

Module:

Biological Foundations of Mental Health

Week 3:

Synaptic transmission and neurotransmitter systems



Dr Jon Robbins

Topic 2:

Neurotransmitters, receptors and pathways

Part 4 of 4

Topic list



This week, we will be looking at the following topics:

- Topic 1: Action potentials and synaptic transmission
- **Topic 2: Neurotransmitters, receptors and pathways**
- Topic 3: Neurotransmission defects and mental health; focus on schizophrenia

Click **Next** to continue

Part 4

5-HT

Week 3 Synaptic transmission and neurotransmitter systems

Topic 3: Neurotransmitters, receptors and pathways

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5-HT

S

S

R

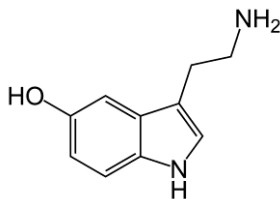
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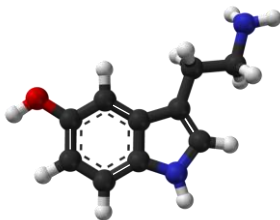
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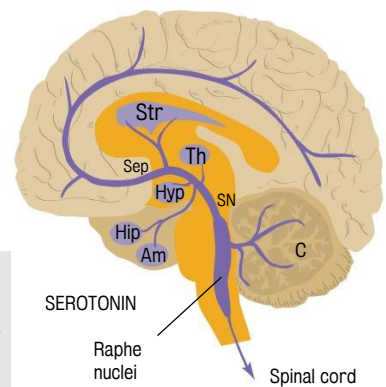
5-HT



serotonin
monoamine
enteric nervous system 80 per cent
platelets



Str – striatum
Th – thalamus
Hyp – hypothalamus
Hip – hippocampus,
Am – amygdala
C – cerebellum
Sep – septum
Sn – substantia nigra



Humphrey et al (2014)

Week 3 Synaptic transmission and neurotransmitter systems

Topic 3: Neurotransmitters, receptors and pathways

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5-HT – synthesis

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D

5-HT synthesis

Tryptophan (diet)



Tryptophan hydroxylase (rate limiting)

5-hydroxytryptophan



Dopa decarboxylase

5-hydroxytryptamine

Week 3 Synaptic transmission and neurotransmitter systems

Topic 3: Neurotransmitters, receptors and pathways

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5-HT – storage

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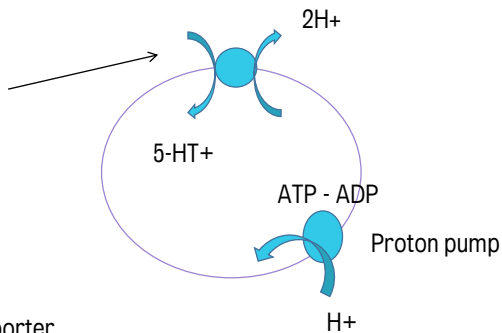
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5-HT storage

● VMAT1
● VMAT2



VMAT - vesicular monoamine transporter
1 or 2 can be cell type specific

Week 3 Synaptic transmission and neurotransmitter systems

Topic 3: Neurotransmitters, receptors and pathways

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5-HT – release

S

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5-HT release

5-HT has a **calcium dependent release** which mainly occurs at the **axon terminal bouton**.

5-HT can also be **co-released with neuropeptides**, such as somatostatin or substance P.

Week 3 Synaptic transmission and neurotransmitter systems

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5-HT – receptors

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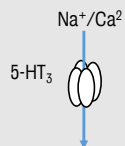
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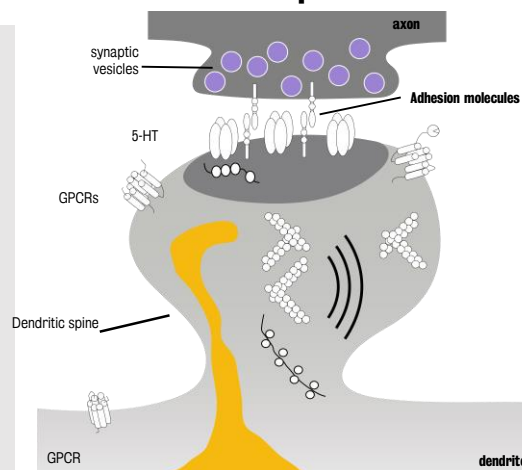
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5-HT receptors

