The Nervous System

• Responds to changes within the internal and external environment for a fast effect.

• Works alongside the endocrine system to maintain homeostasis.
The Nervous System

Consists of:
• Brain
• Spinal cord
• Peripheral nerves

• Nerves are made up of **Nerve Cells** known as **NEURONS**
• **Nerve** = *A bundle of one or more neurons*

Divided into 2 parts:
• **Central Nervous System**: Brain and spinal cord
• **Peripheral nervous system**: All of the nerves outside of the CNS
FUNCTIONS

Sensory, Integrative & Motor

1. Sensory
   • **Detects** internal and external environmental **change**
   • Information carried by *Sensory (afferent)* neurons

2. Integrative:
   • **Processes** sensory information, **analyse** store and cause **perception**.
   • Carried by *Interneurons*

3. Motor
   • **Produces a response** to sensory information (perception) to **effect change**.
   • Impulse carried by *Motor (efferent)* neurons.

http://science.kennesaw.edu/~jdirnber/Bio2108/Lecture/LecPhysio/PhysioNervous.html
Organisation of the NS

Central nervous system

- Autonomic NS
  - Sympathetic NS
  - Parasympathetic NS
  - Enteric NS

Peripheral nervous system

- Somatic NS
- Parasympathetic NS
THE AUTONOMIC NERVOUS SYSTEM

Sympathetic NS
- ‘Fight or flight response’
- Thoraco-lumbar innervation

Parasympathetic NS
- ‘Rest and digest’
- Cranio-sacral innervation
Autonomic Nervous System

- ‘AUTO-PILOT’: maintains homeostasis
- Affects organs, glands, cardiac and smooth muscle

Controls:
- Rate and force of heart beat
- Gland activity
- Vessel diameter- Vasoconstriction and vasodilation
- Bronchi- Bronchoconstriction/dilation
- Pupillary constriction/dilation

Too much stress!!
- Sympathetic & Parasympathetic generally have opposite effects
The Enteric Nervous System

- **Enteric Nervous System** = ‘Brain of the Gut’
- Can (and does) function **autonomously/Independently** BUT Mostly regulated by the **Autonomic NS**.
- Also Usually **interacts extensively** with the **Central Nervous System**
- Links with the **CNS** via the **Sympathetic (Pre-vertebral Ganglia)** and **Parasympathetic (Vagus) Nervous System**
- CNS allows outside information to reach the gut

- **Sensory neurons** of ENS monitor chemical changes (Chemo-receptors) in GI tract and stretching (Stretch receptors) of its walls
- **Motor neurons** of the ENS govern motility and secretions of the GI tract and associated glands.
- **Interneurons** connect the 2 plexuses
HISTOLOGY

• 2 types of nerve cells:
  – **NEURONS** process and transmit information, electrically excitable
  – **NEUROGLIA** (GLIAL CELLS) nourish, support and protect neurons
NERVES & NEURONS

- **Nerve**: A *bundle* of one or more Neurons
- Axons of the Neuron determine Nerve length
- Vary from <1mm (CNS) to ~1m (Sciatic nerve)!!
- Possess electrical excitability- the ability to make an ‘*action potential*’ (nerve impulse)

- ‘*Stimulus*’:
  - Anything able to trigger generation of an action potential in a neuron
  - Can be from the internal or external environment
CELL BODY/ SOMA

- Size and shape varies
- The cell body consist of a nucleus and typical cell organelles
- **Cell bodies & Nuclei** are known collectively as ‘Grey matter’ of the NS.
- Collections of Cell bodies referred to as **Nuclei / Centres** in the CNS & **Ganglia** in the PNS
NERVE FIBRES: AXONS & DENDRITES

• *Nerve fibres*: Collective term for any projection away from the cell body
• *Dendrites* (‘little trees’): The receiving end of a neuron
• *Axon*: Carries nerve impulses towards another neuron, away from the body. Covered by a membrane called the axolemma
• *Axon Terminals*: At the end of the axon.
• Axons and dendrites make up the white matter of the nervous system
• Axon bundles are called ‘nerves’ in PNS
• Axon bundles are called ‘Tracts’ in CNS
MYELIN SHEATH

Multi-layered lipid & Protein covering around the Axons.

