

Module:

Biological Foundations of Mental Health

Week 3:

Synaptic transmission and neurotransmitter systems



Dr Jon Robbins

Topic 2:

Neurotransmitters, receptors and pathways

Part 1 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

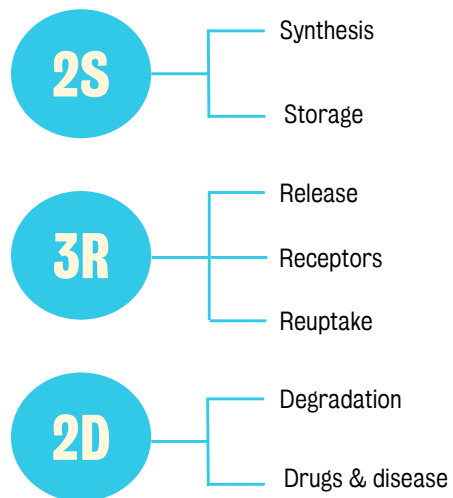
Part 1

Week 3 Synaptic transmission and neurotransmitter systems

Topic 2: Neurotransmitters, receptors and pathways

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The 2S, 3R, 2D (SSRRRDD) system

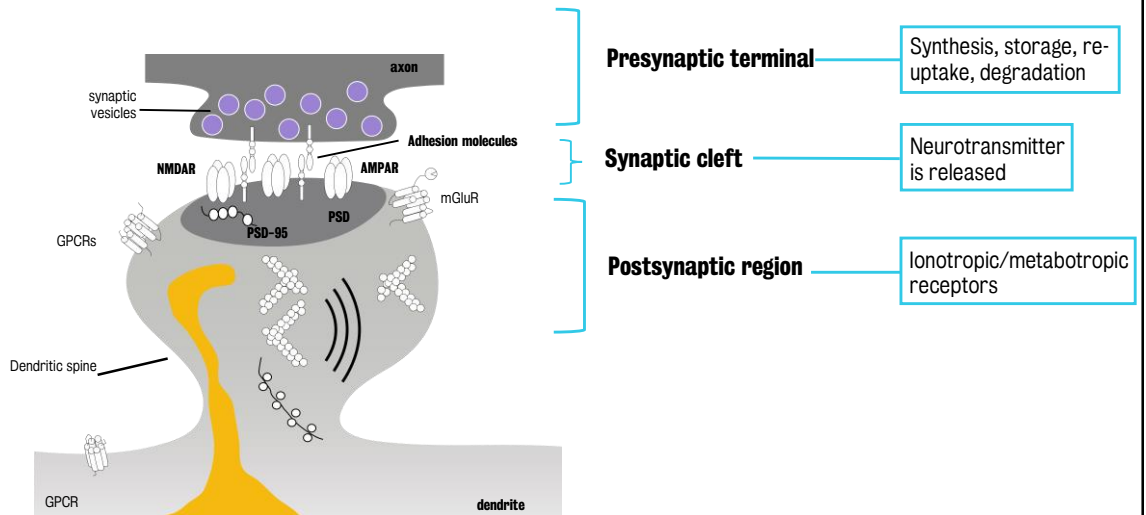


Week 3 Synaptic transmission and neurotransmitter systems

Topic 2: Neurotransmitters, receptors and pathways

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The synapse



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Glutamate

S

S

R

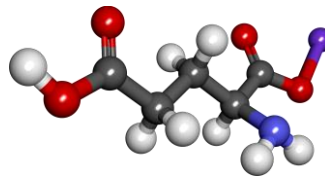
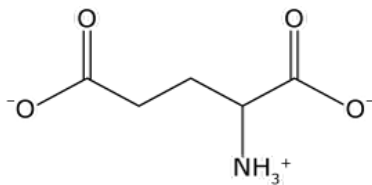
R

R

D

D

Glutamate



- amino acid
- widely distributed in the CNS and it occurs in 70 per cent of all synapses
- very little in the PNS
- the most important excitatory NT in the CNS