Ionotropic receptor



- the only 5-HT receptor that is a ligand-gated ion channel
- mixed cation channel – allows sodium and calcium into cell and potassium out



GPCRs



- 5-HT_{1A}, 1B, 1D, 1E, 1F – Gi/Go (presynaptic)
- 5-HT_{2A}, 2B, 2C – Gq/G11
- 5-HT₄ – Gs
- 5-HT_{5A} – Gi/Go, 5B pseudogene in human
- 5-HT₆ – Gs
- 5-HT₇ – Gs

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Topic 3: Neurotransmitters, receptors and pathways

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5-HT- reuptake

S

S

R

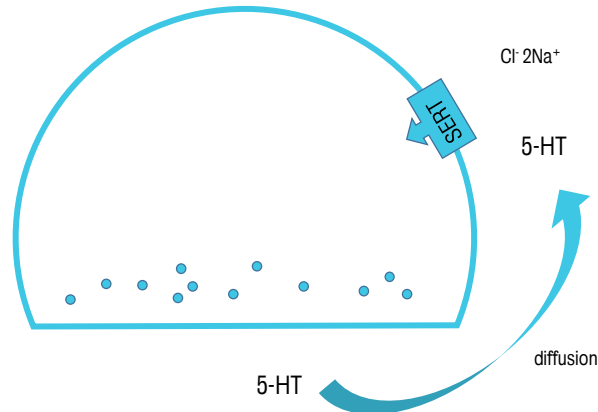
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5-HT reuptake



SERT – serotonin transporter

Week 3 Synaptic transmission and neurotransmitter systems

Topic 3: Neurotransmitters, receptors and pathways

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5-HT – degradation

S

S

R

R

R

D

D

5-HT degradation

5-hydroxytryptamine



Monoamine oxidase

5-hydroxyindolealdehyde



Aldehyde hydrogenase

5-hydroxyindoleacetic acid (5-HIAA)

Week 3 Synaptic transmission and neurotransmitter systems

Topic 3: Neurotransmitters, receptors and pathways

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5-HT – drugs

S

S

R

R

R

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D

5-HT: drugs

Synthesis – p-chlorophenylalanine (TH inhib)

- L-tryptophan (precursor)

Storage – tetrabenazine**Release** – MDMA**Receptors:**

- full agonist – 5-HT, sumatriptan (5-HT_{1D})
- partial agonist – buspirone (5-HT_{1A})
- competitive antagonists - ondansetron (5-HT₃), ketanserin (5-HT_{2A})

Reuptake – SSRI (citalopram), TCAs (imipramine), amphetamine (MDMA)**Degradation** – MAOI (phenelzine)

5-HT – disease

S

S

R

R

R

D

D

5-HT: disease



5-HT is associated with amphetamines and derivatives (eg MDMA), LSD, mescaline and psilocybin (magic mushrooms).



Diseases associated with 5-HT include depression, anxiety and hallucinations.



5-HT is important in mood, the sleep/wake cycle and appetite.

5-HT – fact sheet

5-HT: fact sheet**Drugs**

S	Tryptophan hydroxylase	L-tryptophan
S	Vesicular	Tetrabenazine
R	Calcium dependent, terminal	MDMA
R	5-HT ₃ cation channel 5-HT ₁ , 2, 4, 6, 7 receptors – GPCR (15 subtypes)	Ondansetron Sumatriptan
R	SERT	Citalopram
D	MAO & COMT	Phenelzine

Clinical use

Conclusion

Other neurotransmitters that you may come across in this course:

- acetylcholine
- ATP
- bradykinin
- glycine
- histamine
- neuropeptides
- nitric oxide
- noradrenaline

Create your own fact sheets

References

- Chapters 39 Rang et al (2016) Pharmacology 8th ed
- Humphrey, P. R., Maureen, M. D., & Ritter, J. M. (Eds.). (2012). Rang & Dale's pharmacology. Elsevier.
- <http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=68>
- <http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=1>.

End of topic