• Formed by Neuroglia/ Glial cells (Schwann cells/Oilgodendrocytes) in the Embryo.
• Myelination continues through childhood and peaks in Adolescence
• Covered axons are termed ‘Myelinated’

FUNCTIONS:
1. **Insulates** the Axon
   (covers the Axolemma)
2. **Regeneration** of axons in the **Peripheral NS**
3. **Increases speed** of nerve impulse conduction. (Gaps)
SYNAPSES

- Neurons are **NOT continuous**. Instead they have **Spaces / Gaps** between them called **Synapses**
- The **tips** of axon terminals are called **Synaptic End Bulbs**.
- In **Chemical Synapses**, the SPACE between the Synaptic End Bulb and the Next Neuron = **Synaptic Cleft**
- The Nerve impulse is carried across the Synaptic cleft by Nerve Messengers = **Neurotransmitters**
- In **Electrical Synapses**, CONNECTIONS between the Synaptic End Bulb and the Next Neuron = **Gap Junction**
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 an electrochemical, concentration gradient. E.g. Na+ Channels allow Na+ through and K+ channels allow K+ through.

Channels open in response to a Stimulus which changes the permeability of the neuron membrane to Na+ & K+

There are 4 categories of Stimulus, which cause ion channels to open:

1. Voltage
2. Chemicals (hormones, neurotransmitters etc)
3. Mechanical Pressure
4. Light (photoreceptors of the eye)
Parts of a neuron

- Please label the diagram of the myelinated neurone in your handout.
NEUROGLIA

• Also known as ‘glia’ or ‘glial cells’
• Cells that surround and bind the neurones
• Far smaller than neurones and 3-50x 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)
NEUROGLIA

6 types of neuroglia:

• 4 found in the CNS:
  – Astrocytes, oligodendrocytes, microglia and ependymal cells.

• 2 found in the PNS:
  – Neurolemmocytes (Schwann cells), and satellite cells.

• Satellite cells support neurones in the ganglia.
NEUROGLIA

• 4 main functions:
  – Surround neurons and hold them in place
  – Supply nutrients and oxygen to neurons
  – Insulate one neuron from another
  – Destroy pathogens and remove dead neurons.

http://www.medikidz.com/medipedia/glial-cell
Astrocytes

- Star-shaped with branching processes
- Hold neurons to their blood supply
- Contribute to the Blood Brain Barrier
- Found in the CNS
Astrocytes

Surrounding a blood vessel
Oligodendrocytes

- Smaller than astrocytes
- Found in the CNS
- Form and maintain myelin in the CNS
- Similar role to schwann cells in PNS
Ependymal Cells

- Endothelial - Epithelial Cells which line the **walls** of the:
  - **4 Ventricles** of the Cerebrum,
  - **Central Canal** of Spinal cord
- **Make** Cerebrospinal Fluid
- **Beat** their cilia to **circulate** CSF
- Found in the CNS
Microglia

• Derived from monocytes and migrate before birth
• Found near blood vessels
• Phagocytic – to clean up any mess!
• Mobile in the brain and multiply when the brain is damaged
• Found in the CNS
Schwann Cells and Myelination

- *Schwann cells* produce *myelin sheaths* around neurons in the PNS – specifically the axons.
- Myelin sheath: Multi-layered lipid and protein covering, which insulates the axon and increases speed of nerve impulse conduction.
- Covered axons are termed ‘myelinated’
- Dendrite connections and most myelination is finished by 3yrs – Malnutrition in infancy can cause irreversible damage!
The Node of Ranvier

• The gap between the Schwann cells along a neuron is known as the **Node of Ranvier**.

• These gaps increase the speed of nerve impulse transmission.
Cross Section of Myelin Sheath

http://kageeamy2012.wikispaces.com/04+Neurons+and+Synapses
Satellite Cells

- The Support neurones around the ganglia (cell bodies) of the PNS

1. Body of Neuron (Pericaryon)
2. Nucleus of Neuron
3. Satellite Cells

Not to confuse with Sertoli cells
Group work

Which nervous system cell are you?

- Neuron
- Astrocyte
- Oligodendrocyte
- Ependymal cell
- Microglial cell
- Schwann cell
NERVE REGENERATION
AKA NEUROREGENERATION

• **PNS** can regenerate nerves but **CNS** can’t!?!?

