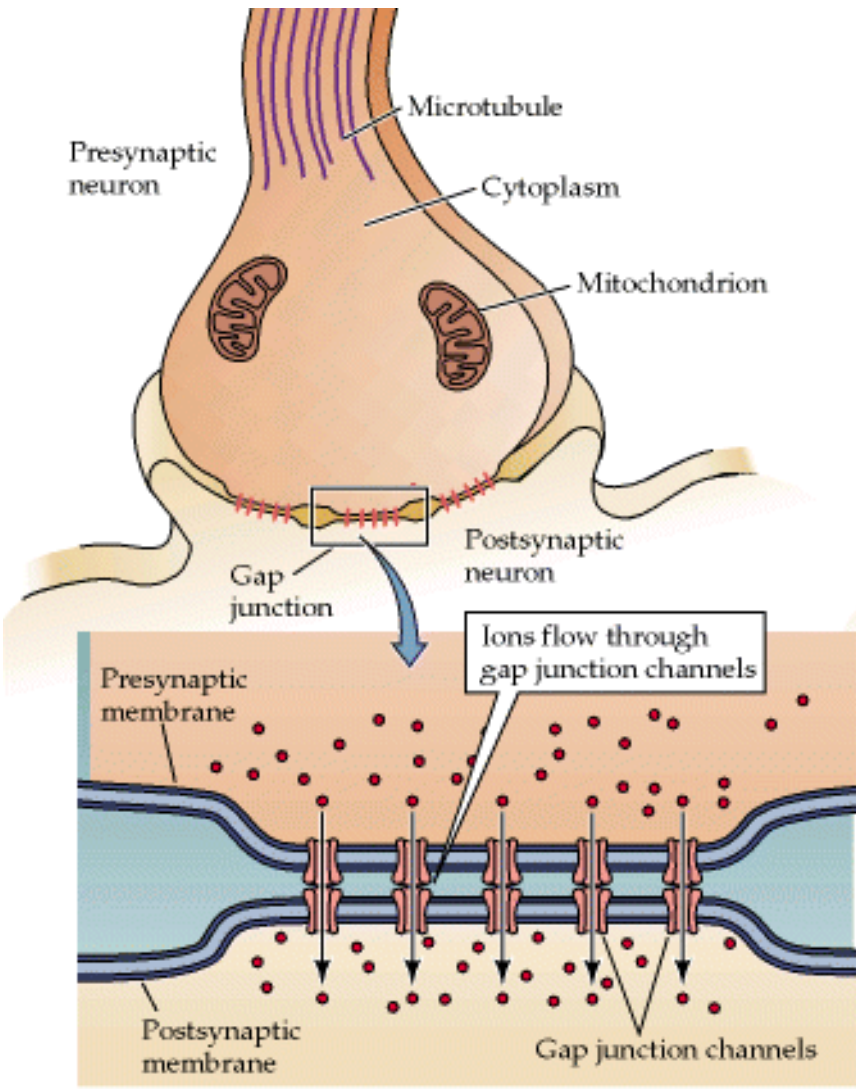
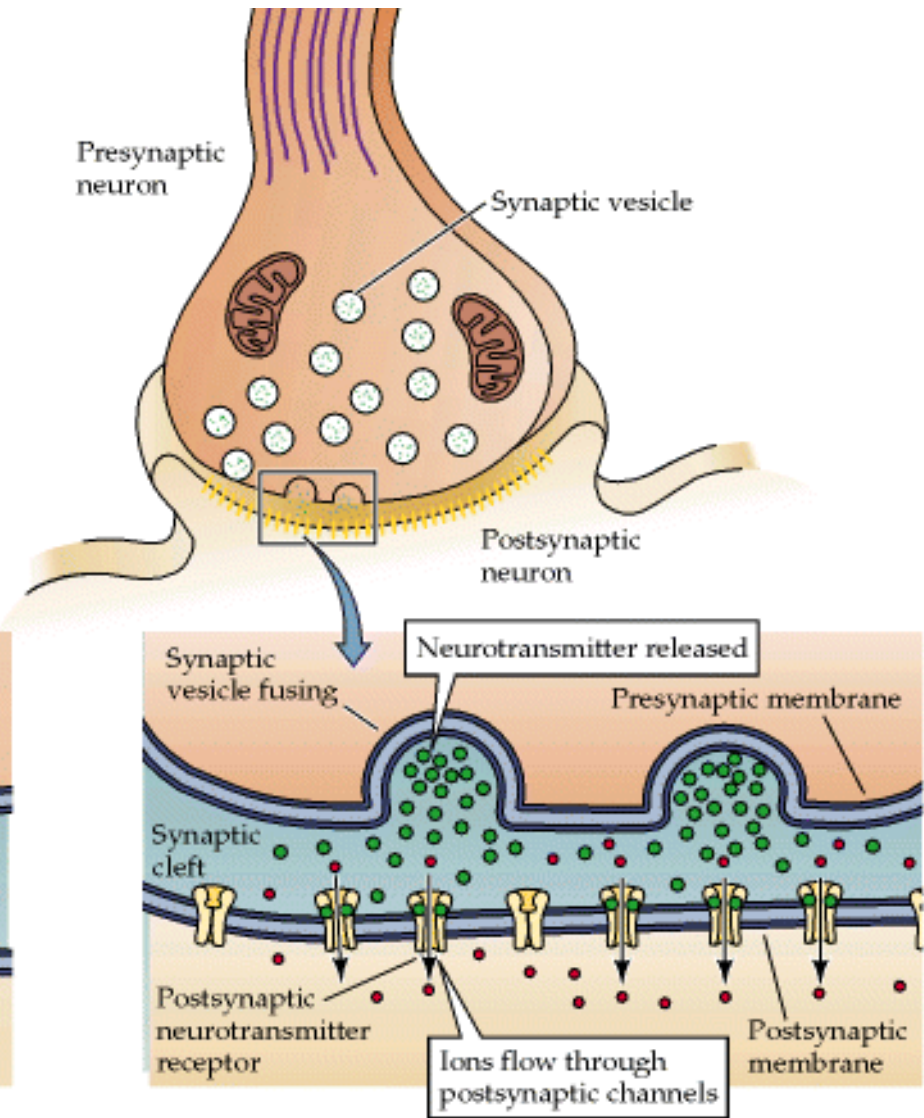


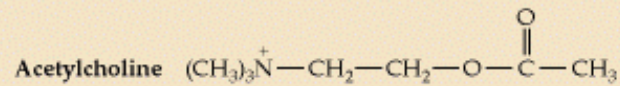
ELECTRICAL SYNAPSE



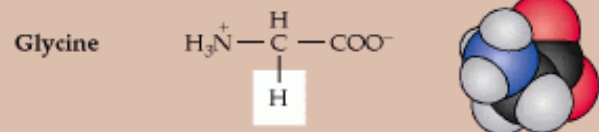
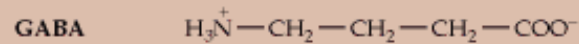
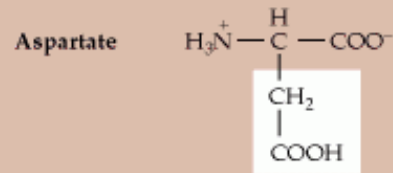
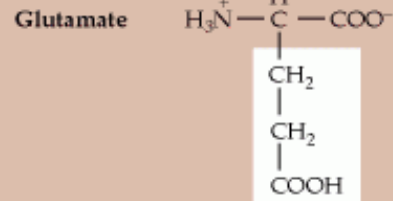
CHEMICAL SYNAPSE



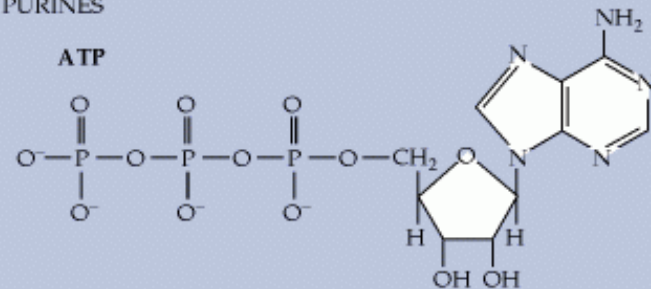
SMALL-MOLECULE NEUROTRANSMITTERS



AMINO ACIDS

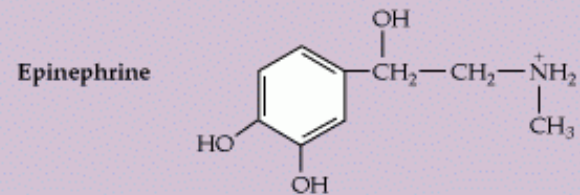
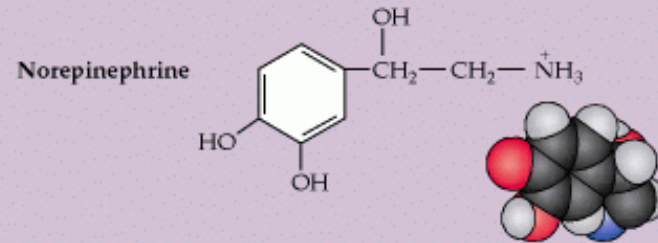
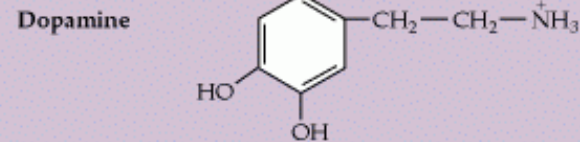


