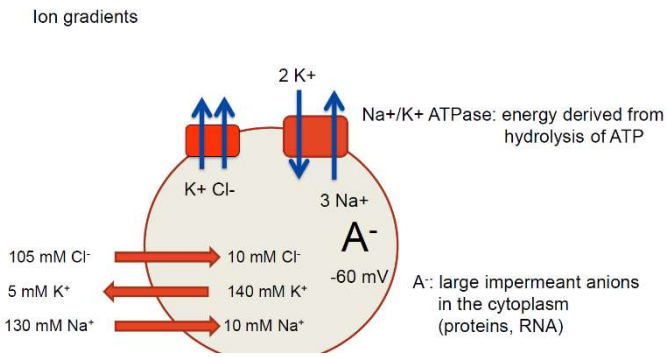
PCOL3922 NOTES

Lecture 1 – Introduction to Synaptic Transmission

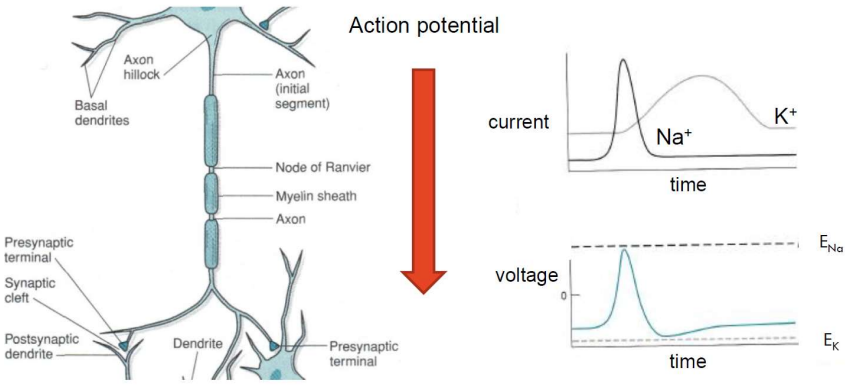
Understand the cellular and ionic basis of synaptic transmission

- Neurons are responsible for communicating signals
  - Cell body (Soma)
  - Dendrites
    - Direct inputs into the neuron
  - Axon
    - Information flows down the axon
    - Can be covered by myelin
  - Synapse
    - Joint between 2 neurons
    - Axo-dendritic, axo-axonic, autoreceptors or complex synapses



Electrical Excitability

- Need to maintain existing ionic gradients to keep the membrane potential at a normal level
  - Calculate this using the Nernst equation
  - Resting membrane is usually -60mV
- Can measure using patch clamp or oocytes



Understand the role of the BBB

- Formed by tight junctions between endothelial cells of the capillaries in the cerebral vascular beds
  - Prevents exchange between the brain ECF and the general circulation
- Allows the control of precise conditions within the CNS and stops the entry of potentially toxic compounds

Describe the roles of glial cells in brain functions

Astrocytes

- Make up 25-50% of cell volume
- Shape varies
- Marked by glial fibrillary acid protein (GFAP)
- Provide structure and form part of the BBB
- Maintain neuronal homeostasis, secrete neurotrophic factors, regulate the extracellular environment
  - Reuptake K+, Glu, GABA

Oligodendrocytes and Schwann Cells

- Produce and ensheath axons with myelin
- Myelin forms an insulating layer for axons to allow rapid electrical conduction

Microglia

- Immune cells of the brain and spinal cord
- Defend against infection
- Respond to insult and injury by changing their morphology and number
- Excessive action can be bad
    - May contribute to neurodegenerative disorders such as AD

Identify major neurotransmitters

- NT are released by the pre-synaptic neuron and act on the post synaptic neuron

Identify major neurotransmitter receptors and transporters

Fast Synaptic Neurotransmission

- Cys-Loop Receptors (pentameric)
    - nAChRs, 5HT-3 receptors
        - induce depolarization through allowing Na and Ca to enter the cell
    - GABAa, Gly
        - Hyperpolarization through passage of Chlorine
- Ligand Gated ion channels – ionotriopic tetramers
    - NMDA receptors, AMPA/Kainate