*(Amphibian CNS can regenerate...what's going on??)*

The PNS and CNS have two distinct types of Glial Cells:

1. **Schwann Cells** in PNS
2. **Oligodendrocytes** and **Astrocytes** in CNS

**CNS** Glial cells **inhibit re-growth** (esp. Astrocytes)
Nerve PATHOLOGIES
BELL’S PALSY = Mononeuropathy

Temporary facial paralysis resulting from damage or trauma of the Facial nerve (Cranial nerve VII)

1. Controls muscles of facial expression
2. Taste to anterior 2/3rds of the tongue
3. Somatosensory info from the ear
BELL’S PALSY

Sx: Sudden facial paralysis, usually unilateral but may be bilateral

C: Mostly viral, e.g. Herpes virus

Rx: According to cause, e.g. Acyclovir, Cortisone etc.

Usually good prognosis i.e. TEMPORARY
Demyelinating Conditions

**NEURITIS**

(GUILLAIN-BARRE SYNDROME) GBS

AIDP = Acute Inflammatory Demyelinating Polyneuropathy

Wide spread, Autoimmune disorder causing acute inflammation and demyelination of Peripheral Nerves usually triggered 1-3 weeks after a Respiratory Tract Infection.

**Cause:** Auto immune

**Sx:** Sudden, acute, progressive, bilateral ascending paralysis.

**Rx:** EMERGENCY! Respirator, Intensive Care

**Complication:**
Death by heart or respiratory failure.
Demyelinating Conditions

MULTIPLE SCLEROSIS

Progressive *demyelination of neurons* (CNS- Brain & Spinal Cord) & damage to the myelin sheath

Thus Impulse conduction and communication between nerves is disturbed.

- Increased risk with *family history*
- M:F 1:2
- ~20-50 years
Multiple Sclerosis (MS)

**Cause:** Unknown, maybe Viral or Auto-immune. Different environmental risk factors have also been found.

**Sx:**
- "Disease of the Thousand Faces"
- Includes Sensory, Motor & Visual Degeneration, leading to:
  - Numbness, burning, tingling,
  - Blurred vision.
  - Progressive Paralysis

**Diagnosis:** No definite test/ MRI scan, CSF analysis.
MULTIPLE SCLEROSIS

DD:
• Disk slip, Sore eyes, Herpes zoster (Shingles), “candida”, mercury poisoning, Motor-Neuron Disease (early stages) etc.
• Beware of constant symptoms, which are therapy resistant!!
• Can be relapsing - remitting or progressive
• Progressive conditions have a poor prognosis

Rx:
• Corticoids, Interferon, Physiotherapy
Motor - Neurone Disease

AKA Amyotrophic Lateral Sclerosis (ALS)

AKA Lou Gehrig's Disease

Progressive degeneration of motor neurons in Brain stem, Spinal cord & Motor Cortex (involved in the planning, control, and execution of voluntary motor functions.)

• Primarily men 60-70yrs
• C: Unknown
• **Early Sx:** Progressive weakness/twitching in hand, arm & shoulder
• **Late Sx:** Later legs and voice are affected.
• **Motor symptoms only!!**
• **Rx:** Specialist treatment & Care
  Currently no cure :-(

Complication: Death by Respiratory Failure

• Typically, death within 3-5yrs (sometimes over 20yrs)
Neurons are electrically excitable, they communicate with each other using 2 types of electrical signal

**Graded Potential** – Short distance communication

**Action Potential** – Long distance communication
Example

TOUCH:
• **Touch** excites a *graded potential* in the *sensory nerve* in your fingers.
• 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* and you can recognise touch.

**TOUCH**
- Excites

**Graded Potential** *(Short distance Communication in the sensory nerves)*
- Triggers

**Action Potential** *(long distance Communication in the Axon of this sensory nerves)*
- Travels into CNS

**Neurotransmitters released at the synapses of CNS Interneurons**

**Perception**- Brain recognises touch
ACTION POTENTIALS

• AKA Nerve impulse

• Able to occur due to 2 characteristics of a cell:

  1. There is an electrical difference across the membrane of the cell known as the *resting potential*

  2. There are specific *ion channels* that can open and close due to stimuli, creating a changing potential and therefore an electrical current.
RECALL: 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 an electrochemical, concentration gradient. E.g. Na+ Channels allow Na+ through and K+ channels allow K+ through