PURINES

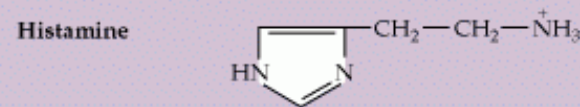


BIOGENIC AMINES

CATECHOLAMINES

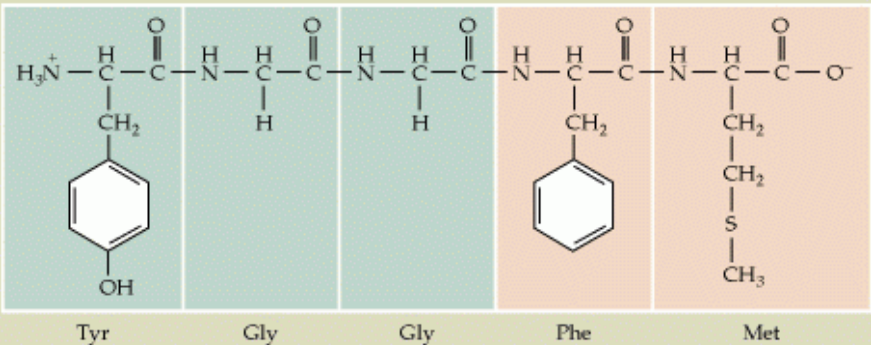
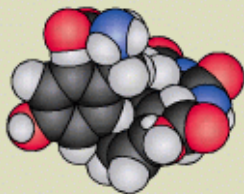


IMIDAZOLEAMINE



PEPTIDE NEUROTRANSMITTERS (more than 100 peptides, usually 3–30 amino acids long)

Example: Methionine enkephalin (Tyr–Gly–Gly–Phe–Met)



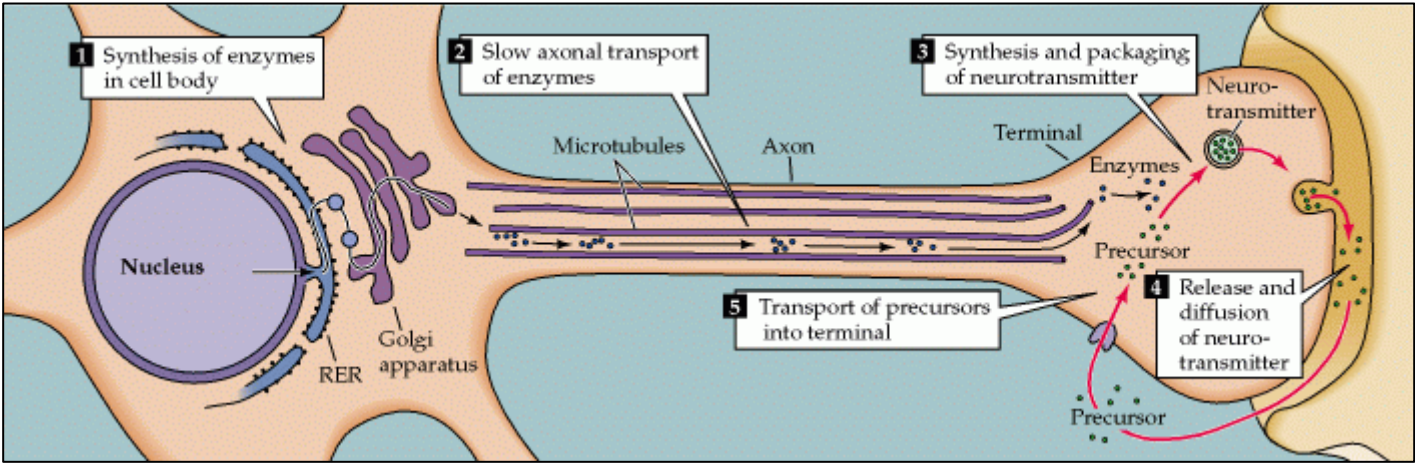
Leucine enkephalin	Tyr Gly Gly Phe Leu
Methionine enkephalin	Tyr Gly Gly Phe Met
α-Endorphin	Tyr Gly Gly Phe Met Thr Ser Glu Lys Ser Gln Thr Pro Leu Val Thr
β-Endorphin	Tyr Gly Gly Phe Met Thr Ser Glu Lys Ser Gln Thr Pro Leu Val Thr Leu Phe Lys Asn Ala Ile Val Lys Asn Ala His Lys Gly Gln
Substance P	Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu Met
Somatostatin-14	Ala Gly Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys
Thyrotropin releasing hormone (TRH)	Glu His Pro
Leutinizing hormone-releasing hormone (LHRH)	Glu His Trp Ser Tyr Gly Leu Arg Pro Gly
Angiotensin-II	Asp Arg Val Tyr Ile His Pro Phe
Vasopressin	Cys Tyr Phe Gln Arg Cys Pro Leu Gly
Oxytocin	Cys Tyr Ile Gln Arg Cys Pro ^{Asp} Leu Gly
Cholecystokinin octapeptide (CCK-8)	Asp Tyr Met Gly Trp Met Asp Phe
Vasoactive intestinal peptide (VIP)	His Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
Neuropeptide-Y	Tyr Pro Ser Lys Pro Asp Asn Pro Gly Glu Asp Ala Pro Ala Glu Asp Leu Ala Arg Tyr Tyr Ser Ala Leu Arg His Tyr Ile Asn Leu Ile Thr Arg Gln Arg Tyr
Neurotensin	Glu Leu Tyr Glu Asn Lys Pro Arg Arg Pro Ile Leu
Bombesin (BBS-14)	Glu Gln Arg Leu Gly Asn Gln Trp Ala Val Gly His Leu Met

Amino acid properties

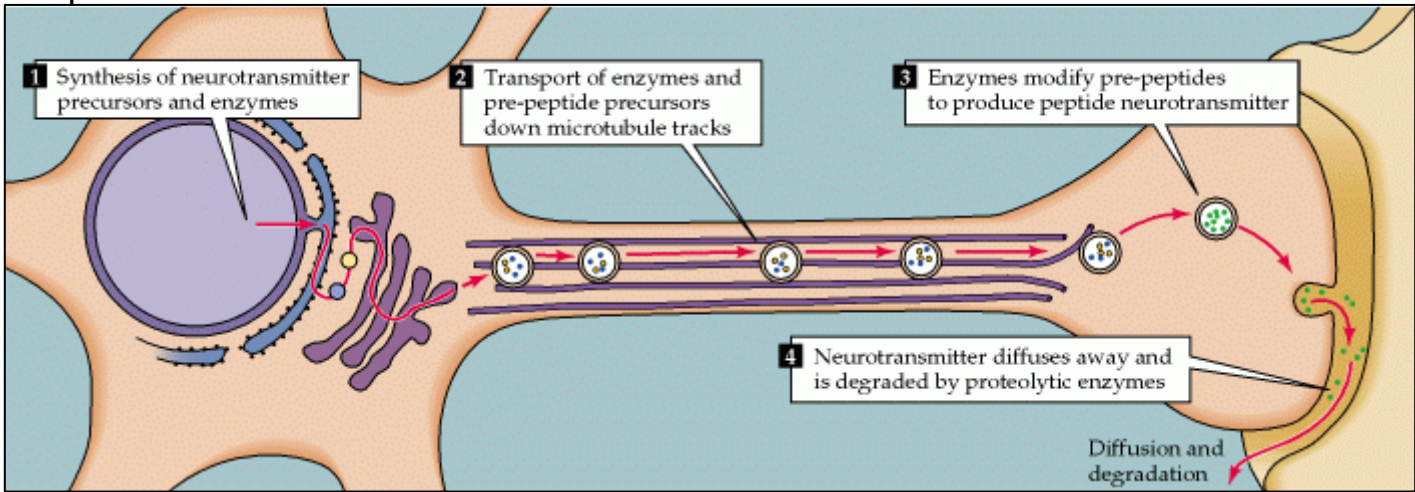
- Hydrophobic
- Polar, uncharged
- Acidic
- Basic

