

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 -adrenoceptor 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-hydroxytryptamine** ($\rightarrow$ requires **KiB6.1**) $\rightarrow$ **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: **$\rightarrow$ 7 GPCR's except for 5HT2, varied distribution**

- 5HT1
 - o Gi (inhibitory) $\rightarrow$ Ca^{2+} channels & K^{+} channels
 - o 5HT1A & 5HT1D – auto-receptors, negative feedback to stop neurotransmitters (5HT1B subtype on vascular smooth muscle $\rightarrow$ vasoconstriction)
- 5HT2
 - o Gq (IP3/ Ca^{2+} 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 Gs (stimulatory) $\rightarrow$ increase secretions & peristalsis
 - CNS, smooth muscle, GI system
- 5HT5,6
- 5HT7

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DP Hallahan



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