Channels open in response to a Stimulus which changes the permeability of the neuron membrane to Na+ & K+

There are 4 categories of Stimulus, which cause ion channels to open:

1. Voltage
2. Chemicals (hormones, neurotransmitters etc)
3. Mechanical Pressure
4. Light (photoreceptors of the eye)
RESTING POTENTIAL

• Neurons at rest, possess an Electrical Difference across the membrane
• This is created by a build up of negative ions on the inside of the cell membrane and positive ions on the other side of the cell membrane in the extra cellular fluid
• Separation of charges creates Potential Energy
• This Resting Potential is approximately -70mV
• Cells exhibiting a membrane potential are said to be Polarised
RESTING POTENTIAL

- The **Extracellular** fluid is rich in Na+ and Cl – ions and carries a **Positive charge**.

- **Inside** the cell is rich in K+ & large negative ions which can NOT leave the cell. The cell thus carries a **Negative charge inside**.

- As the Na+ & K+ try to move back to equalize the charge, the separation of charges (Polarity) is **MAINTAINED** by the **Sodium: Potassium Pump** which pumps 3 Na+ out for every 2 K+ it pumps back in.

- This separation of charges creates a **Potential Energy** = \(-70 \text{ mV}\)
ACTION POTENTIAL
AKA Nerve Impulse

Series of events which decrease and reverse the membrane potential and then restore it to its resting state.

Occurs in 2 phases:

• Depolarisation – The negative membrane potential becomes less negative reaches zero and then becomes positive

• Repolarisation – The membrane is restored to its resting potential of −70mV
DEPOLARISATION

- Triggered by stimulation of a nerve ending
- Depolarisation must reach a threshold value in order to generate an action potential
- Na+ channels open allowing Na+ to flood into the cell
- Positive charge build up inside the cell
REPOLARISATION

• K+ channels open much more slowly than Na+ channels so just as the Na+ channels are closing the K+ ones open.
• This allows K+ to flood out of the cell, restoring the membrane potential to –70mV.
REFRACTORY PERIOD

- Period of time after repolarisation in which a nerve cannot generate another action potential
- Na+ and K+ are on the wrong sides of the membrane!
- During this period the Na-K pump pumps Na+ out and some K+ back into the cell to restore the resting potential
- **Absolute refractory period** = Even a strong impulse can’t generate an action potential
- **Relative refractory period** = Larger than normal stimulus needed to generate an action potential
Action potential
CONDUCTION – Unmyelinated

- **Unmyelinated axons:**
  - The membrane becomes depolarised step-by-step (‘Continuous Conduction’)
  - Conduction spreads away from the cell body, moving down the axon
  - One direction only – Previous section of membrane is in refractory state
CONDUCTION - Myelinated

• *Myelinated axons*- The 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*)

• These “leaps” may cover long intervals, leading to far faster current in myelinated nerves

• These nerves are vital for rapid response reactions (reflexes).
CONDUCTION - Myelinated

- *Saltatory conduction* is also far more energy efficient, with less ATP needed to man the sodium pumps.
- Basic speed of conduction in a nerve is dictated by the width of the nerve. The thicker, the faster.
- Nerves also propagate action potential slower at lower temperature.
Continuous and Saltatory Conduction

**Continuous Conduction**
- Unmyelinated
- Step-by-step depolarisation spread
- Far slower
- Less energy efficient

**Saltatory Conduction**
- Myelinated
- ‘Leaps’ of depolarisation
- Far faster
- More energy efficient
Animations to help your learning

• http://www.blackwellpublishing.com/matthews/channel.html

• http://www.blackwellpublishing.com/matthews/actionp.html
Local Anaesthetics

• Local anaesthetics block the Na+ gates from opening, therefore stopping an action potential from being formed, stopping the nerve from being able to transmit the pain message.
Group Work

• Working in groups or pairs please produce a one page A3 poster to show what happens in a nerve cell when an action potential occurs

Include details of…
• Resting potential
• Depolarisation
• Repolarisation
• Refractory phases

Please also include diagrams to show the difference between continuous and saltatory conduction
SYNAPSES

• Communication between nerve cells
Chemical Synapses

- **Recall**: The gap between the cells is known as the synaptic cleft
- Electrical impulses can not jump the cleft so transmission occurs via chemical means, to then restart the action potential in the post-synaptic neuron
- Chemicals used at this gap are known as *neurotransmitters*
Stages of Chemical Synaptic Transmission