Synthesis, packaging, secretion and removal of NT

Small-molecule NT



Peptide NT

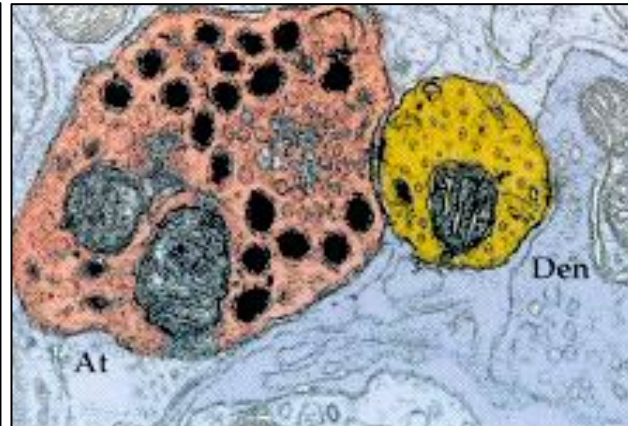


Storage of NT in different types of synaptic vesicles

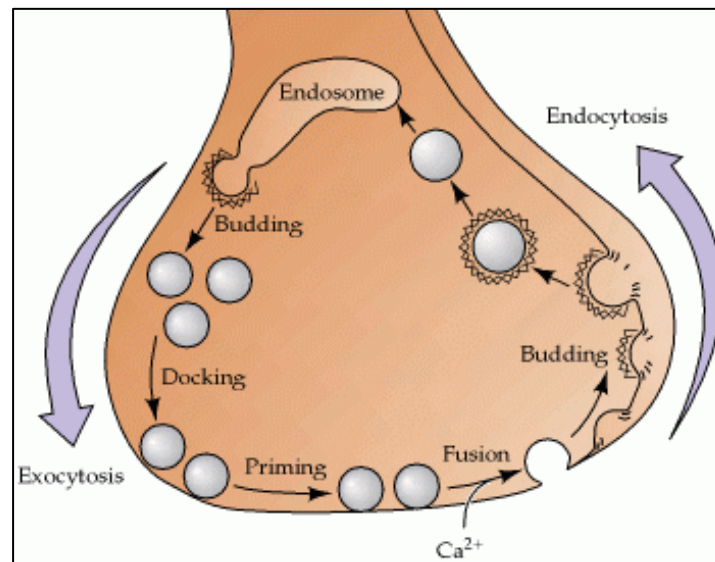
Small clear-core vesicles



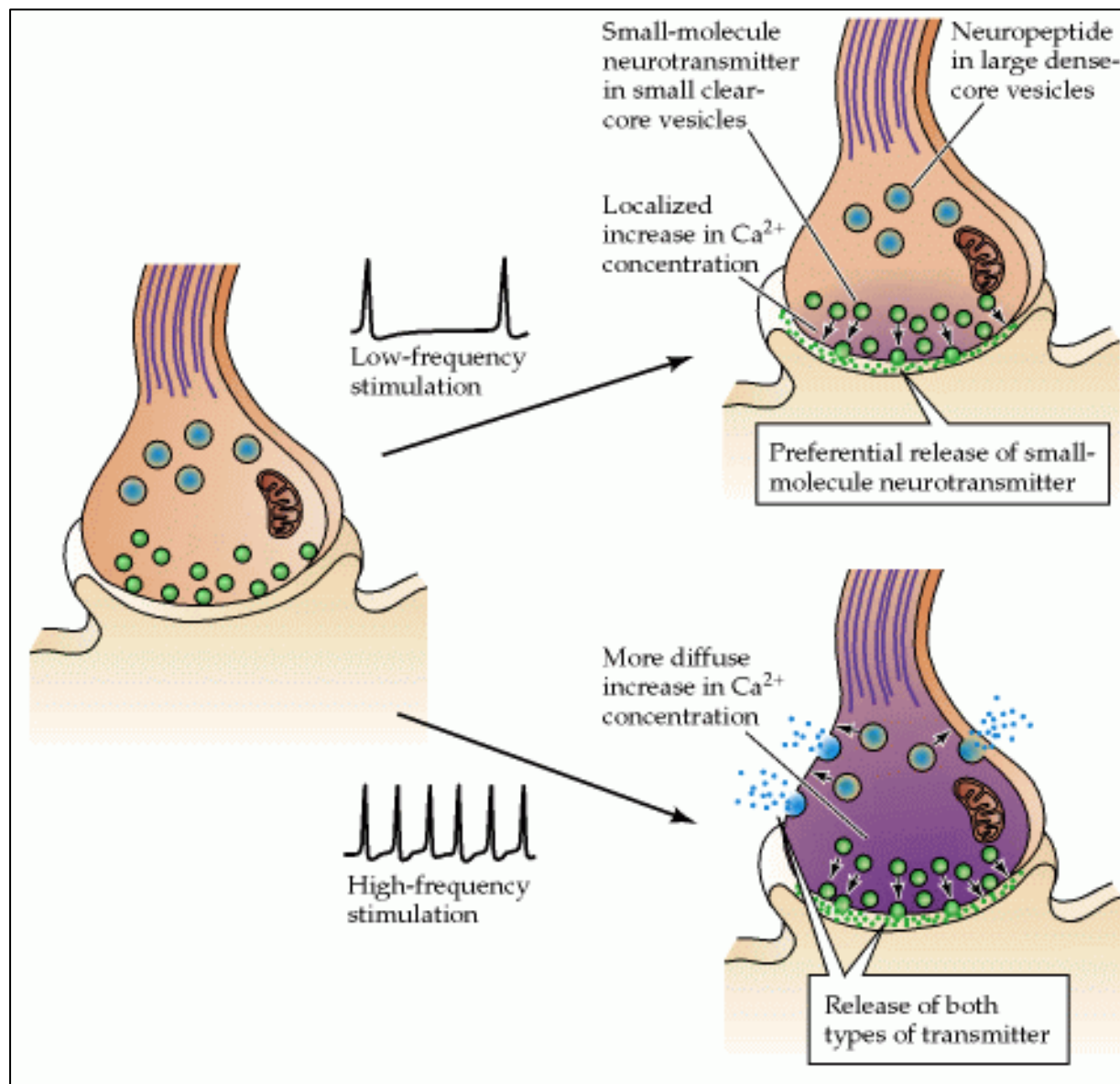
Large dense-core vesicles



