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 3 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

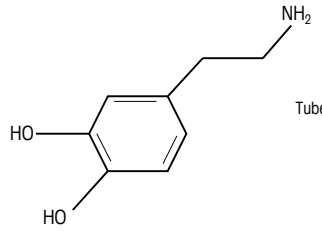
Click **Next** to continue

Part 3

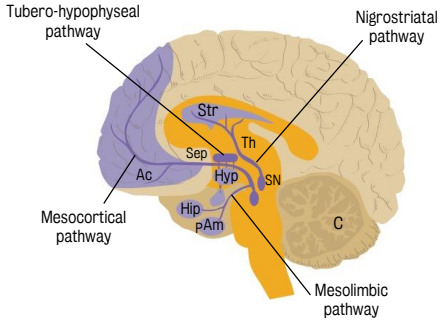
Dopamine

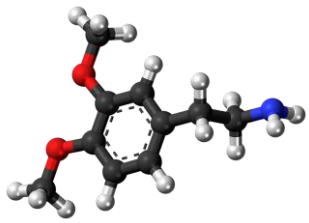
Dopamine

S	S	R	R	R	D	D



Dopamine





Th - thalamus
Hyp – hypothalamus
Am - amygdala
C – cerebellum
Sep – septum
Sn –substantia nigra
Str – striatum
P – pituitary
Ac – nucleus accumbins
Hip – hippocampus

- Monoamine
- Location in CNS

Humphrey et al (2014)

Dopamine – synthesis

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

Dopamine synthesis

Tyrosine (diet)

↓ Tyrosine hydroxylase (rate limiting)

DOPA

↓ Dopa decarboxylase

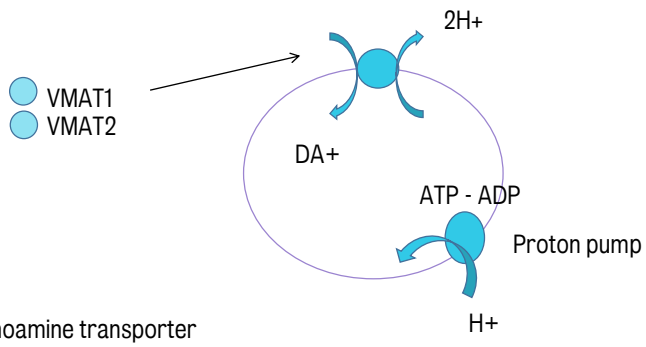
DOPAMINE

DOPA - dihydroxyphenylalamine

Dopamine – storage

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

Dopamine storage



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

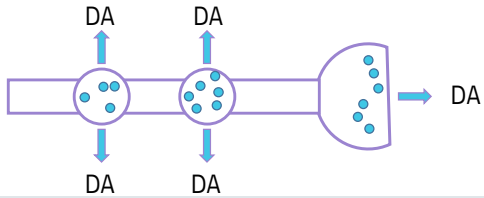
Dopamine – release

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

Dopamine release

Dopamine has a **calcium dependent vesicular release** which mainly occurs at the **axon end terminal bouton**.

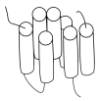
Dopamine can also be released in an **en passant** manner, where small **release sites** are located all the way down the axon, meaning that dopamine can be released **at all these points**.



Dopamine – receptors

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

Dopamine receptors

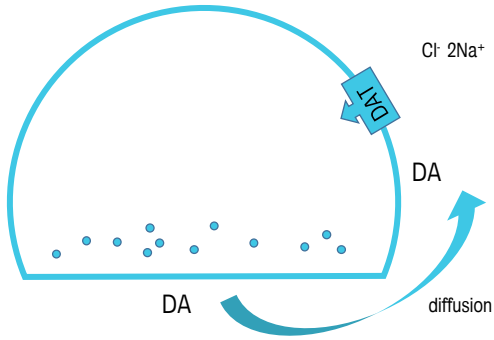


- All GPCRs (Class A, rhodopsin-like)
- 'Dl-like' D1, D5 coupled to Gs
- 'D2-like' D2, D3, D4 coupled to Go/Gi

Dopamine– reuptake

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

Dopamine reuptake

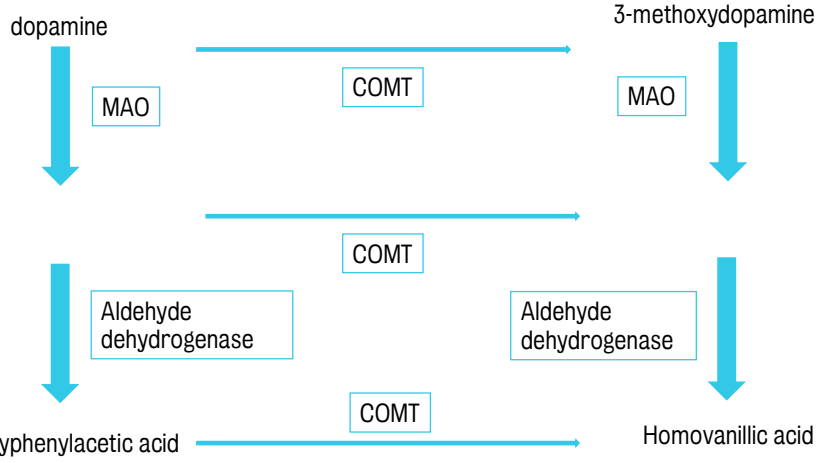


DAT: dopamine active transporter

Dopamine – degradation

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

Dopamine degradation



MAO – monoamine oxidase

COMT – catechol-O-methytranferase

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

Dopamine: drugs

Synthesis - Levodopa

Storage - reserpine, methamphetamine

Release – amantadine

Receptors:
- full agonist - DA, apomorphine, bromocriptine
- competitive antagonists - haloperidol, chlorpromazine

Reuptake – cocaine, bupropion, methylpenidate (Ritalin)

Degradation:
- MAO inhibitors - phenelzine, selegiline (MAO-B)
- COMT inhibitors – entacapone, tolcapone

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

Dopamine: disease

Cocaine, amphetamines and bromocriptine (a fungal contamination of grain) interfere with the dopaminergic system.

Parkinson's, schizophrenia, hormonal disturbances and drug dependence all involve dopamine.

Dopamine is involved in motor control and pituitary control, and may be involved in reward system and thought.

Dopamine: fact sheet

		Drugs	
S	Tyrosine hydroxylase	L-DOPA	
S	Vesicular	Methamphetamine	
R	Calcium dependent terminal and en passant	Amantadine	
R	DA receptors – GPCR (five subtypes)	Apomorphine Haloperidol Chlorpromazine	Clinical use
R	DAT	Methylphenidate	
D	MAO & COMT	Selegiline Tolcapone	

References

- Chapter 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=20

End of Part 3