1. Nerve **impulse arrives** at the end bulb
2. Depolarisation phase causes **calcium channels to open**, sending calcium into the synaptic bulb
3. Increase of concentration of calcium ions 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
Stages of synaptic transmission

5. This **opens the ion channels**, allowing ions to flow across the membrane

6. The change in ions creates a post-synaptic potential, that then **triggers an action potential** in the post-synaptic nerve

Labelling diagram

Please fill in the blanks on your synapse labelling diagram

You may use page 442 of the textbook to help you if you wish
NEUROTRANSMITTERS

• “Chemical, Nerve Messengers”
• Used to create synaptic transmission
• Total number unknown, but >100!!!

Molecules are considered Neurotransmitters if:
1. It exists in the end bulb/synapse
2. It is released in response to Ca
3. Receptors for it in the post-synaptic neuron
NEUROTRANSMITTERS

Neurotransmitters are broadly categorised into 3 Types:

1. **Amino Acids** e.g. GABA & Taurine, Aspartate, Glutamate
2. **Peptides** e.g. Vasopressin, Somatostatin
3. **Monoamines** e.g. Norepinephrine, epinephrine, Dopamine = Catecholamines.
   As well as Serotonin & Melatonin

4. There is also a 4th group which includes all **Unique molecules** making up neurotransmitters e.g. **Acetylcholine**
EXCITATORY or INHIBITORY Post-synaptic Potentials & Neurotransmitters

- **Some** neurotransmitters cause the ligand-gated channels to open, some to close.
- They do this by either causing a **hyperpolarisation** or **depolarisation** at the post-synaptic neuron
- **Hyperpolarisation of the** post-synaptic neurons’ membrane is inhibitory = **IPSP**
- **Depolarisation of the** post-synaptic neurons’ membrane is excitatory = **EPSP**
Removal of Neurotransmitters

For a synaptic cleft to work properly, the neurotransmitters need to be removed for the process to start again.

This can be done by:

1. **Diffusion** out of the cleft into surrounding tissues / circulation

2. **Degradation/Destroyed** by enzymes

3. **Recycled / Re-Uptake** by terminal bulb
Acetylcholine (ACh)

- **Primary Action:** Excitatory

- **Location:** CNS, Neuromuscular Junction, ParaSympNS

- **Role:** Muscle contractions, Learning & Memory

- **Removal:** Degraded / inactivated / Broken down by enzyme Acetylcholinesterase

- **Associated Disorders & Drugs:** Alzheimer’s (Deficiency) 
  *Botulinum blocks Ach. release*
Amino Acids: **Glutamate/Aspartate**

**GABA & Glycine**

**Glutamate/Aspartate**
- **Action**: Excitatory
- **Location**: CNS, brain (most common excitatory neurotransmitter here)
- **Removal**: Re-uptake

**Gamma-aminobutyric acid (GABA) and glycine**
- **Action**: Inhibitory
- **Location**: CNS (Most common inhibitory neurotransmitter)
- **Removal**: Re-uptake
- **Valium** (diazepam) enhances GABA activity
- **Associated disorders & Drugs**: Anxiety

*Valium enhances GABA*
Catecholamines: Epinephrine, Norepinephrine

- **Action**: Excitatory
- **Location**: Sympathetic NS, Motor neurons, Brain
- **Role**: Arousal, Dreaming, Regulating Mood.

- **Removal**: Re-uptake or Degradation by enzymes (Monoamine Oxidase, Catechol-Oxygen-Methyl Transferase)
- Come from amino acid, Tyrosine

- **Associated Disorders & Drugs**: Depression, Sleep problems, ADHD (?)
  Amphetamines - ↑ Norepinephrine
Catecholamines: Dopamine

- **Action**: Excitatory/ Inhibitory
- **Location**: Primarily Substantia Nigra (area of brain for Movement & Co-ordination) but also found in other parts where it is associated with………
- **Role**: Emotional Responses, Addictive behaviours, Pleasurable experiences (Motivation & Drive), (↑ Schizophrenia) Regulates muscle Tone and some aspects of Movement.