Local recycling of synaptic vesicles

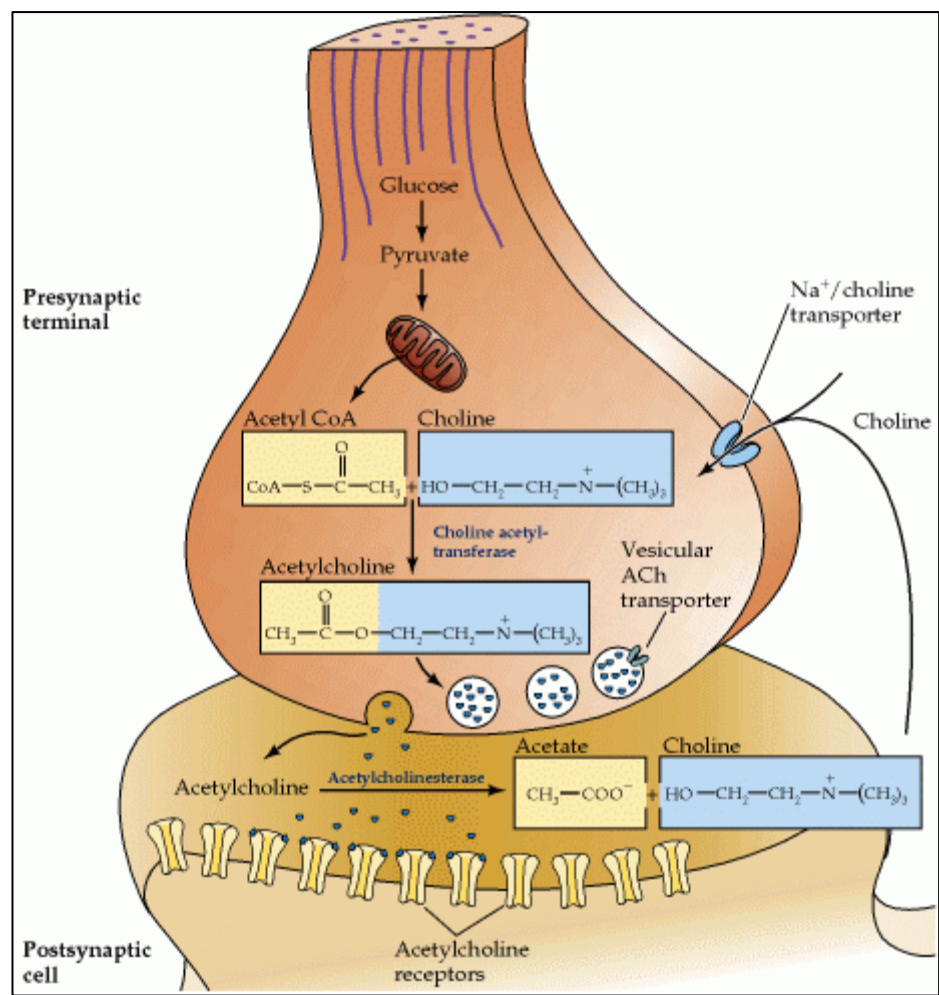


Several NT can be co-released by a given neuron

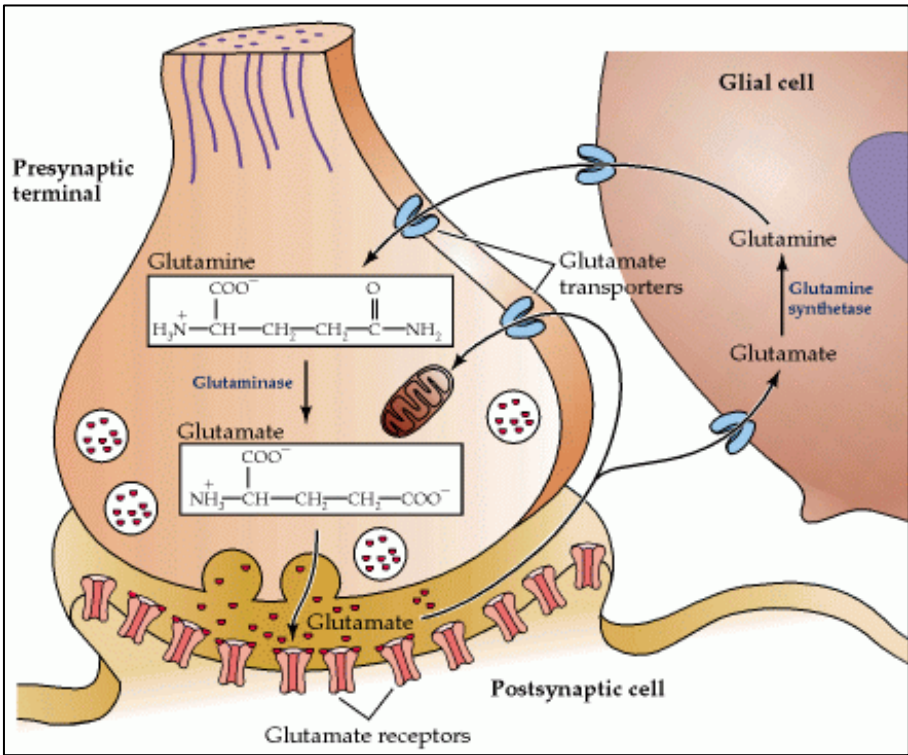


Synthesis and removal of NT

Acetylcholine

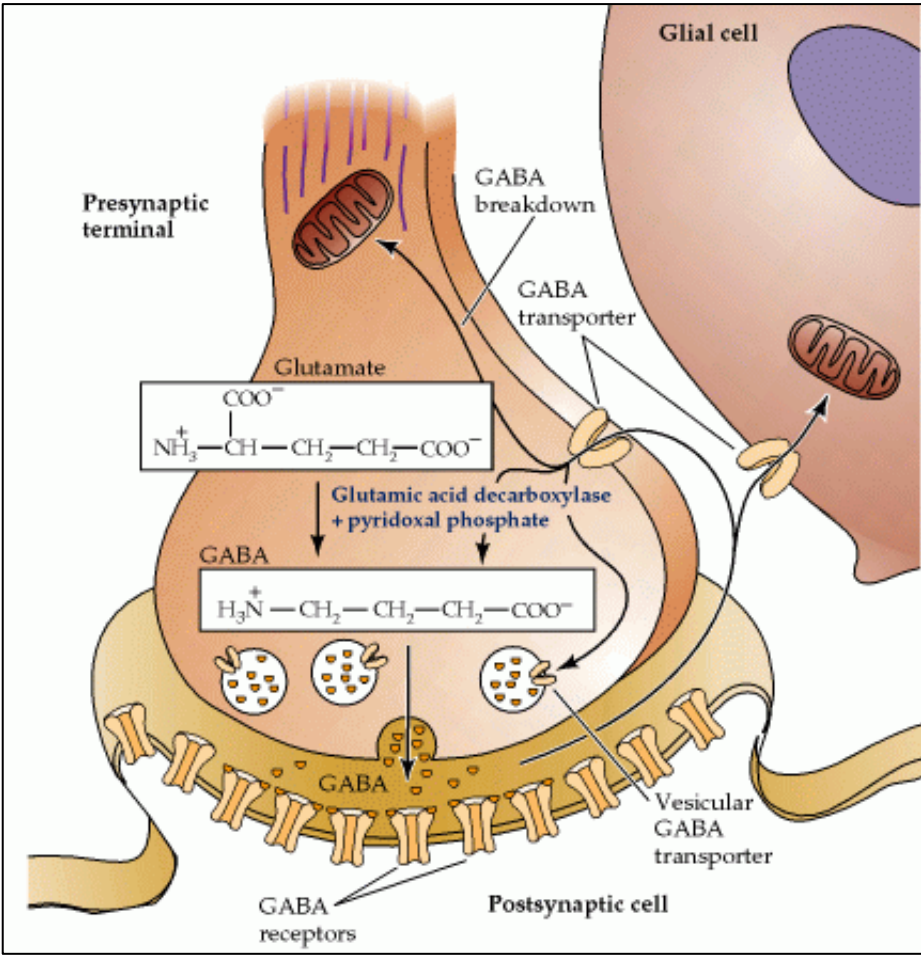


Glutamate

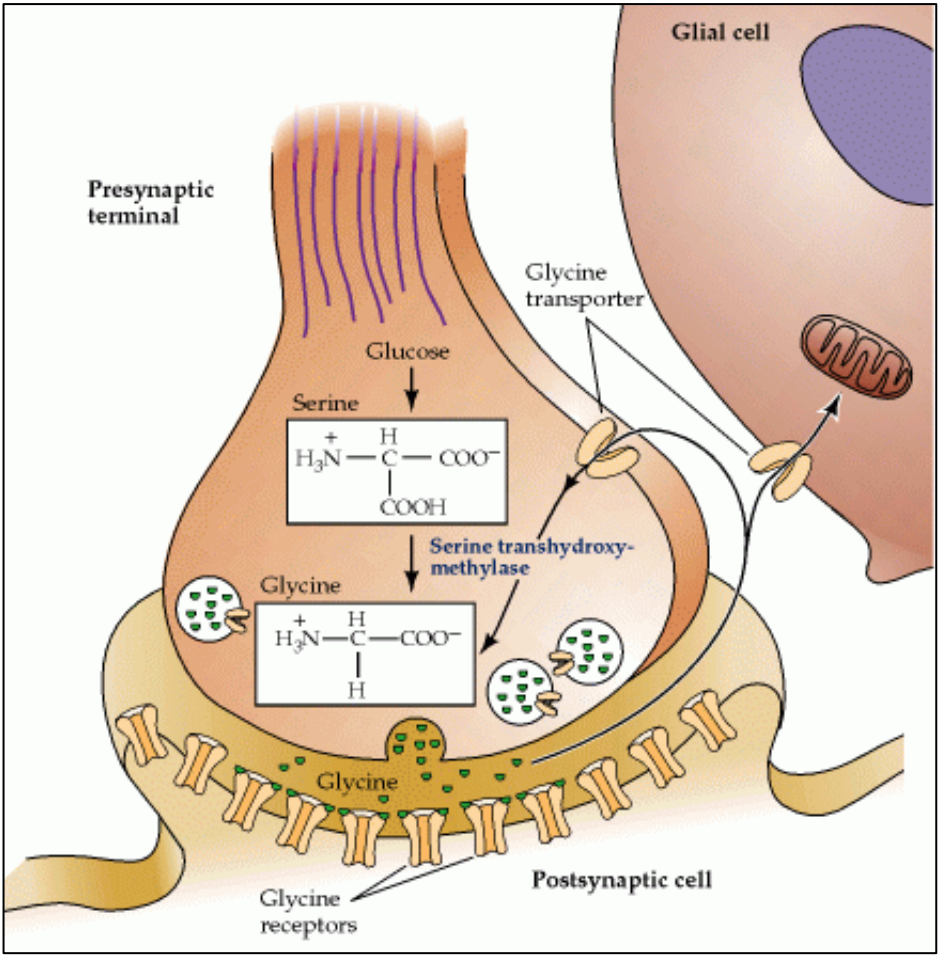


Synthesis and removal of NT

