KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

Module:

Biological Foundations of Mental Health

Week 3:
Synaptic transmission and neurotransmitter systems

Dr Jon Robbins

Topic 2:

Neurotransmitters, receptors and pathways

Part 2 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

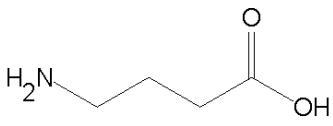
Part 2

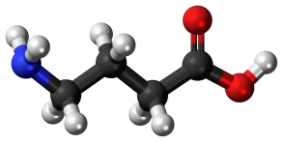
GABA

Gamma aminobutyric acid

S	S	R	R	R	D	D

GABA



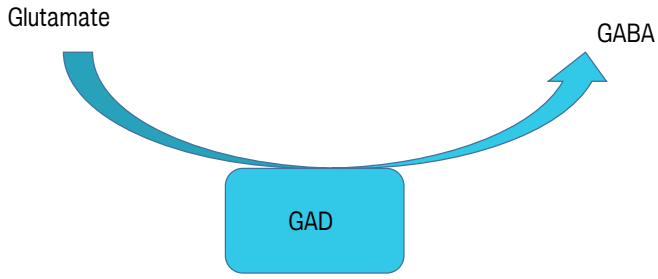


- amino acid
- widely distributed in the CNS (30% of synapses)
- very little in the PNS
- the most important inhibitory NT in the CNS

GABA – synthesis

S | S | R | R | R | D | D

GABA synthesis

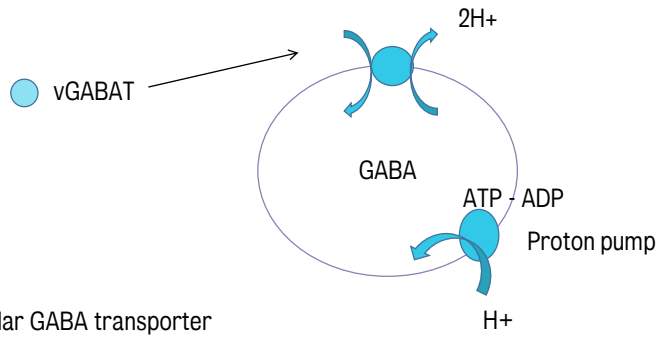


GAD – Glutamic Acid Decarboxylase

GABA – storage

S | S | R | R | R | D | D

GABA storage



vGABAT – vesicular GABA transporter

GABA – release

S | S | R | R | R | D | D

GABA release

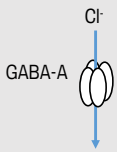
Like glutamate, GABA has a **calcium dependent vesicular release** which mainly occurs at the **axon end terminal bouton**.