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Glutamate – synthesis

S

S

R

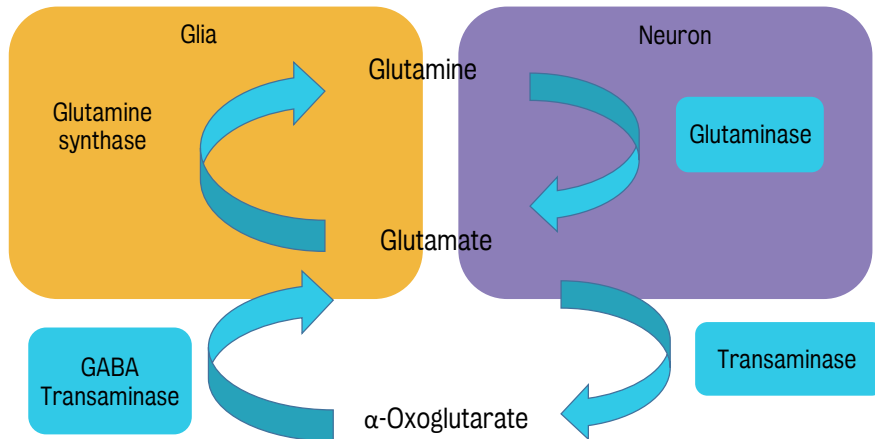
R

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Glutamate synthesis



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Topic 2: Neurotransmitters, receptors and pathways

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Glutamate – storage

S

S

R

R

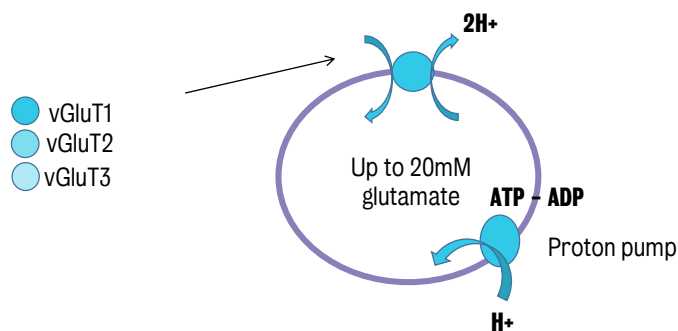
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Glutamate storage

Glutamate is transported by at least three types of vesicular glutamate transporters (vGluT) into vesicles.



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Glutamate – release

S

S

R

R

R

D

D

Glutamate release

Neurotransmitters are released by the nerve terminal at the **axon terminal bouton**.

They are released in a **calcium-dependent process**: calcium is required to move and fuse vesicles with the membrane to allow neurotransmitters into the synaptic cleft.

Glutamate – receptors

S

S

R

R

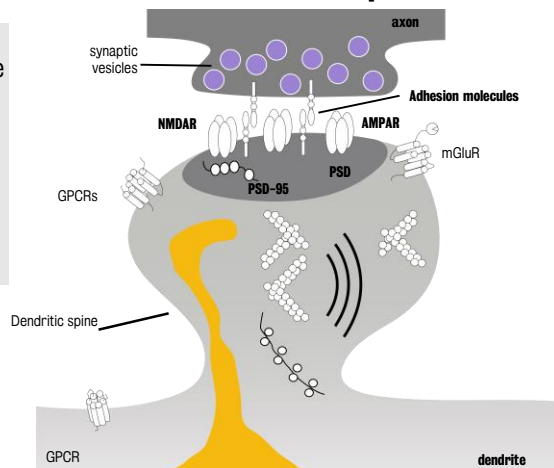
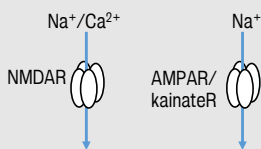
R

D

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Glutamate receptors

Ionotropic receptors iGluR (ion channels activated by glutamate)