GABA



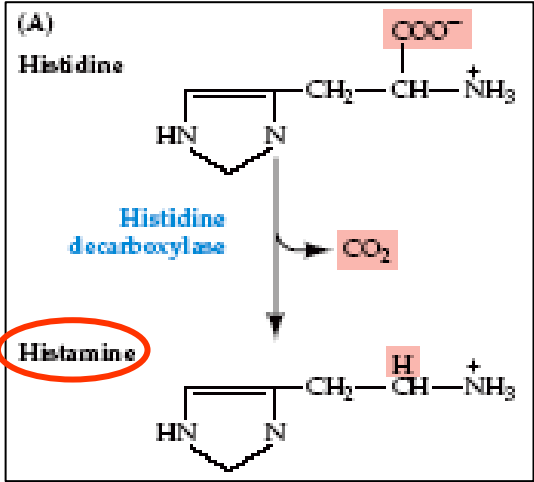
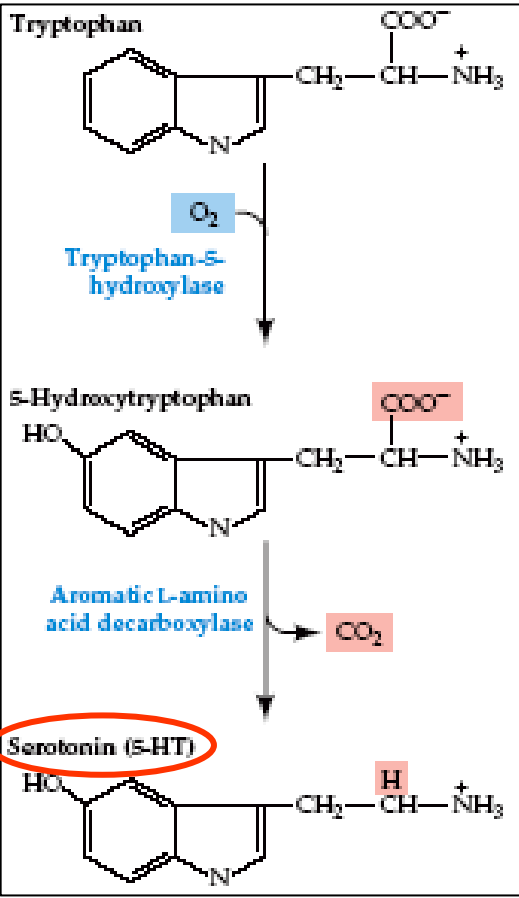
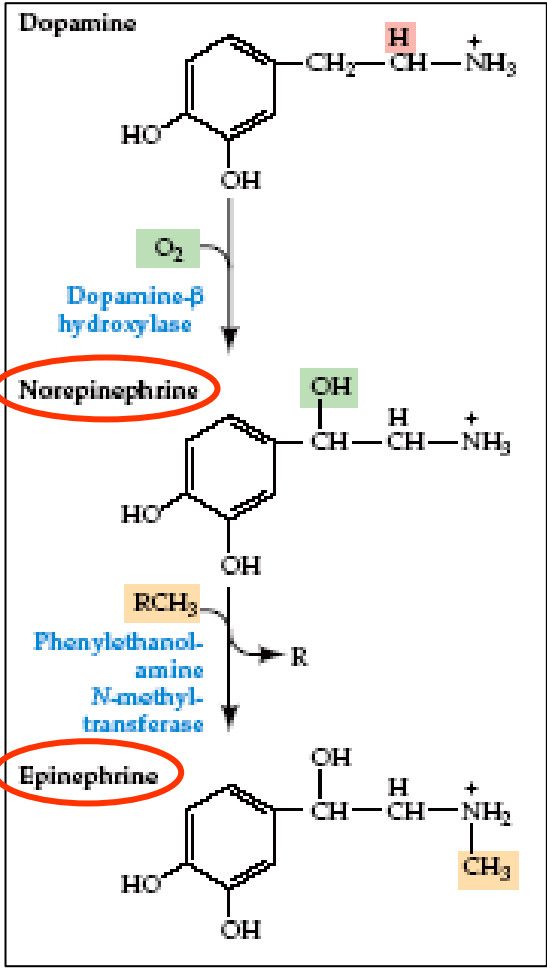
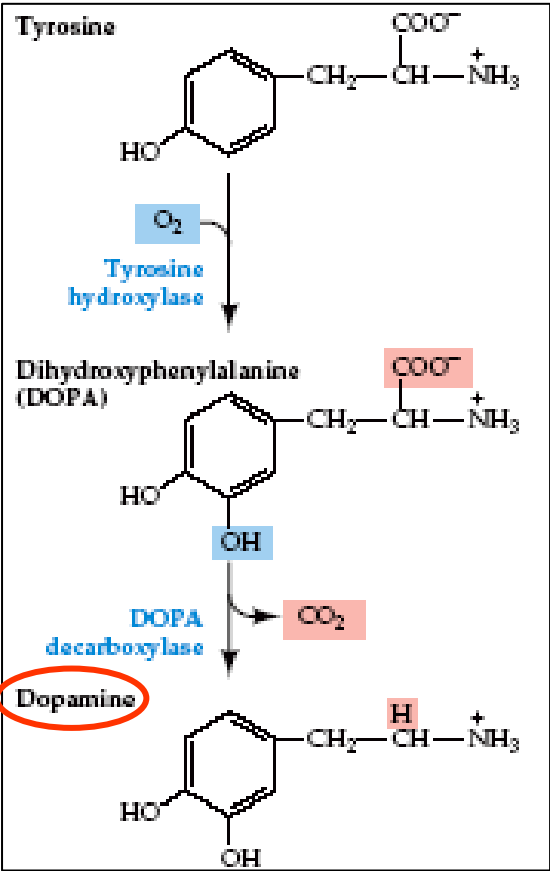
Glycine



Synthesis and removal of NT

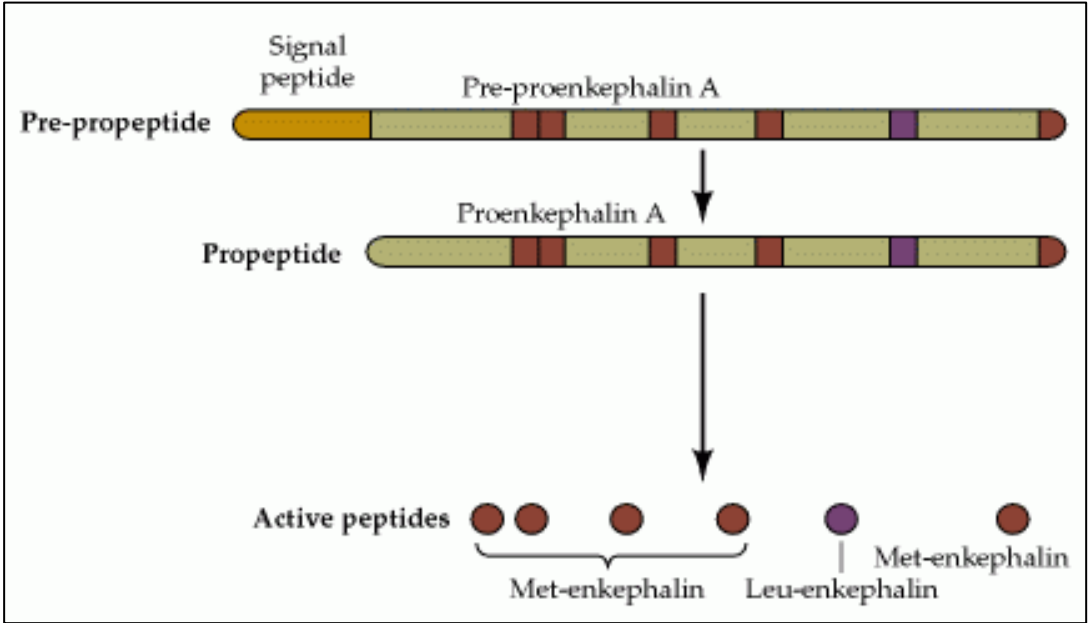
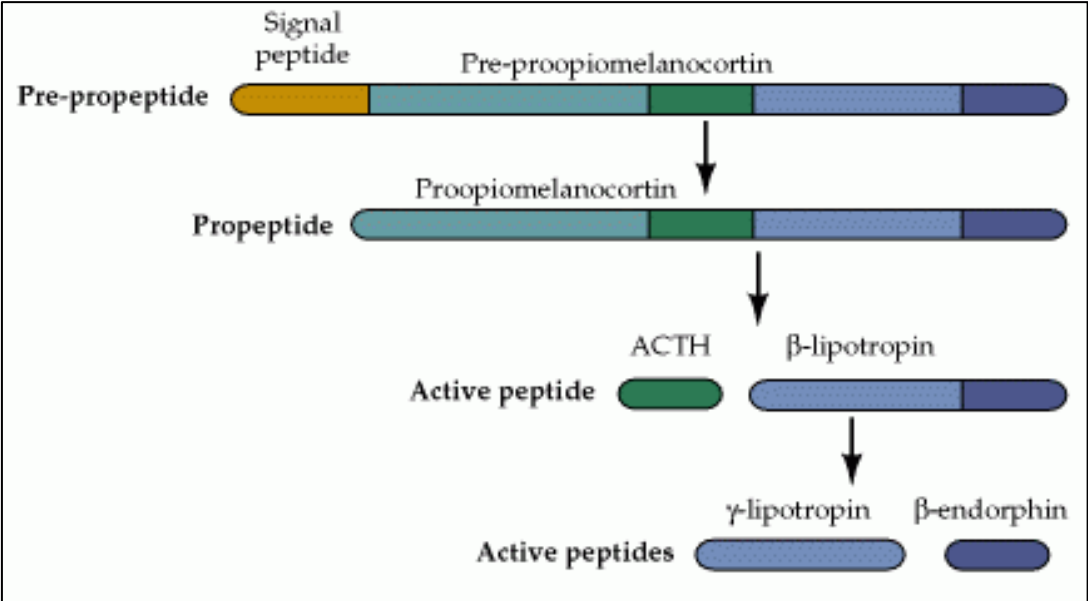
Biogenic amines

