal ganglia areas. Electrical currents modify excitation/inhibition circuits.

ALTERNATIVE TREATMENT:

• Anti-inflammatory, anti-oxidant & mitochondrial support through diet, nutritional supplements, herbs.

Video: www.youtube.com/watch?v=LRGCWIOeTC0
Huntington’s Disease

- Inherited neurodegenerative disorder affecting the basal ganglia.
- Results in loss of muscle co-ordination (abnormal involuntary jerky movements called chorea).
- Also causes cognitive impairment and loss of intellect.
- Poor regulation of mood and emotions: psychiatric symptoms (depression, aggression etc.)
- A genetic (autosomal dominant) disease with a defect on chromosome 4.
- Onset of symptoms is typically 30-50yrs.

Video: www.youtube.com/watch?v=OveGZdZ_sVs
Summary Quiz!

1. List THREE causes of carpal tunnel syndrome
2. Name the nerve involved in carpal tunnel syndrome
3. Describe what happens in multiple sclerosis (MS)
4. List THREE symptoms of MS
5. Name the nerve implicated in Bell’s palsy
6. Define the condition ‘Motor Neuron Disease (MND)’
7. At what age are individuals typically affected by:
   a) Multiple Sclerosis
   b) Motor Neuron disease
8. Describe the presentation of paralysis in Guillain-Barre syndrome
9. Name the part of the brain affected by Parkinson’s disease
10. List FOUR symptoms of Parkinson’s disease