Metabotropic receptors mGluR (G-protein coupled receptors, class C):



- Group I - mGluR1 & mGluR5 couple to Gq & G11 G-proteins
- Group II - mGluR2 & mGluR3 couple to Go and Gi G-proteins
- Group III - mGluR4 & mGluR6-8 couple to Go & Gi G-proteins

Glutamate – reuptake

S

S

R

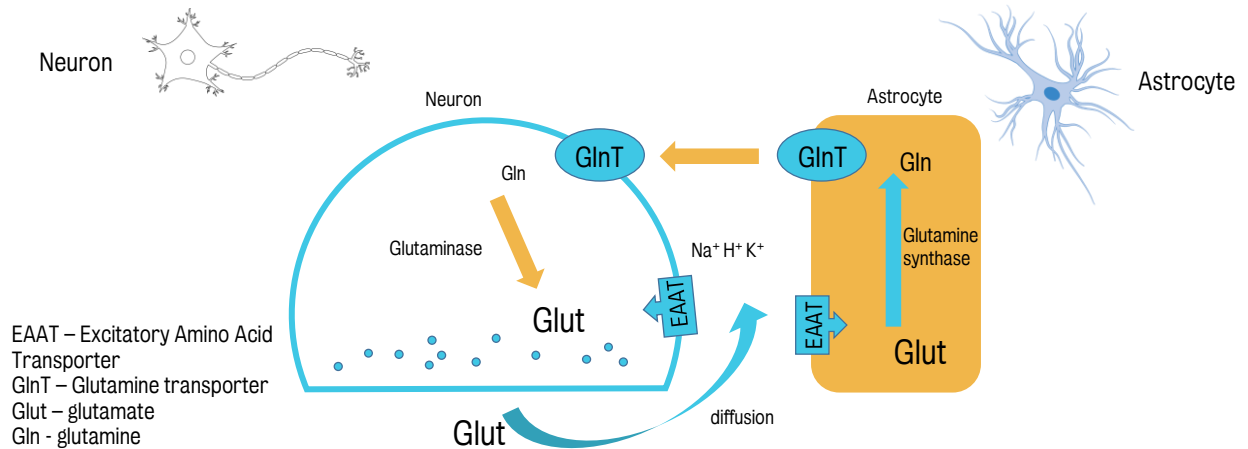
R

R

D

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Glutamate reuptake



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Glutamate – degradation

S

S

R

R

R

D

D

Glutamate degradation

- Glutamate is quickly removed from the synaptic cleft by the EAAT into neurones for recycling or astrocytes (glia).
- In astrocytes it is converted to glutamine by glutamine synthase.
- The glutamine is transferred to the neuron where it is converted back to glutamate by glutaminase to be reused.

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Glutamate – drugs

S

S

R

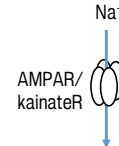
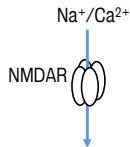
R

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D

Glutamate: drugs



- Ketamine: a dissociative anaesthetic and channel blocker
- Memantine: a competitive antagonist
- Perampanel: a competitive antagonist

Glutamate – disease

S

S

R

R

R

D

D

Glutamate: disease



Recreational use of drugs (PCP, ketamine etc) can lead to drug addiction and dependency.



Epilepsy is associated with the glutamatergic system, as it controls the excitability of the brain.



Glutamate is critical to all CNS functions.

Glutamate – fact sheet

Glutamate: fact sheet**Drugs**

S	Glutaminase	-
S	Vesicular	-
R	Calcium dependent at terminal	-
R	Iono: NMDA, AMPA, kainate; Metabo: mGluR 1-8	Ketamine, pampampanel
R	EAAT	-
D	Glutamine synthase	-

References

- Chapter 38 Rang et al (2016) Pharmacology 8th ed
- <http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=75>
- <http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=40>

End of Part 1