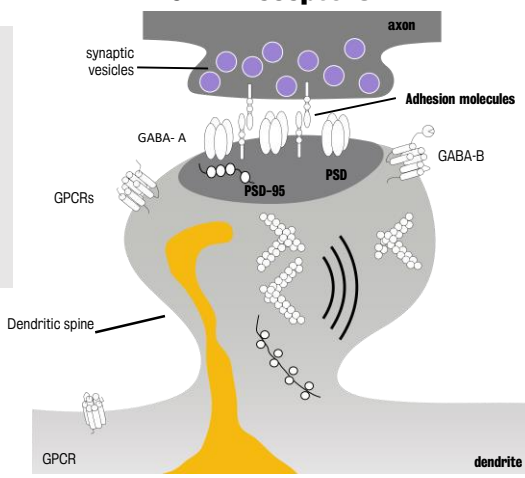
GABA – receptors

S | S | R | R | R | D | D

GABA receptors

Ionotropic receptors





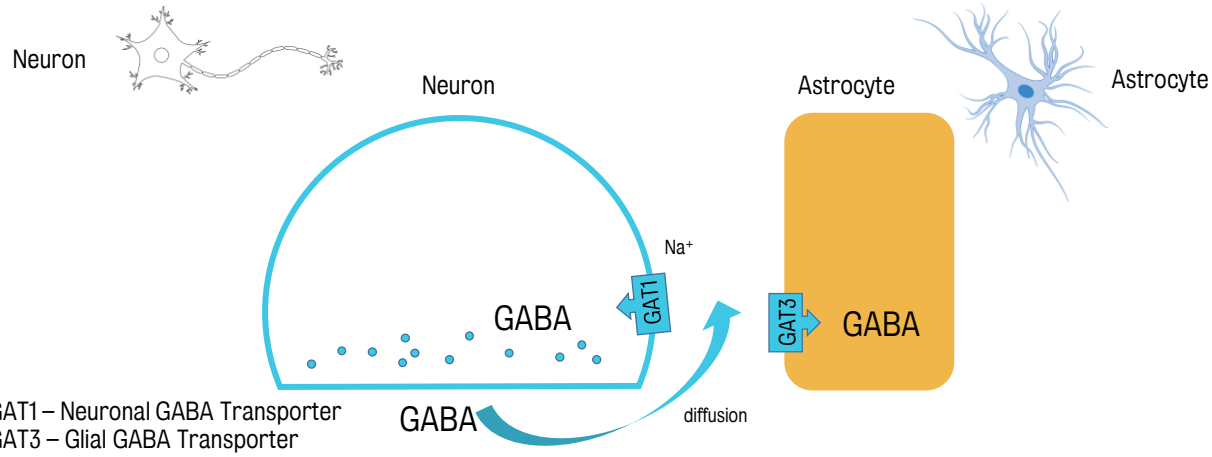
Metabotropic receptors

Coupled to the G-proteins Gi and Go

GABA– reuptake

S | S | R | R | R | D | D

GABA reuptake

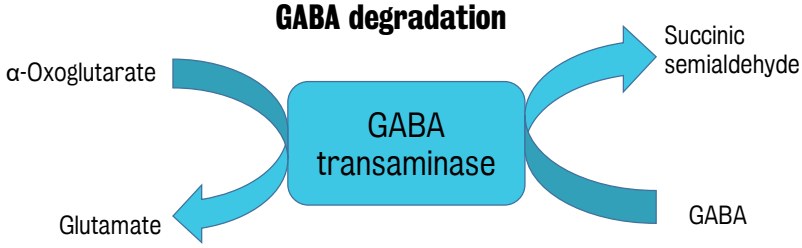


GAT1 – Neuronal GABA Transporter
GAT3 – Glial GABA Transporter

GABA – degradation

S | S | R | R | R | D | D

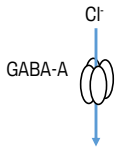
GABA degradation



- occurs in an enzyme called GABA transaminase
- occurs mostly in glial cells eg astrocytes
- α -Oxoglutarate converted to glutamate; GABA converted into succinic semialdehyde

GABA – drugs

S | S | R | R | R | D | D



GABA: drugs

Not used clinically

- muscimol: an agonist which activates the receptor
- bicuculine: a competitive antagonist
- picrotoxin: a GABA-A receptor channel blocker

Clinically useful

- benzodiazepines, ethanol, some general anaesthetics

- baclofen: agonist
- saclofen: competitive antagonist
- tiagabine: interferes with re-uptake by blocking GAT, the GABA transporter
- vigabatrine: blocks GABA transaminase (degradation)

GABA – disease

S | S | R | R | R | D | D

GABA: disease

Barbiturates act on GABA-A receptors.

Epilepsy, anxiety and insomnia are all associated with GABA.

GABA has a major function in the CNS, associated with the brain's inhibitory actions.

GABA: fact sheet

		Drugs	
S	GAD	-	
S	Vesicular	-	
R	Calcium dependent at terminal	-	
R	Ionotropic: GABA-A Metabotropic: GABA-B	Muscimol, bicuculline, benzodiazepines, anaesthetics, baclofen, saclophen	Clinical use
R	GAT	Tiagabine	
D	GABA-t	Vigabatrine	

References

- Chapter 38 Rang et al (2016) Pharmacology 8th ed
- http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=72
- http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=26

End of Part 2