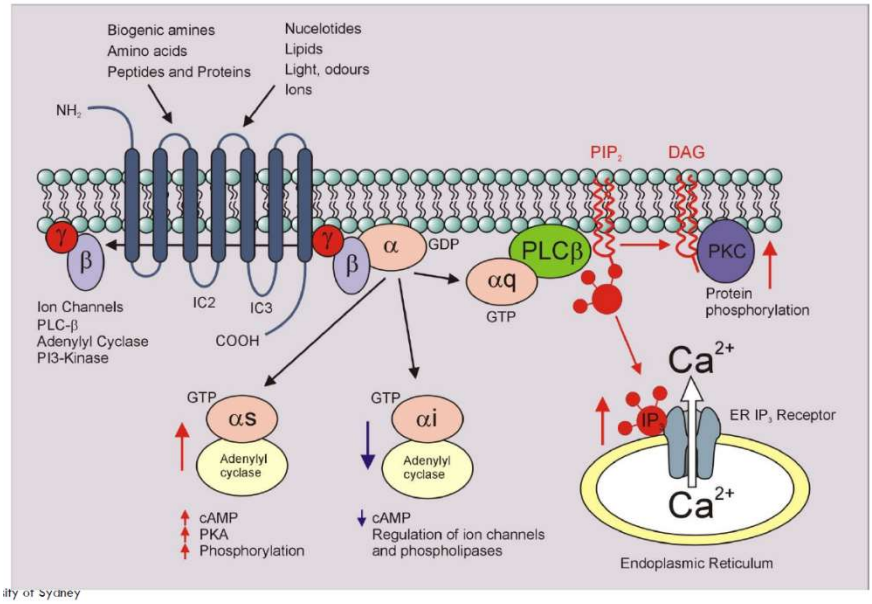
Slow Neurotransmission

- Rely on the action of g-proteins

Neurotransmitter Transporters

- 2 families
    - GABA, Gly, DOPA, NA, 5HT
    - Glu, Aspartate

Neurotransmitter	Ligand-gated ion channels	G-Protein coupled receptors
Glutamate	AMPA-R, NMDA-R	mGluR
Acetylcholine	nACh-R	mACh-R
GABA	$GABA_A$-R	$GABA_B$-R
Glycine	GlyR	
Dopamine Serotonin Noradrenaline	5HT-3 R	D-R 5HT-R A-R
Peptides (enkephalins) Nucleosides (ATP)	P2XR	OR (μ, κ, δ) P2YR

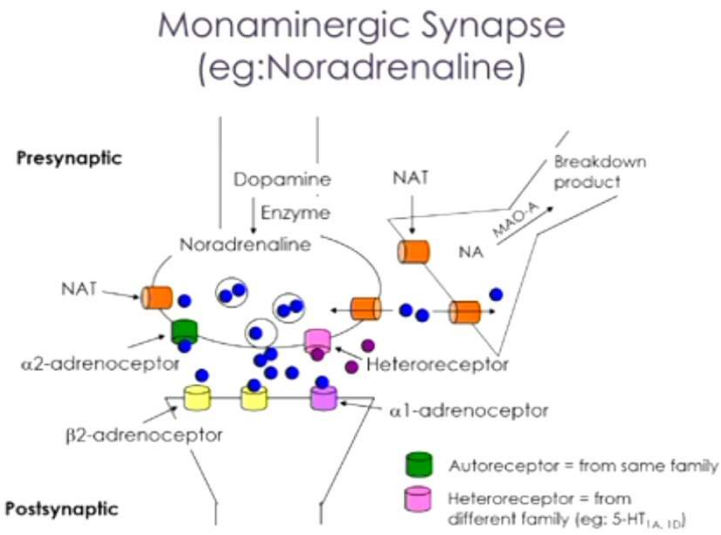


Lecture 2 – Monoamines

Explain the normal synaptic events of monoamines; synthesis, storage, release, receptor action, reuptake and degradation

Transmitter Substances

Classical Transmitters	Neuropeptides	Gases	Others
GABA	Opioids eg: enkephalins	Nitric oxide	Neurosteroids eg: allopregnanolone, DHEA
Glutamate	Neurohypophyseals eg: oxytocin	Carbon monoxide	Purinergics eg: ATP, adenosine
Glycine			Lipid metabolites eg: anandamide, 2-AG
Noradrenaline	Somatostatins		
Dopamine	Tachykinins eg: substance P		
Serotonin (5-HT)			
Histamine			
Acetylcholine			



Synthesis

- DOPA, NA, Adr are synthesized from decarboylated AAs which characterizes the neuron
  - L-tyrosine is a common precursor which is then converted into L-DOPA and then decarboxylated to give DOPA
  - DOPA is hydroxylated to give NA which is then modified with a methyl group to give Adr
    - Adr is most common in the brain while NA is peripheral
- 5HT is synthesized from tryptophan via hydroxylation to 5-hydroxytryptophan and then to 5HT

Storage

- Active transport into vesicles via the vesicular monoamine transporter (VMAT)
- Stored as a bound complex with ARP and proteins plus some ions

Release

- Traditional
  - Terminal depolarization → Ca2+ channels open and Ca2+ influx → vesicles fuse with the terminal membrane → exocytosis
- 5HT and NA release
  - Diffusely projecting neurotransmitters which can be released from varicosities along the axons of the neuron as well as into synapses
    - Raphe nuclei is the main part of serotonin production
    - Important actions in the hypothalamus, hippocampus and amygdala
  - Forms a concentration gradient in these projection areas
    - Similar to an aerosol
- NA release
  - Lots is released in the locus coeruleus and released from there into the forebrain bundle and further into the brain