Catecholamines (dopamine, noradrenaline, adrenaline)
Serotonin
Histamine

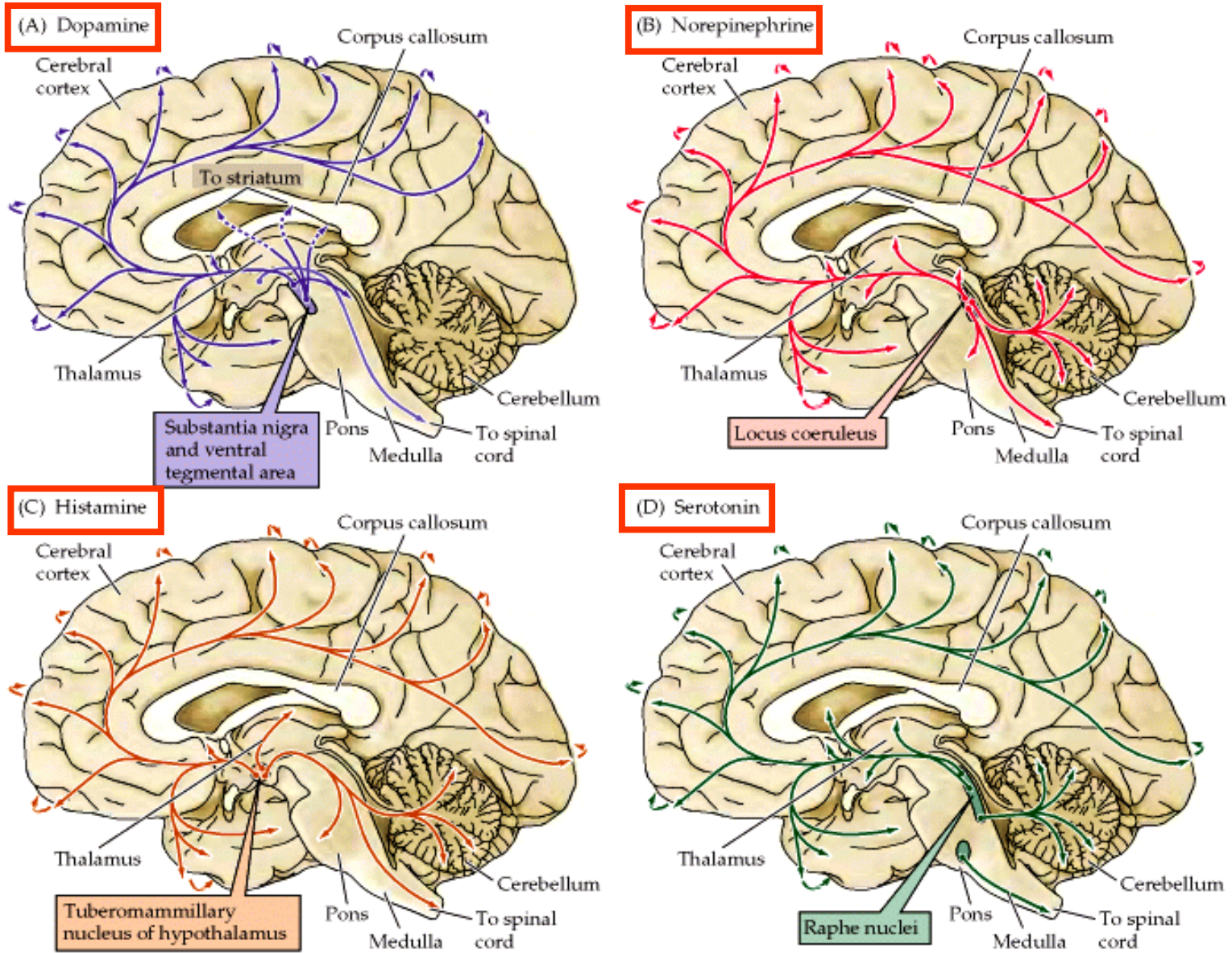


Removal: degradation by MAO/COMT (catecholamines);
MAO (5-HT); MAO/HMT (Histamine)

