

Final Pharmacology Test Study Guide

Antipsychotics & Serotonin

Serotonin – synthesised from Tryptophan

Found in the:

- CNS: sleep & wake cycles... many functions within the CNS
- CV: vasoconstrictor in splanchnic, renal, pulmonary beds, but also stimulates NO which has a vasodilatory effect, also has α -adrenomimetic effect but there is serotonin auto-receptors on the vagus nerve \rightarrow bradycardia & hypotension
- GI: serotonin the primary neurotransmitter of the enteric NS \rightarrow increases motility in the gut, but also has inhibitory effect
- Inflammation: platelet activation/aggregation, increase vascular permeability, chemottractant

Synthesis:

- Tryptophan \rightarrow hydroxylated by Tryptophan hydroxylase \rightarrow **L-tryptophan 5-hydroxy acid decarboxylase** (**requires **Vitamin B6**!) \rightarrow **5-hydroxy-tryptamine, 5-HT, Serotonin** \rightarrow secretory granules
- Serotonin can be converted into Melatonin (circadian rhythms) in **Pineal gland** \rightarrow **Suprachiasmatic nucleus**, (rich in melatonin receptors) regulates sleep/wake cycles

Ramelteon – prescribed for insomnia, agonist at the melatonin receptors in the suprachiasmatic nucleus, has short t_{1/2} (no long-term effects of drowsiness)

Serotonin Receptors: ****GPCRs except for 5HT2, varied distribution**

- 5HT1
 - o **G_i (inhibitory)** \rightarrow **Ca²⁺ channels & K⁺ channels**
 - o 5HT1A & 5HT1D – auto-receptors, negative feedback to stop neurotransmitters (5HT1B subtype on vascular smooth muscle \rightarrow vasoconstriction)
- 5HT2
 - o **G_q (IP3/Ca²⁺ pathway)** \rightarrow smooth muscle contraction, platelet release of granules, CNS neurotransmission
 - o 5HT2A & 5HT2C \rightarrow **PLA2** \rightarrow cleaves arachidonic acid \rightarrow inflammatory response
 - Methysergide
 - Antipsychotic drugs
 - LSD
 - Psilocybin
 - Ayahuasca
- 5HT3
 - o **Ligand-gated Na⁺ channel** \rightarrow depolarisation
 - CNS, GI tract, vagal afference
 - Ondansetron
- 5HT4
 - o **G_s (stimulatory)** \rightarrow increase secretions & peristalsis
 - CNS, smooth muscle, GI system
- 5HT5,6
- 5HT7

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