- **Removal**: Re-uptake or Degraded by enzymes, MAO & COMT
- Comes from amino acid Tyrosine
- Associated Disorders & Drugs: Schizophrenia, Parkinson’s Dx & Addiction.

*Amphetamines*- ↑ Dopamine release.
*Cocaine* = Dopamine Re-uptake Inhibitor
Serotonin

• **Action**: Excitatory
• **Location**: Primarily Brainstem
• **Role**: Regulates Mood, Sensory perception, Temperature & Appetite as well as **Sleep induction** (when converting to Melatonin)
• **Removal**: Re-uptaken (blocked by SSRIs), Degraded by Enzyme MAO

• Made from amino acid **Tryptophan**

• **Associated Disorders & Drugs**: Depression, Overeating
  
  **SSRIs & MAOIs** - ↑ **Serotonin**.
Enzyme - MAO

• Monoamine Oxidase
• **Enzyme** that catalyses the breakdown of some neurotransmitters (Serotonin + Catecholamines)
• *Found in Neurons and Astrocytes*
• Breaks down **Serotonin** + Epinephrine, Norepinephrine, Dopamine

Catecholamines
Enzyme - COMT

- Catechol-Oxygen-Methyl Transferase
- Enzyme that breaks down some neurotransmitters (Catecholamines)
- Breaks down Epinephrine, Norepinephrine, Dopamine
- Interesting fact: **COMT Inhibitors** are found in green tea. (Therefore green tea increases the effect of noradrenaline and dopamine)
Nitric oxide

- **NO** - Formed from Arginine
- Formed on demand and acts immediately
- Highly reactive **Free Radical** (Highly toxic) & **Signalling Molecule**

**Role:**
- **Memory** and **Learning**
- **Vasodilation** - Used for angina, lowering BP and increasing erection in males
NEUROPEPTIDES

• Small amino acids joined together that act as NEUROTRANSMITTERS and sometimes as HORMONES

• Common Neuropeptides:
  ➢ *Enkephalins, Endorphins* and *Dynorphins*:
    Help with Analgesia, mood Stabilisation, Pleasure, Memory and Learning, Mental disorders, Regulation of hormones.
    May act as Neuromodulators—substances that do not propagate nerve impulses directly, but instead affect the synthesis, breakdown, or reabsorption (reuptake) of neurotransmitters. Thereby exerting regulatory effects on many extra-synaptic receptors,
  ➢ *Substance P* is a neurotransmitter that enhances the feeling of pain!
# Summary of Important Neurotransmitters

<table>
<thead>
<tr>
<th>Neurotransmitters</th>
<th>Primary Role / Effect</th>
<th>Associated Disorders &amp; Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td><strong>Excitatory</strong> = Learning, Memory, Voluntary Muscle contractions.</td>
<td>Alzheimer’s (Deficiency)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Botulinum blocks Ach release</em></td>
</tr>
<tr>
<td>Dopamine</td>
<td><strong>Excitatory/ Inhibitory</strong> = Regulates Movement &amp; Muscle Tone (smooth/ coordinated movement) Thought Processes = Addictive Behavior Reward/ Pleasure / Motivation/ Drive</td>
<td>Parkinson’s Dx, Schizophrenia Drug Addiction</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Amphetamines ↑Dopamine release. Cocaine blocks dopamine re-uptake = ↑</em> Dopamine</td>
</tr>
<tr>
<td>Serotonin</td>
<td><strong>Excitatory</strong> = Regulates Emotional States - Mood, &amp; Appetite. Regulates Sleep (Melatonin)</td>
<td>Depression, Overeating</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>SSRI’s &amp; MAOI’s - ↑Serotonin</em></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td><strong>Excitatory</strong> = Stress Response – Flight / Fight Physical Arousal &amp; Mood Learning &amp; Memory</td>
<td>Depression, Sleep</td>
</tr>
<tr>
<td>Epinephrine</td>
<td></td>
<td>ADHD(?)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Amphetamine’s - ↑ Norepinephrine</em></td>
</tr>
<tr>
<td>Glutamate / Aspartate</td>
<td><strong>Excitatory</strong> = Stimulates Brain Activity <em>(most common excitatory neurotransmitter in the Brain)</em></td>
<td>N/A</td>
</tr>
<tr>
<td>Gamma-Amino Butyric Acid / Glycine</td>
<td><strong>Inhibitory</strong> = Inhibition of Brain Activity &amp; Motor Behavior. <em>(Most common inhibitory neurotransmitter in the brain)</em></td>
<td>Anxiety (GABA deficiency)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Valium (Diazepam) enhances GABA</em></td>
</tr>
<tr>
<td>Endorphins (Neuromodulators)</td>
<td>Pain perception - Analgesia # Pain Positive emotions- Pleasure &amp; Stability</td>
<td>Opiate Addiction</td>
</tr>
</tbody>
</table>
Drugs and Neurotransmitters