Peptide neurotransmitters

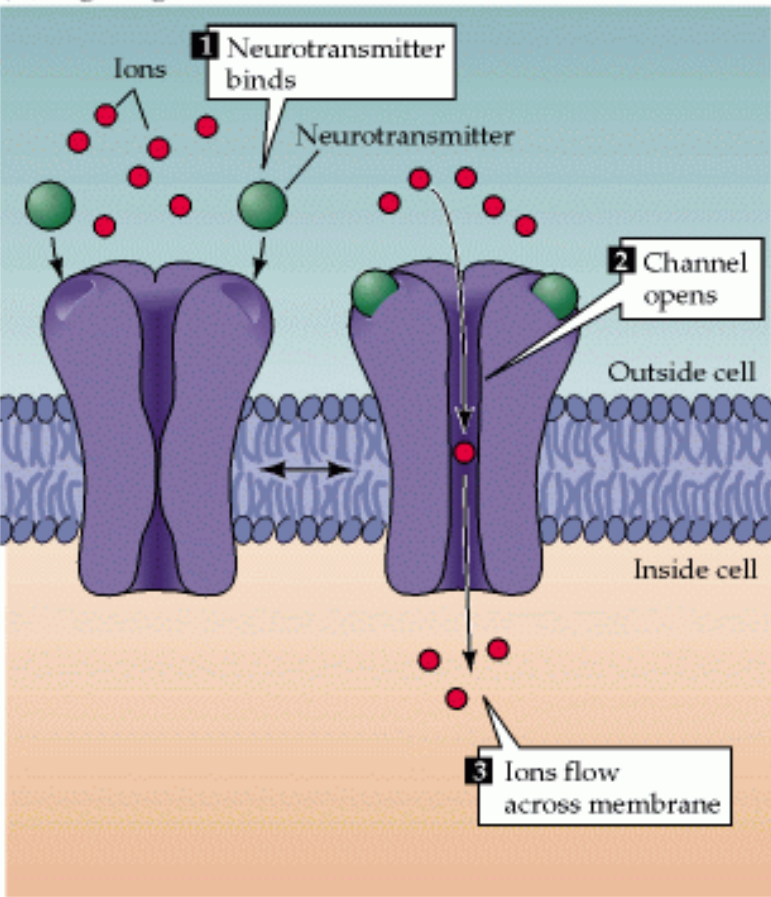


Distribution of neurons and projections containing biogenic amines as NT

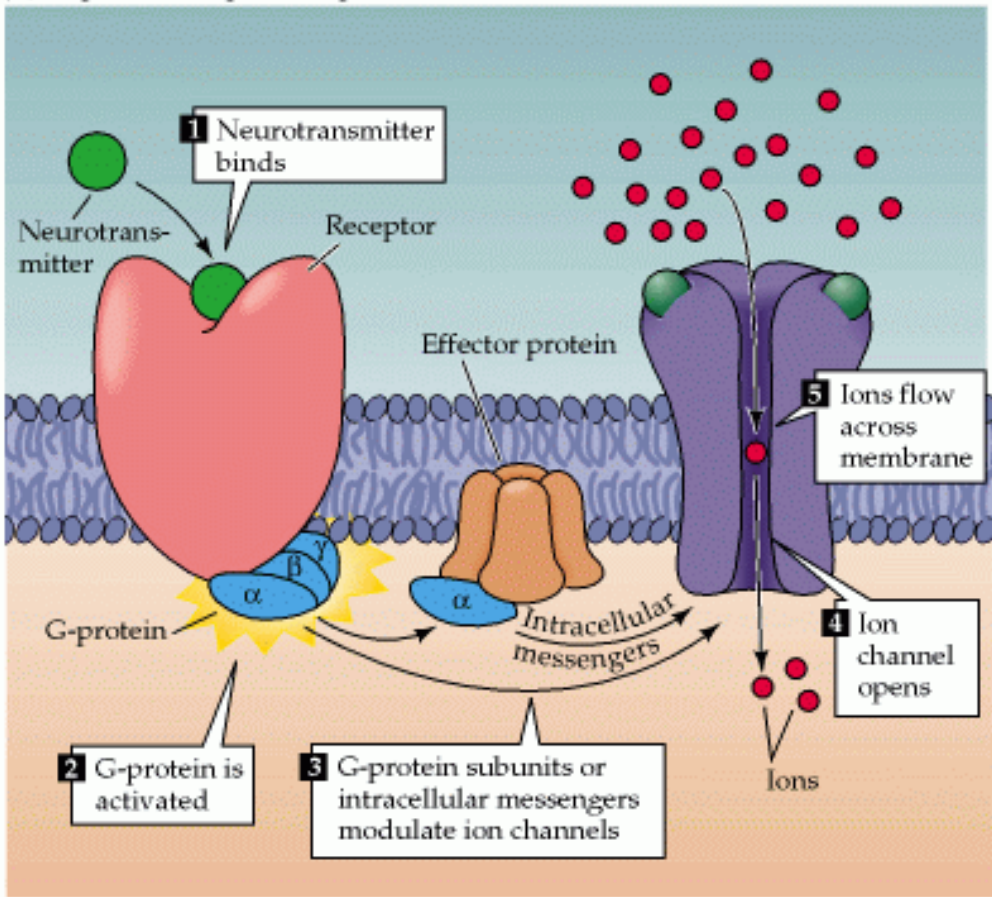


Neurotransmitter receptors

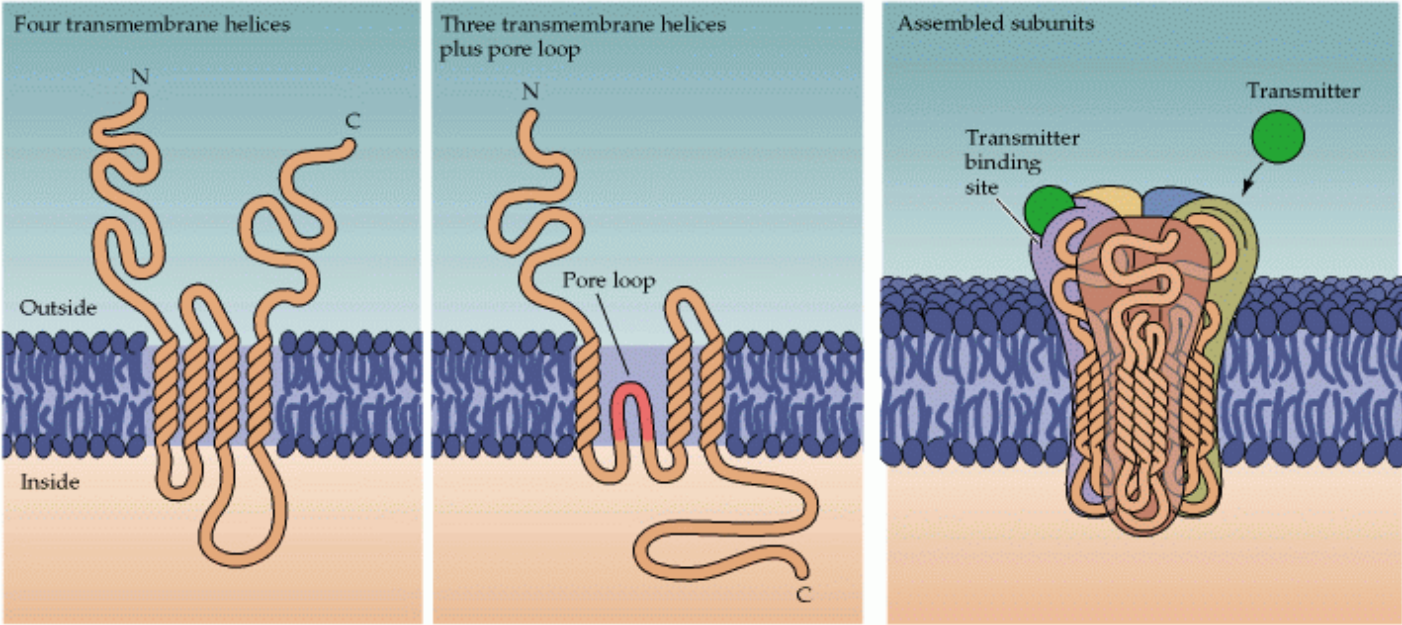
(A) Ligand-gated ion channels



(B) G-protein-coupled receptors



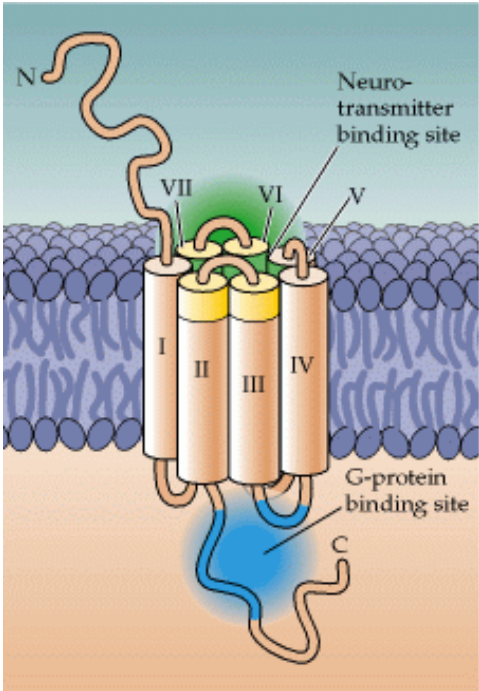
Ionotropic receptors



Glutamate

Receptor	AMPA	NMDA	Kainate	GABA	Glycine	nACh	Serotonin	Purines
Subunits (combination of 4 or 5 required for each receptor type)	Glu R1	NR1	Glu R5	α_{1-7}	$\alpha 1$	α_{2-9}	5-HT ₃	P _{2X1}
	Glu R2	NR2A	Glu R6	β_{1-4}	$\alpha 2$	β_{1-4}		P _{2X2}
	Glu R3	NR2B	Glu R7	γ_{1-4}	$\alpha 3$	γ		P _{2X3}
	Glu R4	NR2C	KA1	δ	$\alpha 4$	δ		P _{2X4}
		NR2D	KA2	ϵ	β			P _{2X5}
				ρ_{1-3}				P _{2X6}
								P _{2X7}

Metabotropic receptors



ACh

Receptor class	Glutamate	GABA _B	Dopamine	NE, Epi	Histamine	Serotonin	Purines	Muscarinic
Receptor subtype	Class I	GABA _B R1	D1 _A	α1	H1	5-HT 1	A type	M1
	mGlu R1	GABA _B R2	D1 _B	α2	H2	5-HT 2	A1	M2
	mGlu R5		D2	β1	H3	5-HT 3	A2a	M3
	Class II		D3	β2		5-HT 4	A2b	M4
	mGlu R2		D4	β3		5-HT 5	A3	M5
	mGlu R3					5-HT 6	P type	
	Class III					5-HT 7	P2x	
	mGlu R4						P2y	
	mGlu R6						P2z	
	mGlu R7						P2t	
	mGlu R8						P2u	

Glutamate

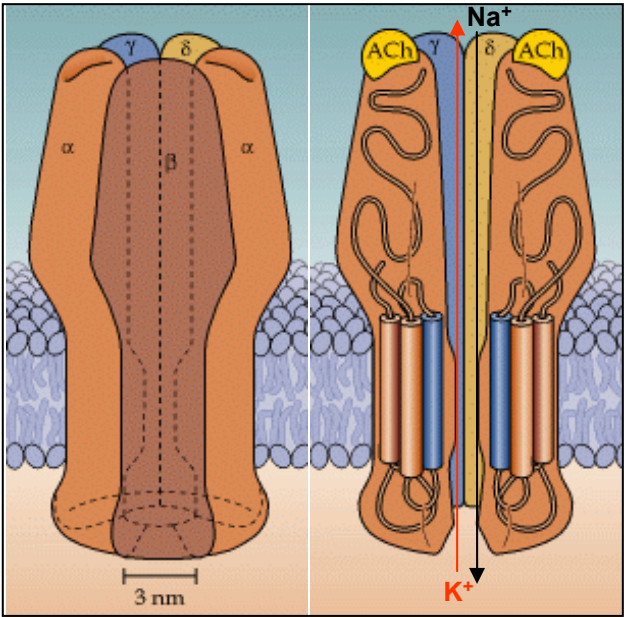
Receptor	AMPA	NMDA	Kainate	GABA	Glycine	nACh	Serotonin	Purines
Subunits (combination of 4 or 5 required for each receptor type)	Glu R1	NR1	Glu R5	α_{1-7}	$\alpha 1$	α_{2-9}	5-HT ₃	P _{2X1}
	Glu R2	NR2A	Glu R6	β_{1-4}	$\alpha 2$	β_{1-4}		P _{2X2}
	Glu R3	NR2B	Glu R7	γ_{1-4}	$\alpha 3$	γ		P _{2X3}
	Glu R4	NR2C	KA1	δ	$\alpha 4$	δ		P _{2X4}
		NR2D	KA2	ϵ	β			P _{2X5}
				ρ_{1-3}				P _{2X6}
								P _{2X7}