• Neurotransmitter production can be stimulated or inhibited e.g. L-dopa
• Neurotransmitter release can be enhanced or blocked e.g. Amphetamine’s ↑ dopamine and norepinephrine, Botulinum blocks Acetylcholine
• Receptors can be activated or blocked (agonist and antagonist)
• Neurotransmitter removal can be stimulated or inhibited (SSRI, Cocaine-blocks dopamine re-uptake)
Links

• Try the link below to watch these neurotransmitters at work!

• http://www.blackwellpublishing.com/matthews/neurotrans.html
Neurotransmitters and Disease
ALZHEIMER’S DISEASE

**Def:** Neurodegenerative disease of the Cerebral Cortex associated with the formation of Amyloid **Plaques** and Neurofibrillary **Tangles** as well as **Acetylcholine deficiency.**

(See Footnotes)

**Sgs & Sxs:** Starts with inability to incorporate new knowledge despite the retention of old information. Eventually leads to Dementia

**Cause:** Unknown. Genetic link. Aluminium ?
Alzheimer’s Disease

- **Alzheimer’s** is the most common form of Dementia in the UK. ([http://www.alzheimers.org.uk](http://www.alzheimers.org.uk))
- There are approx. >700,000 people in the UK with dementia.
- Globally, it affects 5-10% of people over 65yrs. By age 85, the risk doubles.
- Typically **diagnosed by exclusion** & then use of psychiatric/cognitive testing, brain scans
PARKINSON’S DISEASE

Def:
Slow, progressive neurological disorder resulting from the degeneration of neurons in various parts of the brain, primarily the Dopaminergic neurons in the Substantia nigra.

Most frequent neurological disease in older age! Affecting approx. 1% of individuals older than 60 years.

http://parkinsons-tmj.com/the-shaking-palsy-a-review-on-parkinsons-disease/
**Pathophysiology:** There are 2 major neuropathologic findings:

1. **Since Dopamine–generating Neurons in the Substantia Nigra (Midbrain) use Dopamine to allow for coordinated muscle movement, degeneration of these Dopaminergic neurons, creates a Dopamine deficiency,** resulting in abnormal firing of the Motor neurons, leaving patients less able to direct or control their movement.

2. **Accumulation of a protein into nuclear/cytoplasmic aggregations, called Lewy Bodies, in the cerebral neurons** (See Footnotes)
PARKINSON’S DISEASE

Cause:

- Idiopathic.
- Genetic Link.
- Environmental Factors:
  - Carbon monoxide or Manganese Poisoning
  - Exposure to Pesticides & Herbicides
- May develop after Encephalitis

http://www.bostonmagazine.com/health/blog/2013/12/12/pesticides-parkinsons-study-mit/
PARKINSON’S DISEASE

**Sx:** The 3 cardinal signs:

1. **Bradykinesia:** Low voice, Shuffling steps.
2. **Resting Tremors:** Jerky movements.
3. **Rigidity:** Muscle Stiffness, Lack of Movement, Mask-like face.

Other Signs & Sxs include:

**Pill-rolling** of Fingers, **Balance Impairment** & Unstable Moods

**Rx:** Dopamine replacement (Levodopa / L-DOPA) increases Dopamine production. Embryological **Stem Cells.**

[Image of Parkinson's disease symptoms]
HUNTINGTON’S DISEASE /CHOREA

- Inherited Neurodegenerative disorder affecting brain/basal ganglia which affects muscle coordination and some cognitive functions.
- It is the most common Genetic cause of abnormal involuntary writhing movements called Chorea
- Inherited lack of GABA
- ~30-50 yrs. (Often gene passed on by then to child)
Summary Table

• Please fill in the neurotransmitter summary table in your handout using the information in the slides