ACh

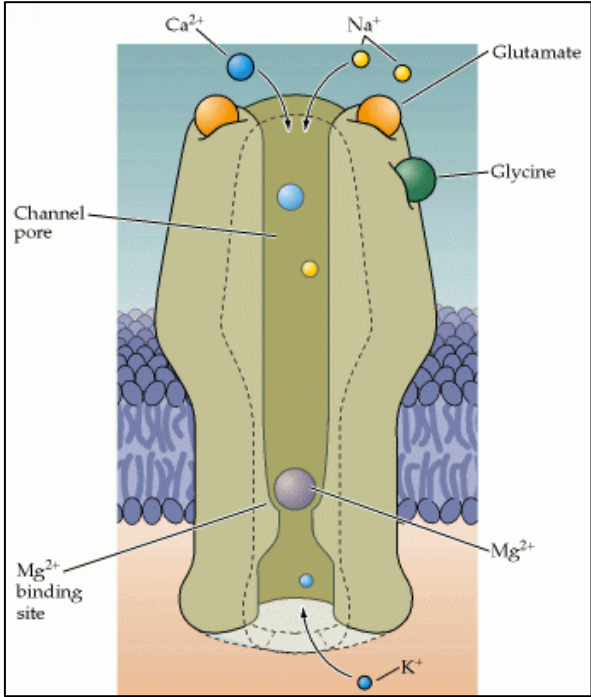
Receptor class	Glutamate	GABA _B	Dopamine	NE, Epi	Histamine	Serotonin	Purines	Muscarinic
Receptor subtype	Class I	GABA _B R1	D1 _A	$\alpha 1$	H1	5-HT 1	A type	M1
	mGlu R1	GABA _B R2	D1 _B	$\alpha 2$	H2	5-HT 2	A1	M2
	mGlu R5		D2	$\beta 1$	H3	5-HT 3	A2a	M3
	Class II		D3	$\beta 2$		5-HT 4	A2b	M4
	mGlu R2		D4	$\beta 3$		5-HT 5	A3	M5
	mGlu R3					5-HT 6	P type	
	Class III					5-HT 7	P2x	
	mGlu R4						P2y	
	mGlu R6						P2z	
	mGlu R7						P2t	
	mGlu R8						P2u	

Ionotropic receptors

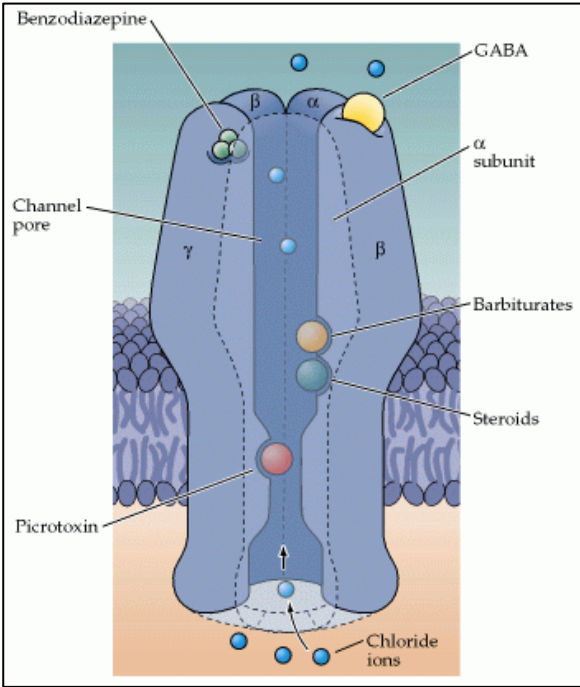
Acetylcholine receptor



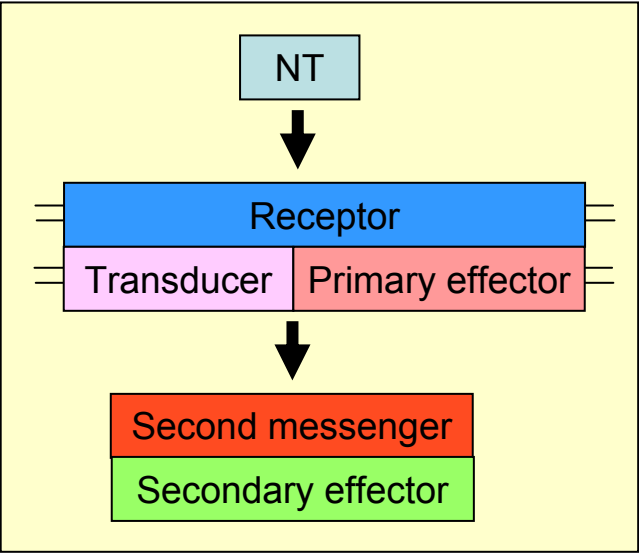
Glutamate NMDA receptor



GABA receptor



Metabotropic receptors



A common plan for synaptic second-messenger systems

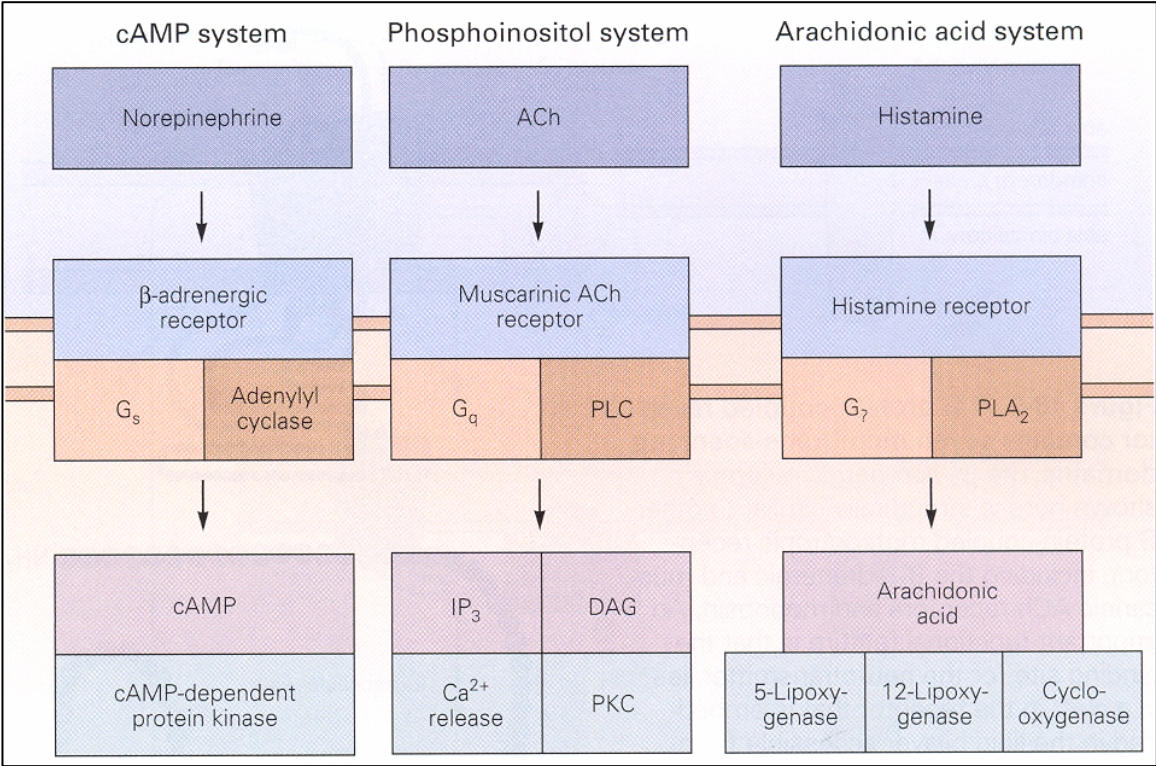


TABLE 6.1
Functional Features of the Major Neurotransmitters

<i>Neurotransmitter</i>	<i>Postsynaptic effect^a</i>	<i>Precursor(s)</i>	<i>Rate-limiting step in synthesis</i>	<i>Removal mechanism</i>	<i>Type of vesicle</i>
ACh	Excitatory	Choline + acetyl CoA	CAT	AChE	Small, clear
Glutamate	Excitatory	Glutamine	Glutaminase	Transporters	Small, clear
GABA	Inhibitory	Glutamate	GAD	Transporters	Small, clear
Glycine	Inhibitory	Serine	Phosphoserine	Transporters	Small, clear
Catecholamines (epinephrine, norepinephrine, dopamine)	Excitatory	Tyrosine	Tyrosine hydroxylase	Transporters, MAO, COMT	Small dense-core, or large irregular dense-core
Serotonin (5-HT)	Excitatory	Tryptophan	Tryptophan hydroxylase	Transporters, MAO	Large, dense-core
Histamine	Excitatory	Histidine	Histidine decarboxylase	Transporters	Large, dense-core
ATP	Excitatory	ADP	Mitochondrial oxidative phosphorylation; glycolysis	Hydrolysis to AMP and adenosine	Small, clear
Neuropeptides	Excitatory and inhibitory	Amino acids (protein synthesis)	Synthesis and transport	Proteases	Large, dense-core

^aThe most common postsynaptic effect is indicated; the same transmitter can elicit postsynaptic excitation *or* inhibition depending on the nature of the ion channels affected by transmitter binding (see Chapter 7).